The Development of New Synthetic Strategies and Methodologies for Complex Alkaloid Total Synthesis. A Concise Synthesis of (+)-Chimonanthine, (+)-WIN 64821, (–)-Ditryptophenaline and Related Alkaloids

by

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To my parents, Donald and Janice

and sister Brianne

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Preface

Portions of this work have been adapted from the following articles that were co-written by the author and are reproduced in part with permission from:

Movassaghi, M.; Schmidt, M. A. "N-Heterocyclic Carbene-Catalyzed Amidation of Unactivated Esters with Amino Alcohols" *Org. Lett.* **2005**, *7*, 2453. Copyright 2005 American Chemical Society.

Schmidt, M. A.; Movassaghi, M. "Synthesis of Optically Active Imidazopyridium Salts and their NHCs" *Tetrahedron Lett.* **2007**, *48*, 101. Copyright 2007 Elsevier Limited.

Movassaghi, M.; Schmidt, M. A. "Concise Total Synthesis of (–)-Calycanthine, (+)-Chimonanthine, and (+)-Folicanthine" *Angew. Chem. Int. Ed.* **2007**, *46*, 3725. Copyright 2007 Wiley-VCH Verlag GmbH & Co. KGaA.

Movassaghi, M.; Schmidt, M. A.; Ashenhurst, J. A. "Concise Total Synthesis of (–)-Ditryptophenaline and (+)-WIN 64821" *Angew. Chem. Int. Ed.* **2008**, *47*, 1485. Copyright 2007 Wiley-VCH Verlag GmbH & Co. KGaA.

Schmidt, M. A.; Movassaghi, M. "New Strategies for the Synthesis of Hexahydropyrroloindole Alkaloids Inspired by Biosynthetic Hypotheses" *Synlett* **2008**, *3*, 313. Copyright 2008 Georg Thieme Verlag Stuttgart • New York.

Schmidt, M. A.; Müller, P.; Movassaghi, M. "On the Interactions of *N*, *N*'-Bismesitylimidazolin-2-yl and Alcohols" *Tetrahedron Lett.* **2008**, *in press*. Copyright 2007 Elsevier Limited.

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by

Michael Anthony Schmidt

Submitted to the Department of Chemistry
on May 16th, 2008 in partial fulfillment of the
requirements for the Degree of Doctor of Philosophy

ABSTRACT

I. The Development of a General Strategy Towards Dimeric Hexahydropyrroloindole Alkaloids. A Concise Total Synthesis of (+)-Chimonanthine, (+)-Folicanthine and (–)-Calycanthine

An efficient and convergent strategy for the synthesis of dimeric hexahydropyrroloindole alkaloids is described. The simultaneous formation of the vicinal quaternary stereocenters using a reductive dimerization reaction provides gram-scale access to an optically active key intermediate employed in the synthesis of (+)-chimonanthine, (+)-folicanthine, and (–)-calycanthine.

II. The Development of a General Strategy Towards Dimeric Hexahydropyrroloindole Alkaloids. A Concise Total Synthesis of (+)-WIN 64821, (–)-Ditryptophenaline and (–)-1'-(2-Phenylethylene)-ditryptophenaline

The concise enantioselective total synthesis of (+)-WIN 64821 and (–)-ditryptophenaline in six and seven steps, respectively, from commercially available amino acid derivatives is described. The gram-scale synthesis of key intermediates and simultaneous introduction of the vicinal quaternary stereocenters provides a highly effective and preparative synthesis of these natural alkaloids. Additionally, the synthesis and structural confirmation of the natural alkaloid (–)-1′-(2-phenylethylene)-ditryptophenaline is described.

III. *N*-Heterocyclic Carbene–Alcohol Hydrogen Bonds. Studies and Application in the Amidation of Unactivated Esters

A single-step and catalytic amidation of unactivated esters with amino alcohols is described. Treatment of equimolar quantities of amino alcohols and unactivated esters with *N,N*-bismestiylimidazolylidene (5 mol%) affords the desired amides in high yield under mild reaction conditions. The compatibility of the present methodology with a wide range of functional groups, heterocycles, and optically active substrates in addition to both aromatic and aliphatic esters is noteworthy. Preliminary data regarding an unprecedented hydrogen–bonded carbene–alcohol complex is reported. Further investigation of this hydrogen bond revealed steric and electronic influences on the nature of this bond, cumulating in discovery of a practical metal free method for the stabilization and storage of these nitrogen heterocyclic carbenes. Also

described is a method for the synthesis of optically active imidazo-[1,5-a]-pyridinium salts as precursors to optically active nitrogen heterocyclic carbenes.

Thesis Supervisor: Professor Mohammad Movassaghi
Title: Assistant Professor of Chemistry

Table of Contents

Abbreviations

2D	Two dimensional
Å	Angstrom
Ac	Acetyl
AIBN	Azobisisobutyronitrile
aq	Aqueous
Boc	*tert*-Butoxycarbonyl
Bn	Benzyl
Bu	Butyl
°C	Degrees Celsius
CAM	Cerric ammonium molybdate
CSA	Camphor sulfonic acid
d	Deuterium
δ	Parts per million
de	Diastereomeric excess
DMA	*N*,*N*-Dimethyl acetamide
DMF	*N*,*N*-Dimethyl formamide
DMPU	1,3-Dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
DMSO	Dimethyl sulfoxide
E	Entgegen
ee	Enantiomeric excess
EDC	1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide
equiv	Equivalent
ESI	Electrospray ionization
Et	Ethyl
Fmoc	9-Fluorenylmethoxycarbonyl
FTIR	Fourier transform infrared spectroscopy
g	Grams
gHMBC	Gradient heteronuclear multiple-bond correlation
gHSQC	Gradient heteronuclear single-quantum correlation
h	Hours
HMDS	Hexamethyldisilazane
HOBt	1-Hydroxybenzotriazole
HPLC	High performance liquid chromatography
HRMS	High resolution mass spectrometry
Hz	Hertz
i	Isopropyl
IMes	*N*,*N*-Bismesitylimidazolylidene
L	Levorotary
m	Meta
M	Molar
Me	Methyl
Mes	Mesityl
mg	Milligrams
MHz	Megahertz

min	Minutes
mL	Milliliters
mmol	millimoles
n	Normal
NHC	Nitrogen-heterocyclic carbene
NMP	1-Methyl-2-pyrrolidone
NMR	Nuclear magnetic resonance
o	Ortho
p	Para
Ph	Phenyl
PIFA	Phenyliodine bistrifluoroacetate
Piv	Pivaloyl
Red-Al	Sodium bis(2-methoxyethoxy)aluminum hydride
R*f*	Retention factor
t	Tertiary
TBAF	Tetrabutylammonium fluoride
Tf	Trifluoromethanesulfonyl
TFA	Trifluoroacetic acid
TFE	2,2,2-Trifluoroethanol
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMSE	Trimethylsilylethyl
μL	Microliters
μmol	Micromoles
UV	Ultraviolet

Chapter I

The Development of a General Strategy Towards Dimeric Hexahydropyrroloindole Alkaloids. A Concise Total Synthesis of (+)-Chimonanthine, (+)-Folicanthine and (–)-Calycanthine

Introduction and Background

The rich history of dimeric hexahydropyrroloindole alkaloids can be traced back to the late 1880's in the southern United States. Hundreds of sheep and cattle died as the result of grazing on the shrub *Calycanthus glaucus.*[1] In 1888, Eccles isolated the active component from these shrubs, the alkaloid (+)-calycanthine (**1**).[2] The correct determination of the structure of calycanthine would wait almost seventy years until R. B. Woodward addressed this problem using a variety of methods including chemical degradation.[3] Contemporaneously the structure of (+)-calycanthine (**1**) was secured by X-ray diffraction analysis, consistent with Woodward's proposed structure.[4]

A striking structural feature of calycanthine is the presence of vicinal quaternary stereocenters adjacent to two aminals (C3a-C3a', sp^3-sp^3). This structural motif can be seen in many other natural products such as (+)-chimonanthine (**2**)[5], (+)-folicanthine (**3**)[5], and dozens of other dimeric hexahydropyrroloindole derived alkaloids. A related and large subset of the bisindole super family of alkaloids contain a diketopiperzaine fused to the hexahydropyrroloindole substructure as seen by the representative derivatives such as (+)-WIN 64821 (**4**),[6] (+)-chaetocin (**5**),[7] and (+)-11,11'-dideoxyverticillin A (**6**).[8] Another closely related group of alkaloids contain two or more hexahydropyrroloindole substructures with an additional interesting C3a-C7' (sp^3-sp^2) connectivity as seen in (–)-idiospermuline (**7**)[9] and (–)-psycholeine (**8**) (Figure 1).[10]

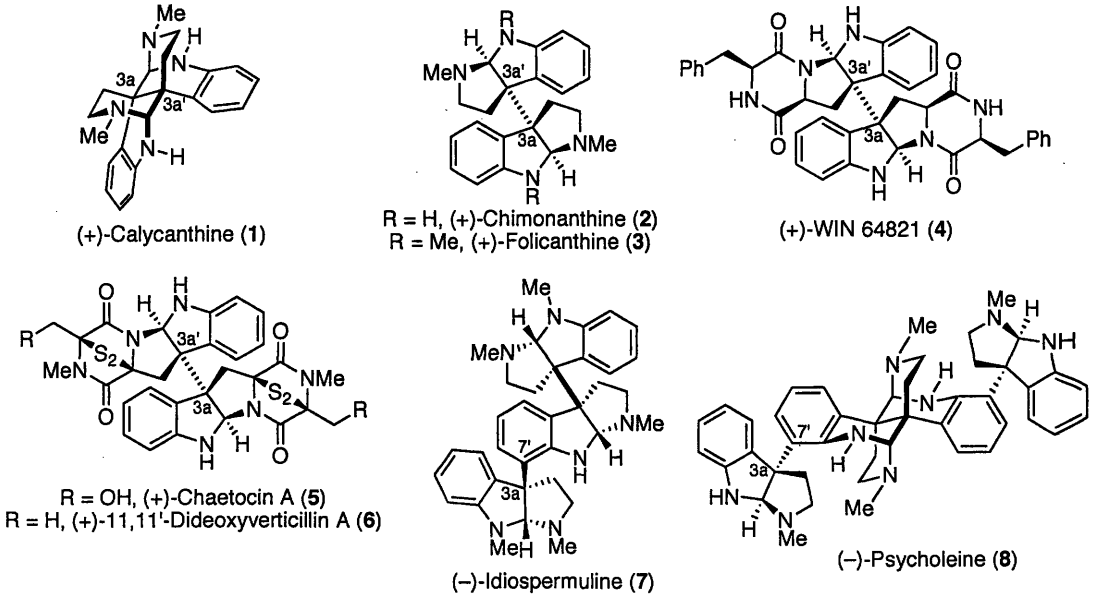
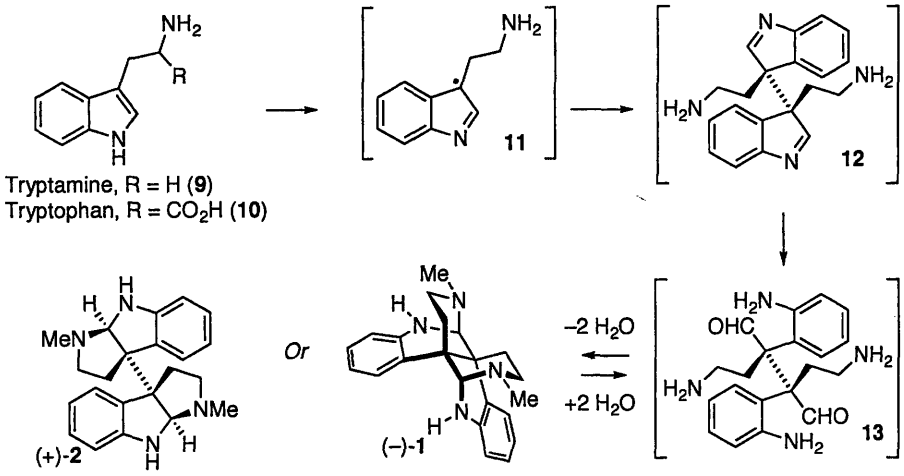


Figure 1. Representative members of the hexahydropyrroloindole alkaloid super family.

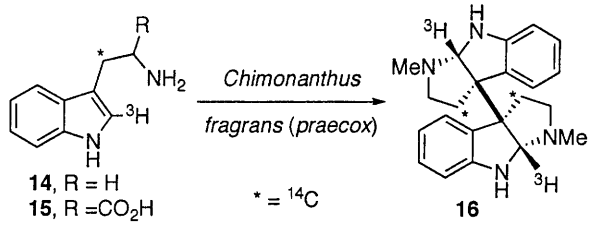
Biosynthetic Hypothesis

In the early 1950's, a hypothesis regarding the biosynthesis of calycanthaceous alkaloids was developed independently by Woodward[3] and Robinson (Scheme 1).[11] A series of structure elucidation studies revealed that (+)-calycanthine (**1**) and (–)-chimonanthine (**2**) were isomers arising from the rearrangement of their respective *N,N*-aminal substructures (Scheme 1). Alkaloids **1** and **2** represent only two of five aminal–arrangement products possible for the hypothetical intermediate **13**. Indeed, several alkaloids containing the other possible arrangements have been isolated.[12] Intermediate **12** is believed to come from a dimerization of tryptamine (**9**) through the intermediacy of the corresponding oxidation product, benzylic radical **11**. Tryptamine (**9**) is in turn derived from the decarboxylation of tryptophan (**10**).



Scheme 1. Woodward's and Robertson's hypothesis for the biosynthesis of the calycanthaceous alkaloids.

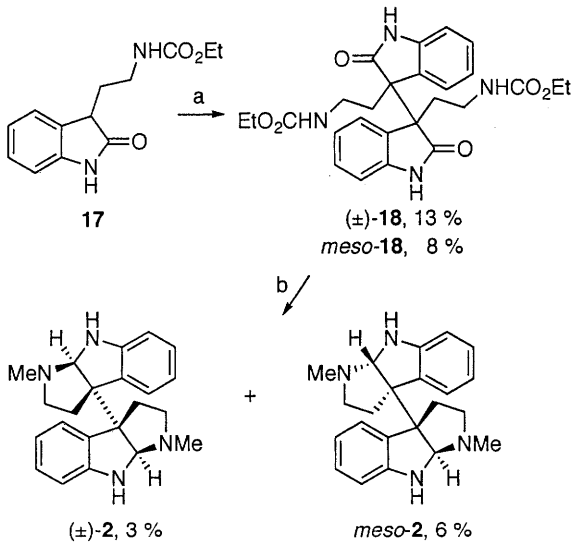
In 1969, Kirby provided experimental evidence for the incorporation of isotopically labeled precursors into (–)-chimonanthine (**2**, Scheme 2).[13] The results of these feeding experiments using doubly labeled tryptamine **14** and racemic tryptophan **15** are consistent with the oxidative dimerization hypothesis outlined in Scheme 1 for the biosynthesis of calycanthaceous alkaloids.



Scheme 2. Feeding experiments using isotopically labeled tryptophan and tryptamine.

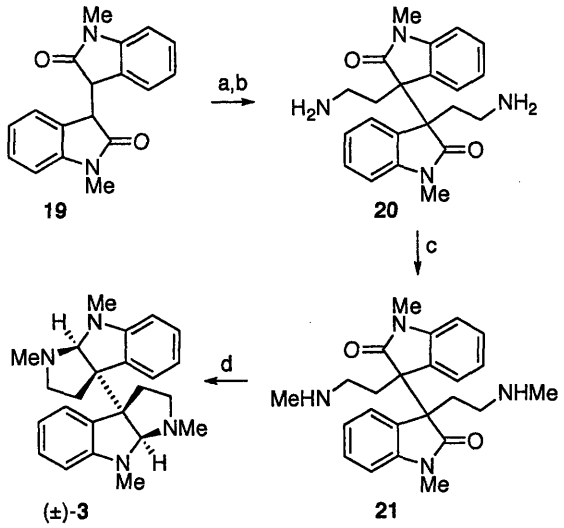
Previous Synthetic Studies

Several synthetic studies in the 1960's were focused on the total synthesis of chimonanthine (**2**). These early routes benefited from the biosynthetic hypothesis described by Woodward and Robinson and focused on the oxidative homodimerization of two suitable indole or oxindole precursors. In 1962, Hendrickson reported the total synthesis of racemic and meso chimonanthine (**2**) by the homodimerization of an oxindole derivative **17** (Scheme 3).[14] The vicinal quaternary centers were formed by treating oxindole **17** with excess sodium hydride followed by the slow addition of iodine in benzene to afford a separable mixture of the two diastereomeric dimers (±)-**18** and *meso*-**18** in 21% combined yield. Exhaustive reduction of each diastereomer with excess lithium aluminum hydride afforded (±)- and *meso*-chimonanthine (**2**) in 3% and 6% yields, respectively (Scheme 3).



Scheme 3. Henderickson's synthesis of the chimonanthines. Conditions: a) NaH, I_2, THF, PhH. b) $LiAlH_4$, THF.

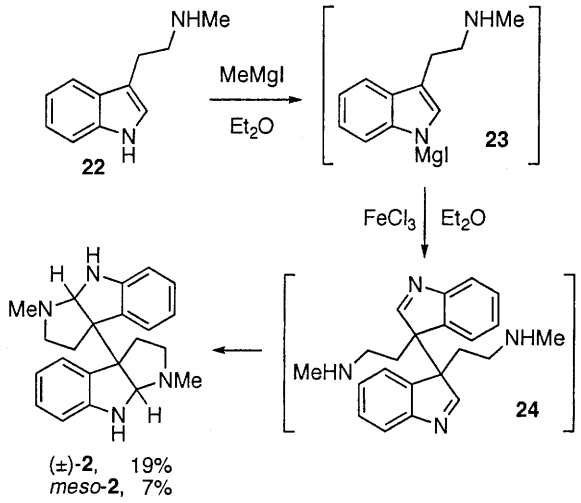
Shortly after the Hendrickson synthesis of chimonanthine, Hino reported a synthesis of folicanthine[15] (**3**) in racemic form through a stepwise introduction of the vicinal quaternary centers (Scheme 4). Bisoxindole **19** was alkylated two times with chloroacetonitrile in the presence of sodium iodide to afford the corresponding bisnitrile that was reduced to the corresponding bisamine **20** with platinum(IV) oxide and dihydrogen. The diamine **20** was converted to a bisphenylimine derivative, *N*-alkylated with methyl iodide to afford the corresponding bisiminium diiodide, and subsequently hydrolyzed to afford the *N*-methyl amine **21**. Reduction of the bisoxindole **21** with lithium aluminum hydride gave folicanthine (**3**) in racemic form (Scheme 4, yield not reported). The stereochemistry of this synthetic folicanthine was assigned as racemic as "the infrared spectrum in carbon tetrachloride solution superimposable with that of natural folicanthine".[15c]



Scheme 4. Hino's synthesis of (±)-folicanthine (**3**). Conditions: a) $ClCH_2CN$, K_2CO_3, NaI. b) PtO_2, H_2, AcOH, 30 % two steps. c) imine formation; MeI, 100 °C; HCl, H_2O, yield and specific conditions not given. d) $LiAlH_4$, 1,4-dioxane, yield not given.

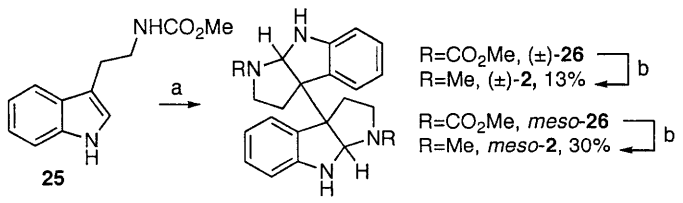
In 1964, Scott, McCapra, and Hall reported an elegant and highly concise total synthesis of chimonanthine taking full advantage of the oxidative dimerization strategy mentioned above and simply starting with *N*-methyl tryptamine (**22**).[16] Treatment of compound **22** with methyl magnesium iodide in diethyl ether provided the corresponding Grignard salt that was rapidly oxidized upon treatment with ferric chloride. The oxidation of the Grignard salt resulted in the oxidative coupling and C–C bond formation to afford 19% yield of (±)-chimonanthine (**2**) along with 7% yield of *meso*-chimonanthine (**2**, Scheme 5). This single-step ferric chloride promoted

oxidative dimerization of tryptamine derivatives to the desired chimonanthines provided a rapid entry to these dimeric alkaloids and further highlighted the challenges associated with stereochemical control in synthesis of the vicinal quaternary stereogenic centers.



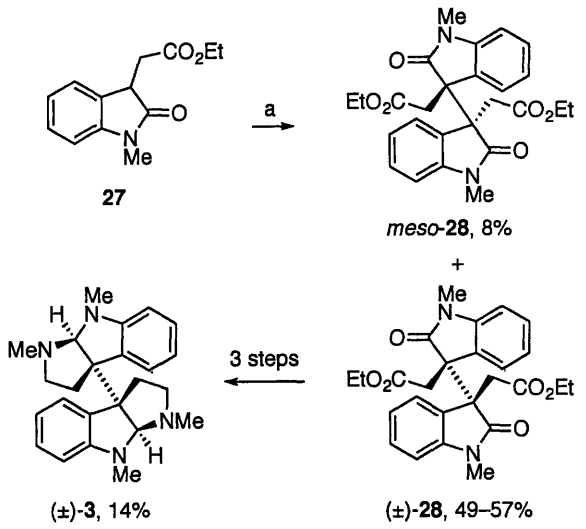
Scheme 5. Scott, McCapra and Hall's elegant synthesis of chimonanthines.

In a related approach, Takayama reported a synthesis of chimonanthines utilizing hypervalent iodine reagents (Scheme 6).[17] Dimerization of *N*-methoxycarbonyl tryptamine (**25**) with phenyliodine bis(trifluoroacetate) (PIFA) in 2,2,2-trifluoroethanol (TFE) afforded a mixture of the racemic carbamate **26** and *meso*-carbamate **26**. Reduction of these methyl carbamates with Red-Al afforded chimonanthine (**2**) in racemic form along with *meso*-chimonanthine (**2**) in 13% and 30% yields, respectively (Scheme 6). In a similar manner, Verotta reported the use of thallium(III) trifluoroacetate as the oxidant in this type of dimerization reaction.[18] The use of a trypamine substrate adorned with a chiral auxiliary enabled them to access optically active derivatives after chromatographic separation of diastereomers.



Scheme 6. Takayama's synthesis of the chimonanthines. Conditions: a) PIFA, TFE. b) Red-Al, PhMe.

In 1994, Rodrigo described a related approach for the synthesis of racemic folicanthine (**3**) by oxidative dimerization of an oxindole-derived enolate (Scheme 7).[19] Treatment of the anion of oxindole **27** with carbon tetraiodide afforded the racemic dimer **28** in 49-57% yield along with 8% yield of *meso*-**28**. Folicanthine (**3**) was prepared in 14% yield and in racemic form following three additional steps from dimer (±)-**28**.

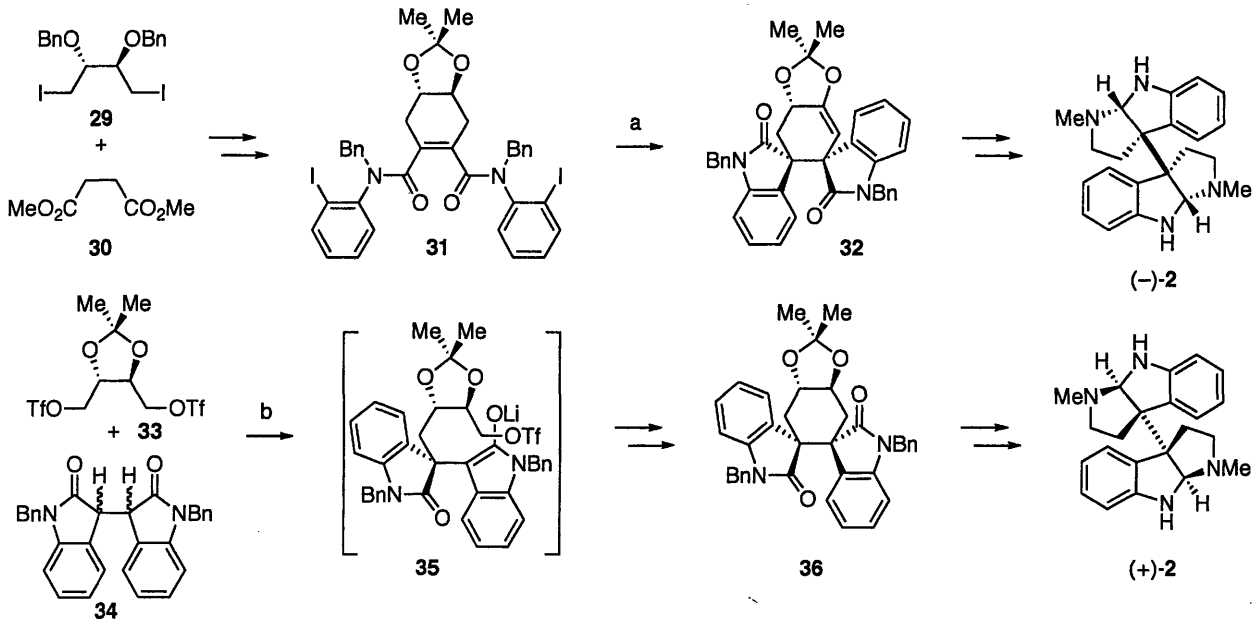


Scheme 7. Rodrigo's synthesis of (±)-folicanthine. Conditions: a) NaH, CI_4.

Prior Enantioselective Synthesis

Overman reported the first enantioselective total synthesis of chimonanthine in 1999.[20a] This elegant synthesis relied on two intramolecular Heck reactions to secure the vicinal quaternary stereocenters (Scheme 8). In this synthesis the enediamide **31** was prepared in six steps from the tartaric acid derived diiodide **29** and the dimethyl butanedioate (**30**). The key transformation proceeds via two intramolecular Heck cyclization reactions to sequentially secure the two quaternary stereocenters and afford the bisoxindole **32** in 90% yield as a single diastereomer. This beautifully designed transformation provided access to optically active and advanced intermediates that were converted to chimonanthine through additional steps. As the result of these studies Overman was also able to revise the absolute stereochemistry of this natural product. Subsequently, the Overman group reported a second approach[20b] to these molecules by utilizing an alkylation reaction as the key step. This approach relied on two alkylation reactions of bisoxindole **34** with bistrifluormethanesulfonate **33** to sequentially introduce the vicinal quaternary stereocenters. The careful choice of the counter ion was found

to be critical in controlling the stereochemistry of the product of this double alkylation reaction. The bisoxindole **36** could be converted to (+)-chimonanthine (**2**) utilizing transformations related to their earlier report.



Scheme 8. Overman's enantioselective total syntheses of (–) and (+)-chimonanthine (**2**). Conditions: a) 10 mol % $Pd(PPh_3)_2Cl_2$, Et_3N, DMA, 100 °C, 90%. b) 2.1 equiv LiHMDS, THF, DMPU, –78 °C, 55%.

Results and Discussion

Early Synthetic Studies of Chimonanthine

The rapid assembly of the chimonanthine core structure utilizing and oxidative dimerization strategy was clearly an exciting approach as illustrated more than four decades ago in the Scott, McCapra, and Hall's single-step synthesis of chimonanthines. These reports inspired our early approach toward the development of general and enantioselective syntheses of these alkaloids. We hoped to address the challenges associated with enantioselective and diastereoselective total synthesis of these alkaloids through the use of rationally designed tethered substrates to bring together two tryptamine or tryptophan units. As the first set of targets for our studies we chose the calycanthaceous alkaloids given the presence of their substructure in many alkaloids in this large family of natural products.

Three scenarios were envisioned for our planed stereoselective synthesis: 1) the use of optically active tethers with trypamine derivatives; 2) the use of achiral tethers with tryptophan derivatives; and 3) identification of appropriate optically active tethers with tryptophan

derivatives to maximize substrate directed stereoselective introduction of the vicinal quaternary stereocenters. The primary amine and the indolyl nitrogen of tryptophan and trypamine along with the carbonyl of tryptophan were expected to serve as suitable attachment points for tethers (Figure 2). We reasoned that if a suitable carbamate based linker (L_2) was employed, it could be removed after dimerization by a reduction step, converting the carbamate carbonyl into the required methyl group found in the chimonanthines. The distance of the tether to the reactive indole C3 position did pose a concern for control of stereochemistry. Linking two tryptophan units together was considered beneficial owing to the resident chiral center. While a carbamate linker (L_2) could be used in conjunction with a tryptophan substrate, an ester (L_3) linker could offer an alternative point for the linker, particularly since the carbonyl groups would be removed later. Lastly, we considered attachment of the tether to the indolyl nitrogen (L_1). This would be advantageous in that the tether would be closer to the reactive indole C3 center; however, at the time the effect of nitrogen substituents on the hypervalent iodine promoted dimerization step was uncertain.

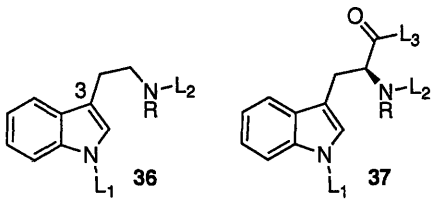
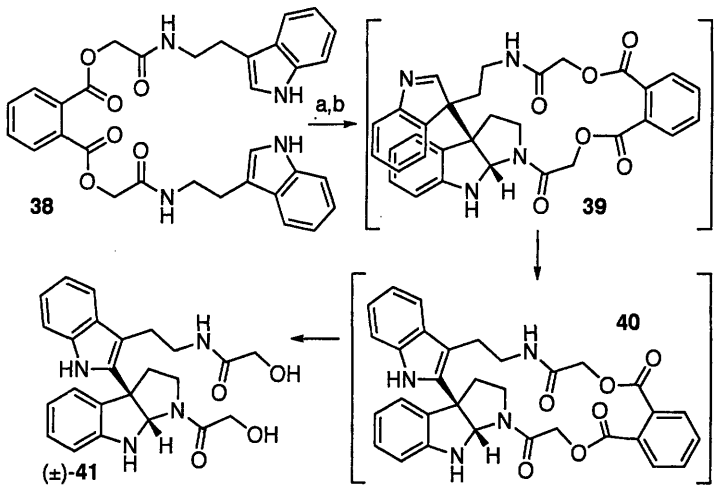


Figure 2. Substrates and points of attachment for tethers.

We first examined tryptamine units linked together through alkyl carbamates using the primary amino group (i.e., **36**, R and L_1= H, L_2= carbamate linker). We prepared carbamate linked tryptamine dimers with simple alkyl linkers such as 1,4-^{n}butyl, 1,4-(*E*)-2-butenyl, and 1,10-^{n}decyl. Unfortunately, these tethered dimeric tryptamines were all insoluble under the optimum conditions for hypervalent iodine mediated dimerization (PIFA, base, TFE, –40 °C), resulting in little conversion to the desired dimerization products and mostly recovered starting material. We reasoned that placement of additional heteroatoms in the linker would provide a more practical tethering scheme.[21] The tethered tryptamine derivative **38** was one of the first substrates to exhibit suitable solubility for the planned oxidative carbon–carbon bond formation. Interestingly, exposure of substrate **38** to the optimum oxidation reaction conditions followed by

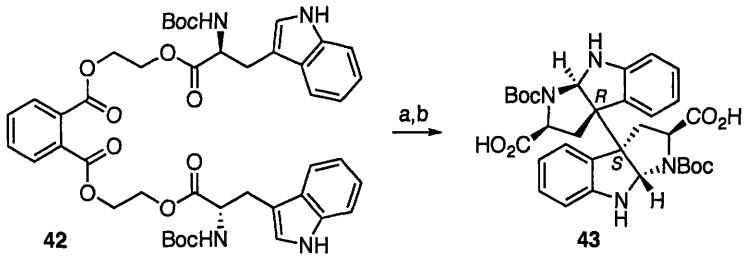
hydrolysis led to the unexpected C3a–C2′ adduct **41** and not the desired C3a–C3a′ adduct (Scheme 9). The structure of compound **41** was determined through the analysis of a series of 2D-NMR spectroscopic data. Based on a range of circumstantial evidence available to us in the context of these and related studies, the formation of compound **41** was best explained by a plausible initial formation of the desired C3a–C3a′ adduct **39** which was likely unable to undergo aminal formation due to the presence of the linker, thereby allowing a competitive C3a′ to C2′ migration to give product **40**. Increasing the tether length by adding additional methylenes between the amide and the ester group (from one methylene to three or five) did not prevent this rearrangement and the corresponding C3a–C2′ adduct were isolated in all cases.



Scheme 9. Representative C–C bond formation with a tethered tryptamine substrate **38**. Conditions: a) PIFA, 2-Cl-pyridine, TFE, 16%, along with 36% recovered **38**. b) KOH_{aq}, 31%.

We next envisioned the use of tethered tryptophan subunits to afford the desired C3a-C3a′ products by positioning the tether on the ester functional group so as to not tie back the amino ethyl fragment. This also provides a more nucleophilic carbamate as compared to an amide function group for trapping of the initial indolenine adduct (i.e., **39**). Furthermore, we were interested to see the extent of diastereoselection in the oxidative bond formation imposed by the C_α-stereocenter of a tethered tryptophan substrate. With these parameters in mind we prepared substrates such as **42** from readily available *N*-Boc L-tryptophan (Scheme 10). Exposure of the tethered tryptophan derivative **42** to the optimum reaction conditions using PIFA as the oxidant afforded a complex mixture of products. From this mixture the major product could be isolated in only 16% yield. Hydrolysis of the major product with potassium hydroxide

afforded a biscarboxylic acid that upon a series of NMR spectroscopic analyses, was found to be consistent with the dimeric hexahydropyrroloindole derivative **43** containing the *R*,*S* configuration at the vicinal quaternary stereocenters (Scheme 10).



Scheme 10. Representative C3a–C3a′ bond formation with a tethered tryptophan substrate **42**. Conditions: a) PIFA, 2-Cl-pyridine, TFE, 16%. b) KOH_{aq}, 93%.

With the successful use of the tethered carbamate **42** to access the desired C3a-C3a′ product seen in dimer **43**, we turned our attention to tethered systems that could be engineered to favor the desired *R*,*R* or *S*,*S* relative stereochemistry at the vicinal quaternary carbons. We next explored tryptamine derived substrates tethered through the indolyl nitrogen with the pendant carbamates free to intercept a plausible C–C coupled indolenine intermediate prior to the undesired C3 to C2 rearrangement mentioned above. The closer proximity of the tether to the indole C3 position was envisioned to impart greater stereochemical control in the dimerization reaction. Two sets of substrates were prepared as represented by structures **44** and **45** in Figure 3. Substrate **44** was prepared by *N*-alkylation of the indolyl nitrogen with 1-iodo-3-'butyldimethylsilyloxypropane followed by TBAF desilylation and linking of the resulting primary alcohol with dichlorodiisopropylsilane. Substrate **45** was prepared in a similar fashion with the exception of using a L-tartaric acid derivative as the electrophile.

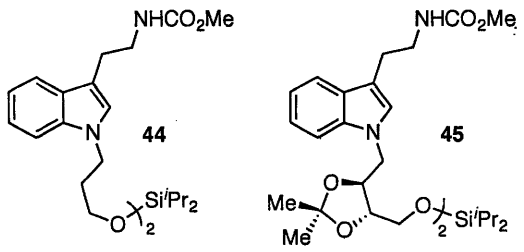
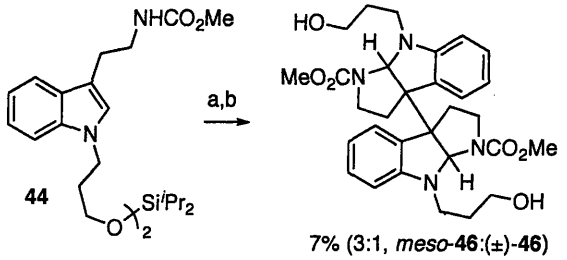


Figure 3. Representative indolyl tethered tryptamine derived substrates.

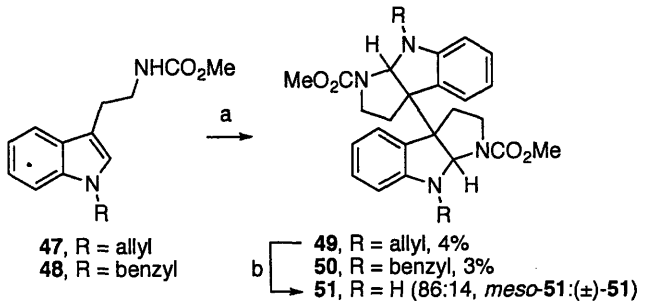
Oxidation of tether dimeric trypamine derivative **44** under optimum reaction conditions with PIFA and subsequent treatment with TBAF afforded a 3:1 mixture of the C3a–C3a' *meso*-**46** and (±)-**46** in only 7% combined yield (Scheme 11). The stereochemistry of the products was rigorously confirmed by NMR experiments in addition to independent synthesis. Synthesis of dimers (±)-**26** and *meso*-**26** using the Takayama protocol (vide supra)[17] and *N*-alkylation with excess 3-'butyldimethylsilyloxypropanal and sodium triacetoxyborohydride followed by desilylation of the alcohol with TBAF afforded authentic samples of diols (±)-**46** and *meso*-**46**.



Scheme 11. C3a–C3a' bond formation with the tethered tryptamine substrate **44**. Conditions: a) PIFA, 2-Cl-pyridine, TFE. b) TBAF, THF, 7% (2 steps).

The low yield of the corresponding product when using substrate **45** (11% yield, of oxidative C–C coupled product) was further complicated due to the failure of various attempts to remove the tartrate based linking group owing to the sensitivity of the dimer to acidic and strong oxidative conditions. The lowered efficiency observed with substrates **44** and **45** in these intramolecular C–C bond forming reactions was due to the presence of the indolyl alkyl substituents. This was illustrated further using the *N*-allyl and *N*-benzyl derived tryptamine derivatives **47** and **48** (Scheme 12). The intermolecular oxidative coupling of these substrates was less effective compared to related systems with no indolyl alkyl groups as described by Takayama (Scheme 6). Upon treatment with PIFA under optimum conditions, the *N*-allyl and *N*-benzyl substrates **47** and **48** afforded the corresponding C–C coupled dimer in only 4% and 3% yield, respectively, as a mixture of diastereomers. In the case of hexacycle **49**, treatment with ruthenium bisisoprene dimer complex[22] in water afforded the hexacycle **51** as a mixture of diastereomers (86:14, *meso*-**51**, (±)-**51**), with stereochemistries confirmed through NMR and by direct comparison with authentic samples prepared through an independent synthesis via previously reported procedures.[17] Interestingly, a series of experiments highlighted the sensitivity of the hexacyclic structures **49** and **50** to oxidative and acidic reaction conditions. A set of

control experiments on (±)-**26** and *meso*-**26** confirmed the high sensitivity of these compounds under the standard PIFA oxidation conditions. For example, exposure of dimer (±)-**26** or *meso*-**26** to PIFA (1 equiv) resulted in decomposition and afforded a complex mixture in less than 5 min.



Scheme 12. C3a–C3a′ bond formation with the *N*-allyl and *N*-benzyl tryptamine derived substrates **47** and **48**. Conditions: a) PIFA, 2-Cl-pyridine, TFE. b) 6 mol% $[RuCl_2(C_{10}H_{18})]_2$, H_2O, 90 °C, 4.5 h, 16%.

Reductive Dimerization Approach

These observations taken collectively in addition to other findings in the context of our early studies all pointed to significant challenges associated with stereochemical control using the above strategy for development of a practical and concise total synthesis of these alkaloids. To decouple the issues of reactivity and stereoselectivity, we sought ways to impart the required stereochemical information to the substrate prior to the dimerization and carbon–carbon bond formation. Importantly, we envisioned the exchange of the single electron oxidation pathways, explored above, to access the C3a centered radical for a single electron reduction of the corresponding alkyl halide.[23] Indeed, an important precedent for this hypothesis was observed by Danishefsky, who, en route to amauromine and the ardeemin natural products, observed dimerization products in the course of radical prenylation of a similar selenide substrate (Figure 4).[24] In this regard, we were inspired by the work of Crich who had successfully utilized cyclic isomers of tryptophan to construct hexahydropyrroloindole alkaloids (Figure 4).[25]

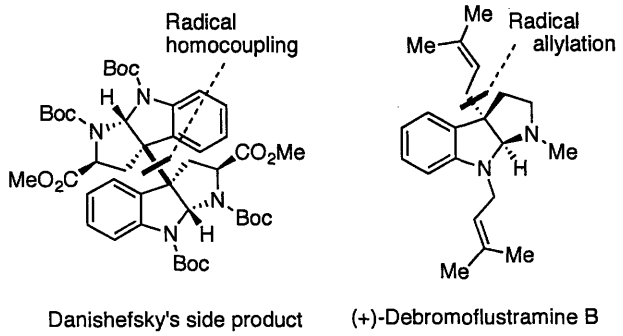
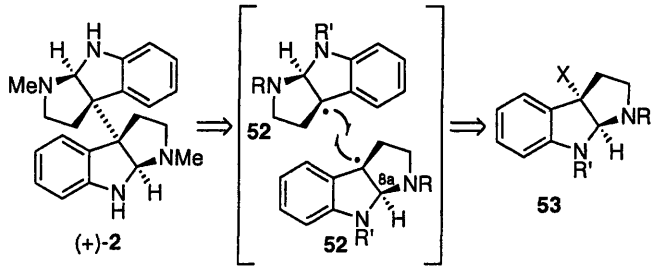


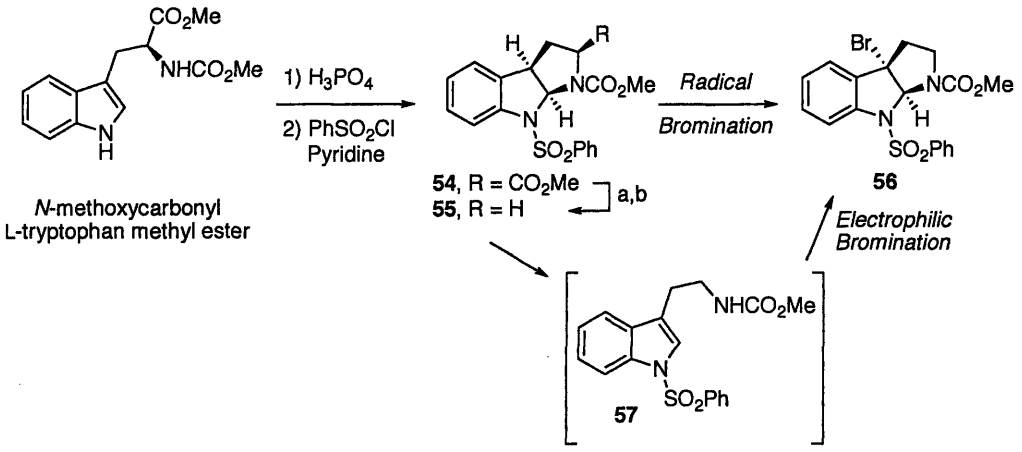
Figure 4. Prior precedent for our reductive homocoupling approach.

Scheme 13 illustrates our retrosynthetic analysis for (+)-chimonanthine [(+)-**2**] based on a reductive homodimerization strategy using a tertiary benzylic halide **53**.



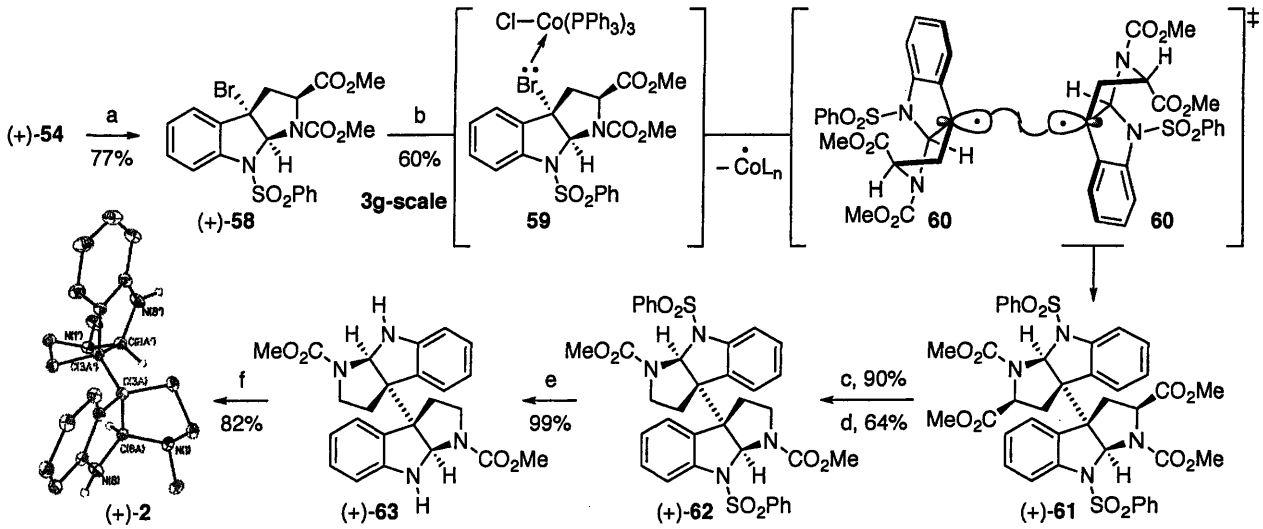
Scheme 13. A reductive homodimerization approach to (+)-chimonanthine (**2**).

Tricycle **54** (Scheme 14) was envisioned to serve as an outstanding precursor for the intermediate **52** (Scheme 13). The strategic positioning of the sulfonyl group on the aniline nitrogen would enable the positioning of the desired halides at the C3a position. Hexahydropyrroloindole derivative **54** was conveniently prepared in two steps from commercially available *N*-methoxycarbonyl tryptophan methyl ester on >20g scale as a single diastereomer with >99% ee (Scheme 14). The decarboxylation of **54** was achieved using the corresponding acid chloride in conjunction with the Chatgilialoglu[26] reagent, affording the tricycle **55** in 84% yield and >99% ee as determined by chiral HPLC analysis.[23] Free radical bromination of **55** under a variety of reaction conditions was problematic, affording the desired product in variable yields and with extensive loss in optical activity. Through a series of control experiments, we recognized the particular sensitivity of the tricycle **55** toward Brønsted acids, and the competitive electrophilic bromination of tryptamine derivative **57** giving rise to the bromide **56** (Scheme 14). Various basic additives did not thwart this undesired pathway. Although this undesired electrophilic bromination reaction was an obstacle in our early studies, the lessons learned from these experiments later proved highly valuable for development of efficient strategies for the synthesis of related alkaloids.



Scheme 14. Synthesis of our initial precursor for the hexahydropyrrolyl radical **52** and the observed competitive electrophilic bromination reaction. Conditions: a) KOH_{aq}. b) oxalyl chloride, DMF (cat.); $(Me_3Si)_3SiH$, AIBN, PhMe, 110 °C, 84% (2 steps), >99% ee.

Given the greater stability of hexahydropyrroloindole derivative **54**[25] as compared to **55**, we decided to postpone the decarboxylation reaction until after the critical dimerization reaction (Scheme 15). Bromination of **55** with 1,3-dibromo-5,5-dimethylhydantoin in the presence of AIBN afforded the desired benzylic bromide **58** in good yield and with complete retention of optical activity (Scheme 15). We next focused on the key dimerization reaction. A variety of reductive conditions were explored for the generation of the C3a radical center including the use of Mg, Li, SmI_2, a wide range of reducing copper complexes, $FeCl_3$–Mg systems, and $^nBu_6Sn_2$ along with heat or photochemical activation. Our first successful dimerization of bromide **58** was achieved using 0.5 equiv of $Mn_2(CO)_{10}$ in dichloromethane under visible light irradiation for 16 h, affording the desired dimer **61** as a single diastereomer in 18% yield and >99% ee (Scheme 15). Using an equimolar quantity of $Mn_2(CO)_{10}$, the yield of the desired product **61** rose to 33%, but no further improvement was observed after an extensive survey of reaction conditions. We reasoned that given the second order dependence of the dimerization rate with respect to the benzylic radical concentration (i.e., **60**, Scheme 15), the reaction time using $Mn_2(CO)_{10}$ (16 h) was too long and non-ideal. We identified a cobalt(I) complex, $Co(PPh_3)_3Cl$[27] as a potential solution due to its more rapid halogen abstraction from benzylic chlorides in benzene.[28]



Scheme 15. Total synthesis of (+)-chimonanthine (**2**). Conditions: a) 1,3-dibromo-5,5-dimethylhydantoin, AIBN, CCl_4, 80 °C, 1 h, 77%. b) $CoCl(PPh_3)_3$, acetone, 23 °C, 15 min, 60%. c) KOH_{aq}–MeOH, 23 °C, 30 min, 90%. d) Oxalyl chloride, DMF, CH_2Cl_2, 23 °C, 1.5 h; $(Me_3Si)_3SiH$, AIBN, toluene, 80 °C, 3.5 h, 64%. e) Na(Hg), Na_2HPO_4, MeOH, 23 °C, 3.5 h, 99%. f) Sodium bis-(2-methoxyethoxy) aluminium hydride, toluene, 110 °C, 1.5 h, 82%.

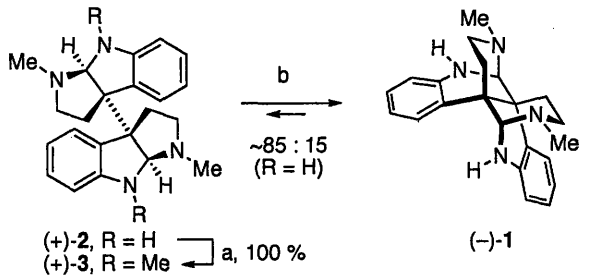
Significantly, treatment of the bromide **58** with 1.2 equiv $Co(PPh_3)_3Cl$ in benzene afforded the product in 34% yield in only 15 min. The dimerization was found to be most sensitive to the choice of reaction solvent. We recognized acetone as the best solvent choice giving the product in 60% yield as a single diastereomer and >99% ee on a 3g scale (Table 1).

Table 1. The effect of solvent on the key dimerization reaction.

Solvent ([**58**] = 0.1 M)	Isolated Yield of **61** (%)
benzene	34
dimethyl formamide	31
dichloromethane	40
3-pentanone	38
butanone	47
acetone	60

After saponification, dimer **61** was subject to double decarboxylation using the Chatgilialoglu procedure we had used earlier on the tricycle (vide supra) to afford the hexacycle **62** in 64% yield. Removal of the benzenesulfonyl groups with sodium amalgam to give product **63** followed by reduction of the methoxycarbonyl groups with Red-Al afforded (+)-chimonanthine (**2**) in eight steps from the commercially available *N*-methoxycarbonyl tryptophan methyl ester.

N-methylation of (+)-**2** yielded the first synthetic sample of (+)-folicanthine (**3**) in quantitative yield. Congruent with Overman's revision[20a] of the absolute stereochemistry of the chimonanthine alkaloids, the absolute stereochemistry of our synthetic (+)-folicanthine (**3**) was antipodal to the originally assigned structure (Scheme 16). Dissolution of (+)-**2** in acetic acid-d_4 and deuterium oxide followed by heating provided isomeric (–)-calycanthine (**1**, Scheme 16).[14b,16b] We monitored this transformation by ^{1}H NMR spectroscopy and observed a ratio (~85:15) in favor of (–)-calycanthine (**1**) in 24 h. Isolation of (–)-**1** and subjection to the identical conditions establishes the same ~85:15 ratio in favor of (–)-**1**, confirming this equilibration.



Scheme 16. Total synthesis of (+)-folicanthine (**3**) and (–)-calycanthine (**1**). Conditions: a) formalin, $NaBH(OAc)_3$, MeCN, 23 °C, 30 min. b) acetic acid-d_4, D_2O, 95 °C, 24 h, 54% (–)-**1**, 5% (+)-**2**.

Conclusion

The concise and efficient total synthesis of (+)-chimonanthine, (+)-folicanthine, and (–)-calycanthine is described. The convergent assembly of these alkaloids utilizes a reductive Co(I)-promoted dimerization of readily available *endo*-bromide (+)-**58**. The gram-scale synthesis of enantiomerically enriched hexacycle (+)-**61** provides ready access to optically active alkaloids **1-3**. This chemistry simultaneously secures the vicinal quaternary stereocenters directed by the C8a-stereochemistry and offers the shortest enantioselective synthesis of these alkaloids from commercially available materials.

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Experimental Section

General Procedures. All reactions were performed in oven-dried or flame-dried round-bottomed flasks. The flasks were fitted with rubber septa and reactions were conducted under a positive pressure of argon. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Where necessary (so noted), solutions were deoxygenated by dinitrogen purging for a minimum of 10 min. Flash column chromatography was performed as described by Still et al. using silica gel (60-Å pore size, 32–63 μm, standard grade, Sorbent Technologies).[1] Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light and iodine vapors or an aqueous solution of ceric ammonium molybdate (CAM). Organic solutions were concentrated on Büchi R-200 rotary evaporators at ~20 Torr (house vacuum) at 25–35 °C.

Materials. Commercial reagents and solvents were used as received with the following exceptions: dichloromethane, acetonitrile and toluene were purchased from J.T. Baker (Cycletainer^{TM}) and were purified by the method of Grubbs et al. under positive argon pressure.[2] Acetone was distilled from anhydrous calcium sulfate. Methanol (>99.9 % HPLC grade, ≤0.020 % water) was purchased from Aldrich chemical company and used as received. CH_2Cl_2 saturated with NH_3 was prepared by agitation of a 2:1 (v/v) biphasic mixture of CH_2Cl_2 and 28-30% aqueous NH_4OH, separation of the organic layer and drying over Na_2SO_4. AIBN was recrystallized from diethyl ether. Na_2HPO_4 was dried by flame–drying under reduced pressure for 5 min.

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with Varian inverse probe 500 INOVA and Varian 500 INOVA spectrometers and are recorded in parts per million from internal tetramethylsilane on the δ scale and are referenced from the residual protium in the NMR solvent ($CHCl_3$: δ 7.27, DMSO-d_6: δ 2.50). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant(s) in Hertz, integration, assignment]. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a Varian 500 INOVA spectrometer and are recorded in parts per million from internal tetramethylsilane on the δ scale and are referenced from the carbon resonances of the solvent ($CDCl_3$: δ 77.23, DMSO-d_6: δ 39.51). Data is reported as follows: chemical shift [assignment]. Infrared data (IR) were obtained with a Perkin-Elmer 2000 FTIR, and are reported as follows: [frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad)]. Optical rotations were measured on a Jasco-1010 polarimeter. Enantiomeric excess was determined by chiral HPLC analysis performed on an Agilent Technologies 1100 series HPLC system with a Daicel Chirapak AD-H column. We are grateful to Dr. Li Li for obtaining the mass spectrometric data at the Department of Chemistry's Instrumentation Facility, Massachusetts Institute of Technology. The structure of (+)-chimonanthine was obtained with the assistance of Dr. Peter Mueller at the X-ray crystallography laboratory of the Department of Chemistry, Massachusetts Institute of Technology.

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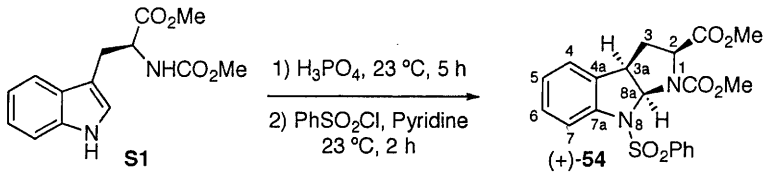


Hexahydropyrroloindole (+)-54:[3]

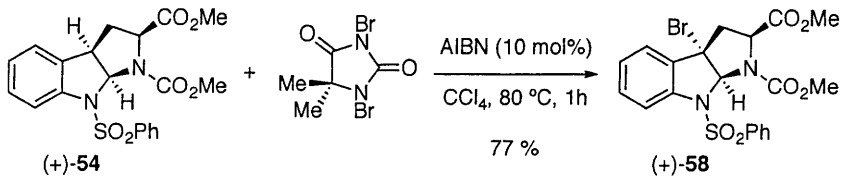
A fine suspension of carbamate **S1** (25.2 g, 95.4 mmol, 1 equiv) in aqueous phosphoric acid (85%) was vigorously stirred. After 5h, a homogenous light tan solution formed. The thick solution was added drop-wise to a vigorously stirred mixture of dichloromethane (600 mL) and an aqueous solution of sodium carbonate (11% wt/wt, 600 ml). The pH of the aqueous layer was monitored throughout the addition, and once it reached pH = 7, another portion of solid sodium carbonate (66 g) was added slowly. The addition was continued in this manner until completion (total Na_2CO_3 added = 198 g). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (4 × 200 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure to afford a white foam (24.3 g, 96%). The hexahydropyrroloindole (1.7 g, 6.4 mmol, 1 equiv) was dissolved in pyridine (8.60 mL) and benzenesulfonyl chloride (1.65 mL, 12.8 mmol, 2.00 equiv) was added and the mixture vigorously stirred. After 2 h, pyridine was removed under reduced pressure and the residue was suspended in ethyl acetate (50 mL). The organic suspension was sequentially washed with aqueous hydrochloric acid solution (1N, 2 × 25 mL), saturated aqueous sodium bicarbonate solution (50 mL), and brine (100 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure to afford a dark red residue. The residue was purified by flash column chromatography (eluent: 50% EtOAc in hexanes) to afford hexahydropyrroloindole (+)-**54** as a white solid (1.7 g, 64%; 61% from **S1**). This compound was determined to be of >99% ee by chiral HPLC analysis (Chirapak AD-H, 90 % hexanes / 10% isopropanol, 3.0 mL/min, 254 nm, t_R (minor, not observed) = 11.9 min, t_R (major) = 23.0 min). All spectral data were in agreement with the literature.[3]

^{1}H NMR (500 MHz, $CDCl_3$, 50 °C): δ 7.76 (d, J = 8.0 Hz, 2H, SO_2Ar-*o*-**H**), 7.51 (t, J = 7.5 Hz, 1H, SO_2Ar-*p*-**H**), 7.46 (d, J = 8.0 Hz, 1H, C_7**H**), 7.40 (t, J = 7.3 Hz, 2H, SO_2Ar-*m*-**H**), 7.23 (app-t, J = 8.0 Hz, 1H, C_6**H**), 7.03-7.07 (m, 2H, C_4**H**, C_5**H**), 6.29 (d, J = 6.0 Hz, 1H, C_{8a}**H**), 4.60 (d, J = 9.0 Hz, 1H, C_2**H**), 3.67 (t, J = 6.8 Hz, 1H, C_{3a}**H**), 3.60 (s, 3H, NCO_2C**H**$_3$), 3.16 (s, 3H, CO_2C**H**$_3$), 2.59 (d, J = 13.0 Hz, 1H, C_3**H**$_{endo}$), 2.46 (ddd, J =13.0, 9.0, 7.5 Hz, 1H, C_3**H**$_{exo}$).

^{13}C NMR (125.8 MHz, $CDCl_3$, 50 °C): 171.5 (**C**=O), 154.9 (N**C**=O), 142.9 (C_{7a}), 140.3 (SO_2Ar-*i*-**C**), 133.1 (C_{4a}), 132.9 (SO_2Ar-*p*-**C**), 129.08 (SO_2Ar-*m*-**C**), 129.07 (C_6), 126.9 (SO_2Ar-*o*-**C**), 125.3 (C_5), 124.5 (C_4), 118.5

[3] C.-O. Chan, C. J. Cooksey, D. Crich, *J. Chem. Soc. Perkin Trans. 1* **1992**, 777.

	($\mathbf{C}_7$), 80.3 ($\mathbf{C}_{8a}$), 59.2 ($\mathbf{C}_2$), 52.9 ($NCO\mathbf{C}H_3$), 52.1 ($CO\mathbf{C}H_3$), 45.9 ($\mathbf{C}_{3a}$), 33.9 ($\mathbf{C}_3$).
FTIR (thin film) cm^{-1}:	3065 (m), 2953 (s) 1753 (s), 1712 (s), 1384 (s), 1359 (s).
HRMS (ESI):	calc'd for $C_{20}H_{21}N_2O_6S$ $[M+H]^+$: 417.1115 found: 417.1105
M.p. (ethyl acetate–hexanes):	160.5–161.5 °C
$[\alpha]^{20}_D$:	+88 ° (c = 1.00, CH_2Cl_2)



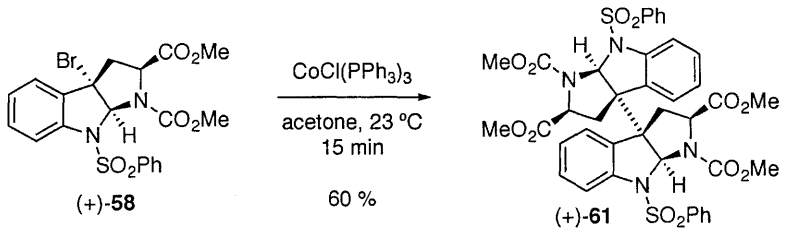
(+)-**54** (+)-**58**

Tricyclic bromide (+)-58:[4]

Dibromohydantoin (2.90 g, 10.0 mmol, 1.00 equiv) followed by AIBN (164 mg, 1.00 mmol, 0.100 equiv) were added to a suspension of the tricycle (+)-**54** (4.16 g, 10.0 mmol, 1 equiv) in CCl_4 (250 mL) at room temperature. The mixture was heated to 80 °C for 1 h at which point the solution became dark orange–red and a white solid precipitated. The reaction mixture was cooled to room temperature, the volatiles were removed under reduced pressure, and the residue was purified by flash column chromatography (eluent: 0 → 40% ethyl acetate in hexanes) to afford the tricyclic bromide (+)-**58** as a white foam (3.80 g, 77%). This compound was determined to be of >99% ee by chiral HPLC analysis (Chirapak AD-H, 10% isopropanol in hexanes, 3.0 mL/min, 254 nm, t_R (minor, not observed) = 8.2 min, t_R (major) = 14.8 min)).

^{1}H NMR (500 MHz, $CDCl_3$, 50 °C):	7.87 (d, J = 7.5 Hz, 2H, SO_2Ph-*o*-**H**), 7.55 (d, J = 8.0 Hz, 1H, C_4**H**), 7.52 (app tt, J = 7.5, 1.0 Hz, 1H, SO_2Ph-*p*-**H**), 7.42 (t, J = 8.0 Hz, 2H, SO_2Ph-*m*-**H**), 7.34 (app td, J = 7.5, 1.0 Hz, 1H, C_6**H**), 7.26 (d, J = 8.0 Hz, 1H, C_7**H**), 7.14, (td, J = 7.5 Hz, 1.0 Hz, 1H, C_5**H**), 6.36 (s, 1H, C_{8a}**H**), 4.62 (d, J = 9.0 Hz, 1H, C_2**H**), 3.70 (s, 3H, NCO_2C**H**$_3$), 3.27 (d, J = 13.0 Hz, 1H, C_3**H**), 3.17 (s, 3H, CO_2C**H**$_3$), 3.04 (dd, J = 13.0, 9.0 Hz, 1H, C_3**H**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 50 °C):	170.2 (**C**=O), 154.3 (N**C**=O), 142.1 (C_{7a}), 140.1 (SO_2Ph-*i*-**C**), 133.5 (C_{4a}), 133.4 (SO_2Ph-*p*-**C**), 131.3 (SO_2Ph-*m*-**C**), 129.2 (C_6), 127.7 (SO_2Ph-*o*-**C**), 125.9 (C_5), 124.8 (C_4), 118.4 (C_7), 87.4 (C_{8a}), 60.2 (C_{3a}), 59.9 (C_2), 53.2 (NCO_2CH_3), 52.4 (CO_2CH_3), 44.9 (C_3).
FTIR (thin film):	2954 (s), 1755 (s), 1716 (s), 1601 (m), 1447 (s).
HRMS-ESI (*m/z*):	calc'd for $C_{20}H_{19}BrN_2NaO_6S$[M+Na]$^+$:517.0039 found: 517.0016.
$[\alpha]_D^{22}$:	+107 (c = 1.00, $CHCl_3$).
TLC (40% EtOAc in hexanes), R*f*:	0.33 (UV, I_2).

[4] a) M. Bruncko, D. Crich, R. Samy, *Heterocycles*, **1993**, *36*, 1735. b) M. Bruncko, D. Crich, R. Samy, *J. Org. Chem.* **1994**, *59*, 5543.

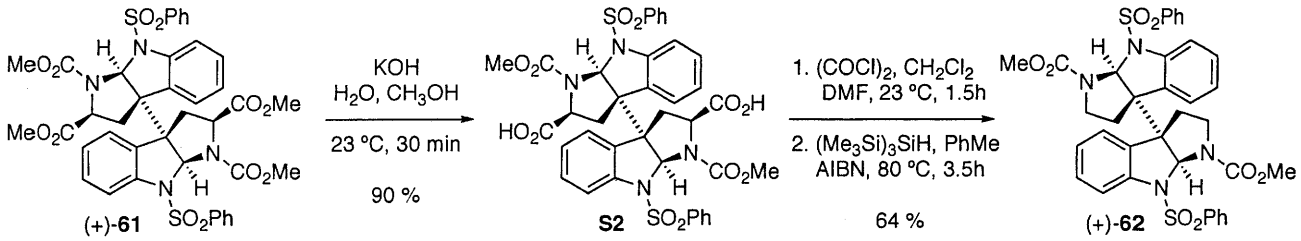


Dimeric hexahydropyrroloindole (+)-61:

A solid sample of freshly prepared tristriphenylphosphine cobalt chloride ($CoCl(PPh_3)_3$[5], 6.40 g, 72.7 mmol, 1.20 equiv) was added rapidly to a degassed (dinitrogen purge, 10 min) solution of tricyclic bromide (+)-**58** (3.00 g, 6.06 mmol, 1 equiv) in acetone (61.0 mL) under an argon atmosphere. The solution immediately turned blue and a precipitate resulted. After 15 min, the reaction mixture was diluted with deionized water (200 mL) and extracted with ethyl acetate (3 × 150 mL). The combined organic extracts were washed with brine (100 mL), were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting yellow oil was purified by flash column chromatography (10% acetone in CH_2Cl_2) to yield the dimeric hexahydropyrroloindole (+)-**61** (1.50 g, 60%) as white foam. The hexacycle (+)-**61** was found to be of >99% ee by chiral HPLC analysis (Chirapak AD-H, 20% isopropanol in hexanes, 3.0 mL/min, 254 nm, t_R (minor, not observed) = 8.3 min, t_R (major) = 13.5 min).

^{1}H NMR (500 MHz, DMSO-d_6, 100 °C):	8.00 (d, J = 7.0 Hz, 4H, SO_2Ph-*o*-**H**), 7.70 (t, J = 7.3 Hz, 2H, SO_2Ph-*p*-**H**), 7.63 (t, J = 7.8 Hz, 4H, SO_2Ph-*m*-**H**), 7.27 (d, J = 7.5 Hz, 2H, C_4**H**), 7.16 (t, J = 7.8 Hz, 2H, C_6**H**), 7.08 (br d, J = 7.5 Hz, 2H, C_7**H**), 6.92 (t, J = 7.5 Hz, 2H, C_5**H**), 6.43 (s, 2H, C_{8a}**H**), 4.67 (d, J = 9.0 Hz, 2H, C_2**H**), 3.31 (br s, 6H, NCO_2C**H**$_3$), 3.12 (s, 6H, CO_2C**H**$_3$), 2.72 (dd, J = 12.8, 9.3 Hz, 2H, C_3**H**), 2.47 (d, J = 13.0 Hz, 2H, C_3**H**).
^{13}C NMR (125.8 MHz, DMSO-d_6, 100 °C):	169.6 (**C**=O), 153.0 (N**C**=O), 142.0 (**C**$_{7a}$), 141.2 (SO_2Ph-*i*-**C**), 132.4 (**C**$_{4a}$), 129.1 (SO_2Ph-*p*-**C**), 129.0 (SO_2Ph-*m*-**C**), 128.7 (SO_2Ph-*o*-**C**), 125.0 (**C**$_6$), 124.3 (**C**$_5$), 122.7 (**C**$_4$), 114.0 (**C**$_7$), 81.0 (**C**$_{8a}$), 60.8 (**C**$_{3a}$), 58.5 (**C**$_2$), 51.8 (NCO_2C**H**$_3$), 51.1 (CO_2C**H**$_3$), 36.8 (**C**$_3$).
FTIR (thin film):	2954 (m), 1750 (s), 1721 (s), 1602 (m), 1447(s).
HRMS-ESI (*m/z*):	calc'd for $C_{40}H_{39}N_4O_{12}S_2$ $[M+H]^+$: 831.2000 found: 831.2025.
$[\alpha]_D^{22}$:	+51 (c = 1.00, $CHCl_3$).
TLC (65% EtOAc in hexanes), R*f*:	0.23 (UV, I_2).

[5] Prepared according to M. Aresta, M. Rossi, A. Sacco, *Inorg. Chem. Acta.* **1969**, *3*, 227.



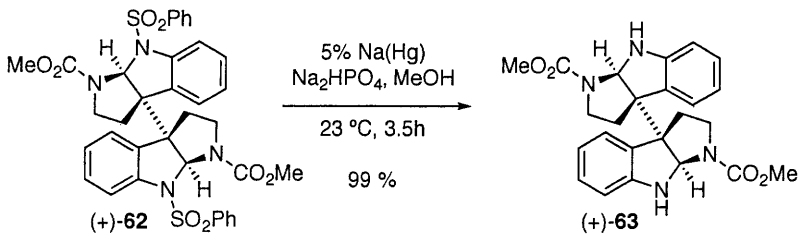
Hexacycle (+)-62:

An aqueous solution of potassium hydroxide (5 N, 10 mL) was added to a solution of dimer (+)-**61** (334 mg, 0.402 mmol, 1 equiv) in methanol (10 ml) at 23 °C. After 30 min, the resulting clear solution was cooled to 0 °C and adjusted to pH ~ 2 by the drop-wise addition of aqueous hydrochloric acid solution (~12N). The reaction mixture was extracted with chloroform (10 × 20 mL) and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure to afford the hexacyclic dicarboxylic acid as a white solid (291.3 mg, 90 %). The dicarboxyclic acid (263 mg, 0.328 mmol, 1 equiv) was concentrated from benzene (2 × 2.5 mL) under reduced pressure. Oxalyl chloride (114 μL, 1.31 mmol, 4.00 equiv) was added to a solution of dicarboxylic acid **S2** in CH_2Cl_2 (2.75 mL) at 23 °C. Dimethylformamide (DMF, 3.8 μL, 0.049 mmol, 0.15 equiv) was added, resulting in vigorous gas evolution. After 1.5 h, the volatiles were removed under reduced pressure and the residue was concentrated from benzene (2 × 3 mL) to remove the remaining oxalyl chloride. Tristrimethylsilylsilane ($(Me_3Si)_3SiH$, 305 μL, 0.985 mmol, 3.00 equiv) followed by AIBN (11 mg, 0.066 mmol, 0.20 equiv) were added to a solution of the crude dicarboxylic acid chloride in toluene (6.60 mL) and the mixture was heated to 80 °C. After 30 min, an additional portion of tristrimethylsilylsilane (305 μL, 0.985 mmol, 3.00 equiv) and AIBN (11 mg, 0.066 mmol, 0.20 equiv) were added. After 1.5 h, an additional portion of AIBN (11 mg, 0.066 mmol, 0.20 equiv) was added. After 1.5 h, the reaction mixture was cooled to 23 °C and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (60% ethyl acetate in hexanes) to afford the hexacycle (+)-**62** as a white solid (149.0 mg, 64%).

^{1}H NMR (500 MHz, DMSO-d_6, 100 °C): 7.91 (app d, J = 7.5 Hz, 4H, SO_2Ph-*o*-**H**), 7.71 (app t, J = 7.5 Hz, 2H, SO_2Ph-*p*-**H**), 7.63 (app t, J = 7.5 Hz, 4H, SO_2Ph-*m*-**H**), 7.38 (d, J = 8.5 Hz, 2H, C_4**H**), 7.19 (app t, J = 8.5 Hz, 2H, C_6**H**), 7.03 (br d, J = 7.5 Hz, 2H, C_7**H**), 6.87 (t, J = 7.5 Hz, 2H, C_5**H**), 6.28 (s, 2H, C_{8a}**H**), 3.74 (dd, J = 11.5, 8.0 Hz, 2H, C_2**H**), 3.56 (s, 6H, NCO_2C**H**$_3$), 2.57 (td, J = 11.8, 5.5 Hz, 2H, C_2**H**), 1.97 (td, J = 12.0, 8.0 Hz, 2H, C_3**H**), 1.85 (dd, J = 12.5, 5.5 Hz, 2H, C_3**H**).

^{13}C NMR (125.8 MHz, DMSO-d_6, 100 °C): 153.1 (**C**=O), 141.7 (C_{7a}), 139.7 (SO_2Ph-*i*-**C**), 132.9 (C_{4a}), 130.2 (SO_2Ph-*p*-**C**), 128.9 (SO_2Ph-*m*-**C**), 128.6 (SO_2Ph-*o*-**C**), 125.6 (C_6), 123.8 (C_5), 123.0 (C_4), 113.0 (C_7), 80.7 (C_{8a}), 62.0 (C_{3a}), 51.9 (CH_3), 43.9 (C_2), 35.1 (C_3).

FTIR (thin film):	2955 (m), 1713 (s), 1599 (w), 1476 (m), 1447 (s).
HRMS-ESI (*m/z*):	calc'd for $C_{36}H_{34}N_4NaO_8S_2$ $[M+Na]^+$: 737.1716 found: 737.1720.
$[\alpha]_D^{22}$:	+161 (*c* = 1.00, CH_2Cl_2).
TLC (50% EtOAc in hexanes), R*f*:	0.53 (UV, I_2).



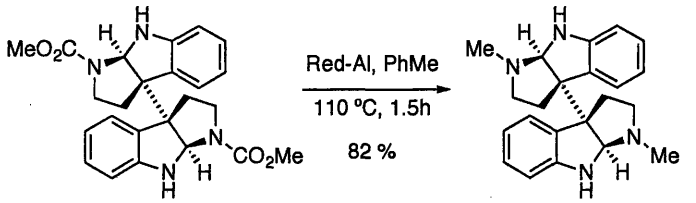
Hexacycle (+)-63:

Anhydrous sodium phosphate dibasic (Na_2HPO_4, 170 mg, 1.20 mmol, 8.00 equiv) followed by freshly prepared 5% Na(Hg)[6] (590 mg, 1.28 mmol, 8.50 equiv) were added to a solution of hexacycle (+)-**62** (107 mg, 0.150 mmol, 1 equiv) in methanol (2.0 mL). The resulting suspension was stirred and an additional sample of Na(Hg) (400 mg) was added approximately every hour until the completion of the reaction as judged by TLC analysis (total time 3.5 h). The reaction mixture was diluted with water (30 mL) and the aqueous layer was separated from the mercury. The aqueous layer was extracted with dichloromethane (3 × 30 mL) and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure to afford a white gel. The residue was purified by flash chromatography (20% ethyl acetate in CH_2Cl_2) to afford the product (+)-**63** (64.6 mg, 99%) as white foam.[7] This hexacycle (+)-**63** was determined to be >99% ee by chiral HPLC analysis (Chirapak AD-H, 10% isopropanol in hexanes, 3.0 mL/min, 254 nm, t_R (minor, not observed) = 7.6 min, t_R (major) = 11.7 min).

^{1}H NMR (500 MHz, DMSO-d_6, 100 °C):	7.23 (d, J = 7.5 Hz, 2H, C_4**H**), 7.02 (td, J = 7.8, 1.2 Hz, 2H, C_6**H**), 6.64 (td, J = 7.5, 1.0 Hz, 2H, C_5**H**), 6.59 (d, J = 7.5 Hz, 2H, C_7**H**), 6.11 (s, 2H, N**H**), 4.91 (s, 2H, C_{8a}**H**), 3.54–3.58 (m, 8H, C_2**H**, NCO_2C**H**$_3$), 2.75 (td, J = 10.8, 6.0 Hz, 2H, C_2**H**), 2.52 (td, J = 12.0, 8.0 Hz, 2H, C_3**H**), 2.12 (dd, J = 12.5, 6.0 Hz, 2H, C_3**H**).
^{13}C NMR (125.8 MHz, DMSO-d_6, 100 °C):	153.4 (**C**=O), 150.4 ($\mathbf{C}_{7a}$), 128.1 ($\mathbf{C}_6$), 128.0 ($\mathbf{C}_{4a}$), 124.0 ($\mathbf{C}_4$), 116.9 ($\mathbf{C}_5$), 108.2 ($\mathbf{C}_7$), 77.4 ($\mathbf{C}_{8a}$), 60.9 ($\mathbf{C}_{3a}$), 51.3 ($\mathbf{C}H_3$), 44.2 ($\mathbf{C}_2$), 31.8 ($\mathbf{C}_3$).
FTIR (thin film):	3365 (br m), 2954 (m), 1695 (s), 1607 (m), 1451 (s).
HRMS-ESI (*m/z*):	calc'd for $C_{24}H_{26}N_4NaO_4$ $[M+Na]^+$: 457.1846 found: 457.1830.
$[\alpha]_D^{22}$:	+474 (c = 1.00, CH_2Cl_2).
TLC (20% EtOAc in CH_2Cl_2), R*f*:	0.38 (UV, CAM).

[6] The reagent was prepared according to R. N. McDonald, C. E. Reineke, *Org. Synth., Coll. Vol. VI* **1988**, 461.

[7] For the synthesis of **16** in racemic form, see: a) M. Nakagawa, H. Sugumi, S. Kodato, H. Hino, *Tetrahedron*, **1981**, *22*, 5323. b) L. Verotta, F. Orsini, M. Sbacchi, M. A. Scheildler, T. A. Amador, E. Elisabetsky, *Bioorg. Med. Chem.* **2002**, *10*, 2133.



(+)-63 (+)-Chimonanthine (2)

(+)-Chimonanthine (2):

Hexacycle (+)-**63** (64 mg, 0.147 mmol, 1 equiv) was concentrated from anhydrous benzene (2.5 ml) and the residue was dissolved in anhydrous toluene (14.7 mL) and placed under an argon atmosphere. A solution of Red-Al (65% wt, 450 μL, 1.47 mmol, 10.0 equiv) in toluene was added via syringe and the reaction mixture was heated to reflux. After 1.5 h, the mixture was cooled to 23 °C and excess reducing agent was quenched by the slow addition of methanol (5:95) in dichloromethane saturated with ammonia. The resulting mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography (5% methanol in dichloromethane saturated with ammonia) to afford (+)-chimonanthine (**2**) as a white solid (41.7 mg, 82 %). X-ray quality crystals were grown by slow evaporation of a benzene solution of (+)-**2**. All spectral data were in agreement with the literature.[8c]

^{1}H NMR (500 MHz, $CDCl_3$, 50 °C):	7.19 (d, J = 7.5 Hz, 2H, C_4**H**), 6.98 (t, J = 7.3 Hz, 2H, C_6**H**), 6.66 (t, J = 7.3 Hz, 2H, C_5**H**), 6.53 (d, J = 7.5 Hz, 2H, C_7**H**), 4.40 (br-s, 2H, C_{8a}**H**), 4.23 (s, 2H, N**H**), 2.51-2.57 (m, 6H, C_2**H**, C_2**H**, C_3**H**), 2.33 (s, 6H, CH_3), 2.05 (app dd, J = 10.5, 5.0 Hz, 2H, C_3**H**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 50 °C):	151.2 (C_{7a}), 133.8 (C_{4a}), 128.2 (C_6), 124.6 (C_4), 118.8 (C_5), 109.4 (C_7), 85.5 (C_{8a}), 63.8 (C_{3a}), 52.9 (C_2), 37.4 (CH_3), 36.1 (C_3).
FTIR (thin film):	3406 (m), 2934 (m), 1603 (m), 1484 (m), 1361 (s).
HRMS-ESI (*m/z*):	calc'd for $C_{22}H_{27}N_4$ $[M+H]^+$: 347.2230 found: 347.2222.
$[\alpha]_D^{22}$:	+254 (c = 1.00, EtOH).[8]
M.p. (C_6H_6):	176-178 °C.

TLC (5% CH_3OH in CH_2Cl_2 saturated with NH_3), R*f*: 0.26 (UV, CAM).

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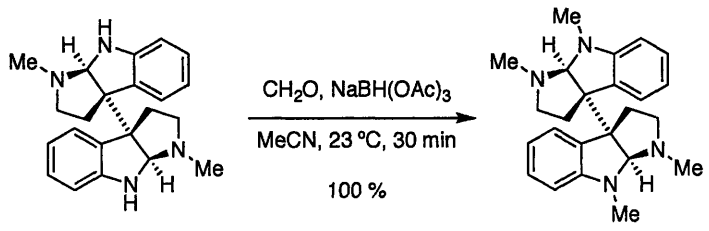
[8] a) $[\alpha]_D^{25}$: +280 (MeOH, concentration not reported), T. Tokuyama, J. W. Daly, *Tetrahedron*, **1983**, *39*, 41. b) $[\alpha]_D$: +224 (conditions not reported), N. H. Lajis, Z. Mahmud, R. F. Toia, *Planta Med.* **1993**, *59*, 383. c) $[\alpha]_D^{20}$: +264.5 (c = 1, EtOH), L. Verotta, T. Pilati, M. Tatò, E. Elisabetsky, T. A. Amador, D. S. Nunes, *J. Nat. Prod.* **1998**, *61*, 392. d) $[\alpha]_D^{23}$: +274 (c = 0.5, EtOH), L. E. Overman, J. F. Larrow, B. A. Stearns, J. M. Vance, *Angew. Chem. Int. Ed.* **2000**, *39*, 213. Data related to (–)-chimonanthine: e) $[\alpha]_D$: –329 (EtOH, conditions not reported), H. F. Hodson, B. Robinson, G. F. Smith, *Proc. Chem. Soc.* **1961**, 465. f) $[\alpha]_D^{25}$: –328 (c = 1.0, EtOH), R. K. Duke, R. D. Allan, G. A. R. Johnston, K. N. Mewett, A. D. Mitrovic, C. C. Duke, T. W. Hambley, *J. Nat. Prod.* **1995**, *58*, 1200. g) $[\alpha]_D^{23}$: –310 (c = 0.5, EtOH), L. E. Overman, D. V. Paone, B. A. Stearns, *J. Am. Chem. Soc.* **1999**, *121*, 7702.

Comparison of our data for (+)-chimonanthine (2) with literature:

Assignment	**Verotta's report**[8c] (+)-chimonanthine (**2**) (^{1}H NMR, 200 MHz, $CDCl_3$)	**This report** (+)-chimonanthine (**2**) (^{1}H NMR, 500 MHz, $CDCl_3$, 50 °C)
C2	2.50 (m)	2.57, (m)
C3	2.50 (m), 2.07 (dt, J = 12.0, 6.4 Hz)	2.57 (m), 2.05 (app dd, J = 10.5, 5.0 Hz)
C3a		
C4a		
C4	7.20, (d, J = 7.4 Hz)	7.19, (d, J = 7.5 Hz)
C5	6.67 (t, J = 7.3 Hz)	6.66 (t, J = 7.3 Hz)
C6	7.00 (t, J = 7.6 Hz)	6.98 (t, J = 7.3 Hz)
C7	6.55, (d, J = 7.7 Hz)	6.53, (d, J = 7.5 Hz)
C7a		
N8	–	4.23 (s)
C8a	4.35 (br s)	4.40 (br s)
N1-CH_3	2.31 (s)	2.33 (s)

Tokuyama's report[8a] (+)-chimonanthine (**2**) (^{13}C NMR, 25.05 MHz, $CDCl_3$)	**This report** (+)-chimonanthine (**2**) (^{13}C NMR, 125.8 MHz, $CDCl_3$, 50 °C)
150.6 (s)	151.1 (C7a)
133.1 (s)	133.8 (C4a)
128.1 (d)	128.2 (C6)
124.4 (d)	124.6 (C4)
118.7 (d)	118.8 (C5)
109.4 (d)	109.4 (C7)
85.2 (d)	85.5 (C8a)
63.2 (s)	63.8 (C3a)
52.7 (t)	52.9 (C2)
37.2 (q)	37.4 (Me)
36.5 (t)	36.1 (C3)



(+)-Chimonanthine (2) (+)-Folicanthine (3)

(+)-Folicanthine (3):

Formalin (37%, 5.5 μL, 0.0734 mmol, 5.2 equiv) followed by solid sodium triacetoxyborohydride (15.6 mg, 0.0734 mmol, 5.2 equiv) were added to a solution of (+)-chimonanthine (**2**, 5.0 mg, 0.0141 mmol, 1 equiv) in acetonitrile (700 μL) at 23 °C and placed under an argon atmosphere. After 30 min, a solution of methanol (5:95) in dichloromethane saturated with ammonia was added slowly. After 5 min, the resulting slurry was concentrated under reduced pressure and the residue was purified by flash column chromatography (1% methanol in dichloromethane saturated with ammonia) to afford (+)-folicanthine (**3**)[9] as a white solid (5.3 mg, 100%). All spectral data were in agreement with the literature.

^{1}H NMR (500 MHz, $CDCl_3$, 50 °C):	6.98 (t, J = 7.5 Hz, 2H, C_6**H**), 6.94 (d, J = 6.5 Hz, 2H, C_4**H**), 6.51 (t, J = 7.0 Hz, 2H, C_5**H**), 6.27 (d, J = 7.5 Hz, 2H, C_7**H**), 4.37 (s, 2H, C_{8a}**H**), 3.00 (s, 6H, N_8C**H**$_3$), 2.62-2.64 (m, 2H, C_2**H**), 2.41-2.50 (m, 10H, C_2**H**, C_3**H**, N_1C**H**$_3$), 1.95-1.99 (m, 2H, C_3**H**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 50 °C):	153.2 (**C**$_{7a}$), 133.2 (**C**$_{4a}$), 128.3 (**C**$_6$), 124.0 (**C**$_4$), 116.9 (**C**$_5$), 106.1 (**C**$_7$), 92.3 (**C**$_{8a}$), 63.0 (**C**$_{3a}$), 52.9 (**C**$_2$), 38.3 (N_8C**H**$_3$), 35.6 (**C**$_3$), 35.5 (N_1C**H**$_3$).
FTIR (thin film):	3047 (w), 2931 (m), 1603 (s), 1493 (s), 1155 (m).
HRMS-ESI (*m/z*):	calc'd for $C_{24}H_{31}N_4$ $[M+H]^+$: 375.2549 found: 375.2547.
$[\alpha]_D^{22}$:	+207 (c = 0.75, MeOH).[10]
M.p. (MeOH-CH_2Cl_2):	184-189 °C.

TLC (5% MeOH in CH_2Cl_2 saturated with NH_3), R*f*: 0.40 (UV, CAM).

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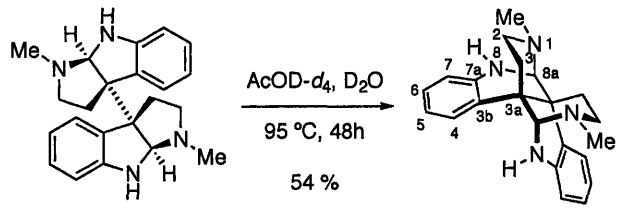
[9] For a synthesis of folicanthine in racemic form, see: C.-l. Fang, S. Horne, N. Taylor, R. Rodrigo, *J. Am. Chem. Soc.* **1994**, *116*, 9480.

[10] Data for (–)-folicanthine is available: a) $[\alpha]_D^{21.5}$: –364.4 (c = 2.043, MeOH), K. Eiter, O. Svierak, *Monatsh. Chem.* **1952**, *83*, 1453. b) $[\alpha]_D$: –364 (EtOH, concentration not reported), see ref. 8e. c) $[\alpha]_D$: –364 (EtOH, concentration not reported), J. E. Saxton, W. G. Bardsley, G. F. Smith, *Proc. Chem. Soc.* **1962**, 148.

Comparison of our data for (+)-folicanthine (3) with literature for (±)-3:

Assignment	Rodrigo's report[9] (±)-folicanthine (**3**) (^{1}H NMR, 250 MHz, $CDCl_3$)	This report (+)-folicanthine (**3**) (^{1}H NMR, 500 MHz, $CDCl_3$, 50 °C)
C2	2.58-2.67 (m), 2.30-2.49 (m)	2.62-2.64, (m), 2.41-2.50 (m)
C3	2.30- 2.49 (m), 1.92-1.98 (m)	2.41-2.50 (m), 1.95-1.99 (m)
C3a		
C4a		
C4	6.89-6.99 (m)	6.94 (d, J = 6.5 Hz)
C5	6.49 (t, J = 7.3 Hz)	6.51 (t, J = 7.0 Hz)
C6	6.89-6.99 (m)	6.98 (t, J = 7.5 Hz)
C7	6.25, (d, J = 7.8 Hz)	6.27, (d, J = 7.5 Hz)
C7a		
N8-CH_3	3.00 (s)	3.00 (s)
C8a	4.38 (s)	4.37 (s)
N1-CH_3	2.40 (s)	2.41-2.50 (m)

Assignment	Rodrigo's report[9] (±)-folicanthine (**3**) (^{13}C NMR, 62.86 MHz, $CDCl_3$)	This report (+)-folicanthine (**3**) (^{13}C NMR, 125.8 MHz, $CDCl_3$, 50 °C)
C2	52.61	52.9
C3	35.28	35.6
C3a	62.65	63.0
C4a	132.78	133.2
C4	123.60	124.0
C5	116.60	116.9
C6	128.02	128.3
C7	105.78	106.1
C7a	152.87	153.2
N8-CH_3	37.90	38.3
C8a	92.95	92.3
N1-CH_3	35.38	35.5



(+)-Chimonanthine (2) (–)-Calycanthine (1)

(–)-Calycanthine (1):

A solution of (+)-chimonanthine (**2**, 10.0 mg, 0.0289 mmol, 1 equiv) in a mixture of acetic acid-d_4 (0.43 M) in deuterium oxide (700 μL) was placed in a J-Young tube and the contents were sealed under an atmosphere of argon and heated to 95 °C. Equilibrium was reached within 24 h, affording a ~85:15 ratio in favor of (–)-calycanthine (**1**). After 48 h, the reaction mixture was cooled to 23 °C and partitioned between dichloromethane (10 mL) and saturated aqueous sodium bicarbonate (10 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (4 × 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure to afford a brown residue. The residue was purified by flash column chromatography (1% methanol in dichloromethane saturated with ammonia) to afford (–)-calycanthine (**1**, 5.4 mg, 54%) as a white solid along with recovered (+)-chimonanthine (**2**, 0.5 mg, 5%).

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	7.01 (d, J = 7.5 Hz, 2H, C_4**H**), 6.82 (app t, J = 7.5 Hz, 2H, C_6**H**), 6.55 (t, J = 7.5 Hz, 2H, C_5**H**), 6.27 (d, J = 8.0 Hz, 2H, C_7**H**), 4.58 (br s, 2H, N**H**), 4.32 (s, 2H, C_{8a}**H**), 3.13 (td, J = 13.3, 5.3 Hz, 2H, C_3**H**), 2.62 (dd, J = 11.3, 5.3 Hz, 2H, C_2**H**), 2.42 (s, 6H, CH_3), 2.27 (dt, J = 12.5, 3.6 Hz, 2H, C_2**H**), 1.29 (dd, J = 13.3, 3.8 Hz, 2H, C_3**H**).
^{13}C NMR (125 MHz, $CDCl_3$, 20 °C):	145.6 (C_{7a}), 126.7 (C_6), 125.2 (C_{4a}), 124.6 (C_4), 116.5 (C_5), 112.2 (C_7), 71.2 (C_{8a}), 46.7 (C_2), 42.8 (CH_3), 36.1 (C_{3a}), 31.9 (C_3).
FTIR (thin film):	3418 (m), 2929 (m), 1678 (w), 1605 (m), 1487 (s).
HRMS-ESI (*m/z*):	calc'd for $C_{22}H_{27}N_4$ $[M+H]^+$: 347.2230 found: 347.2217.
$[\alpha]_D^{22}$:	–612 (c = 0.18, EtOH).[11]
M.p. (EtOH):	230-232 °C.

TLC (5% CH_3OH in CH_2Cl_2 saturated with NH_3), R*f*: 0.53 (UV, CAM).

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[11] For data on (–)-calycanthine, see: a) $[\alpha]_D^{25}$: –570 (MeOH, concentration not reported), see ref. 8a. b) $[\alpha]_D$: –633 (MeOH, concentration not reported), see ref. 8b. c) $[\alpha]_D^{20}$: –463 (c = 1, EtOH), see ref. 8c. For data on (+)-calycanthine, see: d) $[\alpha]_D^{18}$: +684.3 (EtOH, concentration not reported), E. Späth, W. Stroh, *Chem. Ber.* **1925**, *58*, 2131. e) $[\alpha]_D^{25}$: +675 (c = 1.0, $CHCl_3$), see ref. 8f. f) $[\alpha]_D^{25}$: +664 (c = 0.7, EtOH), see ref. 8g.

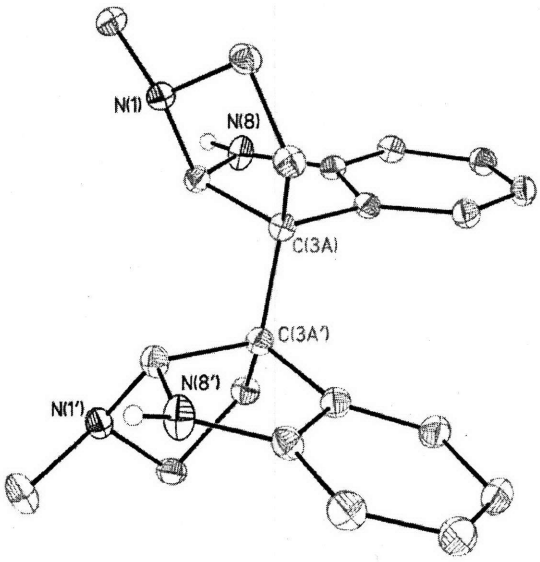
Comparison of our data for (–)-calycanthine (1) with literature:

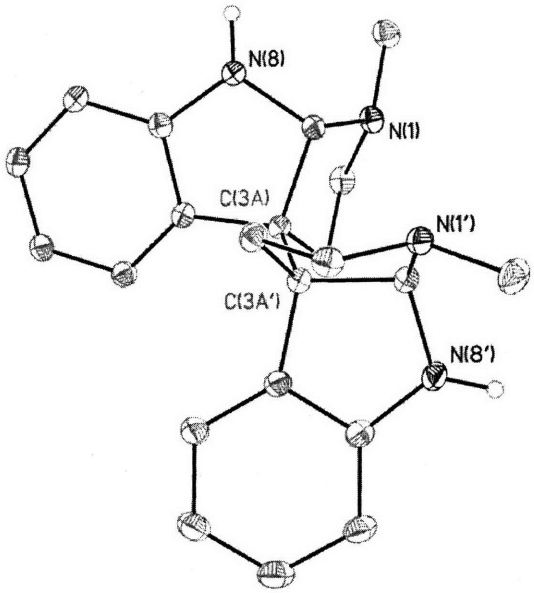
Assignment	**Verotta's report**[8c] (–)-calycanthine (**1**) (^{1}H NMR, 200 MHz, $CDCl_3$)	**This report** (–)-calycanthine (**1**) (^{1}H NMR, 500 MHz, $CDCl_3$,20 °C)
C2	2.63 (ddd, J = 12.0, 5.6, 1.4 Hz), 2.26 (ddd, J = 12.0. 4.1, 1.4 Hz)	2.62 (dd, J = 11.3, 5.3 Hz), 2.27 (dt, J = 12.5, 3.6 Hz)
C3	3.15 (dt, J = 13.2, 5.5 Hz), 1.30 (ddd, J = 13.2, 4.1, 1.4 Hz)	3.13 (app-td, J = 13.3, 5.3 Hz), 1.29 (dd, J = 13.3, 3.8 Hz)
C3a		
C4a		
C4	6.28, (dd, J = 8.0, 1.0 Hz)	7.01, (d, J = 7.5 Hz)[12]
C5	6.55 (td, J = 7.5, 1.0 Hz)	6.55 (t, J = 7.5 Hz)
C6	6.83 (dt, J = 7.5, 1.0 Hz)	6.82 (app t, J = 7.5 Hz)
C7	7.02, (dd, J = 8.0, 1.0 Hz)	6.27, (d, J = 8.0 Hz)[12]
C7a		
N8	1.63 (br s)	4.58 (br s)
C8a	4.33 (s)	4.32 (s)
N1-CH_3	2.42 (s)	2.42 (s)

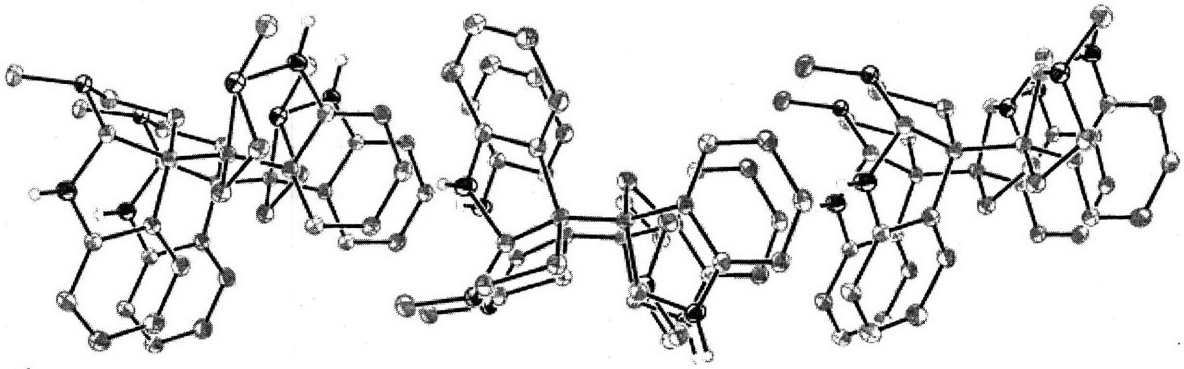
Tokuyama's report[8a] (–)-calycanthine (**1**) (^{13}C NMR, 25.05 MHz, $CDCl_3$)	**This report** (–)-calycanthine (**1**) (^{13}C NMR, 125.8 MHz, $CDCl_3$, 20 °C)
145.3 (s)	145.6 (C7a)
126.5 (d)	126.7 (C6)
125.0 (s)	125.2 (C4a)
124.4 (d)	124.6 (C4)
116.4 (d)	116.5 (C5)
112.0 (d)	112.2 (C7)
71.0 (d)	71.2 (C8a)
46.6 (t)	46.7 (C2)
42.6 (q)	42.8 (Me)
36.0 (s)	36.1 (C3a)
31.7 (t)	31.9 (C3)

[12] Our assignment of C4 and C7 methines is supported by HMBC data.

Crystal Structure of (+)-Chimonanthine (2).







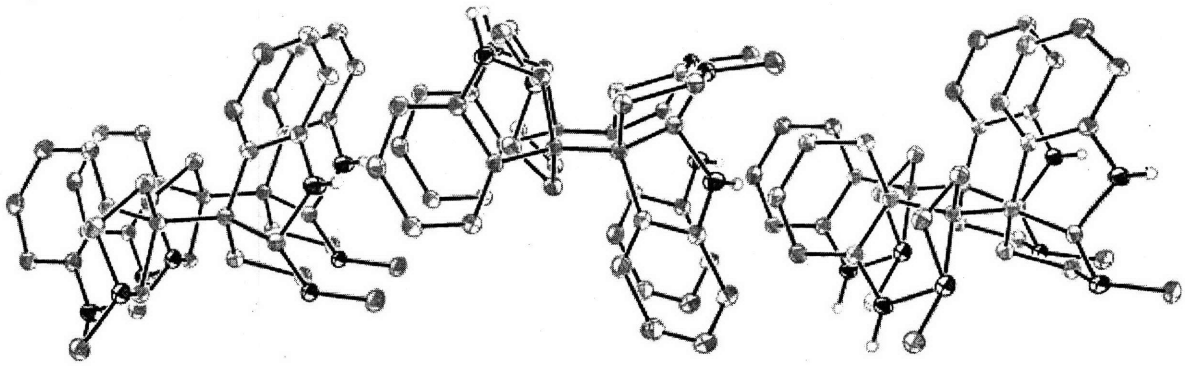


Table 1. Crystal data and structure refinement for (+)-chimonanthine.

Identification code	07003	
Empirical formula	C22 H26 N4	
Formula weight	346.47	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2	
Unit cell dimensions	a = 15.692(2) Å	α= 90°.
	b = 16.844(2) Å	β= 90°.
	c = 7.1828(9) Å	γ = 90°.
Volume	1898.5(4) $Å^3$	
Z	4	
Density (calculated)	1.212 Mg/m^3	
Absorption coefficient	0.073 mm^{-1}	
F(000)	744	
Crystal size	0.30 x 0.25 x 0.20 mm^3	
Theta range for data collection	1.77 to 29.58°.	
Index ranges	-21<=h<=21, -23<=k<=23, -9<=l<=9	
Reflections collected	42252	
Independent reflections	3024 [R(int) = 0.0586]	
Completeness to theta = 29.58°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9855 and 0.9784	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3024 / 2 / 243	
Goodness-of-fit on F^2	1.052	
Final R indices [I>2sigma(I)]	R1 = 0.0361, wR2 = 0.0970	
R indices (all data)	R1 = 0.0407, wR2 = 0.1010	
Absolute structure parameter	No anomalous signal	
Largest diff. peak and hole	0.495 and -0.193 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (+)-chimonanthine. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1')	6023(1)	6635(1)	1369(2)	16(1)
N(1)	6202(1)	4492(1)	-2152(2)	16(1)
C(2)	7067(1)	4195(1)	-2448(2)	18(1)
C(2')	6140(1)	6461(1)	3352(2)	17(1)
C(3A)	7016(1)	4752(1)	612(2)	14(1)
C(3)	7580(1)	4725(1)	-1151(2)	17(1)
C(3A')	7032(1)	5556(1)	1678(2)	14(1)
C(3')	6400(1)	5590(1)	3330(2)	16(1)
C(4A)	7179(1)	4029(1)	1825(2)	14(1)
C(4)	7927(1)	3755(1)	2610(2)	16(1)
C(4')	8435(1)	5559(1)	3720(2)	20(1)
C(4A')	7914(1)	5830(1)	2299(2)	16(1)
C(5)	7915(1)	3066(1)	3706(2)	18(1)
C(5')	9220(1)	5930(1)	4038(3)	24(1)
C(6)	7151(1)	2657(1)	3976(2)	18(1)
C(6')	9467(1)	6572(1)	2947(3)	25(1)
C(7)	6403(1)	2902(1)	3101(2)	16(1)
C(7A')	8147(1)	6508(1)	1294(2)	17(1)
C(7A)	6427(1)	3580(1)	1986(2)	14(1)
C(7')	8934(1)	6877(1)	1569(3)	22(1)
N(8)	5795(1)	3890(1)	880(2)	18(1)
C(8A)	6093(1)	4589(1)	-145(2)	14(1)
C(8A')	6741(1)	6256(1)	373(2)	16(1)
N(8')	7495(1)	6753(1)	152(2)	20(1)
C(9')	5920(1)	7477(1)	956(3)	24(1)
C(9)	5531(1)	4058(1)	-3101(2)	20(1)

Table 3. Bond lengths [Å] and angles [°] for (+)-chimonanthine.

N(1')-C(9')	1.458(2)
N(1')-C(2')	1.466(2)
N(1')-C(8A')	1.4792(19)
N(1)-C(9)	1.4513(19)
N(1)-C(8A)	1.4610(19)
N(1)-C(2)	1.4624(19)
C(2)-C(3)	1.521(2)
C(2')-C(3')	1.524(2)
C(3A)-C(4A)	1.519(2)
C(3A)-C(3)	1.546(2)
C(3A)-C(3A')	1.556(2)
C(3A)-C(8A)	1.571(2)
C(3A')-C(4A')	1.525(2)
C(3A')-C(3')	1.547(2)
C(3A')-C(8A')	1.574(2)
C(4A)-C(4)	1.380(2)
C(4A)-C(7A)	1.4066(19)
C(4)-C(5)	1.402(2)
C(4')-C(4A')	1.385(2)
C(4')-C(5')	1.399(2)
C(4A')-C(7A')	1.400(2)
C(5)-C(6)	1.396(2)
C(5')-C(6')	1.391(3)
C(6)-C(7)	1.393(2)
C(6')-C(7')	1.393(2)
C(7)-C(7A)	1.396(2)
C(7A')-N(8')	1.375(2)
C(7A')-C(7')	1.396(2)
C(7A)-N(8)	1.3737(19)
N(8)-C(8A)	1.4659(19)
C(8A')-N(8')	1.458(2)
C(9')-N(1')-C(2')	113.99(13)
C(9')-N(1')-C(8A')	114.02(13)
C(2')-N(1')-C(8A')	106.75(12)
C(9)-N(1)-C(8A)	115.79(13)
C(9)-N(1)-C(2)	115.68(12)
C(8A)-N(1)-C(2)	106.87(12)
N(1)-C(2)-C(3)	101.63(12)
N(1')-C(2')-C(3')	102.50(12)
C(4A)-C(3A)-C(3)	110.45(12)
C(4A)-C(3A)-C(3A')	114.36(11)
C(3)-C(3A)-C(3A')	114.79(12)

C(4A)-C(3A)-C(8A)	102.36(11)
C(3)-C(3A)-C(8A)	103.86(12)
C(3A')-C(3A)-C(8A)	109.75(12)
C(2)-C(3)-C(3A)	102.45(12)
C(4A')-C(3A')-C(3')	110.26(12)
C(4A')-C(3A')-C(3A)	114.96(12)
C(3')-C(3A')-C(3A)	113.49(11)
C(4A')-C(3A')-C(8A')	102.22(11)
C(3')-C(3A')-C(8A')	104.06(12)
C(3A)-C(3A')-C(8A')	110.71(12)
C(2')-C(3')-C(3A')	102.42(12)
C(4)-C(4A)-C(7A)	119.99(13)
C(4)-C(4A)-C(3A)	130.21(13)
C(7A)-C(4A)-C(3A)	109.63(12)
C(4A)-C(4)-C(5)	119.67(14)
C(4A')-C(4')-C(5')	119.61(15)
C(4')-C(4A')-C(7A')	119.58(14)
C(4')-C(4A')-C(3A')	130.71(14)
C(7A')-C(4A')-C(3A')	109.45(13)
C(6)-C(5)-C(4)	119.80(14)
C(6')-C(5')-C(4')	119.94(16)
C(7)-C(6)-C(5)	121.01(13)
C(5')-C(6')-C(7')	121.34(15)
C(6)-C(7)-C(7A)	118.55(13)
N(8')-C(7A')-C(7')	127.54(15)
N(8')-C(7A')-C(4A')	110.96(13)
C(7')-C(7A')-C(4A')	121.41(15)
N(8)-C(7A)-C(7)	128.53(13)
N(8)-C(7A)-C(4A)	110.80(13)
C(7)-C(7A)-C(4A)	120.61(13)
C(6')-C(7')-C(7A')	117.85(15)
C(7A)-N(8)-C(8A)	111.36(12)
N(1)-C(8A)-N(8)	116.29(13)
N(1)-C(8A)-C(3A)	104.67(12)
N(8)-C(8A)-C(3A)	105.15(11)
N(8')-C(8A')-N(1')	114.95(13)
N(8')-C(8A')-C(3A')	105.02(12)
N(1')-C(8A')-C(3A')	104.91(12)
C(7A')-N(8')-C(8A')	111.50(12)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (+)-chimonanthine. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1')	15(1)	14(1)	20(1)	2(1)	-1(1)	0(1)
N(1)	18(1)	16(1)	14(1)	-1(1)	-1(1)	1(1)
C(2)	19(1)	19(1)	16(1)	-1(1)	3(1)	3(1)
C(2')	18(1)	16(1)	18(1)	-3(1)	0(1)	0(1)
C(3A)	13(1)	14(1)	13(1)	1(1)	1(1)	-1(1)
C(3)	17(1)	18(1)	16(1)	1(1)	3(1)	1(1)
C(3A')	14(1)	14(1)	14(1)	1(1)	0(1)	0(1)
C(3')	17(1)	16(1)	14(1)	0(1)	1(1)	0(1)
C(4A)	14(1)	13(1)	14(1)	0(1)	2(1)	1(1)
C(4)	16(1)	16(1)	18(1)	0(1)	0(1)	0(1)
C(4')	21(1)	16(1)	22(1)	1(1)	-5(1)	-1(1)
C(4A')	16(1)	15(1)	18(1)	0(1)	0(1)	-1(1)
C(5)	17(1)	18(1)	18(1)	2(1)	-2(1)	3(1)
C(5')	22(1)	22(1)	30(1)	-1(1)	-10(1)	0(1)
C(6)	22(1)	15(1)	17(1)	2(1)	0(1)	2(1)
C(6')	18(1)	22(1)	36(1)	-3(1)	-3(1)	-2(1)
C(7)	17(1)	15(1)	16(1)	1(1)	2(1)	-1(1)
C(7A')	16(1)	16(1)	21(1)	0(1)	2(1)	1(1)
C(7A)	16(1)	15(1)	13(1)	-1(1)	0(1)	0(1)
C(7')	17(1)	19(1)	29(1)	1(1)	2(1)	-4(1)
N(8)	14(1)	20(1)	20(1)	6(1)	-2(1)	-2(1)
C(8A)	14(1)	15(1)	13(1)	0(1)	-1(1)	0(1)
C(8A')	16(1)	15(1)	17(1)	3(1)	0(1)	-1(1)
N(8')	15(1)	22(1)	24(1)	10(1)	1(1)	-2(1)
C(9')	20(1)	16(1)	36(1)	5(1)	2(1)	3(1)
C(9)	22(1)	20(1)	17(1)	-2(1)	-4(1)	0(1)

Table 5. Hydrogen coordinates ($x\ 10^4$) and isotropic displacement parameters ($Å^2 x\ 10^3$) for (+)-chimonanthine.

	x	y	z	U(eq)
H(2A)	7248	4260	-3759	21
H(2B)	7117	3629	-2093	21
H(2'1)	5604	6540	4055	21
H(2'2)	6592	6797	3902	21
H(3A)	7658	5261	-1688	20
H(3B)	8146	4491	-878	20
H(3'1)	5903	5240	3113	19
H(3'2)	6680	5435	4511	19
H(4)	8446	4031	2408	20
H(4')	8261	5125	4474	24
H(5)	8426	2878	4264	21
H(5')	9584	5742	4999	29
H(6)	7141	2206	4768	22
H(6')	10009	6808	3145	30
H(7)	5888	2613	3260	19

H(7')	9101	7321	841	26
H(8)	5231(10)	3745(12)	960(30)	21
H(8A)	5715	5053	119	17
H(8A')	6548	6046	-860	19
H(8')	7563(14)	7063(11)	-860(20)	24
H(9'1)	5406	7677	1572	36
H(9'2)	5867	7551	-393	36
H(9'3)	6418	7770	1410	36
H(9A)	5542	3501	-2709	30
H(9B)	5620	4090	-4450	30
H(9C)	4977	4292	-2786	30

Table 6. Hydrogen bonds for (+)-chimonanthine [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(8)-H(8)...N(1')#1	0.918(15)	2.091(15)	3.0072(19)	174.8(19)

Symmetry transformations used to generate equivalent atoms:
#1 -x+1,-y+1,z

Chapter II

The Development of a General Strategy Towards Dimeric Hexahydropyrroloindole Alkaloids. A Concise Total Synthesis of (+)-WIN 64821, (–)-Ditryptophenaline and (–)-1'-(2-Phenylethylene)-ditryptophenaline

Introduction and Background

The development of a cobalt(I)-mediated reductive carbon-carbon bond forming reaction allowed for the rapid construction of the vicinal quaternary stereocenters of the calycanthaceous alkaloids (see Chapter I). Attention was next focused on more complex natural products, the dimeric diketopiperazine alkaloids (Figure 1). This new project was done in collaboration with Dr. James A. Ashenhurst, a post-doctoral researcher in the group.

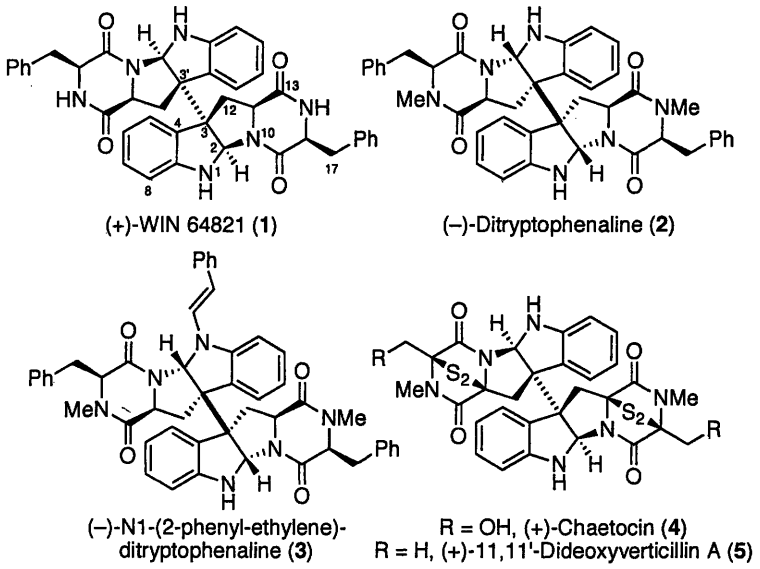
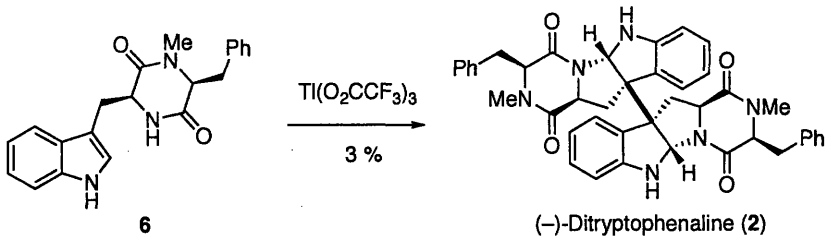


Figure 1. Representative dimeric diketopiperazine alkaloids.

The structurally fascinating and biologically active secondary metabolites (+)-WIN 64821 (**1**) and (–)-ditryptophenaline (**2**), isolated from *Asperigillus flavus* cultures, are members of the dimeric diketopiperazine alkaloid family (Figure 1).[1] Many of these alkaloids, including the closely related (–)-N^1-(2-phenylethylene)-ditryptophenaline (**3**),[2] contain vicinal quaternary stereocenters[3] that connect two hexahydropyrroloindole substructures (Figure 1).[4] Bioactivity-guided studies led to the identification of (+)-**1** as a potent competitive substance P antagonist with submicromolar potency for the human neurokinin 1 and the cholecystokinin B receptors,[2] whereas alkaloids (–)-**2** and (–)-**3** were found to be weaker inhibitors for the former receptor.[1] Many closely related and potently biologically active epidithiodiketopiperazine derivatives[1d] are known, including (+)-chaetocin (**4**) (Figure 1), the first inhibitor of a lysine-specific histone methyltransferase,[1e] and (+)-11,11′-dideoxyverticillin A (**5**) (Figure 1), a tyrosine kinase inhibitor with potent antitumor activity.[1f]

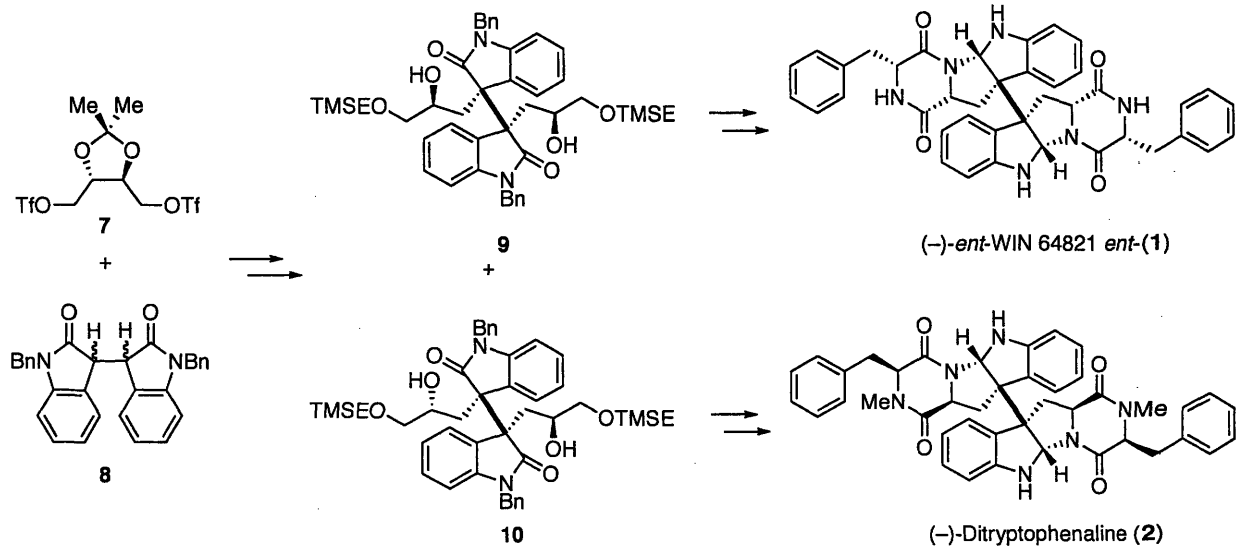
Previous Synthetic Work

Based on the pioneering work of Hino,[4a] Nakagawa reported the first synthesis of (–)-**2** via a thallium(III)-promoted oxidative dimerization of diketopiperazine **6** (3% yield) reaction (Scheme 1).[5]



Scheme 1. Nakagawa's synthesis of (–)-**2**.

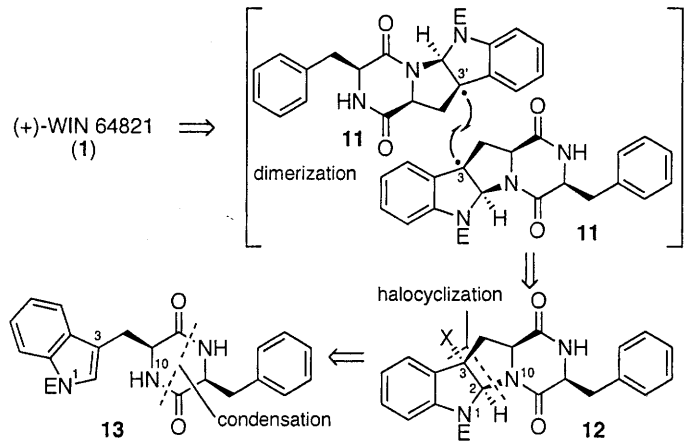
In 2001, Overman reported an elegant total synthesis of (–)-*ent*-WIN 64821 and (–)-(**2**), employing alkylation reactions for introduction of the quaternary stereocenters (see Chapter I) (Scheme 2).[6] Double alkylation of bisoxindole **8** with bistriflate **7** affords the dialkylation product, which after further steps yields diastereomeric diols **9** and **10**. Diol **9** was further elaborated to afford (–)-*ent* WIN 64821 in nine additional steps. Similarly, diol **10** was converted to (–)-ditryptophenaline (**2**) in ten additional steps.



Scheme 2. Overman's synthesis of (–)-*ent*-WIN 64821 *ent*-(**1**) and (–)-ditryptophenaline (**2**).

Retrosynthetic Analysis

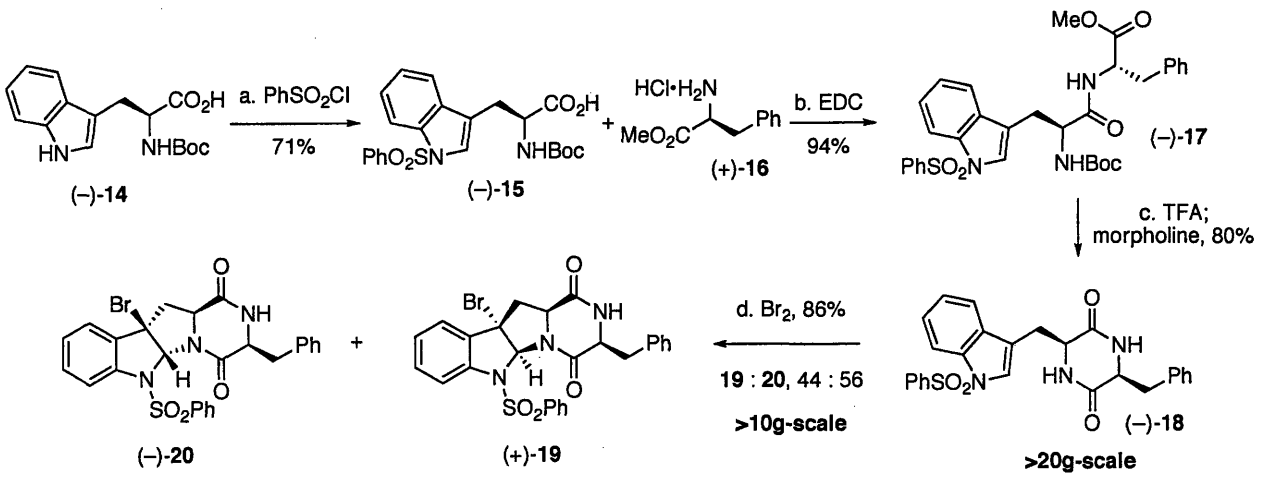
Our retrosynthetic analysis of (+)-WIN 64821 (**1**) illustrates our planned approach to these dimeric diketopiperazines alkaloids (Scheme 3). We envisioned simultaneously securing the imposing vicinal quaternary stereocenters of (+)-**1** by a reductive dimerization[7,8] of a C3-halogenated diketopiperazine **12** (Scheme 3). While diketopiperazine **13** could be readily accessed from L-tryptophan and L-phenylalanine, the strategic positioning of an electron withdrawing group (E) on the indolyl nitrogen atom of **13** could allow the preparation of the desired C3-halogenated derivative **12**. Inspired by the pioneering reports by Hino,[4a] Crich,[4c] and Danishefsky[9] on the synthesis and chemistry of C3a functionalized hexahydropyrroloindoles, we envisioned a C3-halogenated diketopiperazine **12** to serve as a versatile precursor to a fleeting intermediate **11** en route to (+)-(**1**).



Scheme 3. Retrosynthetic analysis of (+)-WIN 64821 (**1**).

Results and Discussion

A short synthesis of the key diketopiperazine is shown in Scheme 4. The direct *N*-sulfonylation of *N*-Boc-L-tryptophan (**14**) was achieved by treatment with LiHMDS (3 equiv)[10] followed by benzenesulfonyl chloride (Scheme 2). Condensation of tryptophan derivative (–)-**15** and L-phenylalanine methyl ester (**16**) provided the desired amide (–)-**17**. Dissolution of (–)-**17** in dichloromethane and sequential treatment with trifluoroacetic acid followed by morpholine resulted in the precipitation of the target diketopiperazine (–)-**18** as a single diastereomer and >99% ee.[11,12] Importantly, attempts to directly *N*-sulfonylate *cyclo*-L-tryptophan-L-phenylalanine (**13**, E = H) were unsuccessful due to its sensitivity toward base promoted epimerization leading to a mixture of diastereomers. The bromides *endo*-(+)-**19** and *exo*-(–)-**20**, which are the key



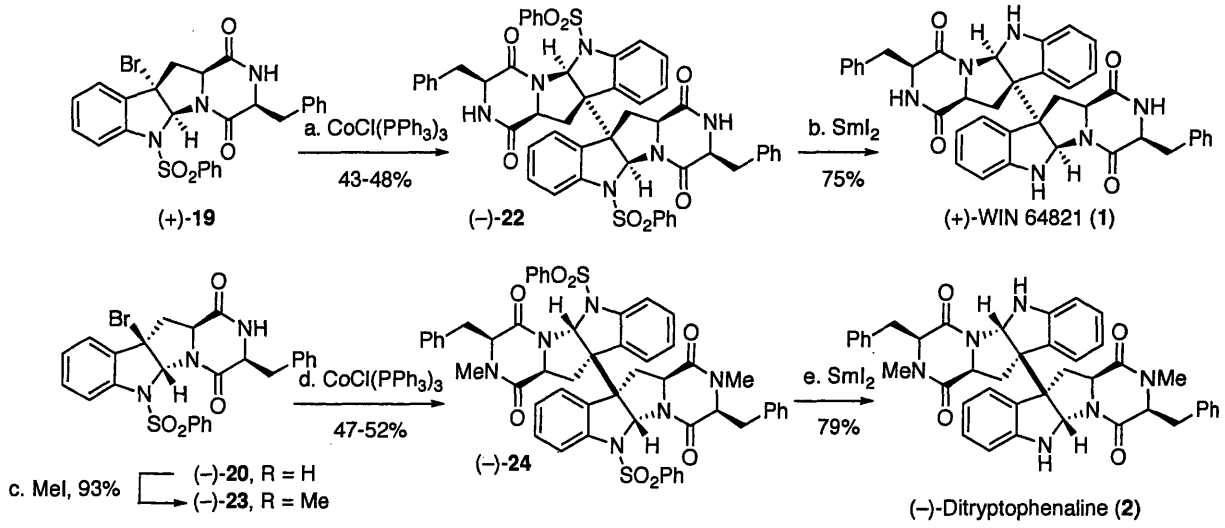
Scheme 4. Synthesis of diastereomeric bromides (+)-**19** and (–)-**20**. Conditions: a) LiHMDS, THF, $PhSO_2Cl$, –78 °C, 71%. b) EDC•HCl, HOBt, Et_3N, CH_2Cl_2, 23 °C, 94%. c) TFA, CH_2Cl_2, 0→23 °C, 3 h; morpholine, CH_2Cl_2, 23 °C, 48 h, 80%. d) Br_2, MeCN, 0 °C, 15 min, 86%. Work done in collaboration with Dr. James Ashenhurst.

precursors for (+)-WIN 64821 (**1**) and (–)-ditryptophenaline (**2**), respectively, were prepared in 86% combined yield by exposure of *N*-benzenesulfonyl diketopiperazine (–)-**18** to bromine in acetonitrile after extensive optimization by Dr. Ashenhurst.[13] The diastereomeric bromides were easily separated and were found to be amenable to storage on >10g-scale.

The total synthesis of (+)-WIN 64821 was completed in two additional steps from the *endo*-bromide (+)-**19** (Scheme 5). After extensive experimentation of various reaction parameters and substrates,[14] a practical set of reaction conditions was identified for the dimerization of diketopiperazines of the general structure **12** (Scheme 3). Under optimal reaction conditions, treatment of (+)-**19** with tris(triphenylphosphine)cobalt chloride (**21** 1.8 equiv)[15] in acetone ([**19**] = 0.1M) at 23 °C provided direct access to the *N*-sulfonylated dimer (–)-**22** as a single diastereomer in 43–48% yield. Importantly, this reductive dimerization exclusively provided the required *cis*-5,5-fused bicycle of the hexahydropyrroloindole substructure.[16] It should be noted that both the dimerization substrate, *endo*-bromide **19**, and to a lesser extent the diketopiperazines in the exo series (e.g., **20**, Scheme 4), along with the corresponding dimerization products were found to be sensitive toward base promoted epimerization and autoxidative decomposition. Ultimately, reductive removal of the *N*-benzenesulfonyl groups in (–)-**22** was achieved using samarium diiodide in a mixture of anhydrous tetrahydrofuran, *N*-methylpyrrolidinone, and ^{t}butanol to give the first synthetic sample of the natural enantiomer (+)-WIN 64821 (**1**, $[\alpha]^{21}_D$ = +230 (*c* = 0.15, MeOH); lit.:[1b] $[\alpha]_D$ = +200

(c = 0.15, MeOH)) in 75% yield.[11] Notably, these conditions did not lead to significant reductive fragmentation of the C3-C3′ bond, nor the epimerization of the base sensitive diketopiperazine substructure.

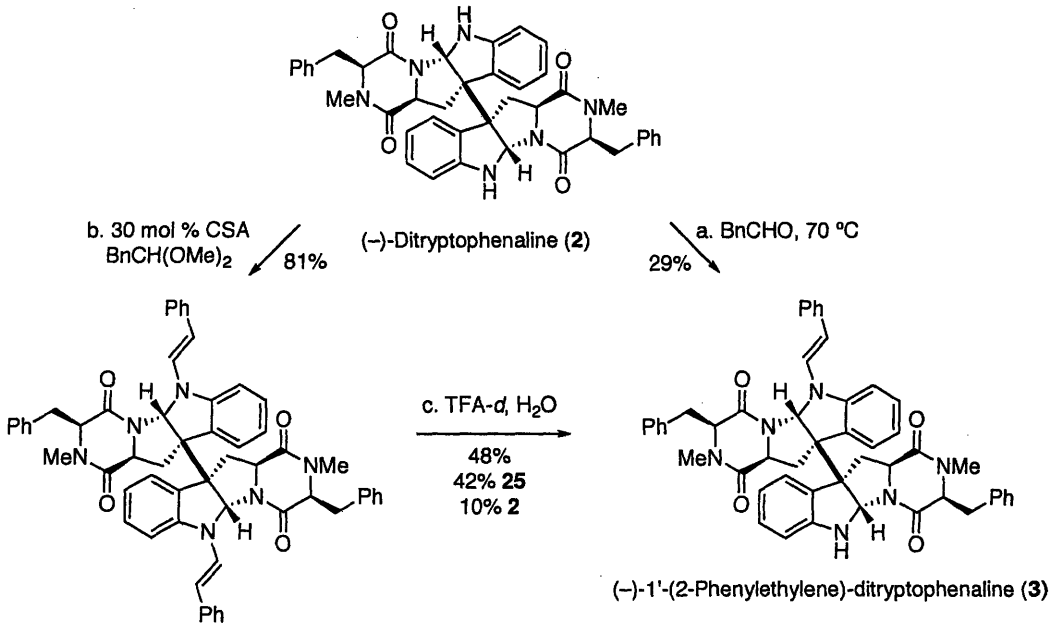
Similarly, the total synthesis of (–)-ditryptophenaline (**2**) was completed in three steps from the (–)-*exo*-bromide **20** (Scheme 5). Treatment of (–)-**20** with methyl iodide and potassium carbonate gave the corresponding N^{14}-Me *exo*-bromide (–)-**23** in 93% yield. Treatment of (–)-**23** with the cobalt(I)-complex **21** in acetone at 23 °C afforded the dimer (–)-**24** as a single diastereomer in 47–52% yield. Reductive removal of the benzenesulfonyl groups provided (–)-ditryptophenaline (**2**, $[\alpha]^{21}_D$ = –292 (c = 0.97, CH_2Cl_2); lit.:[1a] $[\alpha]^{24}_D$ = –330 (c = 0.52, CH_2Cl_2)) in 79% yield.[11] Significantly, the reaction conditions described here for the dimerization event were directly applicable to gram–scale synthesis (e.g., (+)-**19**→(–)-**22**, 43% yield on 1g-scale, and (–)-**23**→(–)-**24**, 47% yield on 2.5g-scale). The successful application of this key transformation to both *endo* and *exo* series of diketopiperazine substrates (Scheme 5) offers a practical route for late stage assembly of related derivatives.



Scheme 5. Concise total synthesis of (+)-WIN 64821 (**1**), (–)-ditryptophenaline (**2**) from bromides (+)-**19** and (–)-**20**. Conditions: a) $CoCl(PPh_3)_3$, acetone, 23 °C, 30 min, 48%. b) SmI_2, NMP, ^{t}BuOH, THF, 23 °C, 1 h , 75%. c) MeI, K_2CO_3, acetone, 23 °C, 3 d, 93%. d) $CoCl(PPh_3)_3$, acetone, 23 °C, 15 min, 52%. e) SmI_2, NMP, ^{t}BuOH, THF, 23 °C, 35 min, 79%. Work done in collaboration with Dr. James Ashenhurst.

Heating a solution of (–)-ditryptophenaline (**2**) at 70 °C with excess phenylacetaldehyde in acetonitrile over 8 hours provided the first synthetic sample of (–)-**3** ($[\alpha]^{22}_D$ = –131.5 (c = 0.36, $CHCl_3$); lit.:[2] $[\alpha]_D$ = –125 (c = 0.05, $CHCl_3$))[11] in 29% yield, accompanied by products derived

from thermal decomposition (Scheme 6). Our synthetic (–)-**3** matched all literature data for this alkaloid, confirming the reported structure for this natural product. The thermal decomposition of (–)-**3** can be avoided using a two–step sequence at ambient temperature. Condensation of (–)-**2** with dimethoxyacetal of phenylacetaldehyde at 23 °C gave the N^1,$N^{1'}$-bis-β-styrene derivative (–)-**25** in 81% yield within 1.5 h. Partial hydrolysis of (–)-**25** at 23 °C cleanly resulted in alkaloid (–)-**3** in 48% yield in 20 min with the majority of the mass balance as recovered (–)-**25**.



Scheme 6. Two routes to monostyrene derivative **3**. Conditions: a) BnCHO, MeCN. 70 °C, 8h, 29%. b) $BnCH(OMe)_2$, 30 mol % CSA, 23 °C, 81 %. c) TFA-*d*, H_2O, C_6D_6, 23 °C, 48 %.

Conclusion

The enantioselective total synthesis of (+)-WIN 64821 (**1**), and (–)-ditryptophenaline (**2**) in six and seven steps, respectively, from commercially available amino acid derivatives is described. The simultaneous introduction of the vicinal quaternary stereocenters in these alkaloids was achieved by a reductive homodimerization of readily available alkyl bromides. In addition to the first synthetic sample of naturally occurring (+)-**1**, we provide structure confirmation of the natural alkaloid (–)-**3**. The gram-scale synthesis of key intermediates and dimerization of bromides (+)-**19** and (–)-**23** provides a concise and preparative route to these

alkaloids. Further development and application of this chemistry to the synthesis of other homo- and hetero-dimeric alkaloids is ongoing and will be reported in due course.

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[11] Please see the experimental section for details.

[12] Under optimized conditions (–)-**18** is readily purified by crystallization allowing the preparation of (–)-**18** on >20-gram scale with equal efficiency and without the use of flash column chromatography.

[13] This bromination reaction was more selective (16:84, **19**:**20**) in favor of the *exo*-diastereomer when performed at –40 °C. Alternatively, bromination reactions conducted at 40 °C led to a slight excess (52:48, **19**:**20**) of the *endo*-diastereomer contaminated with byproducts due to aniline-ring bromination. Work of Dr. James Ashenhurst.

[14] A variety of metal (Mn, V, Ni) and Co(I-III) complexes, reaction solvents (>10), concentration, temperature, addition rate and order, and additives were examined. X=Br was optimal vs. X=Cl or I. E=SO_2Ph was most effective as compared to other sulfonyl derivatives (>5).

[15] a) Aresta, M.; Rossi, M.; Sacco. A. *Inorg. Chim. Acta* **1969**, *3*, 227. b) Baysdon, S. L.; Liebeskind, L. S. *Organometallics* **1982**, *1*, 771.

[16] The mass balance for this reaction is accounted by 10% of the corresponding C3-reduction (**5**, X=H, E=SO_2Ph) product in addition to products (~15%) consistent with radical disproportionation.

Experimental Section

General Procedures. All reactions were performed in oven-dried or flame-dried round-bottomed flasks. The flasks were fitted with rubber septa and reactions were conducted under a positive pressure of argon. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Where necessary (so noted), solutions were deoxygenated by dinitrogen purging for a minimum of 10 min. Flash column chromatography was performed as described by Still et al. using silica gel (60-Å pore size, 32–63 μm, standard grade, Sorbent Technologies).[1] Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light and an aqueous solution of ceric ammonium molybdate (CAM) followed by heating (>1 min) on a hot plate (~250 °C). Organic solutions were concentrated on Büchi R-200 rotary evaporators at ~20 Torr (house vacuum) at 25–35 °C.

Materials. Commercial reagents and solvents were used as received with the following exceptions: dichloromethane, acetonitrile and tetrahydrofuran were purchased from J.T. Baker (Cycletainer^{TM}) and were purified by the method of Grubbs et al. under positive argon pressure.[2] Acetone was distilled from anhydrous calcium sulfate. Methyl iodide was passed through a short column of basic alumina prior to use. 1-methyl-2-pyrrolidinone (NMP) was distilled from calcium hydride.

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with Varian inverse probe 500 INOVA and Varian 500 INOVA spectrometers and are recorded in parts per million from internal tetramethylsilane on the δ scale and are referenced from the residual protium in the NMR solvent ($CHCl_3$: δ 7.27, DMSO: δ 2.50, CHD_2CN: δ 1.94, C_6HD_5: δ 7.19). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant(s) in Hertz, integration, assignment]. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a Varian 500 INOVA spectrometer and are recorded in parts per million from internal tetramethylsilane on the δ scale and are referenced from the carbon resonances of the solvent ($CDCl_3$: δ 77.23, DMSO-d_6: δ 39.51, CD_3CN: δ 118.69, C_6D_6: δ 128.39). Data is reported as follows: chemical shift [assignment]. Infrared data (IR) were obtained with a Perkin-Elmer 2000 FTIR, and are reported as follows: [frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad)]. Optical rotations were measured on a Jasco-1010 polarimeter. We are grateful to Dr. Li Li for obtaining the mass spectrometric data at the Department of Chemistry's Instrumentation Facility, Massachusetts Institute of Technology.

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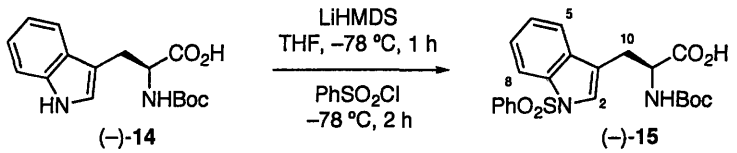


71 %

(–)-(*S*)-2-(ᵗButoxycarbonylamino)-3-(1-(phenylsulfonyl)-1*H*-indol-3-yl)propanoic acid (15):

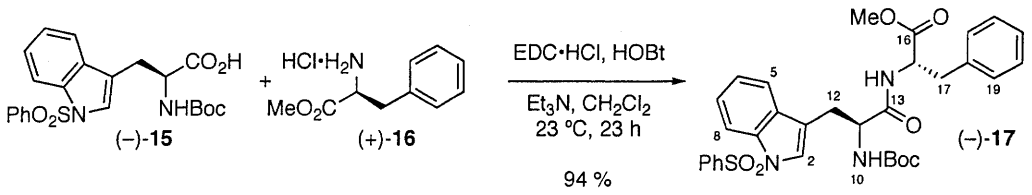
N-Boc-L-tryptophan ((–)-**14**, 5.00 g, 16.4 mmol, 1 equiv) was azeotropically dried by concentration from benzene (20 mL) and the residue dissolved in tetrahydrofuran (34 mL) and cooled to –78 °C. A solution of lithium hexamethyldisilazide (8.25 g, 49.3 mmol, 3.00 equiv) in tetrahydrofuran (30 mL) was added via cannula over 5 min. The reaction mixture was allowed to stir for 1 h before benzenesulfonyl chloride (2.53 mL, 19.7 mmol, 1.20 equiv) was added in one portion. The solution became red and the mixture was stirred for an additional 2 h at –78 °C. Excess base was quenched at this temperature by addition of a solution of acetic acid in ethyl acetate (1:1 v/v, 5 mL) and the resulting mixture was warmed to room temperature. The mixture was diluted with aqueous hydrochloric acid (1 N, 100 mL) and extracted with ethyl acetate (3 × 100 mL). The organic layers were combined and dried over anhydrous sodium sulfate, were filtered, and were concentrated in vacuo to afford a yellow–orange residue. The residue was purified by flash column chromatography on silica gel (eluent: 5% acetic acid, 45% hexanes, 50% dichloromethane). Fractions containing the product (–)-**15** were pooled, concentrated down to approximately 10% of the volume, then diluted with toluene (300 mL) and concentrated. This process was repeated two more times to afford the product as a white solid (5.2 g, 71%). Product (–)-**15** was determined to be of >99% ee by chiral HPLC analysis of the methyl ester ($TMSCHN_2$, PhH, MeOH (3.5:1). Chirapak AD-H, 90% hexanes / 10% isopropanol, 2.0 mL/min, 254 nm, t_R (minor, not observed) = 12.5 min, t_R (major) = 19.2 min).[3]

^{1}H NMR (500 MHz, DMSO, 20 °C):	12.72 (s, 1H, CO_2**H**), 7.86-7.90 (m, 3H, SO_2Ph-*o*-**H**, C_8**H**), 7.66 (t, J = 7.3 Hz, 1H, SO_2Ph-*p*-**H**), 7.53-7.60 (m, 4H, SO_2Ph-*m*-**H**, C_2**H**, C_5**H**), 7.33 (app t, J = 8.1, 7.3 Hz, 1H, C_7**H**), 7.26 (t, J = 7.5 Hz, 1H, C_6**H**), 7.19 (d, J = 8.2 Hz, 1H, N**H**) 4.17 (m, 1H, C_{11}**H**), 3.10 (dd, J = 14.8, 4.3 Hz, 1H, C_{10}**H**), 2.93 (dd, J = 14.8, 10.3 Hz, 1H, C_{10}**H**), 1.31 (s, 9H, $C(CH_3)_3$).
^{13}C NMR (125.8 MHz, DMSO, 20 °C):	173.4 (C_{12}), 155.4 ($C_{carbamate}$), 137.0 (SO_2Ph-*i*-**C**), 134.5, (SO_2Ph-*p*-**C**), 134.3 (C_9), 130.6 (C_4), 129.8 (SO_2Ph-*m*-**C**), 126.6 (SO_2Ph-*o*-**C**), 124.8 (C_7), 124.5 (C_3), 123.4 (C_6), 119.8 (C_5), 119.1 (C_2), 113.2 (C_8), 78.2 (CMe_3), 53.3 (C_{11}), 28.2 ($C(CH_3)_3$), 26.2 (C_{10}).
FTIR (thin film) cm^{-1}:	3309 (br-m), 2979 (m), 1716 (s), 1663 (m), 1175 (s).

[3] On 10-gram scale this same procedure provided the desired product (–)-**15** in 70% yield. Additionally, on 10-gram scale the product was isolated by direct crystallization of the crude reaction mixture from ethyl acetate hexanes (first–crop = 55% yield (Dr. James Ashenhurst)).

HRMS (ESI) (*m/z*):	calc'd for $C_{22}H_{24}N_2NaO_6S$ $[M+Na]^+$: 467.1247 found: 467.1253
$[\alpha]_D^{22}$:	–23.3 (*c* = 1.00, DMF)

TLC (5% acetic acid, 5% CH_3OH, 40% hexanes, 50% CH_2Cl_2), R*f*: 0.57 (UV, CAM)



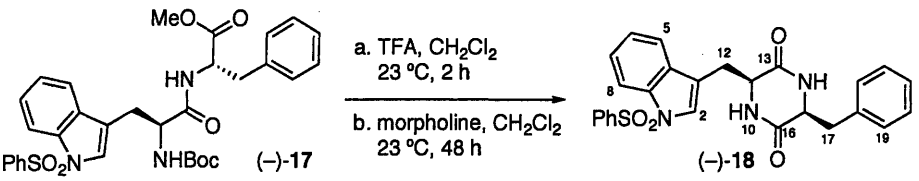
(–)-(*S*)-Methyl 2-((*S*)-2-(ᵗbutoxycarbonylamino)-3-(1-(phenylsulfonyl)-1*H*-indol-3-yl)propanamido)-3-phenylpropanoate (17):

N-Sulfonylated tryptophan (–)-**15** (6.50 g, 14.6 mmol, 1 equiv), L-phenylalanine methyl ester hydrochloride ((+)-**16**, 4.60 g, 21.4 mmol, 1.46 equiv), and 1-hydroxybenzotriazole hydrate (2.89 g, 21.4 mmol, 1.46 equiv) were suspended in dichloromethane (146 mL). Triethylamine (8.93 mL, 64.0 mmol, 4.38 equiv) was added and the suspension was stirred until a golden homogenous solution formed (5 min). To this solution was added EDC•HCl (4.29 g, 22.4 mmol, 1.53 equiv) and the resulting mixture was stirred for 8 h before another portion of EDC•HCl (1.70 g, 8.87 mmol, 0.60 equiv) and triethylamine (4.00 mL, 28.7 mmol, 1.96 equiv) were added. The reaction mixture was allowed to stir for an additional 15 h. The mixture was washed sequentially with an aqueous solution of hydrochloric acid (1 N, 100 mL) and saturated aqueous sodium bicarbonate solution (100 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated in vacuo to afford a yellow foam. The crude product was purified by flash column chromatography on silica gel (eluent: 30% ethyl acetate in hexanes) to yield the product (–)-**17** as a white foam (8.3 g, 94%). On 20-gram scale the purification of (–)-**17** is not necessary; see procedure of (–)-**18**.

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C): δ 7.98 (d, J = 8.5 Hz, 1H, C_8**H**), 7.86 (app dt, J = 7.5, 1.6 Hz, 2H, SO_2Ph-*o*-**H**), 7.56 (d, J = 7.5 Hz, 1H, C_5**H**), 7.52 (tt, J = 7.5, 1.6 Hz, 1H, SO_2Ph-*p*-**H**), 7.44 (s, 1H, C_2**H**), 7.43 (t, J = 8.0 Hz, 2H, SO_2Ph-*m*-**H**), 7.33 (app td, J = 7.0, 1.0 Hz, 1H, C_7**H**), 7.25 (app td, J = 7.5, 0.8 Hz, 1H, C_6**H**), 7.19–7.22 (m, 3H, C_{20}**H**, C_{21}**H**, C_{22}**H**), 6.92 (m, 2H, C_{19}**H**, C_{23}**H**), 6.23 (br d, J = 6.0 Hz, 1H, N_{14}**H**), 5.00 (br d, J = 5.5 Hz, 1Hz, N_{10}**H**), 4.74 (dd, J = 13.5, 6.0 Hz, 1H, C_{15}**H**), 4.40 (br d, J = 6.0 Hz, 1H, C_{11}**H**), 3.68 (s, 3H, O**C**H_3), 3.10–3.18 (m, 2H, C_{12}**H**), 3.02 (dd, J = 14.0, 6.0 Hz, 1H, C_{17}**H**), 2.98 (dd, J = 14.0, 6.0 Hz, 1H, C_{17}**H**), 1.43 (br-s, 9H, C(CH_3)$_3$).

^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C): δ 171.4 (**C**$_{16}$), 170.7 (**C**$_{13}$), 155.4 (**C**$_{carbamate}$), 138.1 (SO_2Ph-*i*-**C**), 135.6 (**C**$_{18}$), 135.2 (**C**$_9$), 133.9 (SO_2Ph-*p*-**C**), 130.8 (**C**$_4$), 129.3 (SO_2Ph-*m*-**C**), 129.2 (**C**$_{19}$, **C**$_{23}$), 128.6 (**C**$_{20}$, **C**$_{22}$), 127.2 (**C**$_{21}$), 126.8 (SO_2Ph-*o*-**C**), 125.0 (**C**$_7$), 124.6 (**C**$_2$), 123.4 (**C**$_6$), 119.8 (**C**$_5$), 117.8 (**C**$_3$), 113.7 (**C**$_8$), 80.4 (**C**Me$_3$), 54.3 (**C**$_{11}$), 53.4 (**C**$_{15}$), 52.5

	($O\mathbf{C}H_3$), 37.9 ($\mathbf{C}_{17}$), 28.3 ($C(\mathbf{C}H_3)_3$), 27.9 ($\mathbf{C}_{12}$).
FTIR (thin film) cm^{-1}:	3307 (br-s), 2979 (m), 1745 (s), 1658 (s), 1523 (br-s).
HRMS (ESI) (*m/z*):	calc'd for $C_{32}H_{35}N_3NaO_7S$ $[M+Na]^+$: 628.2088 found: 628.2064
$[\alpha]_D^{22}$:	–9.7 (*c* = 1.00, DMF)
TLC (40% EtOAc in hexanes), R*f*:	0.56 (UV, CAM)



(–)-(3*S*,6*S*)-3-Benzyl-6-((1-(phenylsulfonyl)-1*H*-indol-3-yl)methyl)piperazine-2,5-dione (18):[4]

Trifluoroacetic acid (6.0 mL) was added to a solution of dipeptide (–)-**17** (3.00 g, 4.95 mmol, 1 equiv) and 1,3-dimethoxybenzene (1.30 mL, 9.90 mmol, 2.00 equiv) in dichloromethane (15.0 mL) at 0 °C. After 2 h, the volatiles were removed and the residue was redissolved in dichloromethane (24 mL). Morpholine (6 mL) was added and the resulting mixture was vigorously stirred for 48 h as the diketopiperazine (–)-**18** precipitated as a white solid. The product was collected by filtration and washed sequentially with dichloromethane (10.0 mL). The filter cake was dissolved in warm dimethylformamide (~55 °C, 100 mL) and triturated by slow addition of deionized water (500 mL). The white gel was collected via filtration and dried under reduced pressure (~20 Torr) at 70 °C to afford the diketopiperazine (–)-**18** as a white solid (1.32 g, 56%). Diketopiperazine (–)-**18** was determined to be >99% ee by chiral HPLC analysis (Chirapak AD-H, 85% hexanes / 15% isopropanol, 3.0 ml/min, 254 nm, t_R (major) = 8.3 min, t_R = (minor, not observed) = 19.3 min).

On 20-gram scale the same procedure provided the desired product (–)-**18** in 82% over all yield starting from the carboxylic acid (–)-**14** without the purification of the amide (–)-**17**.

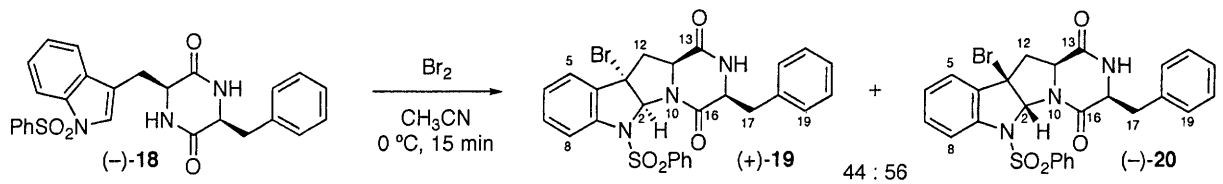
^{1}H NMR (500 MHz, DMSO-d_6, 20 °C): δ 8.14 (br d, J = 2.0 Hz, 1H, N_{14}**H**), 8.02 (br d, J = 2.0 Hz, 1H, N_{10}**H**), 7.94 (app dd, J = 7.8, 1.5 Hz, 2H, SO_2Ph-*o*-**H**), 7.87 (d, J = 8.5 Hz, 1H, C_8**H**), 7.65 (tt, J = 7.5, 1.3 Hz, 1H, SO_2Ph-*p*-**H**), 7.55 (m, 2H, SO_2-*m*-**H**), 7.47 (d, J = 7.5 Hz, 1H, C_5**H**), 7.41 (s, 1H, C_2**H**), 7.34 (td, J = 7.0, 1.0 Hz, 1H, C_7**H**), 7.25 (td, J = 7.5, 1.0 Hz, 1H, C_6**H**), 7.18–7.22 (m, 3H, C_{20}**H**, C_{21}**H**, C_{22}**H**), 6.86 (app dd, J = 8.0, 2.5 Hz, 2H, C_{19}**H**, C_{23}**H**), 3.99–4.03 (m, 2H, C_{11}**H**, C_{15}**H**), 2.61 (dd, J = 14.5, 5.0 Hz, 1H, C_{12}**H**), 2.55 (dd, J = 13.3, 4.8 Hz, 1H, C_{17}**H**), 2.31 (dd, J = 13.5, 5.3 Hz, 1H, C_{17}**H**), 2.29 (dd, J = 14.0 Hz, 6.5 Hz, 1H, C_{12}**H**).

^{13}C NMR (125.8 MHz, DMSO-d_6, 20 °C): δ 166.4 (**C**$_{16}$), 166.3 (**C**$_{13}$), 137.1 (SO_2Ph-*i*-**C**), 136.1 (**C**$_{18}$), 134.5 (SO_2Ph-*p*-**C**), 134.2 (**C**$_9$), 130.6 (**C**$_4$), 129.84, 129.82, 128.1 (**C**$_{20}$, **C**$_{22}$), 126.7 (SO_2Ph-*o*-**C**), 126.6 (**C**$_{21}$), 125.1 (**C**$_2$), 124.7 (**C**$_7$), 123.3 (**C**$_6$), 120.2 (**C**$_5$), 117.6 (**C**$_3$),

[4] Experiment later optimized in collaboration with Dr. James Ashenhurst to afford (–)-**18** in 80 % yield.

	113.0 ($\mathbf{C}_8$), 55.4 ($\mathbf{C}_{15}$), 54.0 ($\mathbf{C}_{11}$), 39.5[5] ($\mathbf{C}_{17}$), 29.3 ($\mathbf{C}_{12}$).
FTIR (nujol) cm^{-1}:	2954 (s), 1675 (s), 1665 (s), 1460 (s), 1376 (s), 1270 (m), 1117 (m), 975 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{26}H_{23}N_3NaO_4S$ $[M+Na]^+$: 496.1301 found: 496.1296
$[\alpha]_D^{22}$:	–145.7 (*c* = 1.00, DMF)
TLC (5% CH_3OH in CH_2Cl_2), R*f*:	0.33 (UV, CAM)

[5] Resonance obscured by DMSO-d_6; however, this signal was observed via gHSQC and gHMBC analysis.



(+)-*endo*–Bromide 19 and (–)-*exo*–Bromide 20:[6]

A solution of bromine in acetonitrile (1.0 M, 1.00 mL, 1.00 mmol, 4.00 equiv) was added to a vigorously stirred suspension of the diketopiperazine (–)-**18** (118 mg, 0.249 mmol, 1 equiv) in acetonitrile (2.50 mL) at 0 °C. The resulting homogeneous red solution and was stirred for 15 min before excess bromide was quenched by the addition of a saturated aqueous solution of sodium thiosulfate (25 ml). The mixture was extracted with dichloromethane (3 × 25 mL) and the organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated in vacuo to afford an orange residue. The residue was purified by flash column chromatography on silica gel (eluent: 5% isopropanol, 45% benzene, 50% hexanes) to provide the (–)-*exo*–bromide **20** (65.7 mg, 48%) and the (+)-*endo*–bromide **19** (51.9 mg, 38%) as a white solids.

(+)-*endo*–Bromide **19**:

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C): 7.99 (d, J = 7.4 Hz, 2H, SO_2-*o*-**H**), 7.61 (d, J = 8.1 Hz, 1H, C_8**H**), 7.55 (t, J = 7.4 Hz, 1H, SO_2Ph-*p*-**H**), 7.44 (app t, J = 8.0, 7.6 Hz, 2H, SO_2Ph-*m*-**H**), 7.29-7.36 (m, 4H, C_5**H**, C_7**H**, C_{20}**H**, C_{22}**H**), 7.25-7.27 (app t, 1H, C_{21}**H**), 7.19 (d, J = 7.1 Hz, 2H, C_{19}**H**, C_{23}**H**), 7.14 (app t, J = 7.6, 7.1 Hz, 1H, C_6**H**), 6.54 (s, 1H, C_2**H**), 5.65 (s, 1H, N_{14}**H**), 4.37 (app t, J = 7.8, 7.5 Hz, 1H, C_{11}**H**), 4.25 (dd, J = 10.6, 3.6 Hz, 1H, C_{15}**H**), 3.66 (dd, J = 14.7, 3.6, 1H, C_{17}**H**), 3.25 (dd, J = 14.4, 6.6, 1H, C_{12}**H**), 3.00 (dd, J = 14.4, 8.8, 1H, C_{12}**H**), 2.85 (dd, J = 14.7, 10.6, 1H, C_{17}**H**).

^{13}C NMR (125 MHz, $CDCl_3$, 20 °C): 167.9 (**C**$_{13}$), 167.1 (**C**$_{16}$), 138.9 (**C**$_9$), 137.9 (SO_2Ph-*i*-**C**), 135.7 (**C**$_{18}$), 133.9 (SO_2Ph-*p*-**C**), 133.6 (**C**$_4$), 131.1 (**C**$_7$), 129.5 (**C**$_{20}$, **C**$_{22}$), 129.2 (**C**$_{19}$, **C**$_{23}$), 129.1 (SO_2Ph-*m*-**C**), 128.5 (SO_2Ph-*o*-**C**), 127.8 (**C**$_{21}$), 126.0 (**C**$_6$), 125.1 (**C**$_5$), 117.1 (**C**$_8$), 87.2 (**C**$_2$), 61.1 (**C**$_3$), 58.5 (**C**$_{11}$), 57.1 (**C**$_{15}$), 40.6 (**C**$_{12}$), 36.2 (**C**$_{17}$).

FTIR (thin film): 3222 (br-w), 1695 (s), 1366 (s), 1169 (s), 1089 (s).

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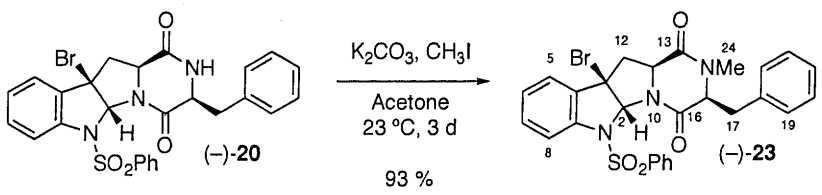
[6] On 12-gram scale this same procedure provided the desired products (–)-*exo*–bromide **20** and (+)-*endo*–bromide **19** in 46% and 42% yield, respectively (88% total yield, 48:52–endo:exo (Dr. James Ashenhurst)).

HRMS-ESI (*m/z*):	calc'd for $C_{27}H_{23}BrN_3O_4S$ $[M+H]^+$: 552.0514 found: 552.0630
$[\alpha]_D^{22}$:	+47.7 (*c* = 1.02, MeOH)
M.p. (CH_2Cl_2):	119-123 °C (dec)
TLC (10% ^{i}PrOH, 40% PhMe, 50% hexanes), R*f*:	0.14 (UV, CAM)

(–)-*exo*–Bromide **20**:

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	7.88 (d, *J* = 7.5 Hz, 2H, SO_2Ph-*o*-**H**), 7.69 (d, *J* = 8.2 Hz, 1H, C_8**H**), 7.56 (t, *J* = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.44 (app t, *J* = 8.0, 7.7 Hz, 2H, SO_2Ph-*m*-**H**), 7.36-7.39 (m, 3H, C_{20}**H**, C_{22}**H**, C_7**H**), 7.31 (app t, 2H, C_{21}**H**, C_5**H**), 7.19-7.22 (m, 3H, C_{19}**H**, C_{23}**H**, C_6**H**), 6.54 (s, 1H, C_2**H**), 5.65 (s, 1H, N_{14}**H**), 4.37 (dd, *J* = 9.5, 3.1 Hz, 1H, C_{15}**H**), 3.78 (dd, *J* = 11.6, 5.0 Hz, 1H, C_{11}**H**), 3.61 (dd, *J* = 14.3, 3.5 Hz, 1H, C_{17}**H**), 3.08 (dd, *J* = 12.7, 5.3 Hz, 1H, C_{12}**H**), 2.95 (dd, *J* = 14.3, 9.6 Hz, 1H, C_{17}**H**), 2.43 (app t, *J* = 12.2, 1H, C_{12}**H**).
^{13}C NMR (125 MHz, $CDCl_3$, 20 °C):	166.0 (**C**$_{13}$), 163.7 (**C**$_{16}$), 141.3 (**C**$_9$), 137.8 (SO_2Ph-*i*-**C**), 135.4 (**C**$_{18}$), 134.0 (SO_2Ph-*p*-**C**), 132.8 (**C**$_4$), 131.4 (**C**$_7$), 129.7 (**C**$_{20}$, **C**$_{22}$), 129.6 (**C**$_{19}$, **C**$_{23}$), 129.3 (SO_2Ph-*m*-**C**), 128.2 (SO_2Ph-*o*-**C**), 128.0 (**C**$_{21}$), 126.7 (**C**$_6$), 124.9 (**C**$_5$), 118.0 (**C**$_8$), 85.7 (**C**$_2$), 58.6 (**C**$_{11}$), 58.1 (**C**$_3$), 56.5 (**C**$_{15}$), 47.0 (**C**$_{12}$), 37.9 (**C**$_{17}$).
FTIR (thin film):	3227 (br-w), 3064 (w), 1684 (s), 1369 (s), 1171 (s).
HRMS-ESI (*m/z*):	calc'd for $C_{27}H_{23}BrN_3O_4S$ $[M+H]^+$: 552.0514 found: 552.0602
$[\alpha]_D^{22}$:	–198 (*c* = 1.00, CH_2Cl_2)
M.p. (CH_2Cl_2):	122–123 °C (dec.)
TLC (10% ^{i}PrOH, 40% PhMe, 50 % hexanes), R*f*:	0.28 (UV, CAM)

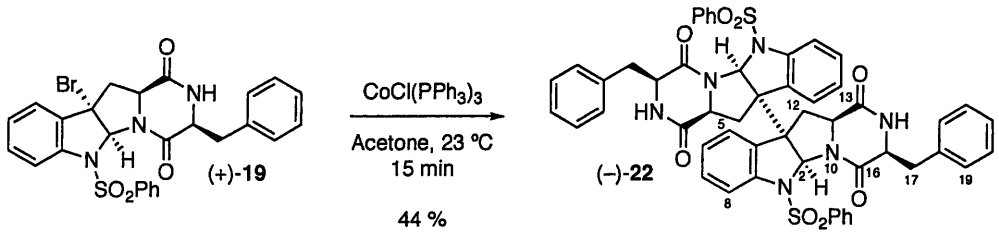


(–)-*N*-Methyl *exo*–bromide 23:

Potassium carbonate (1.86 g, 13.4 mmol, 25.0 equiv) followed by methyl iodide (10.76 mL) were sequentially added to a vigorously stirred solution of the *exo*–bromide (–)-**20** (297 mg, 0.538 mmol, 1 equiv) in acetone (13.45 mL) at 23 °C. The reaction flask containing the resulting suspension was covered in aluminum foil and stirred for 3 d at 23 °C. The volatiles were removed and the resulting white solid residue was partitioned between ethyl acetate (100 mL) and deionized water (100 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated in vacuo to provide crude (–)-**23** as a white solid residue. The residue was purified by flash column chromatography on silica gel (eluent: 2% methanol in dichloromethane) to give the product (–)-**23** as a white solid foam (282 mg, 93%).

On 3-gram scale this same procedure provided the desired product (–)-**23** in 88% yield.

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	δ 7.90 (app ddd, J = 8.5, 2.0, 1.0 Hz, 2H, SO_2Ph-*o*-**H**), 7.62 (d, J = 8.0 Hz, 1H, C_8**H**), 7.57 (tt, J = 7.5, 1.3 Hz, 1H, SO_2Ph-*p*-**H**), 7.47 (app t, J = 7.8 Hz, 2H, SO_2Ph-*m*-**H**), 7.35 (app t, J = 7.3 Hz, 2H, C_{20}**H**, C_{22}**H**), 7.28–7.32 (m, 2H, C_7**H**, C_{21}**H**), 7.16 (app dd, J = 7.5, 1.5 Hz, 1H, C_5**H**), 7.10–7.13 (m, 3H, C_6**H**, C_{19}**H**, C_{23}**H**), 6.41 (s, 1H, C_2**H**), 4.42 (t, J = 3.8 Hz, 1H, C_{15}**H**), 3.52 (dd, J = 13.8, 2.8 Hz, 1H, C_{17}**H**), 3.49 (dd, J = 12.5, 4.5 Hz, 1H, C_{11}**H**), 3.17 (dd, J = 13.8, 4.3 Hz, 1H, C_{17}**H**), 3.12 (s, 3H, C_{24}**H**), 2.48 (dd, J = 12.0, 4.5 Hz, 1H, C_{12}**H**), 0.57 (t, J = 12.5 Hz, C_{12}**H**).
^{13}C NMR (125.8 Hz, $CDCl_3$, 20 °C):	δ 163.42 ($\mathbf{C}_{Amide}$), 163.38 ($\mathbf{C}_{Amide}$), 141.5 ($\mathbf{C}_9$), 137.7 (SO_2Ph-*i*-**C**), 134.5 ($\mathbf{C}_{18}$), 133.9 (SO_2Ph-*p*-**C**), 132.1 ($\mathbf{C}_4$), 131.2 ($\mathbf{C}_7$), 130.2 ($\mathbf{C}_{19}$, $\mathbf{C}_{23}$), 129.7 ($\mathbf{C}_{20}$, $\mathbf{C}_{22}$), 129.3 (SO_2Ph-*m*-**C**), 127.9 ($\mathbf{C}_{21}$), 127.7 (SO_2Ph-*o*-**C**), 126.2 ($\mathbf{C}_6$), 125.4 ($\mathbf{C}_5$), 116.5 ($\mathbf{C}_8$), 85.4 ($\mathbf{C}_2$), 63.6 ($\mathbf{C}_{15}$), 58.7 ($\mathbf{C}_3$), 58.1 ($\mathbf{C}_{11}$), 47.7 ($\mathbf{C}_{12}$), 36.4 ($\mathbf{C}_{17}$), 33.1 ($\mathbf{C}_{24}$).
FTIR (thin film) cm^{-1}:	3063(w), 1681(s), 1664(s), 1447(m), 1172(m).
HRMS (ESI) (*m/z*):	calc'd for $C_{27}H_{24}BrN_3NaO_4S$[M+Na]$^+$:588.0563 found: 588.0546
$[\alpha]_D^{22}$:	–141.5 (c = 1.00, CH_2Cl_2)
TLC (5% CH_3OH in CH_2Cl_2), R*f*:	0.58 (UV, CAM)



(–)-*endo*–Dimer 22:[7]

Freshly prepared tristriphenylphosphine cobalt chloride[8] ($CoCl(PPh_3)_3$, 610 mg, 0.693 mmol, 1.80 equiv) was added rapidly as a solid to a degassed (dinitrogen purge, 10 min) solution of bromide (+)-**19** (319 mg, 0.577 mmol, 1 equiv) in acetone (5.80 mL) at 23 °C under an argon atmosphere. The solution immediately turned blue. After 15 min, the reaction mixture was diluted with deionized water (75 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were washed with brine (50 mL), were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting yellow foam was purified by flash column chromatography on silica gel (eluent: 10% acetone, 90% dichloromethane) to afford the (–)-*endo*-dimer **22** (120 mg, 44%) as a white solid.

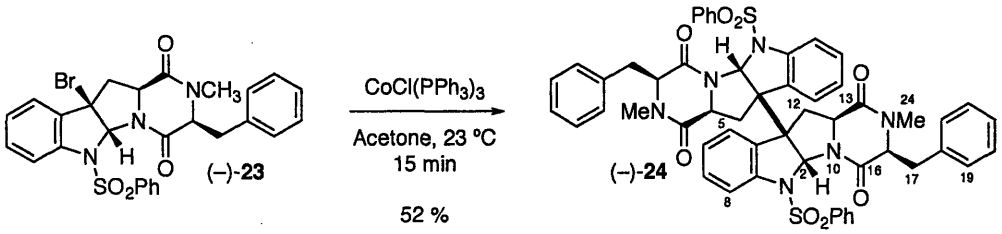
On a gram scale this same procedure provided the desired product (–)-**22** in 43% yield.

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	8.15 (d, J = 7.5 Hz, 4H, SO_2Ph-*o*-**H**), 7.65 (t, J = 7.3 Hz, 2H, SO_2Ph-*p*-**H**), 7.59 (app t, J = 7.85, 7.21, 4H, SO_2Ph-*m*-**H**), 7.35 (t, J = 7.8 Hz, 4H, C_5**H**, C_7**H**), 7.22-7.30 (m, 8H, C_{20}**H**, C_{21}**H**, C_{22}**H**, C_6**H**), 7.13 (d, J = 8.0 Hz, 2H, C_8**H**), 7.08 (d, J = 6.7 Hz, 4H, C_{19}**H**, C_{23}**H**), 6.50 (s, 2H, C_2**H**), 5.36 (s, 2H, N_{14}**H**), 4.67 (t, J = 8.8 Hz, 2H, C_{15}**H**), 4.20 (dd, J = 10.5, 3.6 Hz, 2H, C_{11}**H**), 3.39 (dd, J = 14.5, 3.6 Hz, 2H, C_{17}**H**), 2.74 (dd, J = 15.0, 9.7 Hz, 2H, C_{12}**H**), 2.52 (dd, J = 15.0, 8.3 Hz, 2H, C_{12}**H**), 2.49 (dd, J = 14.5, 10.6 Hz, 2H, C_{17}**H**).
^{13}C NMR (125 MHz, $CDCl_3$, 20 °C):	168.9 (C_{13}), 168.5 (C_{16}), 142.2 (C_9), 141.6 (SO_2Ph-*i*-**C**), 135.6 (C_{18}), 135.3 (C_4), 133.3 (SO_2Ph-*p*-**C**), 129.9 (C_7) , 129.5 (C_{20}, C_{22}), 129.1 (SO_2Ph-*m*-**C**), 129.1 (C_{19}, C_{23}), 127.8 (C_{21}), 127.4 (C_5), 127.3 (SO_2Ph-*o*-**C**), 125.3 (C_6), 117.6 (C_8), 82.0 (C_2), 59.6 (C_3), 57.7 (C_{11}), 57.0 (C_{15}), 36.2 (C_{17}), 33.0 (C_{12}).
FTIR (thin film):	3337 (br-w), 1695 (s), 1388 (m), 1341 (m), 1161 (m).
HRMS-ESI (*m/z*):	calc'd for $C_{52}H_{45}N_6O_8S_2$ $[M+H]^+$: 945.2735 found: 945.2709

[7] Experiment later optimized in collaboration with Dr. James Ashenhurst to afford (–)-**15** in 48 % yield.

[8] a) M. Aresta, M. Rossi, A. Sacco. *Inorg. Chim. Acta* **1969**, *3*, 227. b) Baysdon, S. L.; Liebeskind, L. S. *Organometallics* **1982**, *1*, 771.

$[\alpha]_D^{22}$:	–94.1 (c = 1.00, CH_2Cl_2)
M.p. (CH_2Cl_2):	199–204 °C (dec)
TLC (20% acetone in CH_2Cl_2), R*f*:	0.45 (UV, CAM)



(–)-*exo*-Dimer 24:

Freshly prepared tristriphenylphosphine cobalt chloride ($CoCl(PPh_3)_3$, 790 mg, 0.890 mmol, 1.80 equiv) was added rapidly as a solid to a degassed (dinitrogen purge, 10 min) solution of bromide (–)-**23** (282 mg, 0.498 mmol, 1 equiv) in acetone (5.0 mL) at 23 °C under an argon atmosphere. The solution immediately turned blue. After 15 min, the reaction mixture was diluted with deionized water (100 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic extracts were washed with brine (2 × 20 mL), were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting yellow oil was purified by flash column chromatography on silica gel (eluent: 20% acetone, 30% hexanes, 50% dichloromethane) to afford the (–)-*exo*-dimer **24** (125 mg, 52%) as a white solid.

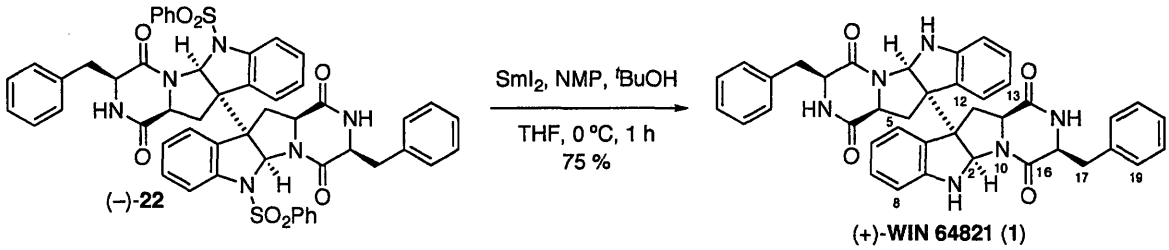
On a 2.5-gram scale this same procedure provided the desired product (–)-**24** in 47% yield.

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	δ 7.97 (app d, J = 7.5 Hz, 4H, SO_2Ph-*o*-**H**), 7.58 (app t, J = 7.5 Hz, 2H, SO_2Ph-*p*-**H**), 7.47 (t, J = 7.8 Hz, 4H, SO_2Ph-*m*-**H**), 7.40 (d, J = 7.5 Hz, 2H, C_5**H**), 7.25 (t, J = 7.8 Hz, 4H, C_{20}**H**, C_{23}**H**), 7.21 (d, J = 8.5 Hz, 2H, C_8**H**), 7.17 (d, J = 7.0 Hz, 4H, C_{19}**H**, C_{23}**H**), 7.09 (t, J = 7.0 Hz, 2H, C_{21}**H**), 7.06 (d, J = 7.3 Hz, 2H, C_7**H**), 6.93 (t, J = 7.3 Hz, 2H, C_6**H**), 6.63 (s, 2H, C_2**H**), 3.97 (dd, J = 4.5, 3.5 Hz, 2H, C_{15}**H**), 3.74 (dd, J = 11.8, 4.8 Hz, 2H, C_{11}**H**), 3.31 (d, J = 4.5 Hz, 4H, C_{17}**H**), 2.98 (s, 6H, C_{24}**H**), 2.59 (dd, J = 12.0, 5.0 Hz, 2H, C_{12}**H**), 1.36 (t, J = 12.0 Hz, 2H, C_{12}**H**).
^{13}C NMR (125.8 Hz, $CDCl_3$, 20 °C):	δ 164.3 (**C**$_{13}$), 162.6 (**C**$_{16}$), 142.6 (**C**$_9$), 141.3 (SO_2Ph-*i*-**C**), 136.5 (**C**$_{18}$), 133.2 (SO_2Ph-*p*-**C**), 130.2 (**C**$_7$), 129.7 (**C**$_{19}$, **C**$_{23}$), 129.2 (SO_2Ph-*m*-**C**), 129.1 (**C**$_{20}$, **C**$_{22}$), 128.2 (**C**$_4$), 127.3 (**C**$_{21}$), 126.8 (SO_2Ph-*o*-**C**), 124.6 (**C**$_5$), 124.3 (**C**$_6$), 113.4 (**C**$_8$), 78.9 (**C**$_2$), 63.0 (**C**$_{15}$), 59.8 (**C**$_3$), 57.7 (**C**$_{11}$), 39.4 (**C**$_{12}$), 36.8 (**C**$_{17}$), 33.0 (**C**$_{24}$).
FTIR (thin film) cm^{-1}:	3063 (w), 2940 (w), 1670 (s), 1447 (m), 1170 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{54}H_{48}N_6NaO_8S_2$ $[M+Na]^+$: 995.2867 found: 995.2870

$[\alpha]_D^{22}$: –214.1 (c = 1.00, CH_2Cl_2)

M.p. (CH_2Cl_2): 168–172 °C (dec.)

TLC (20% acetone, 40% hexanes, 40% CH_2Cl_2), R*f*:0.32 (UV, CAM)



(+)-WIN 64821 (1):

A fresh solution of samarium diiodide in tetrahydrofuran (0.1 M, 3.20 mL, 0.320 mmol, 6.04 equiv) was added dropwise over one hour to a degassed (dinitrogen purge, 10 min) solution of dimer (–)-**22** (50 mg, 53 μmol, 1 equiv), 1-methyl-2-pyrrolidinone (3.15 ml), and *t*butanol (3.15 mL) at 0 °C. After 20 min a white precipitate formed. After complete addition, the dark black reaction mixture was poured into a saturated aqueous sodium carbonate solution (100 mL) and extracted with ethyl acetate (2 × 30 mL). The combined organic layers were washed with water (3 × 50 mL), were dried over anhydrous sodium sulfate, and were concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (eluent: 30% acetone in dichloromethane) to afford (+)-WIN 64821 (1) as a white solid (26.3 mg, 75%). All spectral data were in agreement with those reported in the literature.[9]

^{1}H NMR (500 MHz, CD_3CN, 20 °C):	δ 7.34 (d, J = 7.5 Hz, 2H, C_5**H**), 7.10-7.17 (m, 12H, C_{19}**H**, C_{20}**H**, C_{21}**H**, C_{22}**H**, C_{23}**H**, C_7**H**), 6.73 (t, J = 7.5, 2H, C_6**H**), 6.68 (d, J = 7.8 Hz, 2H, C_8**H**), 5.87 (s, 2H, N_{14}**H**), 5.85 (s, 2H, N_1**H**), 4.86 (s, 2H, C_2**H**), 4.16 (t, J = 5.1 Hz, 2H, C_{15}**H**), 4.06 (t, J = 8.4 Hz, 2H, C_{11}**H**). 3.09 (dd, J = 14.7, 4.9 Hz, 2H, C_{17}**H**), 2.96-3.01 (m, 4H, C_{17}**H**, C_{12}**H**), 2.51 (dd, J = 14.0, 7.9, 2H, C_{12}**H**).
^{13}C NMR (125.8 MHz, CD_3CN, 20 °C):	δ 170.1 (**C**$_{13}$), 169.3 (**C**$_{16}$), 150.4 (**C**$_9$), 137.7 (**C**$_{18}$), 131.8 (**C**$_4$), 130.7 (**C**$_{19}$, **C**$_{23}$), 130.5 (**C**$_7$), 129.7 (**C**$_{20}$, **C**$_{22}$), 128.0 (**C**$_{21}$), 126.4 (**C**$_5$), 120.6 (**C**$_6$), 110.8 (**C**$_8$), 80.9 (**C**$_2$), 61.3 (**C**$_3$), 58.1 (**C**$_{11}$), 57.3 (**C**$_{15}$), 37.1 (**C**$_{12}$), 36.4 (**C**$_{17}$).
FTIR (thin film) cm^{-1}:	3382 (br-w), 1674 (s), 1410 (m), 910 (m), 733 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{40}H_{37}N_6O_4$ [M+H]$^+$: 665.2871 found: 665.2859
$[\alpha]_D^{21}$:	+230 (c = 0.15, MeOH)[9]
M.p. (MeOH):	181–183 °C (dec)
TLC (30% Acetone in CH_2Cl_2), R*f*:	0.33 (UV, CAM).

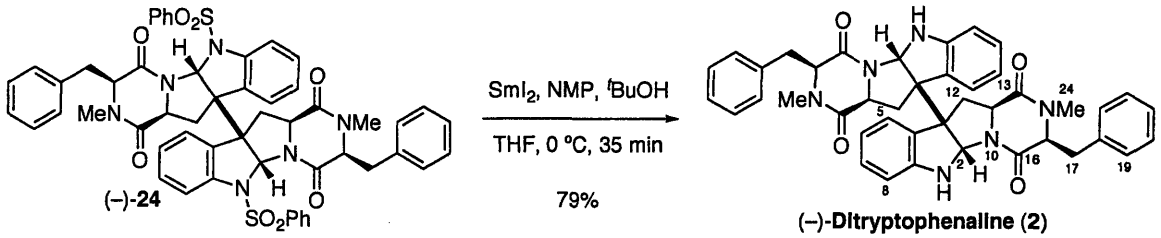
[9] a) $[\alpha]_D$ = +200.0 (c = 0.15, MeOH), Barrow, C. J.; Cai, P.; Snyder, J. K.; Sedlock, D. M.; Sun, H. H.; Cooper, R. *J. Org. Chem.* **1993**, *58*, 6016. b) $[\alpha]_D$ = –200.0 (c = 0.19, MeOH), Overman, L. E.; Paone, D. V. *J. Am. Chem. Soc.* **2001**, *123*, 9465.

Comparison of our data for (+)-WIN-64821 (1) with literature:

Assignment	Barrow's Report[9a] (+)-WIN 64821 (**1**) ^{1}H NMR, 360 MHz, CD_3CN	Overman's Report[9b] (–)-WIN 64821 (**1**) ^{1}H NMR, 500 MHz, CD_3CN	This Work (+)-WIN 64821 (**1**) ^{1}H NMR, 500 MHz, CD_3CN, 20 °C
N1	5.84 (s)	5.86 (s)	5.85 (s)
C2	4.85 (br-s)	4.86 (br-s)	4.86 (s)
C3			
C4			
C5	7.34 (d, J = 8.0 Hz)	7.33 (d, J = 7.6 Hz)	7.34 (d, J = 7.5 Hz)
C6	6.73 (td, J = 8.0, 1.2 Hz)	6.72 (t, J = 7.5 Hz)	6.73 (t, J = 7.5 Hz)
C7	7.10 (td, J = 8.0, 1.2 Hz)	7.10 (t, J = 8.3 Hz)	7.10–7.17 (m)
C8	6.67 (d, J = 8.0 Hz)	6.67 (d, J = 7.8 Hz)	6.68 (d, J = 7.8 Hz)
C9			
C11	4.05 (t, J = 8.5 Hz)	4.05 (br t, J = 8.5 Hz)	4.06 (t, J = 8.4 Hz)
C12	2.98 (dd, J = 14.0, 8.0 Hz) 2.50 (dd, J = 14.0, 7.5 Hz)	2.95–3.00 (m) 2.50 (dd, J = 14.0, 7.9 Hz)	2.96–3.01 (m) 2.51 (dd, J = 14.0, 7.9 Hz)
C13			
C14	5.88 (br-s)	5.94 (s)	5.87 (s)
C15	4.15 (bt, J = 5.5 Hz)	4.14 (br t, J = 5.2 Hz)	4.16 (t, J = 5.1 Hz)
C16			
C17	3.09 (dd, J = 14.5, 5.0 Hz) 2.98 (dd, J = 14.5, 6.0 Hz)	3.09 (dd, J = 14.7, 4.9 Hz) 2.97 (dd, J = 14.7, 6.3 Hz)	3.09 (dd, J = 14.7, 4.9 Hz) 2.96–3.01 (m)
C18			
C19, C23	7.13 (s)	7.12–7.15 (m)	7.10–7.17 (m)
C20, C22	7.13 (s)	7.12–7.15 (m)	7.10–7.17 (m)
C21	7.13 (s)	7.12–7.15 (m)	7.10–7.17 (m)

Assignment	Barrow's Report[9a] (+)-WIN 64821 (1) ^{13}C NMR, CD_3CN	Overman's Report[9b] (–)-WIN 64821 (1) ^{13}C NMR, 125 MHz, CD_3CN[10]	This Work (+)-WIN 64821 (1) ^{13}C NMR, 125.8 MHz, CD_3CN, 20 °C
C2	80.82	81.06	80.9
C3	61.14	61.54	61.3
C4	131.90	131.74	131.8
C5	126.53	126.41	126.4
C6	120.86	120.57	120.6
C7	130.60	130.44	130.5
C8	110.82	110.82	110.8
C9	150.56	150.26	150.4
C11	57.93	58.35	58.1
C12	36.88	37.44	37.1
C13	170.36	169.92	170.1
C15	57.17	57.58	57.3
C16	169.55	169.09	169.3
C17	36.17	36.75	36.4
C18	137.88	137.67	137.7
C19, C23	130.82	130.65	130.7
C20, C22	129.84	129.68	129.7
C21	128.11	127.97	128.0

[10] Professor L. E. Overman, *personal communication* **2007**, and see: Overman, L. E.; Paone, D. V. *J. Am. Chem. Soc.* **2001**, *123*, 9465.



(–)-Ditryptophenaline (2):

A fresh solution of samarium diiodide in tetrahydrofuran (0.1 M, 10.8 mL, 1.08 mmol, 6.58 equiv) was added dropwise over 35 min to a degassed (dinitrogen purge, 10 min) solution of dimer (–)-**24** (160 mg, 164 μmol, 1 equiv), 1-methyl-2-pyrrolidinone (9.85 ml), and *t*butanol (9.85 mL) at 0 °C. During the addition the reaction mixture turned bright yellow and then became clear with a white precipitate. After complete addition, the dark black reaction mixture was poured into a saturated aqueous sodium carbonate solution (300 mL) and extracted with ethyl acetate (2 × 150 mL). The combined organic layers were washed with water (300 mL), were dried over anhydrous sodium sulfate, and were concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (eluent: 100% ethyl acetate) to afford (–)-ditryptophenaline (**2**) as a white solid (90.2 mg, 79%). All spectral data were in agreement with those reported in the literature.[5b,11]

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	δ 7.57 (app t, J = 7.5 Hz, 4H, C_{20}**H**, C_{22}**H**), 7.51 (app t, J = 7.0 Hz, 2H, C_{21}**H**), 7.14 (app d, J = 7.5 Hz, 4H, C_{19}**H**, C_{23}**H**), 7.07 (td, J = 8.0, 1.0 Hz, 2H, C_7**H**), 6.97 (d, J = 7.5 Hz, 2H, C_5**H**), 6.70 (td, J = 7.5, 1.0 Hz, 2H, C_6**H**), 6.55 (d, J = 7.5 Hz, 2H, C_7**H**), 4.81 (s, 2H, C_2**H**), 4.69 (s, 2H, N_1**H**), 4.26 (m, 2H, C_{15}**H**), 3.66 (ddd, J = 12.0, 5.0, 1.5 Hz, 2H, C_{11}**H**), 3.53 (dd, J = 14.5, 3.0 Hz, 2H, C_{17}**H**), 3.25 (dd, J = 14.5, 4.5 Hz, 2H, C_{17}**H**), 3.03 (s, 6H, C_{24}**H**), 2.02 (dd, J = 12.5, 5.0 Hz, 2H, C_{12}**H**), 1.57 (t, J = 12.0 Hz, 2H, C_{12}**H**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 165.6 (C_{13}), 164.1 (C_{16}), 150.3 (C_9), 134.6 (C_{18}), 129.8 (C_7), 129.6 (C_{20}, C_{22}), 129.5 (C_{19}, C_{23}), 128.1 (C_{21}), 126.6 (C_4), 126.0 (C_5), 119.1 (C_6), 109.8 (C_8), 78.8 (C_2), 63.3 (C_{15}), 59.1 (C_3), 58.8 (C_{11}), 36.4 (C_{17}), 36.1 (C_{12}), 32.8 (C_{24}).
FTIR (thin film) cm^{-1}:	3344 (br-m), 2924 (m), 1658 (s), 1454 (s), 1318 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{42}H_{41}N_6O_4$ $[M+H]^+$: 693.3184 found: 693.3192

[11] Maes, C. M.; Potgieter, M.; Steyn, P. S. *J. Chem. Soc. Perkin Trans. 1* **1986**, 861.

$[\alpha]_D^{21}$:	–292 (c = 0.97, CH_2Cl_2)[12]
M.p. ($CDCl_3$):	200–204 °C (dec)
TLC (ethyl acetate), R*f*:	0.37 (UV, CAM)

[12] a) $[\alpha]_D^{23.5}$ = –330 (c = 0.52, CH_2Cl_2), Springer, J. P.; Büchi, G.; Kobbe, B.; Demain, A. L.; Clardy, J. *Tetrahedron Lett.* **1977**, *18*, 2403. b) $[\alpha]_D^{33}$ = –318.1 (c = 0.46, CH_2Cl_2), Nakagawa, M.; Sugumi, H.; Kodato, S.; Hino, T. *Tetrahedron Lett.* **1981**, *22*, 5323. c) $[\alpha]_D$ = –317 (c = 0.11, CH_2Cl_2), Overman, L. E.; Paone, D. V. *J. Am. Chem. Soc.* **2001**, *123*, 9465.

Comparison of our data for (–)-ditryptophenaline (2) with literature:

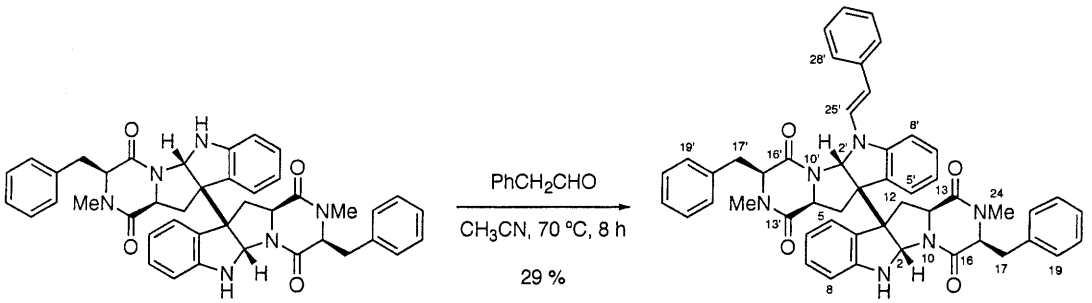
Assignment	Maes's Report[11] (–)-ditryptophenaline (**2**) ^{1}H NMR, 500 MHz, $CDCl_3$	Overman's Report[9b] (–)-ditryptophenaline (**2**) ^{1}H NMR, 500 MHz, $CDCl_3$	This Work[13] (–)-ditryptophenaline (**2**) ^{1}H NMR, 500 MHz, $CDCl_3$, 20 °C
N1	4.70 (s)	4.65 (br s)	4.69 (s)
C2	4.80 (s)	4.79 (s)	4.81 (s)
C3			
C4			
C5	6.94 (d, J = 7.5 Hz)	6.94 (d, J = 7.5 Hz)	6.97 (d, J = 7.5 Hz)
C6	6.66 (br-t, J = 7.4 Hz)	6.66 (ddd, J = 7.5, 7.5, 0.7 Hz)	6.70 (td, J = 7.5, 1.0 Hz)
C7	7.03 (dt, J = 7.6, 0.9 Hz)	7.03 (ddd, J = 7.7, 7.7, 1.1 Hz)	7.07 (td, J = 8.0, 1.0 Hz)
C8	6.51 (d, J = 7.8 Hz)	6.51 (d, J = 7.8 Hz)	6.55 (d, J = 7.5 Hz
C9			
C11	3.63 (ddd, J = 12.0, 4.9, 1.2 Hz)	3.63 (ddd, J = 12.0, 4.9, 1.3 Hz)	3.66 (ddd, J = 12.0, 5.0, 1.5 Hz)
C12	1.99 (dd, J = 4.9, 12.4 Hz) 1.55 (t, J = 12.2 Hz)	1.99 (dd, J = 12.4, 4.9 Hz) 1.55 (t, J = 12.2 Hz)	2.02 (dd, J = 12.5, 5.0 Hz) 1.57 (t, J = 12.0 Hz)
C13			
C15	4.22 (m)	see reference	4.26 (m, 2H)
C16			
C17	3.49 (dd, J = 14.3, 3.1 Hz) 3.21 (dd, J = 4.4, 14.3 Hz)	3.49 (dd, J = 14.3, 3.2 Hz) 3.22 (dd, J = 14.3, 4.4 Hz)	3.53 (dd, J = 14.5, 3.0 Hz) 3.25 (dd, J = 14.5, 4.5 Hz)
C18			
C19, C23	7.10 (d, J = 7.0 Hz)	7.10 (d, J = 7.0 Hz)	7.14 (app d, J = 7.5 Hz)
C20, C22	7.51 (t, J = 7.3 Hz)	7.52 (t, J = 7.0 Hz)	7.57 (app t, J = 7.5 Hz)
C21	7.46 (tt, J = 7.3 Hz)	7.46 (t, J = 7.3 Hz)	7.51 (app t, J = 7.0 Hz)
C24	2.99 (s)	2.99 (s)	3.03 (s)

[13] Data for this report were obtained with the solvent referenced at 7.27 ppm. See the *Instrumentation* section on page S1.

Comparison of our data for (–)-ditryptophenaline (2) with literature continued:

Assignment	Maes's Report[11] (–)-ditryptophenaline (2) ^{13}C NMR, 125.8 MHz, $CDCl_3$	Overman's Report[9b] (–)-ditryptophenaline (2) ^{13}C NMR, 125 MHz, $CDCl_3$	This Work[14] (–)-ditryptophenaline (2) ^{13}C NMR, 125.8 MHz, $CDCl_3$, 20 °C
C2	78.55	78.55	78.8
C3	58.89	58.86	59.1
C4	126.36	126.38	126.6
C5	125.59	125.63	126.0
C6	118.78	118.84	119.1
C7	129.52	129.53	129.8
C8	109.49	109.53	109.8
C9	150.09	150.06	150.3
C11	58.44	58.45	58.8
C12	35.95	35.92	36.1
C13	165.30	165.31	165.6
C15	63.00	63.03	63.3
C16	163.86	163.85	164.1
C17	36.10	36.09	36.4
C18	134.42	134.41	134.6
C19, C23	129.19	129.21	129.5
C20, C22	129.23	129.26	129.6
C21	127.81	127.81	128.1
C24	32.44	32.42	32.8

[14] Data for this report were obtained with the solvent referenced at 77.23 ppm. See the *Instrumentation* section on page S1.



(–)-**Ditryptophenaline** (**2**) (–)-**1'-(2-Phenylethylene)-ditryptophenaline** (**3**)

(–)-1′-(2-Phenylethylene)-ditryptophenaline (3):

To a suspension of (–)-ditryptophenaline (**2**, 40.0 mg, 57.7 μmol, 1 equiv) in acetonitrile (2.80 mL) was added phenylacetaldehyde (72 μL, 0.58 mmol, 10 equiv) and the resulting mixture was heated to 70 °C for 8 h. The mixture was allowed to cool to room temperature and the crude reaction mixture was purified directly by flash column chromatography on silica gel (eluent: 10% Et_3N, 45% hexanes, 45% dichloromethane) to afford the natural product (–)-1′-(2-phenylethylene)-ditryptophenaline (**3**) as a white powder (13.5 mg, 29%). All spectral data were in agreement with those reported in the literature.[15,16]

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C): δ 7.54 (*J* = 7.5 Hz, 2H, $C_{20'}$**H**, $C_{22'}$**H**), 7.43 (d, *J* = 7.0 Hz, 2H, $C_{28'}$**H**, $C_{32'}$**H**), 7.39 (t, *J* = 7.5 Hz, 1H, $C_{21'}$**H**), 7.36 (t, *J* = 7.3 Hz, 2H, $C_{29'}$**H**, $C_{31'}$**H**), 7.36 (d, *J* = 14.5 Hz, 1H, $C_{25'}$**H**), 7.30 (t, *J* = 7.8 Hz, 2H, C_{20}**H**, C_{22}**H**), 7.20 (dd, *J* = 8.0, 1.0 Hz, 2H, $C_{19'}$**H**, $C_{23'}$**H**), 7.15–7.18 (m, 3H, C_{21}**H**, $C_{7'}$**H**, $C_{30'}$**H**), 7.10 (d, *J* = 7.5 Hz, 2H, C_{19}**H**, C_{23}**H**), 7.06 (t, *J* = 7.5 Hz, 1H, C_7**H**), 7.06 (d, *J* = 7.5 Hz, 1H, $C_{5'}$**H**), 6.95 (d, *J* = 7.5 Hz, 1H, C_5**H**), 6.95 (d, *J* = 7.5 Hz, 1H, $C_{8'}$**H**), 6.80 (td, *J* = 7.5, 0.5 Hz, 1H, $C_{6'}$**H**), 6.68 (td, *J* = 7.5, 1.0 Hz, 1H, C_6**H**), 6.56 (d, *J* = 14.5 Hz, 1H, $C_{26'}$**H**), 6.52 (d, *J* = 8.0 Hz, 1H, C_8**H**), 5.52 (s, 1H, $C_{2'}$**H**), 4.89 (s, 1H, C_2**H**), 4.75 (br s, 1H, N_1**H**), 4.40 (app t, *J* = 3.5 Hz, 1H, $C_{15'}$**H**), 4.24 (m, 1H, C_{15}**H**), 3.75 (dd, *J* = 11.5, 4.0 Hz, 1H, C_{11}**H**), 3.72 (dd, *J* = 11.5, 4.5 Hz, 1H, $C_{11'}$**H**), 3.58 (dd, *J* = 14.3, 3.8 Hz, 1H, $C_{17'}$**H**), 3.53 (dd, *J* = 14.5, 3.5 Hz, 1H, C_{17}**H**), 3.25 (app td, *J* = 14.3, 4.5 Hz, 2H,

[15] Barrow, C. J.; Sedlock, D. M. *J. Nat. Prod.* **1994**, *57*, 1239. $CDCl_3$ referenced to 7.25 ppm for ^{1}H NMR analysis and 77.0 ppm for ^{13}C NMR analysis. $[\alpha]_D = -125$ (*c* = 0.05, $CHCl_3$).

[16] We also prepared (–)-1′-(2-phenylethylene)-ditryptophenaline (**3**) by hydrolysis of the corresponding (–)-bisstyrenylditrytophenaline (**25**). In situ ^{1}H NMR monitoring confirmed the formation of **3** within 20 min upon treatment of a solution of **25** in C_6D_6 (0.2M) at 23 °C with water (0.5 equiv) in the presence of trifluoroacetic acid-*d*1 (0.87 equiv). Addition of triethylamine to quench the acid additive followed by chromatography of the reaction mixture on silica gel (eluent: 50% ethyl acetate, 40% hexanes, 10% triethylamine) provided the recovered (–)-bisstyrenylditrytophenaline (**25**, 42%), (–)-1′-(2-phenylethylene)-ditryptophenaline (**3**, 48%), along with (–)-ditryptophenaline (**2**, <10%).

	C_{17}**H**, $C_{17'}$**H**), 3.04 (s, 3H, $C_{24'}$**H**), 3.00 (s, 3H, C_{24}**H**), 2.23 (dd, J = 12.5, 5.0 Hz, 1H, C_{12}**H**), 2.13 (dd, J = 12.0 5.0 Hz, 1H, $C_{12'}$**H**), 1.53 (t, J = 12.0 Hz, 1H, C_{12}**H**), 1.49 (t, J = 12.0 Hz, 1H, $C_{12'}$**H**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 165.5 (**C**$_{13}$), 165.0 (**C**$_{13'}$), 164.4 (**C**$_{16}$), 163.7 (**C**$_{16'}$), 150.2 (**C**$_{9}$), 146.7 (**C**$_{9'}$), 138.2 (**C**$_{27'}$), 135.1 (**C**$_{18'}$), 134.7 (**C**$_{18}$), 130.06, 130.04, 129.8 (**C**$_{19'}$, **C**$_{23'}$), 129.7 (**C**$_{20'}$, **C**$_{22'}$), 129.3 (**C**$_{19}$, **C**$_{23}$), 129.1 (**C**$_{20}$, **C**$_{22}$), 128.9 (**C**$_{29'}$, **C**$_{31'}$), 128.3 (**C**$_{4'}$), 128.1 (**C**$_{21}$), 127.88, 127.86, 126.13 (**C**$_{4}$), 126.1 (**C**$_{5'}$), 125.8 (**C**$_{5}$), 125.6 (**C**$_{30'}$), 125.2 (**C**$_{28'}$, **C**$_{32'}$), 120.5 (**C**$_{6'}$), 119.1 (**C**$_{6}$), 109.9 (**C**$_{8}$), 109.8 (**C**$_{8'}$), 109.1 (**C**$_{26'}$), 81.1 (**C**$_{2'}$), 78.7 (**C**$_{2}$), 63.5 (**C**$_{15'}$), 63.2 (**C**$_{15}$), 59.2 (**C**$_{3}$), 58.65 (**C**$_{3'}$), 58.62 (**C**$_{11'}$), 58.5 (**C**$_{11}$), 37.9 (**C**$_{12'}$), 36.8 (**C**$_{17'}$), 36.40 (**C**$_{17}$), 36.37 (**C**$_{12}$), 33.2 (**C**$_{24'}$), 32.7 (**C**$_{24}$).
FTIR (thin film) cm^{-1}:	3355 (br-w), 1659 (s), 1594 (m), 1484 (m), 1453 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{50}H_{47}N_6O_4$ $[M+H]^+$: 795.3653 found: 795.3655
$[\alpha]_D^{22}$:	–131.5 (c = 0.36, $CHCl_3$)[15]
M.p. (CH_2Cl_2):	193–197 °C (dec)
TLC (10% Et_3N, 45% hexanes, 45% CH_2Cl_2), R*f*:	0.33 (UV, CAM)

Comparison of our data for (–)-1'-(2-Phenylethylene)-ditryptophenaline (3) with literature:

Assignment	Barrow's Report[15] (–)-1'-(2-phenylethylene)-ditryptophenaline (**3**) ^{1}H NMR, 500 MHz, $CDCl_3$	This Work[17] (–)-1'-(2-phenylethylene)-ditryptophenaline (**3**) ^{1}H NMR, 500 MHz, $CDCl_3$, 20 °C
N1	4.78 (s)	4.75 (br s)
C2	4.91 (s)	4.89 (s)
C3		
C4		
C5	6.94 (d, J = 7.5 Hz)	6.95 (d, J = 7.5 Hz)
C6	6.66 (t, J = 7.4 Hz)	6.68 (td, J = 7.5, 1.0 Hz)
C7	7.03 (t, J = 7.6 Hz)	7.06 (t, J = 7.5 Hz)
C8	6.50 (d, J = 7.7 Hz)	6.52 (d, J = 8.0 Hz)
C9		
C11	3.73 (m)	3.75 (dd, J = 11.5, 4.0 Hz)
C12	2.23 (dd, J = 12.3, 5.0 Hz) 1.54 (t, J = 12.0 Hz)	2.23 (dd, J = 12.5, 5.0 Hz) 1.53 (t, J = 12.0 Hz)
C13		
C15	4.22 (t, J = 3.4 Hz)	4.24 (m)
C16		
C17	3.53 (dd, J = 15.0, 3.1 Hz) 3.24 (m)	3.53 (dd, J = 14.5, 3.5 Hz) 3.25 (app td, J = 14.3, 4.5 Hz)
C18		
C19, C23	7.08 (d, J = 7.4 Hz)	7.10 (d, J = 7.5 Hz)
C20, C22	7.28 (t, J = 7.5 Hz)	7.30 (t, J = 7.8 Hz)
C21	7.15 (t, J = 7.5 Hz)	7.15–7.18 (m)
C24	2.98 (s)	3.00 (s)

[17] Data for this report were obtained with the solvent referenced at 7.27 ppm. See the *Instrumentation* section on page S1.

Comparison of our data for (–)-1'-(2-Phenylethylene)-ditryptophenaline (3) with literature continued:

Assignment	Barrow's Report[15] (–)-1'-(2-phenylethylene)-ditryptophenaline (**3**) ^{1}H NMR, 500 MHz, $CDCl_3$	This Work[17] (–)-1'-(2-phenylethylene)-ditryptophenaline (**3**) ^{1}H NMR, 500 MHz, $CDCl_3$, 20 °C
C2'	5.46 (s)	5.52 (s)
C3'		
C4'		
C5'	7.04 (d, J = 7.5 Hz)	7.06 (d, J = 7.5 Hz)
C6'	6.78 (t, J = 7.5 Hz)	6.80 (td, J = 7.5, 0.5 Hz)
C7'	7.13 (t, J = 7.6 Hz)	7.15–7.18 (m)
C8'	6.92 (d, J = 7.7 Hz)	6.95 (d, J = 7.5 Hz)
C9'		
C11'	3.72 (m)	3.72 (dd, J = 11.5, 4.5 Hz)
C12'	2.13 (dd, J = 12.1, 4.6 Hz) 1.48 (t, J = 12.1 Hz)	2.13 (dd, J = 12.0, 5.0 Hz) 1.49 (t, J = 12.0 Hz)
C13'		
C15'	4.37 (t, J = 3.5 Hz)	4.40 (app t, J = 3.5 Hz)
C16'		
C17'	3.54 (dd, J = 15.1, 3.2 Hz) 3.24 (m)	3.58 (dd, J = 14.3, 3.8 Hz) 3.25 (app td, J = 14.3, 4.5 Hz)
C18'		
C19', C23'	7.18 (d, J = 7.5 Hz)	7.20 (dd, J = 8.0, 1.0 Hz)
C20', C22'	7.51 (t, J = 7.6 Hz)	7.54 (t, J = 7.5 Hz)
C21'	7.36 (t, J = 7.6 Hz)	7.39 (t, J = 7.5 Hz)
C24'	3.02 (s)	3.04 (s)
C25'	7.32 (d, J = 14.6 Hz)	7.36 (d, J = 14.5 Hz)
C26'	6.56 (d, J = 14.6 Hz)	6.56 (d, J = 14.5 Hz)
C27'		
C28', C32'	7.40 (d, J = 7.5 Hz)	7.43 (d, J = 7.0 Hz)
C29', C31'	7.33 (t, J = 7.5 Hz)	7.36 (t, J = 7.3 Hz)
C30'	7.28 (m)	7.15–7.18 (m)

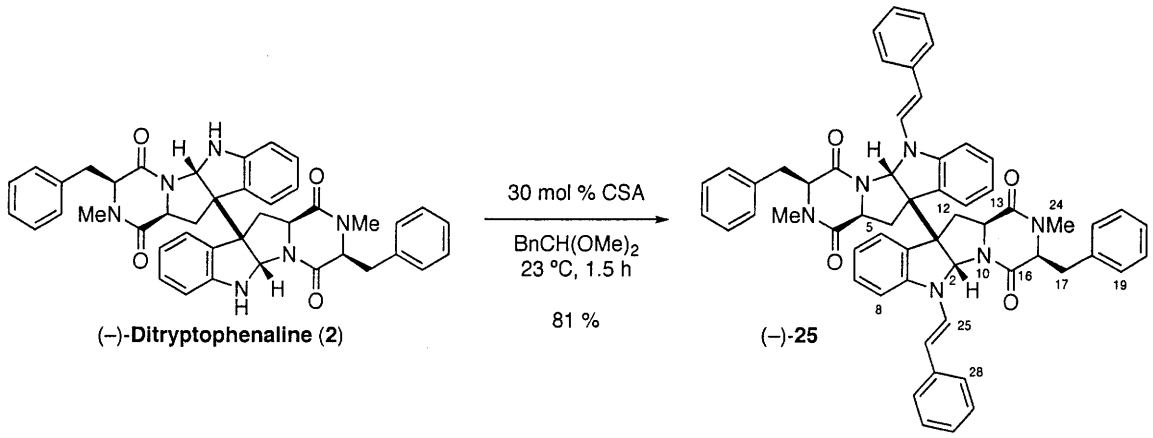
Comparison of our data for (–)-1'-(2-Phenylethylene)-ditryptophenaline (3) with literature continued:

Assignment	Barrow's Report[15] (–)-1'-(2-phenylethylene)-ditryptophenaline (**3**) ^{13}C NMR, $CDCl_3$	This Work[18] (–)-1'-(2-phenylethylene)-ditryptophenaline (**3**) ^{13}C NMR, 125.8 MHz, $CDCl_3$, 20 °C
C2	78.47	78.7
C3	59.06	59.2
C4	125.94	126.13
C5	125.48	125.8
C6	118.83	119.1
C7	129.81	130.06 or 130.04
C8	109.61	109.9
C9	149.96	150.2
C11	58.26	58.5
C12	36.16	36.37
C13	165.30	165.5
C15	63.01	63.2
C16	164.24	164.4
C17	36.25	36.40
C18	134.56	134.7
C19, C23	129.12	129.3
C20, C22	128.91	129.1
C21	127.81	128.1
C24	32.28	32.7

[18] Data for this report were obtained with the solvent referenced at 77.23 ppm. See the *Instrumentation* section on page S1.

Comparison of our data for (–)-1'-(2-Phenylethylene)-ditryptophenaline (3) with literature continued:

Assignment	Barrow's Report[15] (–)-1'-(2-phenylethylene)-ditryptophenaline (3) ^{13}C NMR, $CDCl_3$	This Work[18] (–)-1'-(2-phenylethylene)-ditryptophenaline (3) ^{13}C NMR, 125.8 MHz, $CDCl_3$, 20 °C
C2'	80.92	81.1
C3'	58.48	58.65
C4'	128.13	128.3
C5'	125.80	126.1
C6'	120.26	120.5
C7'	129.81	130.06 or 130.04
C8'	109.53	109.8
C9'	146.48	146.7
C11'	58.42	58.62
C12'	37.79	37.9
C13'	164.77	165.0
C15'	63.23	63.5
C16'	163.49	163.7
C17'	36.62	36.8
C18'	134.97	135.1
C19', C23'	129.53	129.8
C20', C22'	129.45	129.7
C21'	127.62	127.88 or 127.86
C24'	32.91	33.2
C25'	127.62	127.88 or 127.86
C26'	108.94	109.1
C27'	138.04	138.2
C28', C32'	125.02	125.2
C29', C31'	128.62	128.9
C30'	125.39	125.6



(–)-Bisstyrenylditryptophenaline (25):

To a solution of (–)-ditryptophenaline (**2**, 95.4 mg, 0.138 mmol, 1 equiv) in neat phenylacetaldehyde dimethyl acetal (2.76 mL) was added (±)-10-camphorsulfonic acid (9.0 mg, 42 μmol, 0.30 equiv). The mixture was allowed to stir for 1.5 h and then purified directly by flash column chromatography on silica gel (eluent: 10% triethylamine in hexanes → 10% triethylamine, 40% ethyl acetate, 50% hexanes) to afford the desired product as a white powder (100.3 mg, 81%).

^{1}H NMR (500 MHz, C_6D_6, 20 °C): δ 7.64 (d, J = 7.5 Hz, 4H, C_{28}**H**, C_{32}**H**), 7.60 (d, J = 14.5 Hz, 2H, C_{25}**H**), 7.31 (t, J = 7.8 Hz, 4H, C_{29}**H**, C_{31}**H**), 7.28 (t, J = 7.8 Hz, 4H, C_{20}**H**, C_{22}**H**), 7.12-7.17 (m, 8H, C_{19}**H**, C_{21}**H**, C_{23}**H**, C_{30}**H**), 6.95 (d, J = 14.5 Hz, 2H, C_{26}**H**), 6.79 (app td, J = 7.8, 1.5 Hz, 2H, C_7**H**), 6.52 (d, J = 8.0 Hz, 2H, C_8**H**), 6.45-6.48 (m, 4H, C_5**H**, C_6**H**), 5.97 (s, 2H, C_2**H**), 3.48 (dd, J = 14.5, 3.0 Hz, 2H, C_{17}**H**), 3.44 (dd, J = 12.5, 5.0 Hz, 2H, C_{11}**H**), 3.42 (m, 2H, C_{15}**H**), 2.74 (dd, J = 14.5, 4.5 Hz, 2H, C_{17}**H**), 2.60 (s, 6H, C_{24}**H**), 2.48 (dd, J = 12.0, 5.0 Hz, 2H, C_{12}**H**), 1.50 (t, J = 12.0 Hz, 2H, C_{12}**H**).

^{13}C NMR (125.8 MHz, C_6D_6, 20 °C): δ 164.5 (**C**$_{13}$), 163.6 (**C**$_{16}$), 146.8 (**C**$_9$), 139.5 (**C**$_{27}$), 136.7 (**C**$_{18}$), 130.14 (**C**$_{19}$, **C**$_{23}$), 130.07 (**C**$_{21}$), 130.01 (**C**$_7$), 129.7 (**C**$_{25}$), 129.5 (**C**$_{20}$, **C**$_{22}$), 129.4 (**C**$_{29}$, **C**$_{31}$), 129.2 (**C**$_4$), 126.1 (**C**$_{30}$), 125.8 (**C**$_{28}$, **C**$_{32}$), 124.9 (**C**$_5$), 121.0 (**C**$_6$), 109.8 (**C**$_8$), 109.4 (**C**$_{26}$), 81.8 (**C**$_2$), 62.9 (**C**$_{15}$), 59.5 (**C**$_3$), 58.2 (**C**$_{11}$), 38.5 (**C**$_{12}$), 36.6 (**C**$_{17}$), 32.2 (**C**$_{24}$).

FTIR (thin film) cm^{-1}: 3028 (w), 1667 (s), 1594 (m), 1484 (m), 1144 (w).

HRMS (ESI) (*m/z*): calc'd for $C_{58}H_{53}N_6O_4$ $[M+H]^+$: 897.4123

found: 897.4128

$[\alpha]_D^{22}$: -199.6 ($c = 0.58$, CH_2Cl_2)

M.p. (C_6D_6): 161–164 °C (dec)

TLC (10% triethylamine, 40% ethyl acetate, 50% hexanes), R*f*: 0.38 (UV, CAM)

Chapter III

N-Heterocyclic Carbene–Alcohol Hydrogen Bonds. Studies and Application in the Amidation of Unactivated Esters

Introduction and Background

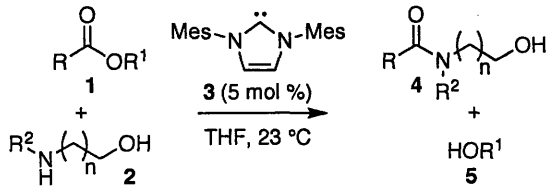
Synthesis of amides is important in many areas of chemistry, including peptide, polymer, and complex molecule synthesis.[1] Condensation products of optically active amino alcohols and carboxylic acids are of particular significance due to their impact in stereoselective synthesis.[2] Dehydration (and oxidation) of *N*-hydroxyalkyl amides affords valuable heterocycles that are present in many biologically active natural products.[3] Mild methods for the synthesis of amides rely on activation of carboxylic acid derivatives using stoichiometric quantities of condensation or activating reagents.[1] Direct coupling of amines and alcohols with unactivated carboxylic acid derivatives is of current interest.[4]

The discovery of stable nitrogen–heterocyclic carbenes (NHCs)[5] has had a large impact on the development of new methodologies for organic synthesis.[6] NHCs have served both as ligands in organometallic catalyst systems[7] and as organic catalysts.[8] Furthermore, fascinating reports regarding the use of NHCs as nucleophilic catalysts[9] for the polymerization of lactones and transesterification reactions have appeared.[10]

Results and Discussion

Catalytic Amidation

As part of a program directed at the discovery of new and efficient methods for target-oriented synthesis, we sought the development of a single-step and catalytic amidation of unactivated esters. In preliminary studies focused on carbene-catalyzed amidation of esters, we discovered that amino alcohols were particularly reactive (Scheme 1). A combination of superb

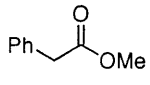
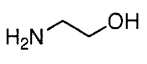
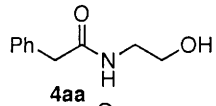
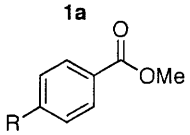
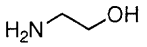
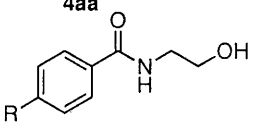
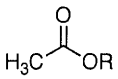
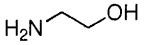
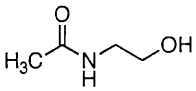
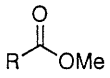
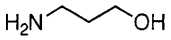
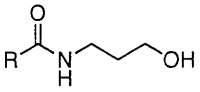
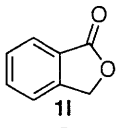
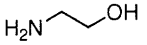
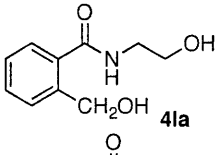
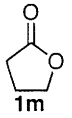
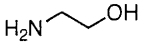
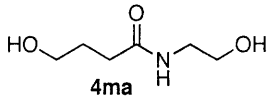
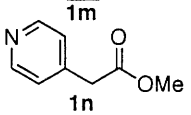
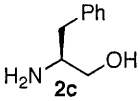
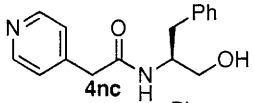
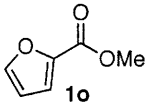
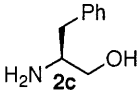
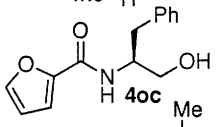
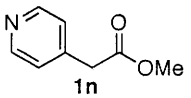
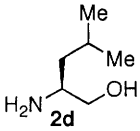
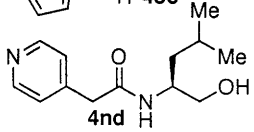


Scheme 1. Carbene-catalyzed amidation of esters with amino alcohols.

reactivity, ready availability, and ease of storage of *N*,*N*-bismesitylimidazolylidene[5b] (**3**, IMes) led to its selection as the catalyst for our amidation studies. Under optimal conditions (tetrahydrofuran, 1.0 M initial concentration of substrates, 23 °C), treatment of an equimolar

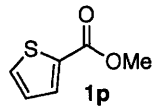
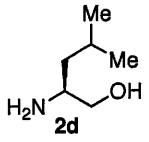
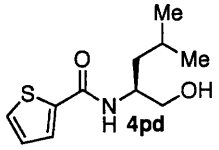
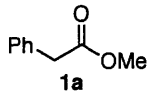
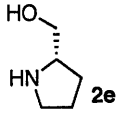
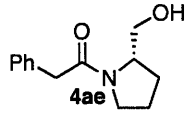
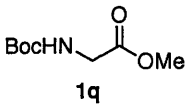
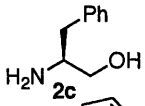
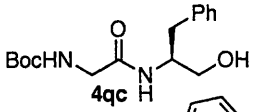
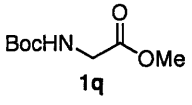
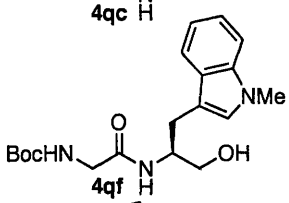
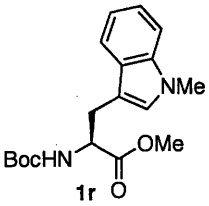
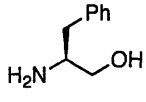
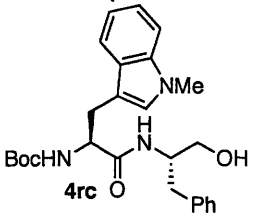
amount of an amino alcohol and an unactivated ester with IMes (**3**, 5 mol %) affords the corresponding amide in high yield (Table 1). Under standard conditions, the coupling of methyl

Table 1. Substrate scope for the amidation of esters by **3**.

Entry	Ester	Aminoalcohol	Amide	Yield (%)[a]
1	 **1a**	 **2a**	 **4aa**	100 (96)[c]
2	 **1b**, R = H	 **2a**	 **4ba**, R = H	75 (94)[b]
3	**1c**, R = COMe		**4ca**, R = COMe	87
4	**1d**, R = CN		**4da**, R = CN	96
5	**1e**, R = CF_3		**4ea**, R = CF_3	95
6	**1f**, R = F		**4fa**, R = F	88
7	**1g**, R = OMe		**4ga**, R = OMe	31 (69)[b]
				
8	**1h**, R = Me	**2a**	**4ha**	99
9	**1i**, R = Bn			95
10	**1j**, R = ^{i}Pr			34
11	**1k**, R = ^{t}Bu			0
				
12	**1a**, R = CH_2Ph	**2b**	**4ab**, R = CH_2Ph	99
13	**1b**, R = Ph		**4bb**, R = Ph	16 (96)[b]
14	 **1l**	 **2a**	 **4la**	66
15	 **1m**	 **2a**	 **4ma**	88
16	 **1n**	 **2c**	 **4nc**	86
17	 **1o**	 **2c**	 **4oc**	89
18	 **1n**	 **2d**	 **4nd**	84

[a] Reaction times 1.5–24 h; isolated yield after purification. [b] In situ generation of IMes (6.5 mol % IMes•HCl, 5.0 mol % ^{t}BuOK). [c]Anhydrous LiCl (5 mol %) used as an additive.

Table 1. Continued.

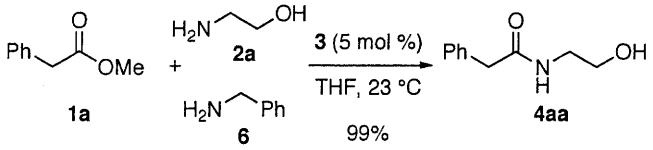
Entry	Ester	Aminoalcohol	Amide	Yield (%)[a]
19	 **1p**	 **2d**	 **4pd**	77
20	 **1a**	 **2e**	 **4ae**	99
21	 **1q**	 **2c**	 **4qc**	83
22	 **1q**	 **2f**	 **4qf**	88
23	 **1r**	 **2c**	 **4rc**	88[d]

[a] Reaction times 1.5–24 h; isolated yield after purification. [d] >94% de, >98% ee.

phenyl acetate (**1a**) and ethanolamine (**2a**) was complete in 8 h while the corresponding reaction with methyl benzoate (**1b**) gave the desired amide in 75% yield after 24 h (Table 1, entries 1 and 2 respectively).[11]

Both aromatic and aliphatic esters with a wide range of functional groups may be employed in this amidation reaction. The amidation reaction is sensitive to both electronic and steric factors (Table 1, entries 2–7 and 8–11, respectively).[12] The presence of heterocycles is tolerated both on the ester and the amino alcohol components (Table 1, entries 16–19 and 22–23, respectively). The IMes (**3**)-catalyzed condensation of optically active *N*-Boc-1-methyl-L-tryptophan methyl ester (**1r**) and L-phenylalaninol (**2c**) provided the corresponding amide **4rc** in good yield (Table 1, entry 23).[13] This catalytic amidation does not require use of excess coupling components, heat, vacuum, molecular sieves or activated esters for completion.[10] The high

reactivity of amino alcohols can be used to an advantage in their selective coupling with unactivated esters in the presence of amines (Scheme 2).

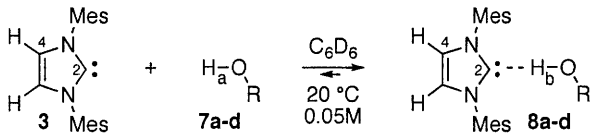


Scheme 2. Selective reaction of amino alcohols in the presence of amines.

Significantly, this amidation reaction proceeds with equal efficiency when a solution of catalyst, IMes (**3**), is prepared by the addition of potassium *t*butoxide (5 mol %) to a suspension of *N*,*N*-bisimidazolium chloride (6.5 mol %) in tetrahydrofuran (Table 1, entry 1).[10c,d] This method is particularly effective for use of NHCs that are more difficult to isolate.[14] Despite the clear practical advantage of using in situ-generated carbene samples, we have relied on recrystallized samples of IMes (**3**) in these preliminary studies to allow thorough mechanistic investigation.

These carbene catalysts have been previously proposed to act as nucleophilic catalysts in transesterification reactions (through activated C2-acylimidazolium intermediates).[10a–f,15] However, our observations regarding the surprising stability of carbene-alcohol complexes prompt consideration of an additional mode of catalysis for NHCs. Mixing an equimolar amount of IMes (**3**) and anhydrous methanol (**7b**) in C_6D_6 (0.05 M, 20 °C) leads to immediate formation of *N*,*N*-bismesitylimidazolylidene-methanol complex **8b** (Table 2, entry 2).[16] The hydroxyl

Table 2. Alcohol-carbene complexes **8a-d**[a]



Entry	R	δ H_a (ppm)[a]	δ H_b (ppm)[a]	Δ (ppm)
1	**a**, ^{t}Bu	0.67	2.81	2.14
2	**b**, Me	0.05	4.37	4.32
3	**c**, $CH_2CH_2NH_2$	~0.70	5.24	~4.5
4	**d**, Bn	0.89	~6.0	~5.1

[a] ^{1}H NMR (500 MHz) data were separately recorded for the alcohols and the IMes-alcohol complexes in C_6D_6 (0.05 M) at 20 °C.

proton of complex **8b** displays a significant downfield shift in the ^{1}H NMR spectrum (Table 2, entry 2).[17] Significantly, the C2 resonance of complex **8b** at 209.7 ppm is upfield by 9.7 ppm compared to the C2 resonance of carbene **3**.[18] We have also prepared the hexadeuterated variant of this complex, IMes-d_2–methanol-d_4 (**8b**-d_6),[14] that displays a C4 resonance (δ 121.1, triplet, J^1_{CD} = 27.0 Hz) and a C2 resonance (δ 203.9, singlet) in C_6D_6, most consistent with an imidazolylidene-d_2 fragment rather than an imidazolium-d_3 substructure.[19] The hydroxyl proton of other alcohols including ^{t}butanol, ethanolamine, and benzyl alcohol, display a similar downfield shift upon complex formation with IMes (**3**) (Table 2). Samples containing unequal ratios of IMes to alcohol(s) exhibit averaged resonances suggesting dynamic systems with exchange rates faster than the NMR time scale. Benzylamine does not show a significant interaction with IMes (**3**), while mixing benzyl mercaptan with **3** leads to rapid precipitation of imidazolium thiolate salts under the conditions described in Table 2. These observations are consistent with the expected basicity of imidazolylidenes (pKa (DMSO) I^{t}BuHCl = 22.7).[20c]

The IMes-methanol complex **8b** represents the first X-ray structure of a carbene-alcohol hydrogen-bonded complex (Figure 1).[21] The distance between the carbene C2 and the oxygen (C-

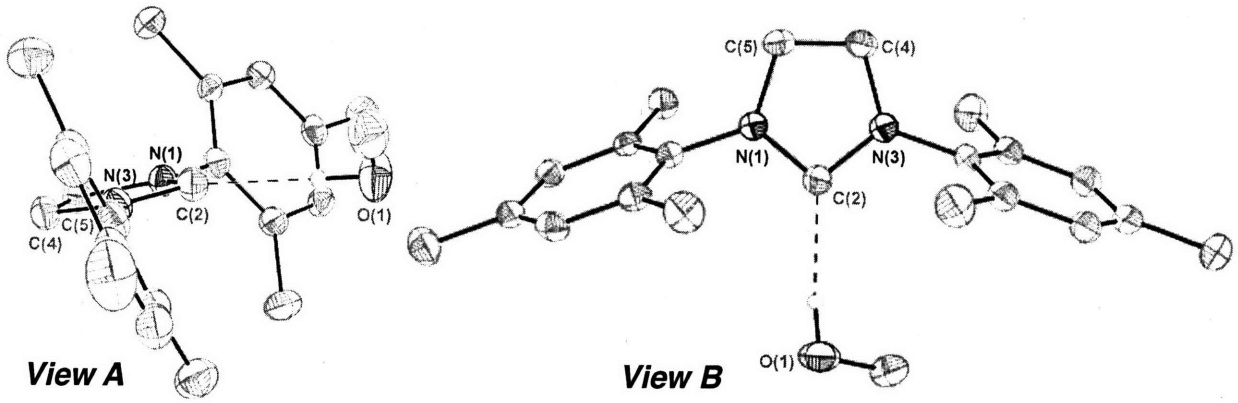
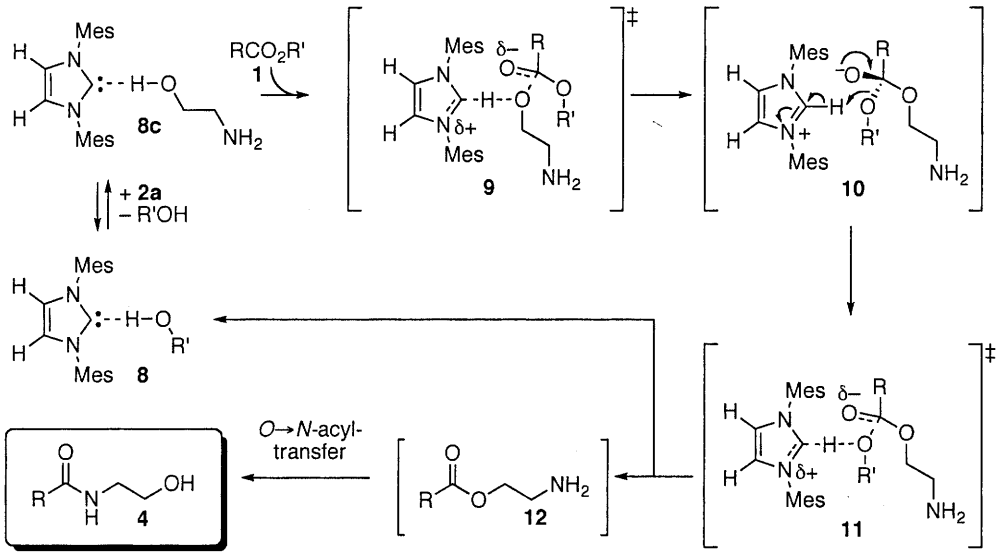


Figure 1. Thermal ellipsoid representation of complex **8b**.

-H–O) is only 2.832(2) Å. The oxygen atom resides only 0.04 Å above the plane defined by the imidazolylidene ring, thus allowing a nearly linear (174°) hydrogen bond interaction. Significantly, the N–C–N bond angle of 102.5° found in complex **8b** is much closer to the same bond angle of 101.4° present in the parent IMes (**3**)[5b] as compared to the bond angle of 108.6° found in the corresponding bismesitylimidazolium chloride.[20a] This carbene-alcohol interaction merits further consideration alongside previously reported modes of reactivity and catalysis for NHCs.

We propose a carbon-centered Brønsted base[20b] nucleophile activation for an initial transesterification followed by a rapid O→N acyl-transfer reaction (Scheme 3) to be operational in our chemistry. Monitoring the IMes-catalyzed coupling of γ-lactone **1m** (Table 1, entry 15, C=O, 1779 cm^{-1}) with ethanolamine (**2a**) by React-IR proceeded to give amide **4ma** (Table 1, entry 15, C=O, 1648 cm^{-1}), while a weak absorbance for a fleeting *O*-(acyl)ethanolamine **12ma** (Scheme 1, **12** R = $(CH_2)_3OH$, C=O, 1736 cm^{-1}) was observed during the reaction.[14] Additionally, monitoring the IMes-catalyzed amidation of methyl benzoate (**1b**) with ethanolamine (**2a**), in THF-d_8 by ^1H NMR spectroscopy clearly demonstrated the intermediacy of *O*-(benzoyl)-ethanolamine **12ba** (Scheme 3, **12** R = Ph).[14,22] Furthermore, the addition of an authentic sample of ester **12ba** (0.12 equiv) to an amidation reaction of methyl benzoate (**1b**) with ethanolamine (**2a**), in progress (at 2h, 41% conversion) under optimal reaction conditions

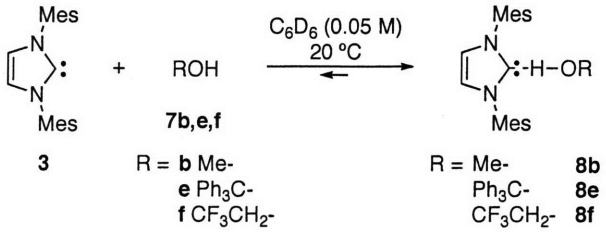


Scheme 3. Proposed reaction mechanism.

led to rapid O→N acyl-transfer within minutes, providing amide **4ba** (Table 1, entry 2) in 90% yield upon completion of the experiment (8 h).[14] The poor reactivity of 6-aminohexan-1-ol, 2-hydroxymethylaniline, and (2*S*,3*S*)-pseudoephedrine in coupling with methyl phenylacetate (**1a**) under our standard conditions may be due to a slow O→N acyl-transfer[23] and/or an unfavorable initial transesterification reaction[10f] in the latter case.[24]

Further Investigations of Carbene–Alcohol Hydrogen–Bonded Complexes

Having identified a carbene-alcohol hydrogen bonded complex, we sought to investigate the steric and electronic effects of the alcohol on the nature of the complex (Scheme 4). For comparison to the IMes-HOMe complex **8b** we examined a bulky alcohol, triphenylmethanol (**7e**) and a more acidic alcohol, 2,2,2-trifluoromethanol (TFE, **7f**).



Scheme 4. Hydrogen-bond interaction between IMes and alcohols. Mes = 2,4,6-trimethylphenyl.

It is interesting to compare the X-ray structure of IMes-HOMe with the more labile X-ray structure of IMes-HOCPh$_3$ (Figure 2).[25] The solid-state structure of complex **8e** revealed a distorted hydrogen-bond between the hydroxyl proton and the carbene. Hydrogen bond formation is expected to relax the N1-C2-N3 bond angle of the carbene toward an

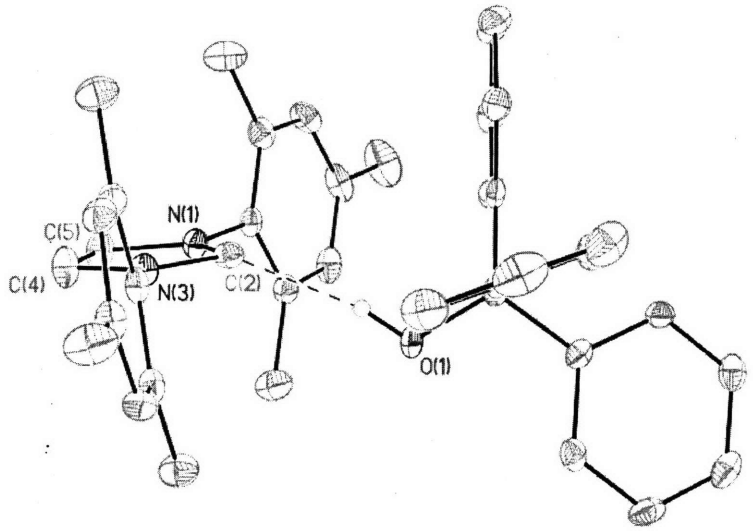


Figure 2. Thermal ellipsoid representation of complex **8e**.

imidazolium ion. It could then be reasoned that the degree of proton transfer (i.e., strength of the hydrogen bond) would be reflected in the N1-C2-N3 bond angle of the carbene. The N1-C2-N3

bond angle of the carbene moiety in **8e** is 101.9(2)°, which is closer to the observed angle in the free carbene (101.4°)[5b] than the imidazolium chloride (108.6°).[20a] This angle is however smaller than that of the methanol complex **8b** at 102.53(16)°. Interestingly, in the triphenylmethanol complex **8e** the hydrogen atom is 0.84(3) Angstrom below the imidazolinyl azaheterocycle plane, a non-optimal orientation for hydrogen-bond interaction with the carbene lone pair (Figure 2, ~26° from planarity).[21] The length of the hydrogen-bond interaction in IMes–triphenylmethanol complex (**8e**) was found to be 2.856(3) Å that is slightly longer than the corresponding hydrogen-bond interaction (2.832(2) Å) in the methanol complex **8b** by 0.02 Å.

We also studied the formation of a complex between IMes (**3**) and TFE (**7f**) to examine electronic effects on such carbene alcohol complexes. This alcohol was expected to be a better proton donor due to the increased acidity of TFE (pKa (DMSO) TFE = 23.5, pKa (DMSO) MeOH = 29.0)[26] compared to other alcohols we had examined. We obtained high quality crystals from toluene solutions containing equal molar ratio of IMes (**3**) and TFE (**7f**). Indeed, the X-ray structure of these crystals clearly illustrated a complete proton transfer to afford an imidazolium ion derivative (Figure 3). Interestingly, rather than a 2,2,2-trifluoroethoxide counter ion another molecule of **3** was bound to the C2-proton of the imidazolium ion. The 2,2,2-trifluoroethoxide was stabilized by a hydrogen-bond interaction with a TFE molecule (Figure 3). Analysis of the structure suggests a hydrogen-bond interaction between the 2,2,2-trifluoroethoxide with the C4-proton of the imidazolinyl fragment while TFE is engaged in a hydrogen-bond interaction with the C4-proton of the imidazolium ion in the crystal structure.

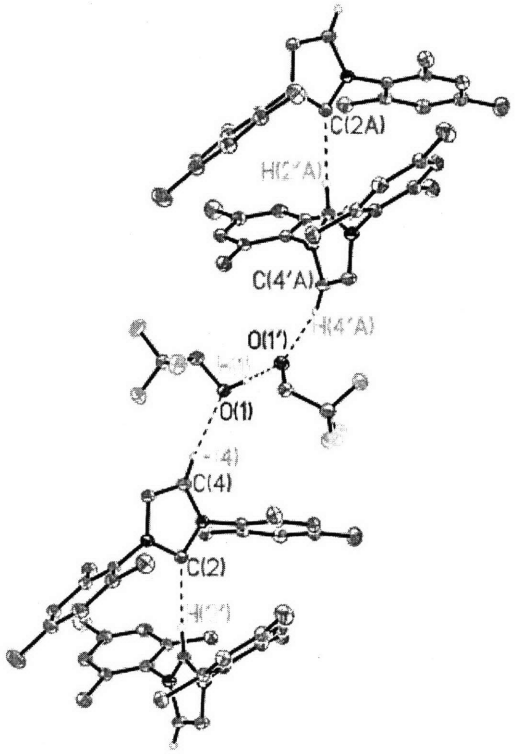
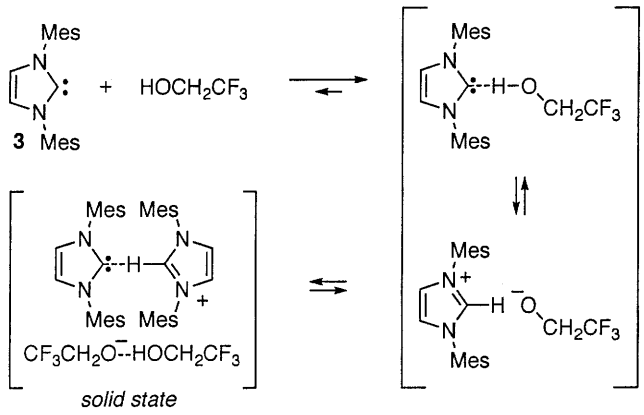


Figure 3. Thermal ellipsoid representation of the crystal obtained from IMes (**3**) and TFE (**7f**). Atoms labeled with an A after the atom name are generated from the parent atom by the symmetry operator $x+1, y, z$.

A carbene–imidazolium interaction was also observed in the solid state by Arduengo[20a] when a 1:1 mixture of **3** and **3•HPF$_6$** (or **3** and **3•HOTf**) were allowed to crystallize. Interestingly, in these structures the C2-carbon of the two heterocycles exhibited an averaged ^{13}C NMR resonance at 175 ppm, midway between the resonances expected for a carbene and an imidazolium ion.[20a] Interestingly, in our studies of the IMes-TFE (1:1) solution in benzene (0.5 M in C_6D_6 at 20 °C) we observe a downfield ^{13}C NMR resonance for the C2-carbon at 194.7 ppm which is closer to the free carbene (219.4 ppm 0.5 M in C_6D_6 at 20 °C). Additionally, all other carbon resonances save those related to the methyl groups appear as two unequal resonances. These appear as a broad minor resonance blending into a sharp major resonance in the ^{13}C NMR spectra. Using variable temperature NMR we observed that at 70 °C in C_6D_6 (0.5 M), all signals appear to sharpen, however not all pair of carbon resonances coalesce.[27] Importantly, upon cooling the sample from 70 °C (after extended heating, >12 h) to 20 °C there was no decomposition, providing spectra identical to those obtained prior to heating. Interestingly, we also examined the ^{1}H NMR of the IMes–TFE (1:1) solution in benzene and observed a

significant dependence as a function of TFE equivalents (from 1.0 to 5.0 equiv).[28] Cumulatively, our observations suggest a dynamic equilibrium in the solution involving multiple species only one of which is seen in the crystal structure shown in Figure 3 (Scheme 5).



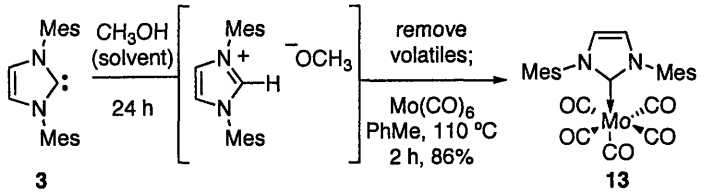
Scheme 5. Dynamic interaction of IMes **3** with TFE (**7f**).

The observation with TFE described above and the effect of solvation paralleled those of IMes (**3**) in protic solvents. Dissolution of IMes (**3**) in MeOD-d_4 led to deuterium incorporation at C4/5 of the azaheterocycle (96.5% at 0.5 M in MeOD-d_4 at 20 °C).[29] A residual protium resonance at 8.13 ppm is similar to the C2-imidazolium chloride signal for the C2-H (8.10 ppm). The ^{13}C NMR resonances corresponding to the C4/5 in methanolic solution of IMes were found at 126 ppm as a triplet (J_{CD} = 32 Hz), similar to the imidazolium chloride salt (126 ppm). The resonance corresponding to the C2 in this methanolic solution of IMes was at 139.9 ppm as a broad singlet[30] and not in the region observed for IMes–HOMe (1:1) in aprotic solvent (i.e., ~200 ppm). These results indicate that dissolution of IMes in methanol provides a solvated imidazolium methoxide in contrast to the hydrogen-bonded complex seen in aprotic solvents.

Given the stability of imidazolium salts we sought to investigate the chemistry of IMes dissolved in MeOD-d_4. A solution of IMes in methanol (0.05 M) persisted unchanged for six weeks at –10 °C under an argon atmosphere by NMR. A methanolic solution of IMes (as the solvated imidazolium methoxide) is also more resistant to hydrolytic decomposition. Addition of deionized and degassed water (1.0 equiv) to a solution of IMes in MeOD-d_4 (0.05 M, 20 °C) did not lead to decomposition over 24 h. Notably, rapid decomposition (<5 min) was observed when deionized and degassed water (1.0 equiv) was added to a solution of IMes in C_6D_6 (0.05 M,

20 °C). The solvated imidazolium methoxide mentioned above is resistant to hydrolytic decomposition even upon addition of large excess of water (30.0 equiv) over 1 week.[31]

The protium/deuterium exchange at C4/5-carbons of the solvated imidazolium methoxide samples described above hinted at a reversible access to the free carbene. This is due to the observation that while such protium/deuterium exchange is very rapid in the case of the carbene structure, it is significantly slower in methanolic solution of imidazolium chloride. Indeed, the IMesNHC•MeOH complex **8b** was accessible after removal of the excess methanol and was used in complex formation with $Mo(CO)_6$ to give IMesNHC•$Mo(CO)_5$ **13** in 86% yield (Scheme 6).[32] These observations suggest an alternative means for the storage of carbenes alongside the formation of BEt_3 adducts[32] and Ag-complexes.[33]



Scheme 6. Synthesis of complex **13** from methanolic IMes (**3**).

The strength and nature of the hydrogen-bond interaction between IMes (as a representative NHC) and alcohols is greatly sensitive to the solvent and the particular alcohol. The more sterically congested the alcohol, the weaker the interaction with the carbene. A more acidic alcohol leads to greater involvement of imidazolium alkoxides in equilibrium with other hydrogen-bond complexes. Dissolution of IMes in methanol leads to formation of a solvated imidazolium methoxide. Evaporation of the volatiles and desolvation of robust imidazolium alkoxide solutions returns the carbene–alcohol (1:1) complex that may be used in organometallic complex formation or used directly in transformations employing them as catalysts.

Synthesis of Optically Active Imidazopyridium Salts

With a broader appreciation of the dynamic interplay between alcohols and NHCs, we considered the possibility of rendering certain reactions enantioselective by utilizing chiral carbene complexes. Chiral carbene complexes are indeed known, and a variety of them have

been successfully used as ligands for organometallic systems or in the free state as organic catalysts (Figure 4).[34]

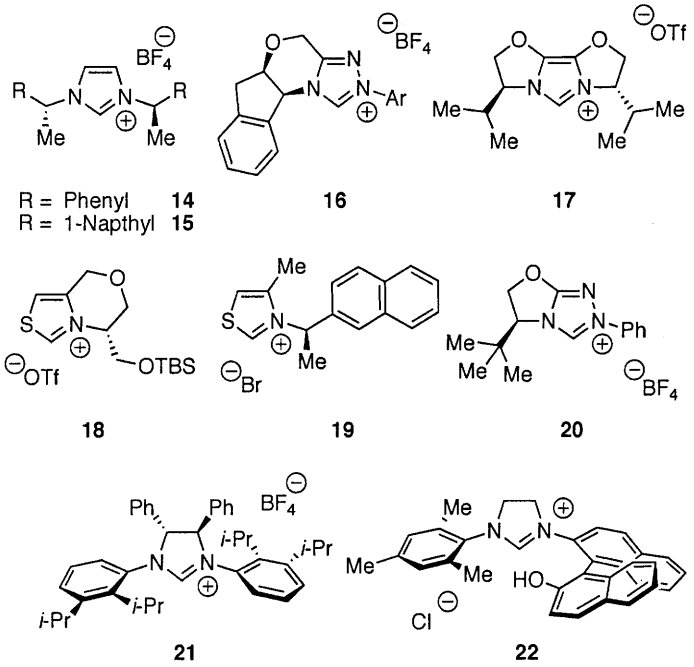


Figure 4. A representative collection of chiral azolium salts.

Subtle electronic and steric effects can often play a dramatic role in the yield and/or enantioselectivity of a NHC reaction. Therefore it is of great interest to have ready access to a wide variety of different NHC's. Recently NHC's based on the imidazo-[1,5-a]-pyridinium ring system **23** were reported by Lassaletta[35] and Glorius[36], and the use of salt **24** as a highly reactive umpolung catalyst was nicely demonstrated by Miyashita (Figure 5).[37] We were drawn to this particular ring system because of the flexibility the pyridinium ring allows for fine-tuning of the electronic and steric properties of the resulting carbenes.

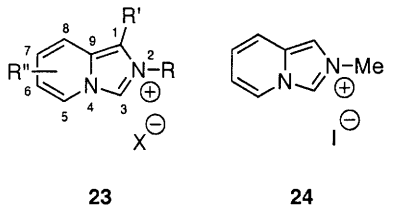
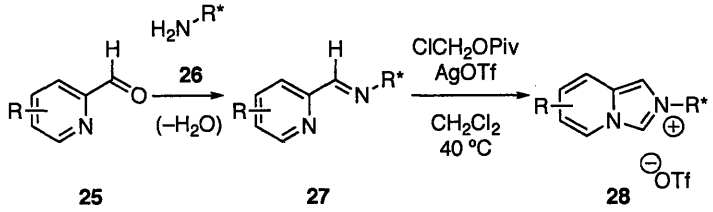


Figure 5. Imidazo-[1,5-a]-pyridinium salts.

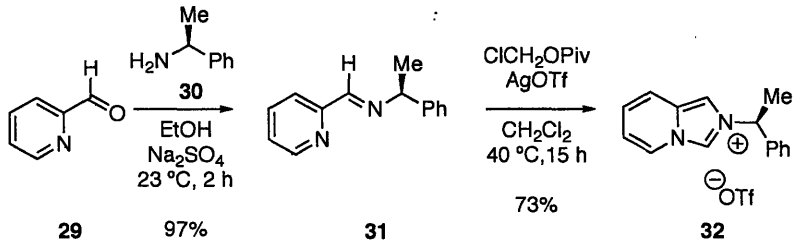
A variety of transformations catalyzed by NHC's have been developed.[8] Many of these methodologies employ an in-situ deprotonation strategy for the generation of the reactive NHC's from chemically robust azolium salt dervatives. Enders[34c] and Rovis[34g] have employed chiral triazolium salt precatalysts **20** and **16** very elegantly in a variety of catalytic asymmetric reactions. Similarly, optically active imidazolium salts **22** and **21** have found applications as precatalysts by Hoveyda[34d] and Grubbs[34i] as precursors to ligands used in organometallic chemistry.

We envisioned a highly convergent and rapid synthesis of chiral salts by the condensation of a chiral primary amine **26** with a suitable pyridine derivative **25** to yield the C2-iminopyridine **27** followed by derivatization to the target triflate salts **28** (Scheme 7).[36,38]



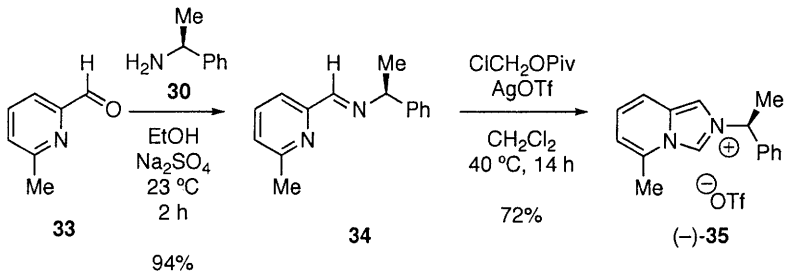
Scheme 7. Synthetic plan for the formation of optically active triflate salts **28**.

Condensation of commercially available 2-formylpyridine (**29**) with *S*-α-methylbenzylamine (98% ee) (**30**) yielded imine **31** in 97% yield. We found that the crude imine was sufficiently pure to be used without purification in the next step. Exposure of the imine **31** to $ClCH_2OPiv$ and anhydrous silver triflate in dichloromethane at 40 °C for 15 h in the dark yielded the triflate **32** in 73% yield. It should be noted that the imidazo-[1,5-a]-pyridinium salts are readily purified by flash column chromatography (Scheme 8).



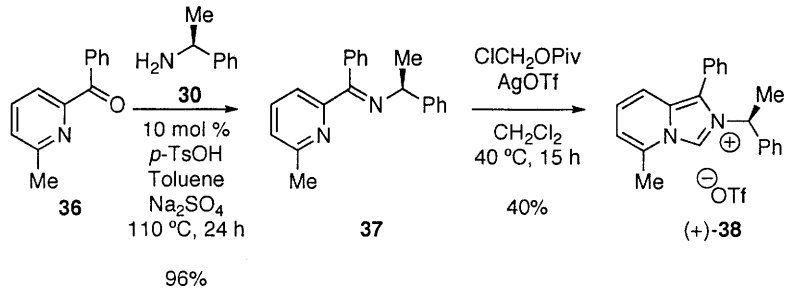
Scheme 8. Synthesis of azolium salt **32**.

The synthesis of chiral salts with substitution around the imidazo-[1,5-a]-pyridinium skeleton were accomplished under identical reaction conditions. We chose to derivatize the C5 position since it was shown to greatly enhance the stability of the resulting carbenes towards decomposition.[35] 2-Formyl-6-methylpyridine (**33**), obtained from commercially available 2,6-dibromopyridine in two steps, was readily condensed with amine **30** to afford imine **34**. Crude **34** was cyclized to give triflate (–)-**35** in 72% yield (Scheme 9). Deprotonation of (–)-**35** (1.0 equiv NaH, 4 mol % KO^{t}Bu, 0.2 M THF, 23 °C, 3 h) afforded the carbene as a thick syrup, with characteristic ^{1}H NMR resonances[39] consistent with those reported by Lassaletta for a related optically inactive derivative.[35]



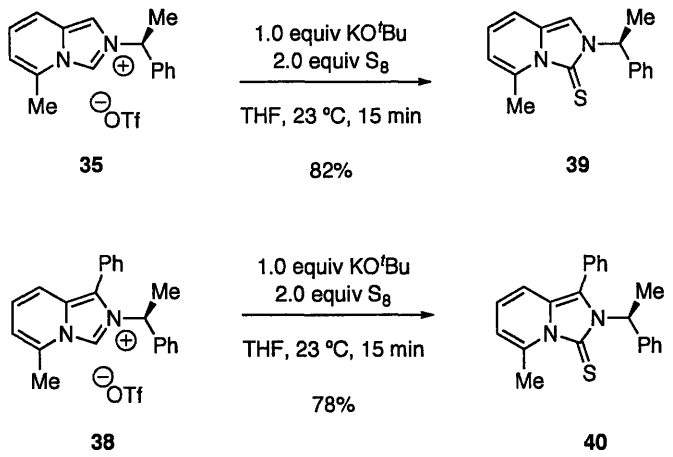
Scheme 9. Synthesis of azolium salt **35**.

In an effort to minimize rotation of the N-C bond bearing the stereogenic center, thus "locking" the chiral arm into a secure configuration, we introduced a phenyl substituent at the C1 position. The bisaryl ketone **36** was prepared from 2,6-dibromopyridine in two steps and condensed with amine **30** in 96% yield. Due to the lowered reactivity of **36**, much more vigorous conditions as compared to **33** were needed to complete the imine formation. Imine **37** was a mixture (47:53) of isomers and was cyclized to give the imidazolium triflate (+)-**38** in 40% yield under the conditions described above (Scheme 10).



Scheme 10. Synthesis of azolium salt **38**.

Direct e.e. determinations of the imidazolium triflates could not be performed by HPLC (normal or reverse phase) analysis. Deprotonation of the triflate salts **35** and **38** with KO^{t}Bu (1.0 equiv) in the presence of elemental sulfur (2.0 equiv) in THF afforded the corresponding thioureas **39** and **40** in 82% and 78% yields respectively. Thiourea derivatives[40] **39** and **40** were both found to be >98% e.e. by HPLC analysis, thus illustrating that 1) the synthetic route maintains optical activity throughout, and 2) the free carbenes generated by the deprotonation of these salts are not epimerized (Scheme 11).



Scheme 11. Synthesis of thiourea derivatives **39** and **40** for e.e. determination.

In conclusion, we have expanded the library of chiral imidazolium salts to include those with the imidazo-[1,5-a]-pyridinium skeleton. We have encountered no obstacles with reaction scale; imidazolium salt **35** was prepared in >4 g without any complications. This route maintains stereochemical integrity throughout the synthesis of the azolium salts and further to the carbenes.

Conclusion

Our initial attempts at expanding the NHC catalyzed transesterification to amidation led to the discovery of a facile amidation reaction with 1,2- and 1,3-amino alcohols. We have shown that with this method, esters are easily converted to ω-hydroxy amides with a broad tolerance of functional groups (Table 1). During the course of our studies, we identified a strong carbene-alcohol hydrogen bond, which prompted an investigation into the mechanism of this reaction. Having investigated this reaction by ^{1}H NMR, React-IR, and through X-ray crystallography, we

propose a nucleophile activation mechanism, allowing for a facile transesterification, followed by an O→N acyl-transfer reaction forming the product amides (Scheme 1). Further studies on this unprecedented carbene-alcohol hydrogen bond by both ^{1}H NMR and X-ray crystallography, revealed that sterically encumbered alcohols such as triphenylmethanol (**7e**) form weaker hydrogen bonds with IMes (**3**) due to the inability of this alcohol to achieve an optimal hydrogen bond geometry with **3**. Reaction of **3** with acidic alcohols such as TFE (**7f**) leads to a dynamic system involving multiply equilibrating species in the solution state, and a carbene-imidazolium hydrogen bonded complex **8f** in the solid state (Scheme 3 and Figure 5). Interestingly, dissolving **3** in neat methanol affords a solvated imidazolium methoxide with greatly enhanced stability relative to parent **3**, which may be utilized for extended storage of NHCs.

Lastly, a rapid and practical synthesis of chiral imidazo-[1,5-a]-pyridinium salts was developed. The present approach affords optically active azolium salts which, lead to optically active carbenes without erosion of optical activity. This protocol is amenable to the large-scale synthesis of these salts without loss of efficiency.

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[11] (a) In the absence of **3**, incubation of equimolar mounts of esters **1a** and **1b** with **2a** at 23 °C provides less than 2 and 1%, respectively, of the corresponding amides in 12 h. (b) The use of sodium methoxide or potassium *tert*-butoxide in place of IMes (**3**) in the coupling of **1a** and **2a** gave 60 and 74% yield of **4aa**, respectively. See experimental section.

[12] Introduction of anhydrous lithium chloride (5 mol %) to the reaction mixture increases the rate of this coupling (Table 1, entries 2, 7, and 13).

[13] *N*-Fmoc-protected glycine methyl ester was found to undergo deprotection in the presence of either **3** or **2a**.

[14] See experimental section for details.

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[16] Similar results were found in THF-d_8.

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[18] For reference, the C2 and C4 resonances of carbene **3** (C_6D_6 , 20 °C) are found at 219.4 and 120.9 ppm, respectively.

[19] (a) While the C2 resonance of imidazolium salts are typically >60 ppm upfield relative to the corresponding carbene C2 resonance, the reversible formation of an undetectable concentration of imidazolium alkoxide cannot be ruled out. (b) In THF-d_8, the C2 and C4 resonances of carbene **3** and the complex **8b**-d_6 are found at 219.9 and 121.6 and at 212.4 and 121.6 (t, J^1_{CD} = 29.4 Hz) ppm, respectively.

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[25] The crystal structure described in Figures 4 and 5 have been deposited at the Cambridge Crystallographic Data Center, please see: CCDC# 626849 and 626850.

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[27] A low temperature experiment was attempted in PhMe-d_8 in an effort to look for two distinct sets of resonances; however, precipitation resulted during sample cooling due to diminished solubility of the solutes.

[28] The proton originating from TFE shifts upfield from 10.75 ppm at 20 °C to 9.85 ppm at 70 °C. Imidazolium cations with coordination anions such as chloride have C2 resonances at 11.1 ppm, while those with non-coordinating anions such as tetrafluoroborate resonate at 8.6 ppm; see: Grasa, G. A.; Singh, R.; Scott, N. M.; Stevens, E. D.; Nolan, S. P. *Chem. Commun.* **2004**, 2890.

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[30] The corresponding imidazolium chloride C2 is completely deuterated upon dissolution in MeOD-d_4 and the corresponding C2-carbon resonates as a triplet in the ^{13}C NMR spectrum at 139.7 ppm (J_{CD} = 34.0 Hz). The signal broadening and the absence of carbon-deuterium spin coupling suggest rapid equilibrium/D-exchange.

[31] Addition of water increases in the intensity of the residual protium resonance corresponding to C4/5 and ROH.

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[37] (a) Miyashita, A.; Suzuki, Y.; Okumra, Y.; Iwamoto, K-i.; Higashino, T. *Chem. Pharm. Bull.* **1996**, *46*, 6-11. (b) Miyashita, A.; Suzuki, Y.; Kobayashi, M.; Kuriyama N.; Higashino, T. *Heterocycles*, **1996**, *43*, 509-512.

[38] (a) Altenhoff, G.; Goddard, R.; Lehmann, C. W.; Glorius, F. *J. Am. Chem. Soc.* **2004**, *126*, 15195-15201. (b) Glorius, F.; Altenhoff, G; Goddard, R.; Lehmann, C. *Chem. Comm.* **2002**, 2704-2705.

[39] ^1H NMR (500 MHz, C_6D_6, 20 °C) δ 7.01–7.15 (m, 5H, Ph**H**), 6.84 (d, J = 9.0 Hz, 1H, C_8**H**), 6.76 (s, 1H, C_1**H**), 6.33 (dd, J = 9.3 Hz, 6.3 Hz, 1H, C_7**H**), 5.87 (d, J = 6.0 Hz, 1H, C_6**H**), 5.74 (q, J = 7.0 Hz, 1H, CH_3C**H**), 2.76 (s, 3H, Pyr-C**H**$_3$), 1.82 (d, J = 7.0 Hz, 3H, C**H**$_3$CH).

[40] A similar strategy was employed in: Seo, H.; Kim, B. Y.; Lee, J. H.; Park, H-j.; Son, S. U.; Chung, Y. K. *Organometallics*, **2003**, *22*, 4783-4791.

Experimental Section

General Procedures. All reactions were performed in oven-dried or flame-dried round bottomed flasks, modified Schlenk (Kjeldahl shape) flasks, or where indicated in modified Schlenk vessels designed for the probe of the React-IR[1] instrument. The flasks were fitted with rubber septa and reactions were conducted under a positive pressure of argon. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Flash column chromatography was performed as described by Still et al. using silica gel (60-Å pore size, 32–63 μm, standard grade, Sorbent Technologies).[2] Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light and/or by exposure to an ethanolic phosphomolybdic acid (PMA), an acidic solution of ^{p}anisaldehyde (Anis), an aqueous solution of ceric ammonium molybdate (CAM), an aqueous solution of potassium permanganate ($KMnO_4$) or an ethanolic solution of ninhydrin followed by heating (<1 min) on a hot plate (~250 °C). Organic solutions were concentrated on Büchi R-200 rotary evaporators at ~20 Torr (house vacuum) at 25–35 °C.

Materials. Commercial reagents and solvents were used as received with the following exceptions: Dichloromethane, diethyl ether, tetrahydrofuran, acetonitrile, and toluene were purchased from J.T. Baker (Cycletainer^{TM}) and were purified by the method of Grubbs et al. under positive argon pressure,[3] Triethylamine and 2,2,2-trifluoroethanol were distilled from calcium hydride at 760 Torr under a nitrogen atmosphere. Methanol was distilled from magnesium methoxide at 760 Torr under a nitrogen atmosphere. Acetic acid was distilled from 5% v/v acetic anhydride and 2% wt/v CrO_3. Perdeuterobenzene was distilled from CaH_2 and stored over 5Å MS pellets. All reagents for NMR experiments were degassed via an argon purge for at least 10 min. ^{i}Propyl acetate, ^{t}butyl acetate, methyl benzoate, L-leucinol , L-prolinol, methyl 2-furate and benzyl alcohol were distilled from K_2CO_3. Ethanolamine and methylphenyl acetate were distilled from KOH. Methyl 4-methoxybenzoate was purified by bulb–to–bulb distillation. Phthalide (**1j**) was recrystallized from toluene. Triphenylmethanol was recrystallized from dry hexanes. LiCl was dried at 200 °C under vacuum (~1 Torr) for 24 h then flame dried and stored in a glove box.

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with Varian inverse probe 500 INOVA and Varian 500 INOVA spectrometers and are recorded in parts per million from internal tetramethylsilane on the δ scale and are referenced from the residual protium in the NMR solvent ($CHCl_3$: δ 7.27, C_6D_6: δ 7.16, DMSO-d_6: δ 2.50, THF-d_8: δ 1.73, δ 3.58). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet), coupling constant(s) in Hertz, integration, assignment]. Carbon-13 nuclear magnetic resonance spectra were recorded with a Varian 500 INOVA spectrometer and are recorded in parts per million from internal tetramethylsilane on the δ scale and are referenced from the carbon resonances of the solvent ($CDCl_3$: δ 77.23, DMSO-d_6: δ 39.51, C_6D_6: δ 128.39, THF-d_8: δ 67.57, δ 25.37). Data is reported as follows: chemical shift [multiplicity (s = singlet, d

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[1] www.asirxn.com

[2] W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923–2925.

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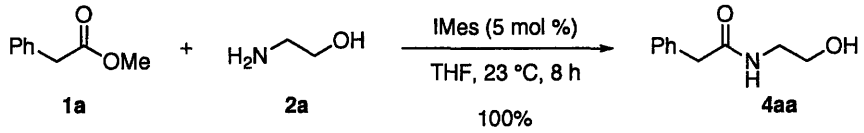
= doublet, q = quartet, m = multiplet), coupling constant(s) in Hertz, assignment]. Infrared data were obtained with a Perkin-Elmer 2000 FTIR and are reported as follows: [frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad), assignment]. React-IR experiments were performed on an ASI ReactIR 1000 fitted with a silicon probe. Infrared (IR) spectra were obtained using a Perkin Elmer System 2000 FT-IR spectrophotometer referenced to a polystyrene standard. Data are represented as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak) and assignment where appropriate. Melting points were determined on an Electrothermal Mel-Temp melting point apparatus. Gas chromatograpy was performed on an Agilent Technologies 6890N Network GC System with a HP-5 5% Phenyl Methyl Siloxane column. We are grateful to Dr. Li Li for obtaining the mass spectroscopic data at the Department of Chemistry's Instrumentation Facility, Massachusetts Institute of Technology. The structure of *N*,*N*-bismesitylimidazolylidene–methanol complex **8b**, bismesitylimidazolylidene–triphenylmethanol complex **8e** and bismesitylimidazolylidene–2,2,2-trifluoroethanol complex **8f** were obtained with the assistance of Dr. Peter Müller at the X-ray crystallography laboratory of the Department of Chemistry, Massachusetts Institute of Technology.

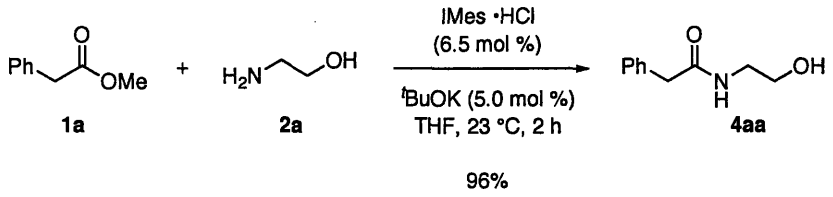
Procedure A
Use of Recrystallized IMes as Catalyst:



N-(2-Hydroxyethyl)-2-phenyl acetamide (4aa, Table 1, entry 1):

To a solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv.) in THF (1.95 mL) was added ester **1a** (285 μL, 1.97 mmol, 1 equiv) and ethanolamine **2a** (120 μL, 1.97 mmol, 1.00 equiv) sequentially via a gas-tight syringe. Monitoring the reaction mixture by TLC and GC analysis indicated complete conversion after 8 h. The volatiles were removed under reduced pressure on a rotary evaporator, and the resulting residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4aa** as a white powder (355 mg, 100%). For characterization data, please see below.

Procedure B
***In Situ* Generation of IMes as Catalyst:**



N-(2-Hydroxyethyl)-2-phenyl acetamide (4aa):

A flame-dried flask was charged with IMes•HCl (44 mg, 128 μmol, 0.065 equiv) and ^{t}BuOK (11 mg, 98 μmol, 0.050 equiv) and sealed under an argon atmosphere. THF (1.95 mL) was added via a gas-tight syringe and the resulting suspension was vigorously stirred for 30 min. Ester **1a** (285 μL, 1.97 mmol, 1 equiv) and ethanolamine **2a** (120 μL, 1.97 mmol, 1.00 equiv) were sequentially added via a gas-tight syringe. After 2 h, the yellow homogenous mixture was concentrated under reduced pressure on a rotary-evaporator. The resulting residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4aa** as a white solid (340 mg, 96%).

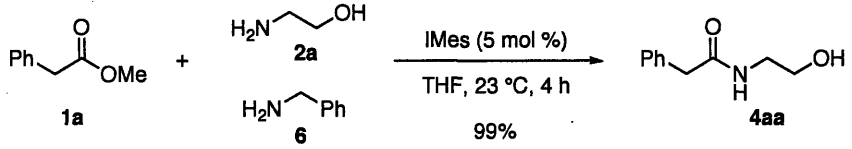
Use of 1,3-dimethylimidazolium iodide (IMe•HI) and 1,3-dicyclohexyl-imidazolium chloride (I^{c}Hx•HCl) in place of IMes•HCl provided the desired product in 95 and 88% yield, respectively.

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C): δ 7.35–7.38 (m, 2H, Ph**H**$_m$), 7.26–7.32 (m, 3H, Ph**H**$_{o,p}$), 5.97 (br-s, 1H, N**H**), 3.66 (app-q, J = 5.0 Hz, 2H, CH_2OH), 3.59 (s, 2H, PhCH_2), 3.37 (app-q, J = 5.0 Hz, 2H, NCH_2), 2.87 (br-s, 1H, O**H**).

^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 172.7 ($\mathbf{C}_{amide}$), 134.8 ($\mathbf{PhC}_{ipso}$), 129.7 ($\mathbf{PhC}_{orrtho}$), 129.3 ($\mathbf{PhC}_{meta}$), 127.7 ($\mathbf{PhC}_{para}$), 62.7 ($\mathbf{CH_2OH}$), 43.9 ($\mathbf{PhCH_2}$), 42.9 ($\mathbf{NCH_2}$).
FTIR (thin film) cm^{-1}:	3293 (s, O-H), 3087 (w), 2925 (m), 1645 (s, C=O), 1550 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{10}H_{13}NO_2$ $[M+H]^+$: 180.1019 found: 180.1018
M.p.:	65–66 °C
TLC (5% MeOH in CH_2Cl_2) R*f*:	0.40 (UV, $KMnO_4$).

Control Experiments:
All experiments were conducted under standard conditions used above for direct comparison. In the absence of IMes (**3**), incubation of equimolar amounts of esters **1a** and **1b** with **2a** at 23 °C for 12 h provides less than 2 and 1% respectively, of the corresponding amides **4aa** and **4ba**. The use of sodium methoxide and potassium ^{t}butoxide in place of IMes (**3**) in the coupling of **1a** and **2a** resulted in complete consumption of **1a** within 5 h and gave 60% and 74% isolated yield of **4aa**, respectively. Use of 1,3-bis(2,4,6-trimethylphenyl)imidazoin-2-ylidene (SIMes), prepared by in situ deprotonation (SIMes•HCl 6.5 mol% and potassium ^{t}butoxide 5 mol%) did not provide a detectable amount (<2%) in 5h and returned the starting ester **1a**.

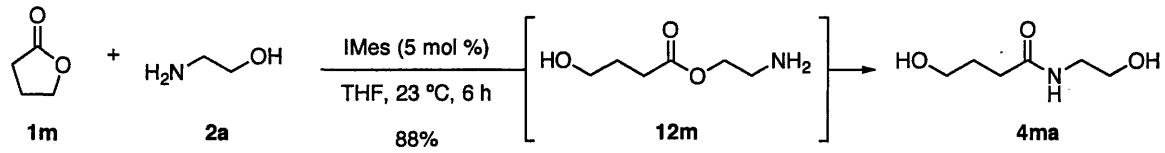
Competition Experiment (Figure 2):



<u>*N*-(2-Hydroxyethyl)-2-phenyl acetamide (4aa):</u>

To a solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) in THF (1.95 mL) was added the ester **1a** (255 μL, 1.97 mmol, 1 equiv), ethanolamine (**2a**, 120 μL, 1.97 mmol, 1.00 equiv), and benzylamine (**6**, 215 μL, 1.97 mmol, 1.00 equiv) sequentially via a gas-tight syringe under an argon atmosphere. After 4 h, TLC analysis indicated complete conversion of ester **1a** to the desired amide **4a.** The volatiles were removed under reduced pressure on a rotary-evaporator. ^1H NMR analysis of the residue indicated an equal mixture of amide **4a** and benzylamine (**6**). To facilitate chromatographic separation, acetic acid (100 μL, 1.75 mmol, 0.89 equiv) was added and the residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4aa** as a white solid (350 mg, 98.5%). For characterization data, please see above.

React-IR Monitoring of the Amidation Reaction



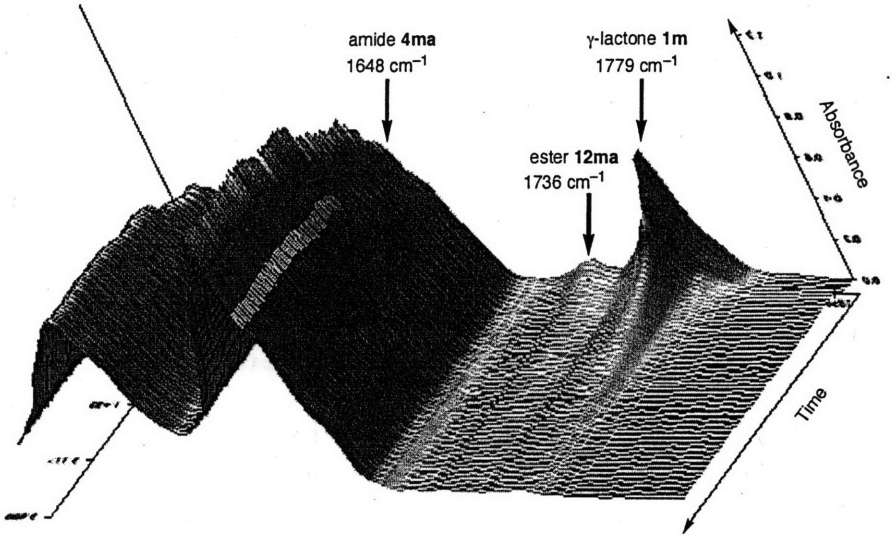
1m 2a 12m 4ma

4-Hydroxy-*N*-(2-hydroxyethyl)-butyramide (4ma, Table 1, entry 15):

An oven-dried React-IR flask was charged with IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) under a nitrogen atmosphere and the reaction vessel was sealed, moved out of the glove-box, and fitted to the React-IR probe under a stream of Argon. Anhydrous and deoxygenated THF (1.95 mL) was added to dissolve the IMes. A background spectrum was collected, ester **1m** (150 μL, 1.97 mmol, 1 equiv) followed by ethanolamine (**2a**, 120 μL, 1.97 mmol, 1.00 equiv) were added sequentially via a gas-tight syringe, and the reaction progress was monitored. After 6 h, the reaction was complete, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4ma** as a solid (261 mg, 88%).

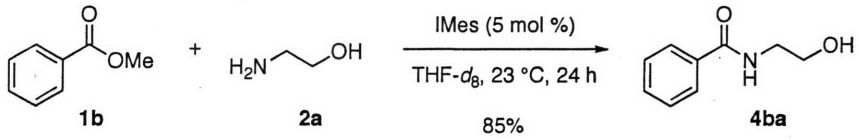
^{1}H NMR (500 MHz, DMSO-d_6, 20°C):	δ 7.78 (br-t, J = 5.0 Hz, 1H, CONH), 4.61 (t, J = 5.5 Hz, 1H, OH), 4.45 (t, J = 5.5 Hz, 1H, OH), 3.34–3.38 (m, 4H, NCH_2CH_2OH, $CH_2CH_2CH_2OH$), 3.08 (q, J = 6.0 Hz, 2H, NCH_2), 2.09 (t, J = 7.5 Hz, 2H, CH_2CONH), 1.61 (app-quintet, J = 7.3 Hz, 2H, $CH_2CH_2CH_2$).
^{13}C NMR (125.8 MHz, DMSO-d_6, 20 °C):	δ 172.3 (C_{amide}), 60.4 (CH_2OH), 60.0 (CH_2OH), 41.5 (NCH_2), 32.1 (CH_2CONH), 28.7 ($CH_2CH_2CH_2$).
FTIR ($CHCl_3$) cm^{-1}:	3447 (m, O-H), 3006 (w), 2946 (w), 1648 (s, C=O), 1525 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_6H_{13}NO_3$ $[M+Na]^+$: 170.0788 found: 170.0786
M.p.:	55.5–56.5 °C
TLC (5% MeOH in CH_2Cl_2) R*f*:	0.18 (UV, $KMnO_4$)

React-IR Monitoring of IMesNHC–catalyzed amidation of γ-lactone **1m** to amide **4ma**.



The intermediate ester **12ma** was observed within 2 min. Although ester **12ma** proved to be exceedingly difficult to isolate for direct verification of the absorbance at 1736 cm^{-1}, a similar ester ($Ph(CH_2)_{14}CO_2CH_2CH_2N(CH_3)_2$) has been reported to have an absorbance at 1730 cm^{-1} (T. Siatra-Prpastaikoudi, A. Papadaki-Valiraki, A. Tsantili-Kakoulidou, L. Tzouvelekis, A. Mentis, *Chem. Pharm. Bull.* **1994**, *42*, 392–394). Additionally, we have prepared samples of *O*-benzoylethanolamine (see below) and *O*-4-hydroxybutanoyl-*N*,*N*-dimethylethanolamine and detected their carbonyl absorbances at 1721cm^{-1} and 1741 cm^{-1}, respectively.

^{1}H NMR Monitoring of the Amidation Reaction



1b **2a** **4ba**

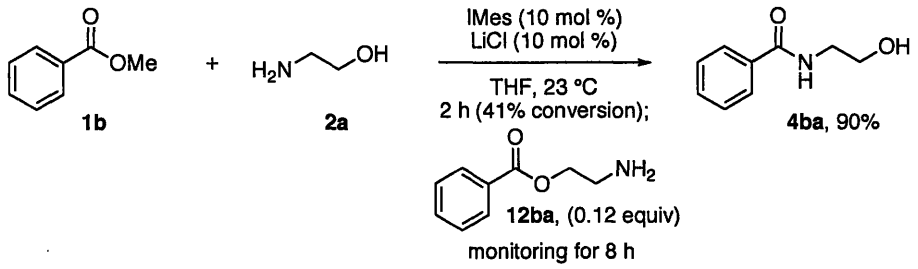
<u>*N*-(2-Hydroxyethyl)-benzamide (4ba):</u>

An NMR tube was charged with IMes (**3**, 11 mg, 35 μmol, 0.05 equiv) and THF-d_8 (700 μL) and sealed under a nitrogen atmosphere in a glove–box. Methyl benzoate **1b** (87 μL, 0.71 mmol, 1 equiv) and ethanolamine (**2a**, 43 μL, 0.71 mmol, 1.0 equiv) were added sequentially via a gas-tight syringe and the reaction progress was monitored by ^{1}H NMR spectroscopy over 24 h. The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting yellow residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4ba**[4] as a white solid (101 mg, 85%).

[4] For a previous synthesis of amide **4ba** using benzoyl chloride, see: A. Morcuende, M. Ors, S. Valverde, B. Herrandón, *J. Org. Chem.* **1996**, *61*, 5264–5270.

^{1}H NMR (500 MHz, $CDCl_3$, 20°C):	δ 7.78–7.79 (m, 2H, Ph**H**$_o$), 7.49–7.53 (m, 1H, Ph**H**$_p$), 7.27–7.45 (m, 1H, Ph**H**$_m$), 6.74 (br-s, 1H, N**H**), 3.83 (app-q, J = 6.0 Hz, 2H, **C**H_2OH), 3.64 (app-q, J = 5.5 Hz, 2H, NCH_2), 2.89 (br-s, 1H, O**H**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 168.8 (**C**$_{amide}$), 134.3 (Ph**C**$_{ipso}$), 131.9 (Ph**C**$_p$), 128.8 (Ph**C**$_m$), 127.2 (Ph**C**$_o$), 62.7 (**C**H_2OH), 43.1 (N**C**H_2).
FTIR (thin film) cm^{-1}:	3326 (s, O–H), 2936 (w), 2879 (w), 1636 (s, C=O), 1542 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_9H_{11}NO_2$ $[M+Na]^+$: 188.0682 found: 188.0678
M.p.:	54–55 °C
TLC (5% MeOH in CH_2Cl_2) R*f*:	0.43 (UV, $KMnO_4$)

React-IR Monitoring of the Amidation Reaction



<u>*N*-(2-Hydroxyethyl)-benzamide (4ba):</u>

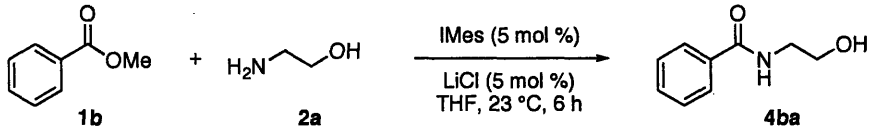
A flame dried React-IR cell was charged with IMes (**3**, 60.0 mg, 197 μmol, 0.100 equiv) and anhydrous LiCl (8 mg, 0.2 mmol, 0.1 equiv), and was sealed under a nitrogen atmosphere in a glove-box. The reaction vessel was placed onto the probe under a stream of Argon and THF (1.95 mL) was added via a gas-tight syringe to give a clear colorless solution. Methyl benzoate **1b** (246 μL, 1.97 mmol, 1 equiv) and ethanolamine (**2a**, 120 μL, 1.97 mmol, 1.00 equiv) were added sequentially via a gas-tight syringe. The reaction progress was monitored for 2 h (41% conversion). A solution of the sensitive ester **12ba** (0.12 equiv, the sample was a 43:57 ratio of **12ba**:**4ba**, see below for preparation; 27% expected increase in final product) in THF (535 μL) was added to the reaction in progress. Monitoring of the reaction mixture (IR and TLC) was continued for an additional 8 h. The conversion to amide **4ba** proceeded as expected after an initial burst upon addition of ester **12ba**. The ester **12ba** was rapidly consumed and within 20 min the ester was no longer detectable by TLC (the carbonyl frequencies of esters **12ba** and **1b** were not sufficiently resolved for clear monitoring by IR). The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting crude orange residue was purified by

flash column chromatography on silica gel (100% THF) to afford the amide **4ba** as a white solid (370 mg, 90%). For characterization data, please see above.

Preparation of the ester **12ba**: A suspension of *O*-benzoyl-*N*-Cbz-ethanolamine (197 mg, 657 μmol, 1.00 equiv) and palladium on carbon (5% wt/wt, 197 mg, 92.6 μmol, 0.14 equiv) in THF (650 μL) was vigorously stirred under a hydrogen atmosphere. Monitoring the reaction mixture by TLC indicated complete removal of the nitrogen protective group and formation of ester **12ba** in 2 h. To avoid IMes deactivation in the amidation reaction, the ester **12ba** was purified under a nitrogen-atmosphere (glove-box) by flash column chromatography (0.5 × 2.5 cm, 100% THF) on dry silica gel (dehydrated by heating 200 °C for 48 h) to give a sample of the sensitive ester **12ba** along with the corresponding amide **4ba** as a clear oil (88.5 mg, 82%, 536 μmol, 43:57 ratio of **12ba**:**4ba**) which was diluted with THF (535 μL) and used above.

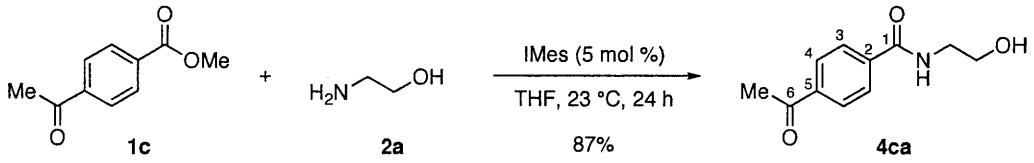
^{1}H NMR (500 MHz, $CDCl_3$, 20°C, 43:57 mixture of **12ba**:**4ba**, ester **12ba** noted by *): δ 8.06–8.08 (m, 2H, Ph$\mathbf{H}_o$*), 7.78–7.80 (m, 2H, Ph$\mathbf{H}_o$), 7.58 (tt, J = 7.5 Hz, 1.5 Hz, 1H, Ph$\mathbf{H}_p$*), 7.53 (tt, J = 7.0 Hz, 1.5 Hz, 1H, Ph$\mathbf{H}_p$), 7.44–7.48 (m, 4H, Ph$\mathbf{H}_m$, Ph$\mathbf{H}_m$*), 6.61 (br s, 1H, N**H**) 4.37 (app-t, J = 5.5 Hz, 2H, O$\mathbf{CH}_2$*), 3.86 (app-t, J = 5.0 Hz, 2H, $\mathbf{CH}_2$OH), 3.66 (app-q, J = 5.2 Hz, 2H, N$\mathbf{CH}_2$), 3.10 (app-t, J = 5.5 Hz, 2H, N$\mathbf{CH}_2$*), 1.72 (br-s, 3H, $\mathbf{NH}_2$*, O**H**).

Experimental Procedures for Remainder of Compounds in Table 1



<u>*N*-(2-Hydroxyethyl)-benzamide (4ba, Table 1, entry 2):</u>

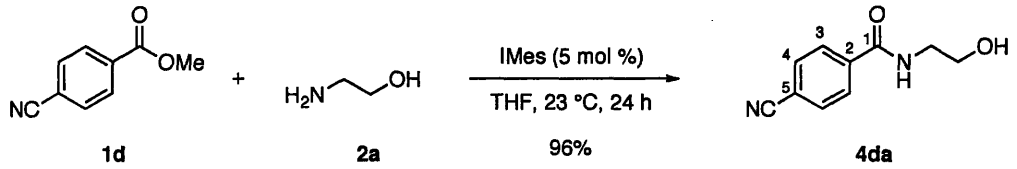
To a solution of IMes (**3**, 30 mg, 66 μmol, 0.05 equiv) and anhydrous lithium chloride (3 mg, 7 μmol, 0.05 equiv) in THF (1.30 mL) was added methyl benzoate **1b** (190 μL, 1.31 mmol, 1 equiv) and ethanolamine (**2a**, 80 μL, 1.9 mmol, 1.0 equiv) sequentially via a gas-tight syringes at 23 °C under an Argon atmosphere. After 9.5 h, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting orange residue was purified by flash column chromatography on silica gel (100 % THF) to afford the amide **4ba** as a white solid (205 mg, 94%). For characterization data, please see above.



4-Acetyl-*N*-(2-hydroxyethyl)-benzamide (4ca, Table 1, entry 3):

A solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) in THF (1.95 mL) followed by ethanolamine (**2a**, 120 μL, 1.97 mmol, 1.00 equiv) was added sequentially via a gas-tight syringe to a flame-dried round bottom flask containing the ester **1c** (351 mg, 1.97 mmol, 1 equiv) under an argon atmosphere. Amide **4ca** began to precipitate after 40 min. After 24 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting red residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4ca** as a white powder (354 mg, 87%).

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	δ 8.02 (dt, J = 8.0 Hz, 1.5 Hz, 2H, C_4**H**), 7.88 (dt, J = 8.0 Hz, 1.5 Hz, 2H, C_3**H**) 6.71 (br-s, 1H, N**H**), 3.88 (app-q, J = 5.0 Hz, 2H, CH_2OH), 3.67 (app-q, J = 5.2 Hz, 2H, NCH_2), 2.64 (s, 3H, CH_3), 2.43 (t, J = 4.8 Hz, 1H, O**H**).
^{13}C NMR (125.8 MHz, CD_3OD, 20 °C):	δ 199.8 (C_{ketone}), 169.6 (C_{amide}), 140.6 (C_5), 139.9 (C_2), 129.7 (C_4), 128.8 (C_3), 61.6 (CH_2OH), 43.8 (NCH_2), 27.0 (COCH_3).
FTIR ($CHCl_3$) cm^{-1}:	3452 (m, O–H), 3020 (w), 2995 (w), 1687 (s, C=O), 1660 (s, C=O).
HRMS (ESI) (*m/z*):	calc'd for $C_{11}H_{13}NO_3$ $[M+H]^+$: 208.0968 found: 208.0968
M.p.:	136–137 °C
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.44 (UV, $KMnO_4$)

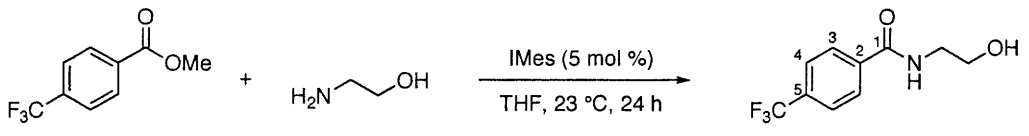


1d 2a 4da

4-Cyano-*N*-(2-hydroxyethyl)-benzamide (4da, Table 1, entry 4):

A solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) in THF (1.95 mL) followed by ethanolamine (**2a**, 120 μL, 1.97 mmol, 1.00 equiv) was added sequentially via a gas-tight syringe to a flame-dried round bottom flask containing the ester **1d** (317 mg, 1.97 mmol, 1 equiv) under an argon atmosphere to give a maroon mixture. After 24 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4da** as a white powder (361 mg, 96%).

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	δ 7.90 (d, J = 7.5 Hz, 2H, C_4**H**), 7.75 (d, J = 8.0 Hz, 2H, C_3**H**), 6.69 (br-s, 1H, N**H**), 3.87 (app-q, J = 4.8 Hz, 2H, C**H**$_2$OH), 3.66 (app-q, J = 5.2 Hz, 2H, NC**H**$_2$), 2.26 (br-t, J = 4.3 Hz, 1H, O**H**).
^{13}C NMR (125.8 MHz, DMSO-d_6, 20 °C):	δ 165.0 (**C**$_{amide}$), 138.6 (**C**$_2$), 132.4 (**C**$_4$), 128.1 (**C**$_3$), 118.4 (**C**N), 113.5 (**C**$_5$), 59.6 (**C**H$_2$OH), 42.4 (N**C**H$_2$).
FTIR ($CHCl_3$) cm^{-1}:	3451 (m, O–H), 2995 (w), 2940 (w), 2234 (m, nitrile), 1664 (s, C=O).
HRMS (ESI) (*m/z*):	calc'd for $C_{10}H_{10}N_2O_2$ $[M+H]^+$: 191.0815 found: 191.0816
M.p.:	108–109 °C
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.58 (UV, $KMnO_4$)

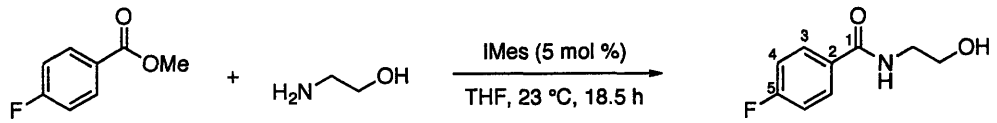


1e 2a 4ea

***N*-(2-Hydroxyethyl)-4-trifluoromethyl benzamide (4ea, Table 1, entry 5):**

A flame dried React-IR cell was charged with IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) and sealed under a nitrogen atmosphere in a glove-box. The reaction vessel was placed onto the probe under a stream of Argon and THF (1.95 mL) was added via a gas-tight syringe to give a clear colorless solution. Ester **1e** (317 μL, 1.97 mmol, 1 equiv) and ethanolamine (**2a**, 120 μL, 1.97 mmol, 1.00 equiv) were added sequentially via a gas-tight syringe. The reaction progress was monitored for 24 h. The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting orange residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4ea** as a white powder (436 mg, 95%).

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	δ 7.89 (dd, J = 8.5 Hz, 1.0 Hz, 2H, C_4**H**), 7.70 (dd, J = 8.3 Hz, 1.0 Hz, C_3**H**), 6.76 (br-s, 1H, N**H**), 3.86 (app q, J = 5.0 Hz, 2H, C**H**$_2$OH), 3.66 (app-q, J = 5.3 Hz, 2H, NC**H**$_2$), 2.56 (t, J = 5.0 Hz, 1H, O**H**).
^{13}C NMR (125.8 MHz, DMSO-d_6, 20 °C):	δ 165.2 (**C**$_{amide}$), 138.3 (**C**$_2$), 131.0 (q, J^2_{CF} = 31.9 Hz, **C**$_5$), 128.1 (**C**$_3$), 125.3 (app-t, J^3_{CF} = 3.8 Hz, **C**$_4$), 124.0 (q, J_{CF} = 272.6 Hz, **C**F$_3$), 59.6 (**C**H$_2$OH), 42.3 (NCH$_2$).
FTIR ($CHCl_3$) cm^{-1}:	3452 (m O–H), 2997 (w), 2943 (w), 1662 (s, C=O), 1327 (s, C–F).
HRMS (ESI) (*m/z*):	calc'd for $C_{10}H_{10}F_3NO_2$ $[M+H]^+$: 234.0736 found: 234.0735
M.p.:	118–119.5 °C
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.42 (UV, $KMnO_4$)



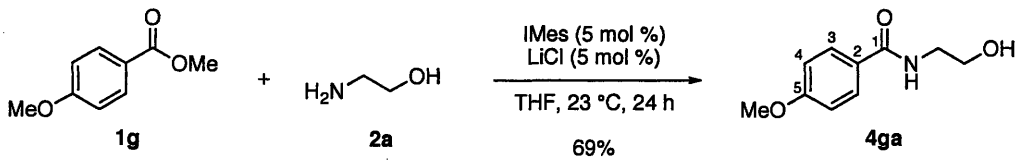
1f 2a 4fa

4-Fluoro-*N*-(2-hydroxyethyl)-benzamide (4fa, Table 1, entry 6):

To a solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) in THF (1.95 mL) at 23 °C, was added ester **1f** (255 μL, 1.97 mmol, 1.00 equiv) followed by ethanolamine (**2a**, 120 μL, 1.97 mmol, 1 equiv) sequentially via a gas-tight syringe. After 18.5 h, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4fa**[5] as a white solid (318 mg, 88%).

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	δ 7.80 (m, 2H, C_4**H**), 7.10 (m, 2H, C_3**H**), 6.70 (br-s, 1H, N**H**), 3.83 (app-t, J = 5.0 Hz, 2H, CH_2OH), 3.62 (app-q, J = 5.2 Hz, 2H, NCH_2), 2.82 (br-s, 1H, O**H**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 167.7 (C_{amide}), 165.0 (d, J_{CF} = 252.2 Hz, C_5), 130.5 (d, J^4_{CF} = 3.5 Hz, C_2), 129.5 (d, J^3_{CF} = 8.6 Hz, C_3), 115. 8 (d, J^2_{CF} = 21.9 Hz, C_4), 62.4 (CH_2OH), 43.0 (NCH_2).
FTIR (thin film) cm^{-1}:	3292 (s, O–H), 2980 (w), 1636 (s, C=O), 1560 (m), 854 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_9H_{10}FNO_2$ $[M+H]^+$: 184.0768 found: 184.0769
M.p.:	91.5–92.5 °C
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.56 (UV, $KMnO_4$)

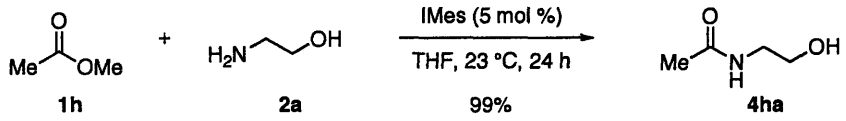
[5] For an alternative synthesis of amide **4fa** using an electrochemical method starting with ester **1f**, see: K. Arai, S. Tamura, T. Masumizu, K.-i. Kawai, S. Nakajima, A. Ueda, *Can. J. Chem.* **1990**, *68*, 903–907.



***N*-(2-Hydroxyethyl)-4-methoxy benzamide (4ga, Table 1, entry 7):**

A solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) and anhydrous lithium chloride (4 mg, 0.1 mmol, 0.05 equiv) in THF (1.95 mL) followed by ethanolamine (**2a**, 120 μL, 1.97 mmol, 1.00 equiv) was added sequentially via a gas-tight syringe to a flame-dried round bottom flask containing the ester **1g** (327 mg, 1.97 mmol, 1 equiv) under an argon atmosphere to give a maroon mixture. After 24 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4ga** as a white powder (264 mg, 69%).

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	δ 7.76 (d, J = 8.5 Hz, 2H, C_3**H**), 6.93 (d, J = 8.5 Hz, 2H, C_4**H**), 6.57 (br-s, 1H, N**H**), 3.86 (s, 3H, O**C**H$_3$), 3.84 (m, 2H, **C**H$_2$OH), 3.63 (app-q, J = 5.2 Hz, 2H, N**C**H$_2$), 2.79 (br-s, 1H, O**H**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 168.5 (**C**$_{amide}$), 162.5 (**C**$_5$), 129.0 (**C**$_3$), 126.5 (**C**$_2$), 113.9 (**C**$_4$), 62.6 (**C**H$_2$OH), 55.6 (O**C**H$_3$), 43.1 (N**C**H$_2$).
FTIR (thin film) cm^{-1}:	3332 (s, O–H), 2940 (w), 1633 (s, C=O), 1559 (m), 1252 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{10}H_{13}NO_3$ $[M+H]^+$: 196.0968 found: 196.0964
M.p.:	97–98 °C
TLC (5% MeOH in CH_2Cl_2) R*f*:	0.38 (UV, $KMnO_4$)



***N*-(2-Hydroxyethyl)-acetamide (4ha, Table 1, entry 8):**

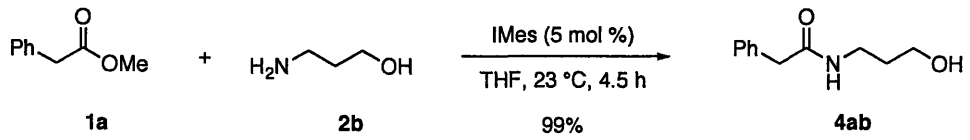
A flame dried React-IR cell was charged with IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) and sealed under a nitrogen atmosphere in a glove-box. The reaction vessel was placed onto the probe under a stream of Argon and THF (1.95 mL) was added via a gas-tight syringe to give a clear colorless solution. Ester **1h** (265 μL, 1.97 mmol, 1 equiv) and ethanolamine (**2a**, 120 μL, 1.97 mmol, 1.00 equiv) were added sequentially via a gas-tight syringe. The reaction progress was monitored for 24 h. The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting orange residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4ha**[6] (200 mg, 99%).

^{1}H NMR (500 MHz, $CDCl_3$, 20°C):	δ 6.29 (br-s, 1H, N**H**), 3.72 (t, J = 4.5 Hz, 2H, CH_2OH), 3.41 (app-q, J = 5.2 Hz, 2H, NCH_2), 3.25 (br-s, 1H, O**H**), 2.02 (s, 3H, CH_3).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 171.7 (C_{amide}), 62.3 (CH_2OH), 42.7 (NCH_2), 23.4 (CH_3).
FTIR (thin film) cm^{-1}:	3298 (s, O–H), 2963 (m), 1652 (s, C=O), 1559 (m), 1261 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_4H_9NO_2$ [M+Na]$^+$: 126.0525 found: 126.0531
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.29 ($KMnO_4$)

***N*-(2-Hydroxyethyl)-acetamide (4ha, Table 1, entries 9-11):**

The same procedure as above was used for entries 9–11 (Table 1). For consistency all experiments were allowed to proceed only for 24 h prior to isolation of the product. The experiments with benzyl acetate, ^{i}propyl acetate, and ^{t}butyl acetate gave 95, 34, and 0% yield of the desired amide **4ha**. For characterization data, please see above.

[6] For a previous synthesis of amide **4ha** using acetic acid, Ph_3SbO, and P_4S_{10} at 50 °C, see: R. Nomura, T. Nakano, Y. Yamada, H. Matsuda, *J. Org. Chem.* **1991**, *56*, 4076–4078.

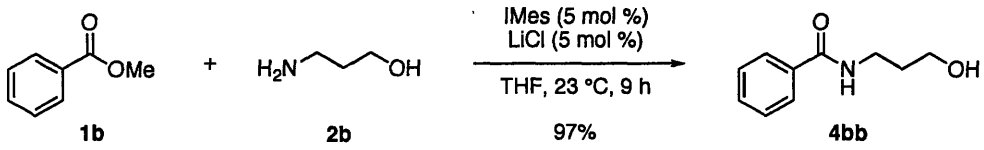


***N*-(3-Hydroxypropyl)-2-phenyl acetamide (4ab, Table 1, entry 12):**

To a solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) in THF (1.95 mL) at 23 °C, was added ester **1a** (285 μL, 1.97 mmol, 1 equiv) and 1-amino-3-propanol **2b** (151 μL, 1.97 mmol, 1.00 equiv) sequentially via a gas-tight syringes. After 4.5 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4ab**[7] as a white solid (379 mg, 99%).

^{1}H NMR (500 MHz, $CDCl_3$, 20°C):	δ 7.36–7.39 (m, 2H, Ph**H**$_m$), 7.30–7.33 (m, 2H, Ph**H**$_o$), 7.27–7.27 (m, 1H, Ph**H**$_p$), 5.76 (br-s, 1H, N**H**), 3.61 (s, 2H, PhC**H**$_2$), 3.58 (app-q, J = 5.5 Hz, 2H, C**H**$_2$OH), 3.38 (app-q, J = 6.5 Hz, 2H, NC**H**$_2$), 3.09 (td, J = 6.5 Hz, 3.0 Hz, 1H, O**H**), 1.61 (app-pentet, J = 6.0 Hz, 2H, $CH_2CH_2CH_2$).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 172.6 (**C**$_{amide}$), 134.9 (Ph**C**$_{ipso}$), 129.6 (Ph**C**$_o$), 129.2 (Ph**C**$_m$), 127.6 (Ph**C**$_p$), 59.3 (**C**H$_2$OH), 43.8 (Ph**C**H$_2$), 36.6 (N**C**H$_2$), 32.3 ($CH_2CH_2CH_2$).
FTIR (thin film) cm^{-1}:	3247 (s, O–H), 3084 (m), 2946 (m) , 1630 (s, C=O), 1567 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{11}H_{15}NO_2$ [M+Na]$^+$: 216.0995 found: 216.0994
M.p.:	62.5–63.5 °C
TLC (5% MeOH in CH_2Cl_2) R*f*:	0.31 (UV, $KMnO_4$)

[7] For an alternative synthesis of amide **4ab** at 150 °C using phenylacetic acid, see: J. Cossy, C. Pale–Grosdemange, *Tetrahedron Lett.* **1989**, *30*, 2771–2774.



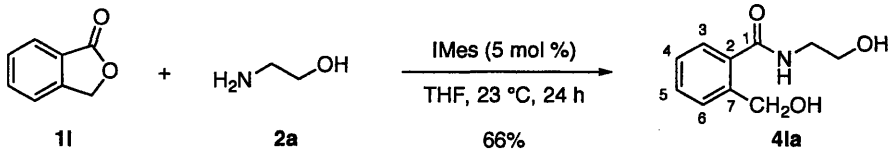
1b **2b** 97% **4bb**

***N*-(3-Hydroxypropyl)-benzamide (4bb, Table 1, entry 13):**

To a solution of IMes (**3**, 20 mg, 66 μmol, 0.05 equiv) and anhydrous LiCl (3 mg, 0.07 mmol, 0.05 equiv) in THF (1.30 mL) was added ester **1b** (164 μL, 1.31 mmol, 1 equiv) and 1-amino-3-propanol **2b** (100 μL, 1.31 mmol, 1.00 equiv) sequentially via a gas-tight syringe. After 9 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4bb**[8] as a clear oil (229 mg, 97%).

^{1}H NMR (500 MHz, $CDCl_3$, 20°C):	δ 7.78–7.79 (m, 2H, Ph**H**$_o$), 7.52 (tt, J = 7.0, 1.5 Hz, 1H, Ph**H**$_p$), 7.44–7.47 (m, 2H, Ph**H**$_m$), 6.64 (br-s, 1H, N**H**), 3.73 (app-q, J = 6.0 Hz, 2H, C**H**$_2$OH), 3.66 (app-q, J = 6.0 Hz, 2H, NC**H**$_2$), 3.15 (br-t, J = 6.0 Hz, 1H, O**H**), 1.81 (app-quintet, J = 6.0 Hz, 2H, CH$_2$C**H**$_2$CH$_2$).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 168.8 (**C**$_{amide}$), 134.2 (Ph**C**$_{ipso}$), 131.6 (Ph**C**$_p$), 128.5 (Ph**C**$_m$), 127.0 (Ph**C**$_o$), 59.9 (**C**H$_2$OH), 37.4 (N**C**H$_2$), 31.8 (CH$_2$**C**H$_2$CH$_2$).
FTIR (thin film) cm^{-1}:	3323 (s, O–H), 3066 (m), 2944 (s), 1639 (s, C=O), 1545 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{10}H_{13}NO_2$ [M+Na]$^+$: 202.0838 found: 202.0837
TLC (5% MeOH in CH_2Cl_2) R*f*:	0.22 (UV, $KMnO_4$)

[8] For a previous synthesis of amide **4bb** using benzoyl chloride, see: A. Morcuende, M. Ors, S. Valverde, B. Herrandón, *J. Org. Chem.* **1996**, *61*, 5264–5270.

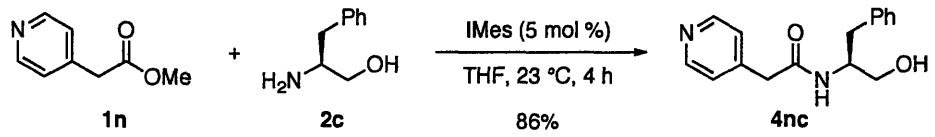


1l **2a** **4la**

***N*-(2-Hydroxyethyl)-2-hydroxymethyl benzamide (4la, Table 1, entry 14):**

A flame dried React-IR cell was charged with IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) and sealed under a nitrogen atmosphere in a glove-box. The reaction vessel was placed onto the probe under a stream of Argon and THF (1.00 mL) was added via a gas-tight syringe to give a clear colorless solution. A solution of ester **1l** (264 mg, 1.97 mmol, 1 equiv) in THF (0.95 mL) was added to the cell followed by ethanolamine (**2a**, 120 μL, 1.97 mmol, 1.00 equiv) via a gas-tight syringe. The reaction progress was monitored for 24 h. The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting yellow residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4la** as a solid (105 mg, 66%).

^{1}H NMR (500 MHz, DMSO-d_6, 20°C):	δ 8.34 (br-t, J = 5.3 Hz, 1H, N**H**), 7.52 (d, J = 7.5 Hz, 1H, C_3**H**), 7.42–7.44 (m, 2H, C_5**H** and C_6**H**), 7.29 (t, J = 7.5 Hz, 1H, C_4**H**), 5.28 (t, J = 6.5 Hz, 1H, ArCH_2O**H**), 4.73 (t, J = 6.5 Hz, 1H, CH_2O**H**), 4.58 (d, J = 6.0 Hz, 2H, Ar**C**H_2OH), 3.49 (app-q, J = 6.5 Hz, 2H, **C**H_2OH), 3.29 (app-q, J = 6.0 Hz, 2H, N**C**H_2).
^{13}C NMR (125.8 MHz, DMSO-d_6, 20 °C):	δ 168.8 ($\mathbf{C}_{amide}$), 140.2 ($\mathbf{C}_7$), 135.2 ($\mathbf{C}_2$), 129.7 ($\mathbf{C}_5$), 127.6 ($\mathbf{C}_3$), 127.4 ($\mathbf{C}_4$), 126.6 ($\mathbf{C}_6$), 61.1 (**C**H_2OH), 59.8 (Ar**C**H_2OH), 42.0 (N**C**H_2).
FTIR ($CHCl_3$) cm^{-1}:	3442 (m, O–H), 3003 (w), 2940 (w), 1644 (s, C=O), 1526 (w).
HRMS (ESI) (*m/z*):	calc'd for $C_{10}H_{13}NO_3$ $[M+Na]^+$: 218.0788 found: 218.0783
M.p.:	63–64 °C
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.40 (UV, $KMnO_4$)

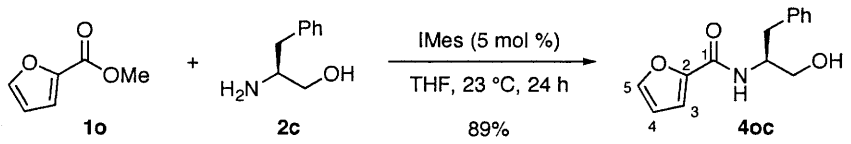


1n 2c 86% 4nc

***N*-(1-(*S*)-Benzyl-2-hydroxyethyl)-pyridin-4-yl acetamide (4kc, Table 1, entry 16):**

Ester **1n** (265 μL, 1.97 mmol, 1.00 equiv) was added via a gas-tight syringe to a solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv.) in THF (1.95 mL) at 23 °C under an argon atmosphere. The resulting bright-yellow solution was transferred via cannula to a flask containing solid L-phenylalaninol (**2c**, 298 mg, 1.97 mmol, 1 equiv) under an argon atmosphere and the resulting mixture was set to stir vigorously. After 15 min, a yellow–homogenous solution resulted and after an additional 30 min, the amide product **4nc** began to precipitate. After 4 h, monitoring of the reaction mixture by TLC indicated complete conversion to the desired amide **4nc**. The volatiles were removed under reduced pressure on a rotary-evaporator and the resulting beige-residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4nc** as an off–white solid (461 mg, 86%).

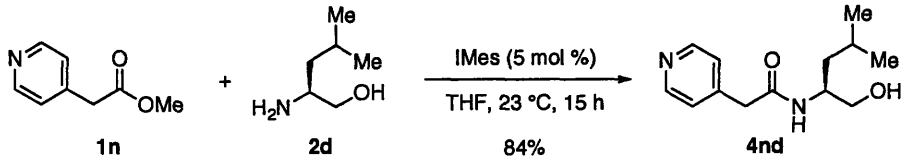
^{1}H NMR (500 MHz, DMSO-d_6, 20°C):	δ 8.40 (d, J = 5.8 Hz, 2H, $CH_{2,6\text{-pyr}}$), 8.07 (d, J = 8.5 Hz, 1H, NH), 7.21–7.24 (m, 2H, PhCH_m), 7.16–7.19 (m, 3H, PhC$H_{o,p}$), 7.08 (d, J = 6.1 Hz, 2H, $CH_{3,5\text{-pyr}}$), 4.86 (t, J = 5.5 Hz, 1H, OH), 3.91 (m, 1H, NCH), 3.30–3.43 (m, 4H, CH_2CONH, CH_2OH), 2.85 (dd, J = 13.7, 5.2 Hz, 1H, PhCH_2), 2.60 (dd, J = 13.6, 9.1 Hz, 1H, PhCH_2).
^{13}C NMR (125.8 MHz, DMSO-d_6, 20 °C):	δ 168.4 (C_{amide}), 149.2 ($C_{2,6\text{-pyr}}$), 145.3 ($C_{4\text{-pyr}}$), 139.1 (PhC_{ipso}), 129.1 (PhC_o), 128.1 (PhC_m), 125.9 (PhC_p), 124.3 ($C_{3,5\text{-pyr}}$), 62.7 (CH_2OH), 52.5 (NCH), 41.6 (CH_2CONH), 36.6 (CH_2Ph).
FTIR (thin film), cm^{-1}:	3316 (s, O–H), 3059 (w), 2919 (w), 1637 (s, C=O), 1538 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{16}H_{18}N_2O_2$ $[M+H]^+$: 271.1441 found: 271.1433
M.p.:	144.5–145 °C
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.30 (UV, $KMnO_4$)



***N*-(2-Furoyl) L-Phenylalaninol (4lc, Table 1, entry 17):**

Ester **1o** (211 μL, 1.97 mmol, 1 equiv) was added via a gas-tight syringe to a solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv.) in THF (1.95 mL) at 23 °C under an argon atmosphere. The resulting bright-yellow solution was transferred via cannula to a flask containing solid L-phenylalaninol (**2c**, 298 mg, 1.97 mmol, 1.00 equiv) under an argon atmosphere. After 24 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting beige-residue was purified by flash column chromatography on silica gel (2% MeOH in CH_2Cl_2) to afford the amide **4oc** as an off–white solid (428 mg, 89%).

^{1}H NMR (500 MHz, $CDCl_3$, 20°C):	δ 7.42 (m, 1H, C_3**H**), 7.31–7.34 (m, 2H, Ph$\mathbf{H}_m$), 7.23-7.28 (m, 3H, Ph$\mathbf{H}_{o,p}$), 7.10 (m, 1H, C_5**H**), 6.65 (br-d, J = 6.0 Hz, 1H, N**H**), 6.49 (dd, J = 3.2, 2.5 Hz, 1H, C_4**H**), 4.35 (m, 1H, NC**H**), 3.77 (m, 1H, C$\mathbf{H}_2$OH), 3.67 (m, 1H, C$\mathbf{H}_2$OH), 2.99 (d, J = 7.5 Hz, 2H, PhC$\mathbf{H}_2$), 2.74–2.77 (br-d, 1H, O**H**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 158.8 ($\mathbf{C}_{amide}$), 147.7 ($\mathbf{C}_2$), 144.2 ($\mathbf{C}_5$), 137.7 (Ph$\mathbf{C}_{ipso}$), 129.4 (Ph$\mathbf{C}_o$), 128.7 (Ph$\mathbf{C}_m$), 126.8 (Ph$\mathbf{C}_p$), 114.6 ($\mathbf{C}_3$), 112.3 ($\mathbf{C}_4$), 63.5 ($\mathbf{C}H_2$OH), 52.6 (N$\mathbf{C}H_2$), 37.2 ($\mathbf{C}H_2$Ph).
FTIR ($CHCl_3$) cm^{-1}:	3425 (m, O–H), 3000 (w), 2948 (w), 1653 (s (C=O), 1595 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{14}H_{15}NO_3$ $[M+H]^+$: 246.1125 found: 246.1126
M.p.:	94.5–95.5 °C
TLC (5% MeOH in CH_2Cl_2) R*f*:	0.34 (UV, $KMnO_4$)

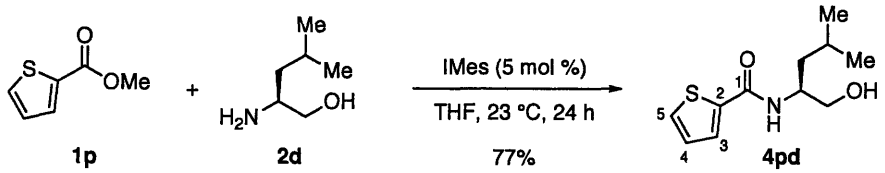


1n 2d 84% 4nd

***N*-(1-(*S*)-Hydroxymethyl-3-methylbutyl)-2-pyridin-4-yl acetamide (4nd):**

Ester **1n** (265 μL, 1.97 mmol, 1.00 equiv) was added via a gas-tight syringe to a solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv.) in THF (1.95 mL) at 23 °C under an argon atmosphere. To the resulting bright-yellow solution was added L-leucinol (**2d**, 255 μL, 1.97 mmol, 1 equiv) under an argon atmosphere and the resulting mixture was set to stir vigorously. After 1.5 h, the amide product **4nd** began to precipitate. After 15 h, monitoring of the reaction mixture by TLC indicated complete conversion to the desired amide **4nd**. The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting beige residue was purified by flash column chromatography on silica gel (5→10% MeOH in CH_2Cl_2) to afford the amide **4nd** as an off–white solid (391 mg, 84%).

^{1}H NMR (500 MHz, DMSO-d_6, 20°C)	δ 8.46 (d, J = 5.0 Hz, 2H, **C**$H_{2,6\text{-pyr}}$), 7.90 (d, J = 8.5 Hz, 1H, N**H**), 7.26 (d, J = 5.5 Hz, 2H, **C**$H_{3,5\text{-pyr}}$), 4.70 (t, J = 5.3 Hz, 1H, O**H**), 3.77 (m, 1H, NC**H**), 3.47 (d, J = 14.5 Hz, 1H, **C**H_2CONH), 3.43 (d, J = 14.0 Hz, 1H, **C**H_2CONH), 3.32 (m, 1H, **C**H_2OH), 3.24 (m, 1H, **C**H_2OH), 1.55 (septet, J = 6.5 Hz, 1H, CH_3**C**HCH_3), 1.29 (m, 2H, **C**H_2*i*-Pr), 0.84 (d, J = 6.5 Hz, 3H, **C**H_3), 0.79 (d, J = 6.5 Hz, 3H, **C**H_3).
^{13}C NMR (125.8 MHz, DMSO-d_6, 20 °C)	δ 168.5 (**C**$_{amide}$), 149.4 (**C**$_{2,6\text{-pyr}}$), 145.6 (**C**$_{4\text{-pry}}$), 124.4 (**C**$_{3,5\text{-pyr}}$), 63.8 (**C**H_2OH), 48.8 (**C**H_2CONH), 41.7 (N**C**H), 24.3 (**C**H$(CH_3)_2$), 23.3 (**C**H_2*i*-Pr), 21.8 (**C**H_3)
FTIR ($CHCl_3$) cm^{-1}:	3430 (m, O–H), 2993 (m), 2959 (m), 1666 (s, C=O), 1603 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{13}H_{20}N_2O_2$ $[M+H]^+$: 237.1598 found: 237.1608
M.p.	106.5–107.5 °C
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.22 (UV, $KMnO_4$)

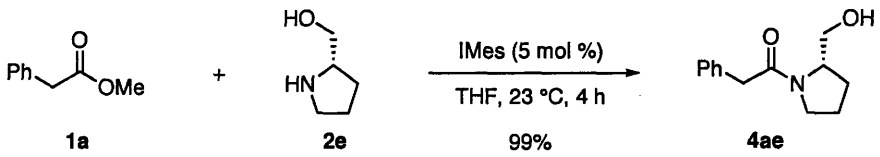


1p 2d 77% 4pd

N-(2-thiophenecarbonyl) L-Leucinol (4pd, Table 1, entry 19):

Ester **1p** (228 μL, 1.97 mmol, 1.00 equiv) was added via a gas-tight syringe to a solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) in THF (1.95 mL) at 23 °C under an argon atmosphere. To the resulting bright-yellow solution was added L-leucinol (**2d**, 255 μL, 1.97 mmol, 1 equiv) under an argon atmosphere. After 24 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting yellow-residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4pd** as a white solid (343 mg, 77%).

^{1}H NMR (500 MHz, $CDCl_3$, 20°C):	δ 7.51 (m, 1H, C_3**H**), 7.48 (dd, *J* = 5.0, 1.0 Hz, 1H, C_5**H**), 7.07, (m, 1H, C_4**H**), 6.19 (br-s, 1H, N**H**), 4.32 (m, 1H, NC**H**), 3.78 (d, *J* = 11.0 Hz, 1H, CH_2OH), 3.65 (dd, *J* = 10.5 Hz, 5.0 Hz, 1H, CH_2OH) 2.82, (br-s, 1H, O**H**), 1.70 (m, 1H, CH_3CHCH_3), 1.54 (ddd, *J* = 9.5, 6.0, 5.5 Hz, 1H, CH_2*i*-Pr), 1.44 (ddd, *J* = 5.5, 5.5, 8.5 Hz, CH_2*i*-Pr), 0.97 (d, *J* = 1.5 Hz, 3H, CH_3), 0.96 (dd, *J* = 1.5 Hz, 3H, CH_3).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 162.8 (C_{amide}), 139.1 (C_2), 130.4 (C_5), 128.4 (C_3), 127.8 (C_4), 65.8 (CH_2OH), 50.5 (NCH), 40.4 (CH_3CHCH_3), 25.2 (C*i*-Pr), 23.2 (CH_3), 22.5 (CH_3).
FTIR ($CHCl_3$) cm^{-1}:	3438 (m, O–H), 3003 (w), 2959 (w), 1641 (s, C=O), 1537 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{11}H_{17}NO_2S$ $[M+H]^+$: 228.1053 found: 228.1045
M.p.:	67-70 °C
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.53 (UV, $KMnO_4$)



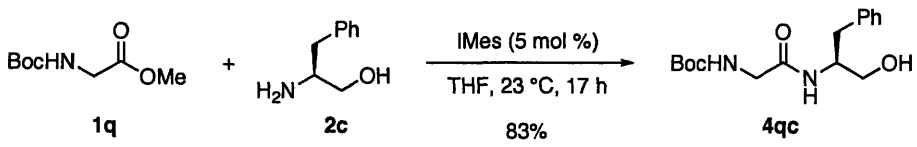
1a **2e** 99% **4ae**

<u>*N*-Phenylacetyl-L-Prolinol (4ae, Table 1, entry 20):</u>

Ester **1a** (283 μL, 1.97 mmol, 1.00 equiv) and L-prolinol (**2e**, 192 μL, 1.97 mmol, 1 equiv) were added sequentially via a gas-tight syringe to a solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) in THF (1.95 mL) at 23 °C under an argon atmosphere. After 4 h, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting yellow-residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4ae**[9] as a pale yellow oil (428 mg, 99%).

^{1}H NMR (500 MHz, $CDCl_3$, 20°C):	δ 7.33–7.36 (m, 2H, Ph**H**$_m$), 7.26–7.29 (m, 3H, Ph**H**$_{o,p}$), 5.08 (dd, *J* = 8.0, 2.5 Hz, 1H, O**H**), 4.25 (ddd, *J* = 14.1, 8.5, 2.5 Hz, 1H, NC**H**CH$_2$OH), 3.66–3.71 (m, 3H, PhC**H**$_2$, C**H**$_2$OH), 3.56–3.62 (m, 2H, C**H**$_2$OH, NC**H**$_2$), 3.45 (dt, *J* = 10.5, 7.0 Hz, 1H, NC**H**$_2$), 2.05 (dt, *J* = 19.9, 7.5 Hz, 1H, NCHC**H**$_2$CH$_2$), 1.91 (app-septet, *J* = 7.0 Hz, 1H, NCHC**H**$_2$CH$_2$), 1.85 (m, 1H, NCHCH$_2$C**H**$_2$), 1.57 (sextet, *J* = 7.0 Hz, 1H, NCHCH$_2$C**H**$_2$).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 172.7 (**C**$_{amide}$), 134.5 (Ph**C**$_{ipso}$), 129.1 (Ph**C**$_o$), 129.0 (Ph**C**$_m$), 127.2 (Ph**C**$_p$), 67.8 (NCHCH$_2$OH), 61.8 (NCH**C**H$_2$OH), 48.2 (N**C**H$_2$), 42.7 (Ph**C**H$_2$), 28.6 (NCH**C**H$_2$CH$_2$), 24.7 (NCHCH$_2$**C**H$_2$).
FTIR (thin film) cm^{-1}:	3383 (s, O–H), 3062 (w), 2954 (m), 1620 (s, C=O), 1429 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{13}H_{17}NO_2$ [M+Na]$^+$: 242.1151 found: 242.1148
TLC (5% MeOH in CH_2Cl_2) R*f*:	0.33 (UV, $KMnO_4$)

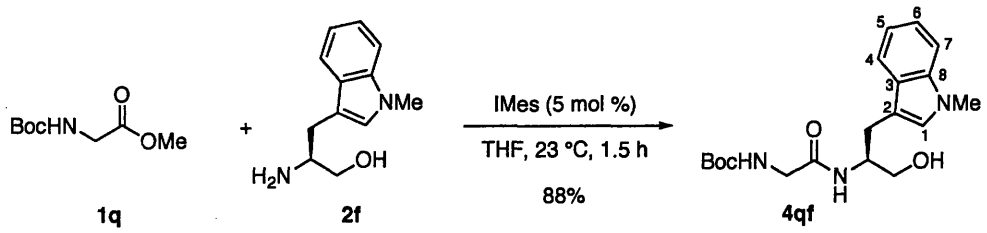
[9] For a previous synthesis of amide **4ae** by acylation of the phenylacetyl chloride, see: F. A. Davis, L. C. Vishwakarma, *Tetrahedron Lett.* **1985**, *26*, 3539–3542.



N-(N-Boc-Glycyl)-L-Phenylalaninol (4qc, Table 1, entry 21):

A solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) in THF (1.95 mL) was added to a suspension of *N*-Boc-glycine methyl ester (**1q**, 373 mg, 1.97 mmol, 1.00 equiv) and L-phenylalaninol (**2c**, 298 mg, 1.97 mmol, 1 equiv) via a gas-tight syringe under an argon atmosphere. Within 5 min, amide **4qc** began to precipitate. After 17 h, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting yellow-residue was purified by flash column chromatography on silica gel (5 →10% MeOH in CH_2Cl_2) to afford the amide **4qc** as a white crystalline solid (506 mg, 83%).

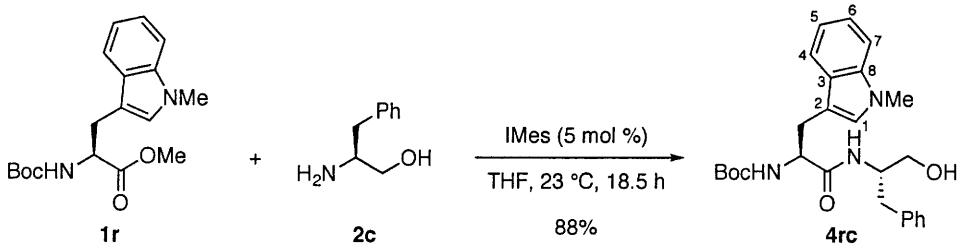
^{1}H NMR (500 MHz, $CDCl_3$, 20°C):	δ 7.30–7.33 (m, 2H, Ph**H**$_m$), 7.21–7.26 (m, 3H, Ph**H**$_{p,o}$), 6.34 (br-d, 1H, N$_{amide}$**H**), 5.10 (br-s, 1H, N$_{carbamate}$**H**), 4.19 (m, 1H, NC**H**), 3.75 (d, J = 5.5 Hz, 2H, C**H**$_2$CONH), 3.70 (m, 1H, C**H**$_2$OH), 3.59 (m, 1H, C**H**$_2$OH), 2.92 (d, J = 7.5 Hz, 1H, C**H**$_2$Ph), 2.89 (dd, J = 7.5, 4.5 Hz, 2H, C**H**$_2$Ph), 2.58–2.75 (br-d, 1H, O**H**), 1.46 (s, 9H, (C**H**$_3$)$_3$).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 170.1 (**C**$_{amide}$), 156.5 (**C**$_{carbamate}$), 137.7 (Ph**C**$_{ipso}$), 129.4 (Ph**C**$_o$), 128.8 (Ph**C**$_m$), 126.9 (Ph**C**$_p$), 80.6 (**C**(CH$_3$)$_3$), 63.7 (**C**H$_2$OH), 53.0 (N**C**H), 44.6 (BocNH**C**H$_2$), 37.2 (Ph**C**H$_2$), 28.5 (**C**H$_3$)$_3$).
FTIR ($CHCl_3$) cm^{-1}:	3424 (m, O–H), 2984 (m), 2935 (m), 1699 (s, C=O), 1674 (s, C=O).
HRMS (ESI) (*m/z*):	calc'd for $C_{16}H_{24}N_2O_4$ [M+H]$^+$: 309.1809 found: 309.1811
M.p.:	134–135 °C
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.49 (UV, ninhydrin)



N-(N-Boc-Glycyl)-L-1-Methyl-Tryptophanol (4qf, Table 1, entry 22):

A solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) in THF (1.95 mL) was added via a gas–tight syringe to a suspension of *N*-Boc-glycine methyl ester (**1q**, 373 mg, 1.97 mmol, 1.00 equiv) and L-1-methyl-tryptophanol (**2f**, 402 mg, 1.97 mmol, 1 equiv) under an argon atmosphere at 23 °C. After 1.5 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting yellow residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4qf** as a white foam (628 mg, 88%).

^{1}H NMR (500 MHz, DMSO-d_6, 20°C)	δ 7.61 (m, 2H, C_4**H**, N_{amide}**H**), 7.36 (d, J = 8.0 Hz, 1H, C_7**H**), 7.12 (t, J = 7.8 Hz, 1H, C_6**H**), 7.08 (s, 1H, C_1**H**), 7.01 (t, 1H, C_5**H**), 6.91 (br-t, J = 5.8 Hz, 1H, $N_{carbamate}$**H**), 4.76 (br-t, J = 5.0 Hz, 1H, O**H**), 3.94 (m, 1H, NC**H**), 3.72 (s, 3H, NC**H**$_3$), 3.54 (dd, J = 16.5, 6.5 Hz, 1H, BocNHC**H**$_2$) 3.49 (dd, J = 16.5, 6.0 Hz, 1H, BocNHC**H**$_2$), 3.30–3.40 (m, 2H, C**H**$_2$OH), 2.29 (dd, J = 14.5, 6.5 Hz, 1H, C**H**$_2$Ar), 2.74 (dd, J = 14.0, 6.3 Hz, 1H, C**H**$_2$Ar), 1.38 (s, 9H, (C**H**$_3$)$_3$).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 170.2 (C_{amide}), 156.4 ($C_{carbamate}$), 137.1 (C_8), 128.2 (C_3), 127.7 (C_1), 121.9 (C_4), 119.3 (C_5), 119.0 (C_6), 110.1 (C_7), 109.5 (C_2), 80.5 (**C**(CH$_3$)$_3$), 64.0 (CH$_2$-OH), 52.5 (NHCH), 44.6 (BocNHCH$_2$), 32.9 (NCH$_3$), 28.5 (C(**C**H$_3$)$_3$), 26.6 (**C**H$_2$Ar).
FTIR ($CHCl_3$) cm^{-1}:	3424 (m, O–H), 3004 (m), 2935 (m), 1706 (s, C=O), 1673 (s, C=O).
HRMS (ESI) (*m/z*):	calc'd for $C_{19}H_{27}N_3O_4$ $[M+H]^+$: 362.2074 found: 362.2077
M.p.:	64–66 °C
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.42 (UV, ninhydrin).



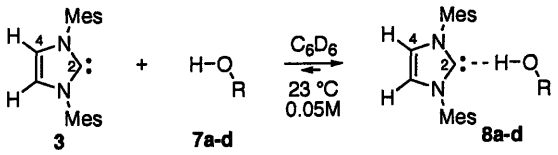
1r 2c 4rc

N-(N-Boc-1-Methyl-L-Tryptophanoyl)-L-Phenylalaninol (4rc-(*S*,*S*), Table 1, entry 23):

A solution of IMes (**3**, 30 mg, 98 μmol, 0.05 equiv) in THF (1.95 mL) was added via a cannula to a suspension of *N*-Boc-1-methyl-tryptophan methyl ester (**1r**, 655 mg, 1.97 mmol, 1.00 equiv) and L-phenylalaninol (**2c**, 298 mg, 1.97 mmol, 1 equiv) under an argon atmosphere. After 18.5 h, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting yellow-residue was purified by flash column chromatography on silica gel (2% MeOH in CH_2Cl_2) to afford the amide **4rc** as a white crystalline solid (781 mg, 88%). Chromatographic enrichment of amide **4rc** was not attempted (crude product, >94%de). The product was found to be >94%de and >98%ee by chiral HPLC analysis [Chirapak AD-H; 3.0 mL/min; 10% *i*-PrOH in hexanes; t_R(major-**4rc-*S*,*S***) = 8.12 min, t_R(minor-**4rc-*R*,*S***) = 11.8 min. t_R(not present-**4rc-*S*,*R***) = 9.9 min t_R(not present-**4rc-*R*,*R***) = 14.8 min]. The L-phenylalaninol (**2c**) and the precursor to ester **1r**, 1-methyl L-tryptophan, were used as received from Aldrich (>98%ee).

^{1}H NMR (500 MHz, $CDCl_3$, 20°C)	δ 7.66 (d, *J* = 8.0 Hz, 1H, C_4**H**), 7.14–7.33 (m, 6H, Ar**H**), 7.01 (m, 2H, Ar**H**), 6.90 (s, 1H, C_1**H**), 5.78 (br-s, 1H, N_{amide}**H**), 5.16 (br-s, 1H, $N_{carbamate}$**H**), 4.36 (br-s, 1H, BocNHC**H**), 4.01 (br-s, 1H, NC**H**) 3.74 (s, 3H, NC**H**$_3$), 3.32 (m, 3H, C**H**$_2$Ar and C**H**$_2$OH), 3.10 (dd, *J* = 14.0, 7.5 Hz, 1H, C**H**$_2$OH), 2.67 (dd, *J* = 14.0, 8.0 Hz, 1H, C**H**$_2$Ph), 2.60 (m, 1H, C**H**$_2$Ph), 2.08 (br-s, 1H, O**H**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 172.0 (**C**$_{amide}$), 155.7 (**C**$_{carbamate}$), 137.6 (**C**$_8$), 137.1 (Ph**C**$_{ipso}$), 129.3 (**C**$_3$), 128.6 (Ph**C**$_m$), 128.0 (**C**$_1$, Ph**C**$_o$), 126.7 (Ph**C**$_p$), 122.1 (**C**$_4$), 119.5 (**C**$_5$), 119.1 (**C**$_6$), 109.5 (**C**$_7$), 109.2 (**C**$_2$), 80.3 (**C**(CH$_3$)$_3$), 63.3 (**C**H$_2$OH), 55.8 (BocNH**C**H), 52.9 (NH**C**H), 36.8 (**C**H$_2$Ph), 32.8 (N**C**H$_3$), 28.6 (**C**H$_2$Ar), 28.4 (C(**C**H$_3$)$_3$).
FTIR ($CHCl_3$) cm^{-1}:	3422 (m, O–H), 3005 (m), 2935 (m), 1705 (s, C=O), 1669 (s, C=O).
HRMS (ESI) (*m/z*):	calc'd for $C_{26}H_{33}N_3O_4$ [M+H]$^+$: 452.2544 found: 452.2541
M.p.:	149–150 °C
TLC (10% MeOH in CH_2Cl_2) R*f*:	0.50 (UV, $KMnO_4$)

IMes–Alcohol Complexes (Table 2)



Representative Experimental Procedure for Complex 8b (Table 2, entry 2):

Anhydrous methanol (14.0 μL, 32 μmol, 1.0 equiv) was added to a solution of IMes (**3**, 100 mg, 32.0 μmol, 1 equiv) and C_6D_6 (700 μL) in an NMR-tube under a nitrogen atmosphere in a glove-box. Alternatively, this complex is quantitatively formed upon removal of excess methanol from a solution of IMes in methanol under reduced pressure. Slow crystallization of complex **8b** from toluene affords high quality crystals that have the same ^{1}H NMR (C_6D_6) spectrum as complexes formed in solution.

IMes–HOMe (8b):

^{1}H NMR (500 MHz, C_6D_6, 20 °C, 0.05M): δ 6.78 (s, 4H, Ar**H**), 6.38 (s, 2H, C_4**H**), 4.37 (s, 1H, O**H**), 3.10 (s, 3H, CH_3OH), 2.13 (s, 18H, ArCH_3).

^{13}C NMR (125.8 MHz, C_6D_6, 20 °C, 0.5M): δ 209.7 (**C**$_2$), 138.5 (Ar**C**$_{ipso}$), 138.1 (Ar**C**$_o$), 135.6 (Ar**C**$_p$), 129.5 (Ar**C**$_m$), 121.2 (**C**$_4$), 48.1 (**C**H_3OH), 21.4 (p-**C**H_3), 18.2 (o-**C**H_3).

The IMes–*tert*-butanol, –ethanolamine and –benzyl alcohol complexes (Table 2, entries 1 and 3-4) were prepared as described above and the data is shown below. For completeness and direct comparison, the relevant ^{1}H and ^{13}C NMR data for IMes (**3**) is listed below:

IMes–HO^{t}Bu (8a):

^{1}H NMR (500 MHz, C_6D_6, 20 °C, 0.05M): δ 6.80 (s, 4H, Ar**H**), 6.43 (s, 2H, C_4**H**), 2.81 (s, 1H, O**H**), 2.16 (s, 12H, **C**H_3), 2.15 (s, 6H, **C**H_3), 1.07 (s, 3H, C(**C**H_3)$_3$).

IMes–HOCH$_2$CH$_2$NH$_2$ (8c):

^{1}H NMR (500 MHz, C_6D_6, 20 °C, 0.05M): δ 6.78 (s, 4H, Ar**H**), 6.37 (s, 2H, C_4**H**), 5.24 (s, 1H, O**H**), 3.27 (t, J = 5.3 Hz, **C**H_2OH), 2.45 (t, J = 5.0 Hz, **C**H_2NH$_2$), 2.14 (s, 6H, Ar(**C**H_3)$_p$), 2.12 (s, 12H, Ar(**C**H_3)$_o$).

IMes–HOCH$_2$Ph (8d):

^{1}H NMR (500 MHz, C_6D_6, 20 °C, 0.05M): δ 7.05–7.21 (m, 5H, C_6**H**$_5$), 6.76 (s, 4H, Ar**H**), 6.33 (s, 2H, C_4**H**), 5.8–6.2 (br-s, 1H, O**H**),

4.38 (s, 2H, CH_2), 2.14 (s, 6H, Ar(CH_3)$_p$), 2.08 (s, 12H, Ar(CH_3)$_o$).

IMes–HOCPh$_3$ (8e):

^{1}H NMR (500 MHz, C_6D_6, 20 °C, 0.05M): δ 7.30 (m, 6H, Ph_3H_o), 7.01 (m, 9H, Ph_3H_p,Ph_3H_m), 6.79 (s, 4H, ArH), 6.34 (s, 2H, C_4H), 5.93 (br s, 1H, OH), 2.16 (s, 6H, Ar(CH_3)$_p$), 2.09 (s, 12H, Ar(CH_3)$_o$).

IMes–HOCH$_2$CF$_3$ (8f):

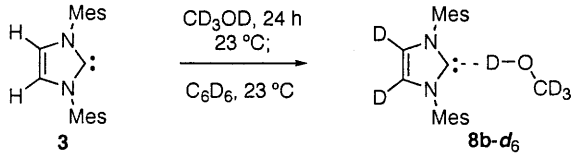
^{1}H NMR (500 MHz, C_6D_6, 20 °C, 0.5M) major resonances: δ 10.75 (br s, 1H, OH), 6.73 (s, 4H, ArH), 6.49 (s, 2H, C_4H), 3.66 (q, J_{HF} = 9.7 Hz, 2H, CF_3CH_2), 2.12 (s, 6H, Ar(CH_3)$_p$), 1.95 (s, 12H, Ar(CH_3)$_o$).

^{13}C NMR (125.8 MHz, C_6D_6, 20 °C, 0.5M) major resonances: δ 194.7 (C_2), 138.8 (ArC_{ipso}), 137.0 (ArC_o), 135.3 (ArC_p), 129.6 (ArC_m), 127.3 (q, J^1_{CF} = 280.9 Hz, CF_3) 121.9 (C_4), 60.4 (app q, J^2_{CF} = 32.4 Hz, CH_2CF_3), 21.3 (*p*-CH_3), 17.9 (*o*-CH_3).

IMes (3):

^{1}H NMR (500 MHz, C_6D_6, 20 °C, 0.5 M): δ 6.81 (s, 4H, ArH), 6.50, (s, 2H, C_4H), 2.15 (s, 6H, Ar(CH_3)$_p$), 2.07 (s, 12H, Ar(CH_3)$_o$).

^{13}C NMR (125.8 MHz, C_6D_6, 20 °C, 0.5 M): δ 219.4 (C_2), 139.6 (ArC_{ipso}), 137.6 (ArC_o), 135.7 (ArC_p), 129.5 (ArC_m), 120.9 (C_4), 21.4 (*p*-CH_3), 18.4 (*o*-CH_3).



IMes (**3**, 100 mg, 32.0 μmol, 1.0 equiv) was dissolved in methanol-d_4 (700 μL) and kept under argon atmosphere for 24 h. Removal of the methanol-d_4 under reduced pressure quantitatively afforded the hexadeuterated complex **8b-d_6**.[10] Dissolution of the residue in C_6D_6 (700 μL) followed by NMR analysis indicated that the complex was >95% deuterated at the $C_{4,5}$.

IMes-d_2–DOMe-d_4 (8b-d_6):

^{1}H NMR (500 MHz, C_6D_6, 20 °C, 0.5M): δ 6.77 (s, 4H, ArH), 6.39, (s, <0.1H, $C_{4,5}$H-residual), 5.88 (br-s, OH-residual), 3.11 (pentet, J = 1.5 Hz, CD_2HOD-residual), 2.11 (s, 6H, *p*-CH_3), 2.06 (s, 12H, *o*-CH_3).

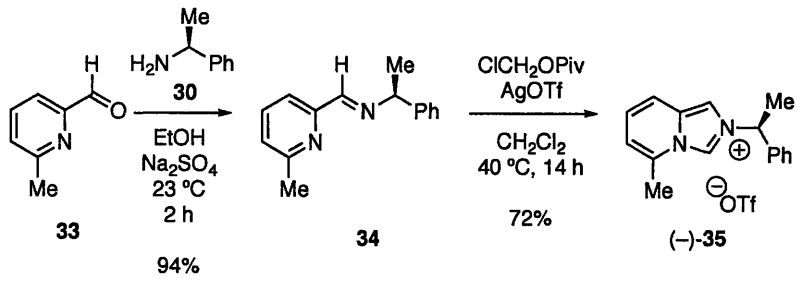
[10] For prior reports regarding preparation of doubly deuterated NHCs, see: M. K. Denk, J. M. Rodezno, *J. Organometal. Chem.* **2000**, *608*, 122-125 and M. L. Cole, C. Jones, P. C. Junk, *New J. Chem.* **2002**, *262*, 1296–1303.

^{13}C NMR (125.8 MHz, C_6D_6, 20 °C, 0.5M): δ 203.9 (**C**$_2$), 138.4 (Ar**C**$_o$), 137.9 (Ar**C**$_{ipso}$), 135.5 (Ar**C**$_p$), 129.5 (Ar**C**$_m$), 121.1 (t, J_{CD} = 27.0 Hz, **C**$_4$), 48.0 (heptet, J_{CD} = 20.9 Hz, **C**D_3OD), 21.3 (p-**C**H_3), 18.2 (o-**C**H_3).

IMes-d_2– DOMe-d_4 (8b-d_6):

^{1}H NMR (500 MHz, THF-d_8, 20 °C, 0.5 M): δ 6.96 (s, 4H, Ar**H**), 7.11, (s, <0.15H, $C_{4,5}$**H**-residual), 5.33 (br-s, O**H**-residual), 2.31 (s, 6H, p-**C**H_3), 2.09 (s, 12H, o-**C**H_3).

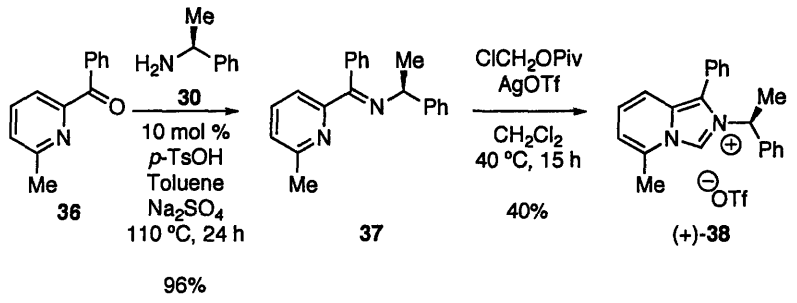
^{13}C NMR (125.8 MHz, THF-d_8, 20 °C, 0.5 M): δ 212.4 (**C**$_2$), 139.3 (Ar**C**$_{ipso}$), 138.2 (Ar**C**$_p$), 136.0 (Ar**C**$_o$), 129.6 (Ar**C**$_m$), 121.6 (t, J_{CD} = 29.4 Hz, **C**$_4$), 47.3 (heptet, J_{CD} = 20.8 Hz, **C**D_3OD), 21.3 (p-**C**H_3), 18.2 (o-**C**H_3).



5-Methyl-2-(1-*S*-phenylethyl)-imidazo[1,5-a]pyridin-2-ium triflate ((–)-35):

To a solution of the aldehyde **33** (1.99 g, 16.43 mmol, 1 equiv) in absolute EtOH (32 mL) was added *S*-α-methylbenzylamine **30** (2.09 mL, 16.43 mmol, 1.00 equiv) followed by Na_2SO_4 (3.2 g). The suspension was stirred for 2 h, and the Na_2SO_4 was removed by gravity filtration. The resulting solution was concentrated in vacuo to yield 3.47 g of a light orange oil that was used without further purification (94 % crude yield). To a solution of the imine **34** (3.47 g, 15.47 mmol, 1 equiv) in CH_2Cl_2 (150 mL) was added chloromethylpivalate (3.14 mL, 21.66 mmol, 1.40 equiv) and AgOTf (4.77 g, 18.56 mmol, 1.2 equiv). The suspension was heated to 40 °C in the dark for 14 h. The dark suspension was cooled to 23 °C and was filtered through a plug of Celite (3" diameter × 1" height). The filter cake was rinsed with MeOH (2 × 20 mL) and the filtrate was concentrated in vacuo to yield 8.8 g of a dark purple oil. Purification of the crude by flash column chromatography (1" × 10.5", 100 % CH_2Cl_2 → 2 % MeOH in CH_2Cl_2) afforded triflate **35** as a light beige powder (4.14 g, 72 %). The e.e. of the salt was determined to be 98.6 % by conversion to the thiourea **39** and analysis by HPLC (Chirapak AD-H, 30 % isopropanol in hexanes, 1.0 mL/min, t_{major} = 6.99 min, t_{minor} = 4.83 min).

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C):	δ 10.80 (s, 1H, C_3**H**), 7.61 (s, 1H, C_1**H**), 7.52-7.54 (m, 2H, Ph**H**), 7.41-7.48 (m, 4H, Ph**H** and C_8**H**), 7.16 (dd, *J* = 9.5 Hz, 7.0 Hz, 1H, C_7**H**), 6.86 (dt, *J* = 7.0 Hz, 1.0 Hz, 1H, C_6**H**), 6.30 (q, *J* = 7.0 Hz, 1H, CH_3**CH**), 2.83 (s, 3H, Pyr-CH_3), 2.13 (d, *J* = 7.0 Hz, 3H, CH_3CH).
^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C):	δ 137.9, 133.5, 131.1, 129.7, 129.6, 127.4, 125.6, 123.5, 120.9 (q, J_{CF} = 320.2 Hz, CF_3), 116.9, 116.1, 111.8, 61.4 (CH_3CHPh), 21.0 (CH_3-Pyr), 18.2 (CH_3CHPh).
FTIR (neat) cm^{-1}:	3106 (m), 1662 (w), 1562 (w), 1457 (w), 1259 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{16}H_{17}N_2$ [M+]: 237.1386 found: 237.1393
$[\alpha]^{20}_D$:	–43 (*c* = 0.49, $CHCl_3$)
TLC (10 % MeOH in CH_2Cl_2), R*f*:	0.48 (UV, $KMnO_4$)



5-Methyl-1-phenyl-2-(1-*S*-phenylethyl)-imidazo[1,5-a]pyridin-2-ium triflate ((+)-38):

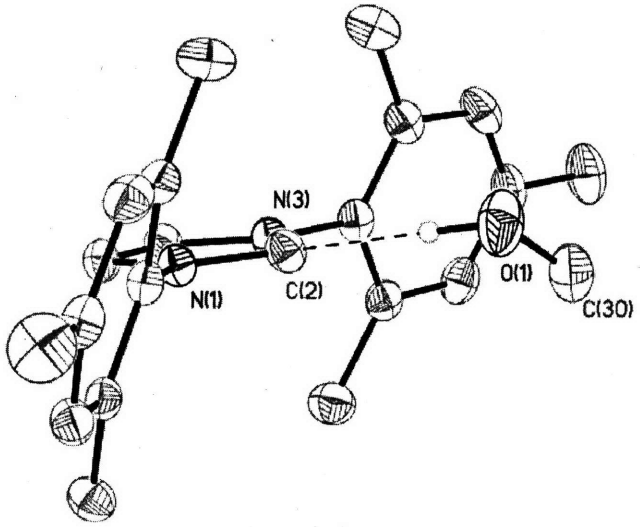
To a solution of the ketone **36** (150 mg, 0.760 mmol, 1 equiv) in toluene (4.00 mL) was added *S*-α-methylbenzylamine **30** (107 μL, 0.837 mmol, 1.10 equiv) followed by *p*-TsOH•H_2O (14.5 mg) and Na_2SO_4 (1.00 g). The suspension was heated to 110 °C for 24 h then allowed to cool to 23 °C whereupon the ammonium tosylate precipitated as long white needles. The solvent was concentrated in vacuo and the light orange gel was diluted with hexanes (2.0 mL) and gravity filtered. The filter cake was washed with hexanes (3 × 2 mL) and the filtrate was concentrated in vacuo to yield 220 mg (96 %) of an orange oil which was used without further purification. The imine was found to be a 47:53 ratio of isomers by ^{1}H NMR. To a solution of the imine **37** (220 mg, 0.732 mmol, 1 equiv) in CH_2Cl_2 (7.00 mL) was added chloromethylpivalate (150 μL, 1.02 mmol, 1.40 equiv) and AgOTf (226 mg, 0.878 mmol, 1.2 equiv). The suspension was heated to 40 °C in the dark for 15 h. The black suspension was cooled to 23 °C and was filtered through a plug of Celite (1" diameter × 0.5" height). The filter cake was rinsed with MeOH (3 × 3 mL) and the filtrate was concentrated in vacuo to yield a thick red oil. Purification of the crude by flash column chromatography (1" × 10", 1 % MeOH in CH_2Cl_2 → 10 % MeOH in CH_2Cl_2) afforded a red oil which was diluted with CH_2Cl_2 (1 mL) and the product was precipitated by addition of Et_2O (10 mL). Evaporation of the solvents yielded the triflate **38** as an off-white solid (136 mg, 40 %). The e.e. of the salt was determined to be 98.3 % by conversion to the thiourea **40** and analysis by HPLC (Chirapak AD-H, 100% hexanes to 30 % isopropanol in hexanes over 10 min, 2.0 mL/min, t_{major} = 5.14 min, t_{minor} = 4.75 min).

^{1}H NMR (500 MHz, $CDCl_3$, 20 °C): δ 10.07 (s, 1H, C_3**H**), 7.63, (app tt, *J* = 7.8 Hz, 1.3 Hz, 1H, Pyr-Ph$\mathbf{H}_{para}$), 7.56 (t, *J* = 7.8 Hz, 2H, CHPh**H**), 7.24-7.28 (m, 5H, CHPh**H** and Pyr-Ph**H**), 7.25 (d, *J* = 10.0 Hz, 1H, C_8**H**), 7.16 (m, 2H, Pyr-Ph**H**), 7.12 (dd, *J* = 9.5 Hz, 7.0 Hz, 1H, C_7**H**), 6.90 (dt, *J* = 6.5 Hz, 0.5 Hz, 1H, C_6**H**), 5.80 (q, *J* = 7.0 Hz, 1H, C**H**Ph), 2.95 (s, 3H, Pyr-C$\mathbf{H}_3$), 2.24 (d, *J* = 7.5 Hz, 3H, CHC$\mathbf{H}_3$).

^{13}C NMR (125.8 MHz, $CDCl_3$, 20 °C): δ 138.4, 134.5, 131.2, 129.8, 129.5, 129.3, 129.1, 126.9, 125.9, 125.6, 124.9, 123.3, 120.9 (q, *J* = 320.5 Hz, **C**F_3), 117.1, 115.2, 60.3 (CH_3**C**HPh), 21.7 (**C**H_3-Pyr), 18.3 (**C**H_3CHPh).

FTIR (neat) cm^{-1}:	3106 (m), 2989 (w), 1661 (m), 1554 (m), 1456 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{22}H_{21}N_2$ [M+]: 313.1699 found: 313.1692
$[\alpha]^{20}_D$:	+5 (*c* = 0.505, $CHCl_3$)
TLC (10 % MeOH in CH_2Cl_2), R*f*:	0.48 (UV, $KMnO_4$)

X-ray crystal structure of *N,N*-bismesitylimidazolylidene-methanol complex 8b:



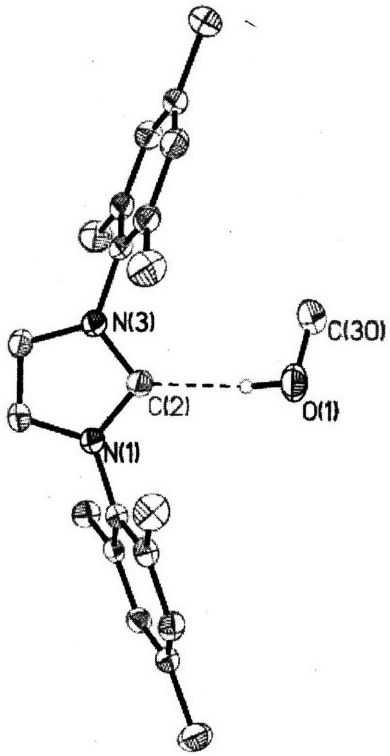


Table 1. Crystal data and structure refinement for 04152final.

Identification code	04152final	
Empirical formula	C22 H28 N2 O	
Formula weight	336.46	
Temperature	123(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 14.9026(16) Å	α= 90°.
	b = 16.6125(17) Å	β= 94.235(2)°.
	c = 7.8304(8) Å	γ = 90°.
Volume	1933.3(3) $Å^3$	
Z	4	
Density (calculated)	1.156 Mg/m^3	
Absorption coefficient	0.071 mm^{-1}	
F(000)	728	
Crystal size	0.15 x 0.10 x 0.08 mm^3	
Theta range for data collection	1.84 to 25.00°.	
Index ranges	-17<=h<=17, 0<=k<=19, 0<=l<=9	
Reflections collected	25954	
Independent reflections	3411 [R(int) = 0.0501]	
Completeness to theta = 25.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9944 and 0.8925	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3411 / 1 / 234	
Goodness-of-fit on F^2	1.175	
Final R indices [I>2sigma(I)]	R1 = 0.0509, wR2 = 0.1134	
R indices (all data)	R1 = 0.0676, wR2 = 0.1214	
Largest diff. peak and hole	0.588 and -0.167 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 04152final. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	6662(1)	746(1)	7418(2)	22(1)
N(3)	7698(1)	67(1)	6389(2)	25(1)
C(2)	7305(1)	195(1)	7881(2)	25(1)
C(4)	7307(1)	522(1)	5047(2)	26(1)
C(5)	6654(1)	952(1)	5695(2)	25(1)
C(11)	8447(1)	-475(1)	6261(2)	25(1)
C(12)	8299(1)	-1212(1)	5450(2)	27(1)
C(13)	9030(1)	-1725(1)	5386(3)	33(1)
C(14)	9878(1)	-1525(1)	6096(3)	33(1)
C(15)	9996(1)	-783(1)	6878(3)	33(1)
C(16)	9291(1)	-243(1)	6988(2)	28(1)
C(17)	7386(1)	-1448(1)	4676(3)	37(1)
C(18)	10660(2)	-2099(2)	6002(3)	47(1)
C(19)	9440(1)	553(1)	7864(3)	40(1)
C(21)	6076(1)	1074(1)	8633(2)	22(1)
C(22)	5174(1)	852(1)	8531(2)	21(1)
C(23)	4633(1)	1157(1)	9750(2)	24(1)
C(24)	4969(1)	1669(1)	11035(2)	25(1)
C(25)	5872(1)	1874(1)	11096(2)	27(1)
C(26)	6443(1)	1585(1)	9914(2)	25(1)
C(27)	4777(1)	295(1)	7165(2)	28(1)
C(28)	4367(2)	1991(1)	12337(3)	38(1)
C(29)	7421(1)	1816(1)	10038(3)	35(1)
O(1)	7891(1)	-406(1)	11145(2)	42(1)
C(30)	8177(2)	-1189(1)	10717(3)	40(1)

Table 3. Bond lengths [Å] and angles [°] for 04152final.

N(1)-C(2)	1.355(2)	C(26)-C(29)	1.503(3)
N(1)-C(5)	1.392(2)	O(1)-C(30)	1.415(3)
N(1)-C(21)	1.444(2)		
N(3)-C(2)	1.363(2)	C(2)-N(1)-C(5)	112.42(15)
N(3)-C(4)	1.388(2)	C(2)-N(1)-C(21)	121.90(15)
N(3)-C(11)	1.442(2)	C(5)-N(1)-C(21)	125.67(15)
C(4)-C(5)	1.338(3)	C(2)-N(3)-C(4)	112.37(16)
C(11)-C(12)	1.389(3)	C(2)-N(3)-C(11)	122.76(15)
C(11)-C(16)	1.396(3)	C(4)-N(3)-C(11)	124.87(15)
C(12)-C(13)	1.388(3)	N(1)-C(2)-N(3)	102.53(16)
C(12)-C(17)	1.500(3)	C(5)-C(4)-N(3)	106.33(16)
C(13)-C(14)	1.384(3)	C(4)-C(5)-N(1)	106.35(16)
C(14)-C(15)	1.381(3)	C(12)-C(11)-C(16)	122.49(18)
C(14)-C(18)	1.512(3)	C(12)-C(11)-N(3)	118.99(17)
C(15)-C(16)	1.389(3)	C(16)-C(11)-N(3)	118.52(17)
C(16)-C(19)	1.498(3)	C(13)-C(12)-C(11)	117.43(18)
C(21)-C(22)	1.390(3)	C(13)-C(12)-C(17)	121.00(19)
C(21)-C(26)	1.396(3)	C(11)-C(12)-C(17)	121.58(18)
C(22)-C(23)	1.390(3)	C(14)-C(13)-C(12)	122.2(2)
C(22)-C(27)	1.503(3)	C(15)-C(14)-C(13)	118.38(19)
C(23)-C(24)	1.382(3)	C(15)-C(14)-C(18)	120.8(2)
C(24)-C(25)	1.387(3)	C(13)-C(14)-C(18)	120.9(2)
C(24)-C(28)	1.504(3)	C(14)-C(15)-C(16)	122.16(19)
C(25)-C(26)	1.388(3)	C(15)-C(16)-C(11)	117.32(19)

C(15)-C(16)-C(19)	120.73(18)
C(11)-C(16)-C(19)	121.95(18)
C(22)-C(21)-C(26)	121.91(17)
C(22)-C(21)-N(1)	119.43(16)
C(26)-C(21)-N(1)	118.62(16)
C(23)-C(22)-C(21)	118.13(17)
C(23)-C(22)-C(27)	119.70(16)
C(21)-C(22)-C(27)	122.17(16)
C(24)-C(23)-C(22)	121.80(18)
C(23)-C(24)-C(25)	118.35(17)
C(23)-C(24)-C(28)	120.68(18)
C(25)-C(24)-C(28)	120.97(18)
C(24)-C(25)-C(26)	122.23(18)
C(25)-C(26)-C(21)	117.58(17)
C(25)-C(26)-C(29)	120.51(18)
C(21)-C(26)-C(29)	121.91(17)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 04152final. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	22(1)	25(1)	20(1)	1(1)	1(1)	2(1)
N(3)	22(1)	30(1)	22(1)	3(1)	3(1)	3(1)
C(2)	22(1)	30(1)	24(1)	1(1)	2(1)	1(1)
C(4)	26(1)	31(1)	21(1)	3(1)	1(1)	-1(1)
C(5)	27(1)	27(1)	22(1)	4(1)	-1(1)	1(1)
C(11)	23(1)	31(1)	21(1)	5(1)	8(1)	4(1)
C(12)	27(1)	32(1)	24(1)	6(1)	6(1)	0(1)
C(13)	38(1)	31(1)	30(1)	4(1)	9(1)	6(1)
C(14)	29(1)	46(1)	24(1)	8(1)	7(1)	12(1)
C(15)	21(1)	54(1)	25(1)	5(1)	2(1)	3(1)
C(16)	25(1)	38(1)	23(1)	4(1)	4(1)	1(1)
C(17)	32(1)	38(1)	43(1)	-2(1)	3(1)	-3(1)
C(18)	42(1)	60(2)	40(1)	8(1)	5(1)	24(1)
C(19)	32(1)	48(1)	39(1)	-6(1)	0(1)	-5(1)
C(21)	24(1)	20(1)	20(1)	3(1)	2(1)	3(1)
C(22)	24(1)	19(1)	20(1)	2(1)	-2(1)	1(1)
C(23)	22(1)	25(1)	25(1)	2(1)	1(1)	2(1)
C(24)	31(1)	21(1)	22(1)	2(1)	3(1)	4(1)
C(25)	37(1)	22(1)	21(1)	-3(1)	-1(1)	-2(1)
C(26)	27(1)	22(1)	26(1)	4(1)	-1(1)	-1(1)
C(27)	26(1)	31(1)	26(1)	-5(1)	-2(1)	-1(1)
C(28)	44(1)	39(1)	34(1)	-7(1)	9(1)	3(1)
C(29)	31(1)	37(1)	37(1)	-5(1)	0(1)	-10(1)
O(1)	60(1)	37(1)	29(1)	0(1)	-2(1)	7(1)
C(30)	41(1)	43(1)	36(1)	9(1)	-1(1)	7(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 04152final.

	x	y	z	U(eq)
H(4)	7471	528	3897	31
H(5)	6262	1325	5097	30
H(13)	8945	-2233	4836	39
H(15)	10577	-638	7357	40
H(17A)	7383	-2024	4404	56
H(17B)	7245	-1138	3625	56
H(17C)	6934	-1337	5492	56
H(18A)	10453	-2591	5407	71
H(18B)	10904	-2233	7164	71
H(18C)	11130	-1844	5376	71
H(18D)	11205	-1854	6557	71
H(18E)	10754	-2212	4800	71
H(18F)	10528	-2602	6588	71
H(19A)	10085	675	7973	59
H(19B)	9212	531	9005	59
H(19C)	9121	975	7187	59
H(23)	4015	1010	9699	29
H(25)	6109	2224	11977	32
H(27A)	4631	599	6109	42
H(27B)	4227	50	7546	42
H(27C)	5212	-129	6950	42
H(28A)	4717	2341	13144	58
H(28B)	4119	1541	12962	58
H(28C)	3875	2299	11754	58
H(28D)	3757	1780	12096	58
H(28E)	4355	2580	12278	58
H(28F)	4599	1822	13485	58
H(29A)	7603	1953	8897	53
H(29B)	7783	1363	10501	53
H(29C)	7514	2282	10799	53
H(1O)	7683	-195	10176	51
H(30A)	8559	-1156	9753	60
H(30B)	7650	-1524	10395	60
H(30C)	8519	-1428	11706	60

Table 6. Torsion angles [°] for 04152final.

C(5)-N(1)-C(21)-C(26)	-109.9(2)
C(4)-N(3)-C(11)-C(16)	106.2(2)
C(2)-N(1)-C(5)-C(4)	0.0(2)
C(2)-N(3)-C(4)-C(5)	0.3(2)
C(2)-H(1O)-O(1)-C(30)	-25.1(12)
N(1)-C(2)-H(1O)-O(1)	175.6(10)

Symmetry transformations used to generate equivalent atoms:

X-ray crystal structure of *N*,*N*-bismesitylimidazolylidene-triphenylmethanol complex 8e:

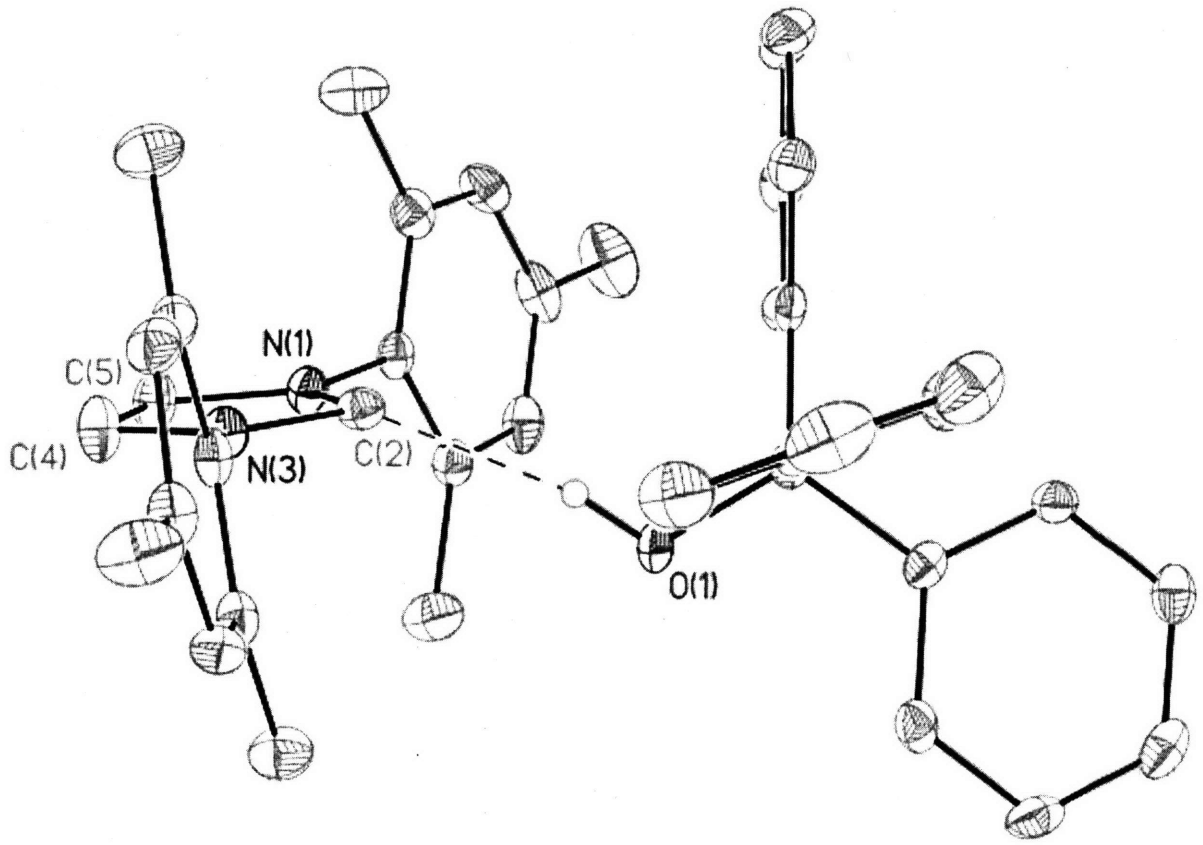


Table 7. Crystal data and structure refinement for 04150.

Identification code	04150	
Empirical formula	C40 H40 N2 O	
Formula weight	564.74	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 10.5053(9) Å	α= 76.44(3)°.
	b = 10.7511(9) Å	β= 83.54(3)°.
	c = 16.2815(14) Å	γ = 63.13(3)°.
Volume	1594.5(2) $Å^3$	
Z	2	
Density (calculated)	1.176 Mg/m^3	
Absorption coefficient	0.070 mm^{-1}	
F(000)	604	
Crystal size	0.08 x 0.08 x 0.05 mm^3	
Theta range for data collection	2.17 to 26.73°.	
Index ranges	-13<=h<=13, -13<=k<=13, 0<=l<=20	
Reflections collected	6758	
Independent reflections	6758 [R(int) = 0.0000]	
Completeness to theta = 26.73∞	99.7 %	
Max. and min. transmission	0.9965 and 0.9944	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6758 / 1 / 396	
Goodness-of-fit on F^2	1.148	
Final R indices [I>2sigma(I)]	R1 = 0.0793, wR2 = 0.1571	
R indices (all data)	R1 = 0.1060, wR2 = 0.1672	
Largest diff. peak and hole	0.400 and -0.317 $e.Å^{-3}$	

Table 8. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å ^{2}x 10^3) for 04150. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	3935(2)	7613(2)	3268(1)	19(1)
C(30)	3275(3)	7074(3)	2820(2)	16(1)
C(31)	4299(3)	6313(3)	2150(2)	16(1)
C(32)	5576(3)	6399(3)	1949(2)	24(1)
C(33)	6501(3)	5691(3)	1356(2)	29(1)
C(34)	6161(3)	4881(3)	959(2)	30(1)
C(35)	4884(3)	4792(3)	1149(2)	29(1)
C(36)	3966(3)	5498(3)	1739(2)	23(1)
C(41)	2996(3)	5937(3)	3478(2)	15(1)
C(42)	1760(3)	5763(3)	3492(2)	17(1)
C(43)	1577(3)	4690(3)	4087(2)	21(1)
C(44)	2622(3)	3793(3)	4673(2)	23(1)
C(45)	3861(3)	3950(3)	4667(2)	23(1)
C(46)	4047(3)	5009(3)	4072(2)	19(1)
C(51)	1881(3)	8306(3)	2429(2)	16(1)
C(52)	854(3)	9062(3)	2975(2)	20(1)
C(53)	-419(3)	10193(3)	2669(2)	23(1)
C(54)	-679(3)	10610(3)	1809(2)	24(1)
C(55)	331(3)	9882(3)	1265(2)	24(1)
C(56)	1606(3)	8735(3)	1573(2)	19(1)
C(2)	4305(3)	10119(3)	2542(2)	16(1)
N(1)	3572(2)	11252(2)	2919(1)	16(1)
C(11)	2163(3)	11626(3)	3287(2)	16(1)
C(12)	995(3)	12580(3)	2777(2)	20(1)
C(13)	-353(3)	12995(3)	3149(2)	24(1)
C(14)	-543(3)	12457(3)	3991(2)	25(1)
C(15)	648(3)	11496(3)	4467(2)	23(1)
C(16)	2020(3)	11060(3)	4129(2)	19(1)
C(17)	1187(3)	13113(3)	1854(2)	32(1)
C(18)	-2026(3)	12915(4)	4374(2)	41(1)
C(19)	3306(3)	10022(3)	4657(2)	29(1)
C(5)	4287(3)	12081(3)	2874(2)	23(1)
C(4)	5500(3)	11471(3)	2457(2)	23(1)
N(3)	5500(2)	10288(2)	2256(1)	17(1)
C(21)	6632(3)	9370(3)	1780(2)	16(1)
C(22)	7705(3)	8110(3)	2212(2)	17(1)
C(23)	8805(3)	7280(3)	1738(2)	18(1)
C(24)	8865(3)	7665(3)	862(2)	19(1)
C(25)	7758(3)	8906(3)	459(2)	19(1)
C(26)	6632(3)	9780(3)	902(2)	18(1)
C(27)	7667(3)	7672(3)	3159(2)	23(1)
C(28)	10108(3)	6763(3)	367(2)	27(1)
C(29)	5468(3)	11148(3)	438(2)	25(1)

Table 9. Bond lengths [Å] and angles [°] for 04150.

O(1)-C(30)	1.423(3)
O(1)-H(1O)	0.851(17)
C(30)-C(51)	1.538(4)
C(30)-C(41)	1.539(3)
C(30)-C(31)	1.542(4)
C(31)-C(32)	1.383(4)
C(31)-C(36)	1.395(4)
C(32)-C(33)	1.385(4)
C(32)-H(32)	0.9500
C(33)-C(34)	1.379(4)
C(33)-H(33)	0.9500
C(34)-C(35)	1.382(4)
C(34)-H(34)	0.9500

C(35)-C(36)	1.378(4)
C(35)-H(35)	0.9500
C(36)-H(36)	0.9500
C(41)-C(42)	1.390(4)
C(41)-C(46)	1.394(4)
C(42)-C(43)	1.394(4)
C(42)-H(42)	0.9500
C(43)-C(44)	1.376(4)
C(43)-H(43)	0.9500
C(44)-C(45)	1.385(4)
C(44)-H(44)	0.9500
C(45)-C(46)	1.384(4)
C(45)-H(45)	0.9500
C(46)-H(46)	0.9500
C(51)-C(56)	1.381(4)
C(51)-C(52)	1.395(4)
C(52)-C(53)	1.382(4)
C(52)-H(52)	0.9500
C(53)-C(54)	1.386(4)
C(53)-H(53)	0.9500
C(54)-C(55)	1.373(4)
C(54)-H(54)	0.9500
C(55)-C(56)	1.391(4)
C(55)-H(55)	0.9500
C(56)-H(56)	0.9500
C(2)-N(1)	1.359(3)
C(2)-N(3)	1.364(3)
N(1)-C(5)	1.388(3)
N(1)-C(11)	1.445(3)
C(11)-C(16)	1.386(4)
C(11)-C(12)	1.392(4)
C(12)-C(13)	1.390(4)
C(12)-C(17)	1.504(4)
C(13)-C(14)	1.387(4)
C(13)-H(13)	0.9500
C(14)-C(15)	1.381(4)
C(14)-C(18)	1.514(4)
C(15)-C(16)	1.389(4)
C(15)-H(15)	0.9500
C(16)-C(19)	1.503(4)
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(18)-H(18D)	0.9800
C(18)-H(18E)	0.9800
C(18)-H(18F)	0.9800
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(5)-C(4)	1.332(4)
C(5)-H(2)	0.9500
C(4)-N(3)	1.386(3)
C(4)-H(3)	0.9500
N(3)-C(21)	1.442(3)
C(21)-C(26)	1.395(4)
C(21)-C(22)	1.397(4)
C(22)-C(23)	1.385(4)
C(22)-C(27)	1.506(4)
C(23)-C(24)	1.390(4)
C(23)-H(23)	0.9500
C(24)-C(25)	1.387(4)
C(24)-C(28)	1.510(4)
C(25)-C(26)	1.387(4)
C(25)-H(25)	0.9500
C(26)-C(29)	1.513(4)
C(27)-H(27A)	0.9800
C(27)-H(27B)	0.9800
C(27)-H(27C)	0.9800
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800
C(29)-H(29A)	0.9800
C(29)-H(29B)	0.9800
C(29)-H(29C)	0.9800

C(30)-O(1)-H(1O)	112(2)
O(1)-C(30)-C(51)	109.0(2)
O(1)-C(30)-C(41)	105.7(2)
C(51)-C(30)-C(41)	111.8(2)
O(1)-C(30)-C(31)	110.9(2)
C(51)-C(30)-C(31)	112.1(2)
C(41)-C(30)-C(31)	107.1(2)
C(32)-C(31)-C(36)	118.3(3)
C(32)-C(31)-C(30)	121.3(2)
C(36)-C(31)-C(30)	120.4(2)
C(31)-C(32)-C(33)	120.9(3)
C(31)-C(32)-H(32)	119.6
C(33)-C(32)-H(32)	119.6
C(34)-C(33)-C(32)	120.2(3)
C(34)-C(33)-H(33)	119.9
C(32)-C(33)-H(33)	119.9
C(33)-C(34)-C(35)	119.6(3)
C(33)-C(34)-H(34)	120.2
C(35)-C(34)-H(34)	120.2
C(36)-C(35)-C(34)	120.1(3)
C(36)-C(35)-H(35)	119.9
C(34)-C(35)-H(35)	119.9
C(35)-C(36)-C(31)	120.9(3)
C(35)-C(36)-H(36)	119.5
C(31)-C(36)-H(36)	119.5
C(42)-C(41)-C(46)	118.4(2)
C(42)-C(41)-C(30)	123.0(2)
C(46)-C(41)-C(30)	118.6(2)
C(41)-C(42)-C(43)	120.7(2)
C(41)-C(42)-H(42)	119.6
C(43)-C(42)-H(42)	119.6
C(44)-C(43)-C(42)	120.0(3)
C(44)-C(43)-H(43)	120.0
C(42)-C(43)-H(43)	120.0
C(43)-C(44)-C(45)	120.0(3)
C(43)-C(44)-H(44)	120.0
C(45)-C(44)-H(44)	120.0
C(46)-C(45)-C(44)	120.0(3)
C(46)-C(45)-H(45)	120.0
C(44)-C(45)-H(45)	120.0

C(45)-C(46)-C(41)	120.9(3)
C(45)-C(46)-H(46)	119.5
C(41)-C(46)-H(46)	119.5
C(56)-C(51)-C(52)	118.3(2)
C(56)-C(51)-C(30)	124.2(2)
C(52)-C(51)-C(30)	117.5(2)
C(53)-C(52)-C(51)	120.9(3)
C(53)-C(52)-H(52)	119.6
C(51)-C(52)-H(52)	119.6
C(52)-C(53)-C(54)	120.1(3)
C(52)-C(53)-H(53)	119.9
C(54)-C(53)-H(53)	119.9
C(55)-C(54)-C(53)	119.4(3)
C(55)-C(54)-H(54)	120.3
C(53)-C(54)-H(54)	120.3
C(54)-C(55)-C(56)	120.5(3)
C(54)-C(55)-H(55)	119.8
C(56)-C(55)-H(55)	119.8
C(51)-C(56)-C(55)	120.8(3)
C(51)-C(56)-H(56)	119.6
C(55)-C(56)-H(56)	119.6
N(1)-C(2)-N(3)	101.9(2)
C(2)-N(1)-C(5)	112.8(2)
C(2)-N(1)-C(11)	124.6(2)
C(5)-N(1)-C(11)	122.4(2)
C(16)-C(11)-C(12)	122.5(2)
C(16)-C(11)-N(1)	119.5(2)
C(12)-C(11)-N(1)	118.0(2)
C(13)-C(12)-C(11)	117.6(3)
C(13)-C(12)-C(17)	121.4(3)
C(11)-C(12)-C(17)	121.0(3)
C(14)-C(13)-C(12)	121.7(3)
C(14)-C(13)-H(13)	119.1
C(12)-C(13)-H(13)	119.1
C(15)-C(14)-C(13)	118.5(3)
C(15)-C(14)-C(18)	121.0(3)
C(13)-C(14)-C(18)	120.5(3)
C(14)-C(15)-C(16)	122.1(3)
C(14)-C(15)-H(15)	119.0
C(16)-C(15)-H(15)	119.0
C(11)-C(16)-C(15)	117.6(3)
C(11)-C(16)-C(19)	121.0(2)
C(15)-C(16)-C(19)	121.5(3)
C(12)-C(17)-H(17A)	109.5
C(12)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(12)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(14)-C(18)-H(18A)	109.5
C(14)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(14)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(14)-C(18)-H(18D)	109.5
H(18A)-C(18)-H(18D)	141.1
H(18B)-C(18)-H(18D)	56.3
H(18C)-C(18)-H(18D)	56.3
C(14)-C(18)-H(18E)	109.5
H(18A)-C(18)-H(18E)	56.3
H(18B)-C(18)-H(18E)	141.1
H(18C)-C(18)-H(18E)	56.3
H(18D)-C(18)-H(18E)	109.5
C(14)-C(18)-H(18F)	109.5
H(18A)-C(18)-H(18F)	56.3
H(18B)-C(18)-H(18F)	56.3
H(18C)-C(18)-H(18F)	141.1
H(18D)-C(18)-H(18F)	109.5
H(18E)-C(18)-H(18F)	109.5
C(16)-C(19)-H(19A)	109.5
C(16)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(16)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(4)-C(5)-N(1)	106.2(2)
C(4)-C(5)-H(2)	126.9
N(1)-C(5)-H(2)	126.9
C(5)-C(4)-N(3)	106.7(2)
C(5)-C(4)-H(3)	126.7
N(3)-C(4)-H(3)	126.7
C(2)-N(3)-C(4)	112.5(2)
C(2)-N(3)-C(21)	124.6(2)
C(4)-N(3)-C(21)	123.0(2)
C(26)-C(21)-C(22)	122.0(2)
C(26)-C(21)-N(3)	118.8(2)
C(22)-C(21)-N(3)	119.2(2)
C(23)-C(22)-C(21)	117.7(2)
C(23)-C(22)-C(27)	121.2(2)
C(21)-C(22)-C(27)	121.1(2)
C(22)-C(23)-C(24)	122.2(3)
C(22)-C(23)-H(23)	118.9
C(24)-C(23)-H(23)	118.9
C(25)-C(24)-C(23)	118.1(2)
C(25)-C(24)-C(28)	121.0(2)
C(23)-C(24)-C(28)	120.9(3)
C(24)-C(25)-C(26)	122.1(2)
C(24)-C(25)-H(25)	118.9
C(26)-C(25)-H(25)	118.9
C(25)-C(26)-C(21)	117.8(2)
C(25)-C(26)-C(29)	120.4(2)
C(21)-C(26)-C(29)	121.8(2)
C(22)-C(27)-H(27A)	109.5
C(22)-C(27)-H(27B)	109.5
H(27A)-C(27)-H(27B)	109.5
C(22)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5
C(24)-C(28)-H(28A)	109.5
C(24)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
C(24)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
C(26)-C(29)-H(29A)	109.5
C(26)-C(29)-H(29B)	109.5
H(29A)-C(29)-H(29B)	109.5

C(26)-C(29)-H(29C)	109.5
H(29A)-C(29)-H(29C)	109.5
H(29B)-C(29)-H(29C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 10. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 04150. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	23(1)	16(1)	22(1)	-4(1)	-2(1)	-13(1)
C(30)	16(1)	16(1)	18(1)	-3(1)	0(1)	-9(1)
C(31)	17(1)	12(1)	16(1)	2(1)	-2(1)	-5(1)
C(32)	21(2)	22(2)	25(2)	-2(1)	-3(1)	-8(1)
C(33)	20(2)	34(2)	27(2)	-3(1)	4(1)	-9(1)
C(34)	30(2)	23(2)	23(2)	-7(1)	9(1)	0(1)
C(35)	41(2)	20(2)	24(2)	-9(1)	4(1)	-11(1)
C(36)	25(2)	22(1)	22(2)	-5(1)	3(1)	-12(1)
C(41)	19(1)	11(1)	14(1)	-6(1)	3(1)	-5(1)
C(42)	20(1)	16(1)	16(1)	-2(1)	-3(1)	-7(1)
C(43)	26(2)	23(1)	21(1)	-10(1)	6(1)	-15(1)
C(44)	37(2)	17(1)	16(1)	-5(1)	6(1)	-14(1)
C(45)	30(2)	13(1)	19(1)	-3(1)	-7(1)	-3(1)
C(46)	18(1)	16(1)	25(2)	-9(1)	0(1)	-8(1)
C(51)	17(1)	14(1)	21(1)	-3(1)	1(1)	-11(1)
C(52)	23(1)	18(1)	19(1)	-3(1)	-1(1)	-11(1)
C(53)	19(1)	19(1)	32(2)	-9(1)	8(1)	-9(1)
C(54)	14(1)	17(1)	34(2)	5(1)	-5(1)	-5(1)
C(55)	25(2)	27(2)	19(1)	3(1)	-3(1)	-14(1)
C(56)	18(1)	20(1)	20(1)	-5(1)	4(1)	-10(1)
C(2)	13(1)	18(1)	15(1)	-2(1)	0(1)	-5(1)
N(1)	14(1)	15(1)	19(1)	-4(1)	3(1)	-6(1)
C(11)	15(1)	12(1)	21(1)	-7(1)	3(1)	-6(1)
C(12)	21(1)	17(1)	25(2)	-9(1)	0(1)	-8(1)
C(13)	16(1)	19(1)	35(2)	-10(1)	-6(1)	-2(1)
C(14)	16(1)	28(2)	36(2)	-21(1)	7(1)	-10(1)
C(15)	28(2)	27(2)	22(2)	-11(1)	9(1)	-18(1)
C(16)	18(1)	17(1)	22(1)	-5(1)	1(1)	-8(1)
C(17)	31(2)	30(2)	24(2)	0(1)	-6(1)	-7(1)
C(18)	21(2)	51(2)	57(2)	-31(2)	14(2)	-15(2)
C(19)	27(2)	28(2)	24(2)	0(1)	-1(1)	-9(1)
C(5)	26(2)	20(1)	28(2)	-11(1)	7(1)	-13(1)
C(4)	22(2)	26(2)	28(2)	-11(1)	8(1)	-16(1)
N(3)	15(1)	18(1)	18(1)	-6(1)	3(1)	-8(1)
C(21)	15(1)	17(1)	22(1)	-8(1)	5(1)	-10(1)
C(22)	17(1)	20(1)	17(1)	-5(1)	3(1)	-12(1)
C(23)	16(1)	17(1)	19(1)	-2(1)	-3(1)	-6(1)
C(24)	18(1)	20(1)	22(1)	-8(1)	4(1)	-11(1)
C(25)	24(2)	22(1)	13(1)	-3(1)	2(1)	-13(1)
C(26)	17(1)	17(1)	21(1)	-4(1)	0(1)	-9(1)
C(27)	23(2)	26(2)	17(1)	-3(1)	2(1)	-8(1)
C(28)	24(2)	24(2)	21(2)	-5(1)	3(1)	-2(1)
C(29)	24(2)	20(1)	22(2)	-3(1)	0(1)	-4(1)

Table 11. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å ^{2}x 10^3) for 04150.

	x	y	z	U(eq)
H(1O)	4010(30)	8340(20)	2972(17)	22
H(32)	5821	6952	2220	28
H(33)	7372	5763	1223	35
H(34)	6799	4387	557	36
H(35)	4640	4244	873	35
H(36)	3093	5427	1867	27
H(42)	1032	6383	3091	21
H(43)	731	4577	4088	25
H(44)	2494	3066	5081	27
H(45)	4583	3331	5072	27
H(46)	4903	5105	4068	23
H(52)	1032	8796	3565	24
H(53)	-1117	10685	3050	28
H(54)	-1550	11392	1597	28
H(55)	159	10165	674	28
H(56)	2296	8240	1190	23
H(13)	-1164	13664	2818	29
H(15)	525	11120	5043	28
H(17A)	253	13766	1599	47
H(17B)	1651	12304	1571	47
H(17C)	1782	13617	1790	47
H(18A)	-2732	13598	3945	62
H(18B)	-2096	13366	4847	62
H(18C)	-2212	12080	4580	62
H(18D)	-1961	12431	4969	62
H(18E)	-2597	12663	4068	62
H(18F)	-2481	13949	4334	62
H(19A)	3015	9850	5250	43
H(19B)	3996	10418	4605	43
H(19C)	3747	9122	4461	43
H(2)	3974	12916	3096	27
H(3)	6225	11786	2323	28
H(23)	9543	6418	2020	22
H(25)	7771	9165	-141	23
H(27A)	8443	6719	3343	35
H(27B)	6749	7659	3337	35
H(27C)	7783	8354	3415	35
H(28A)	11002	6628	588	40
H(28B)	10016	7242	-229	40
H(28C)	10112	5833	422	40
H(29A)	5645	11955	471	37
H(29B)	4541	11274	698	37
H(29C)	5464	11101	-156	37

X-ray crystal structure of *N*,*N*-bismesitylimidazolylidene-trifluoroethanol complex 8f:

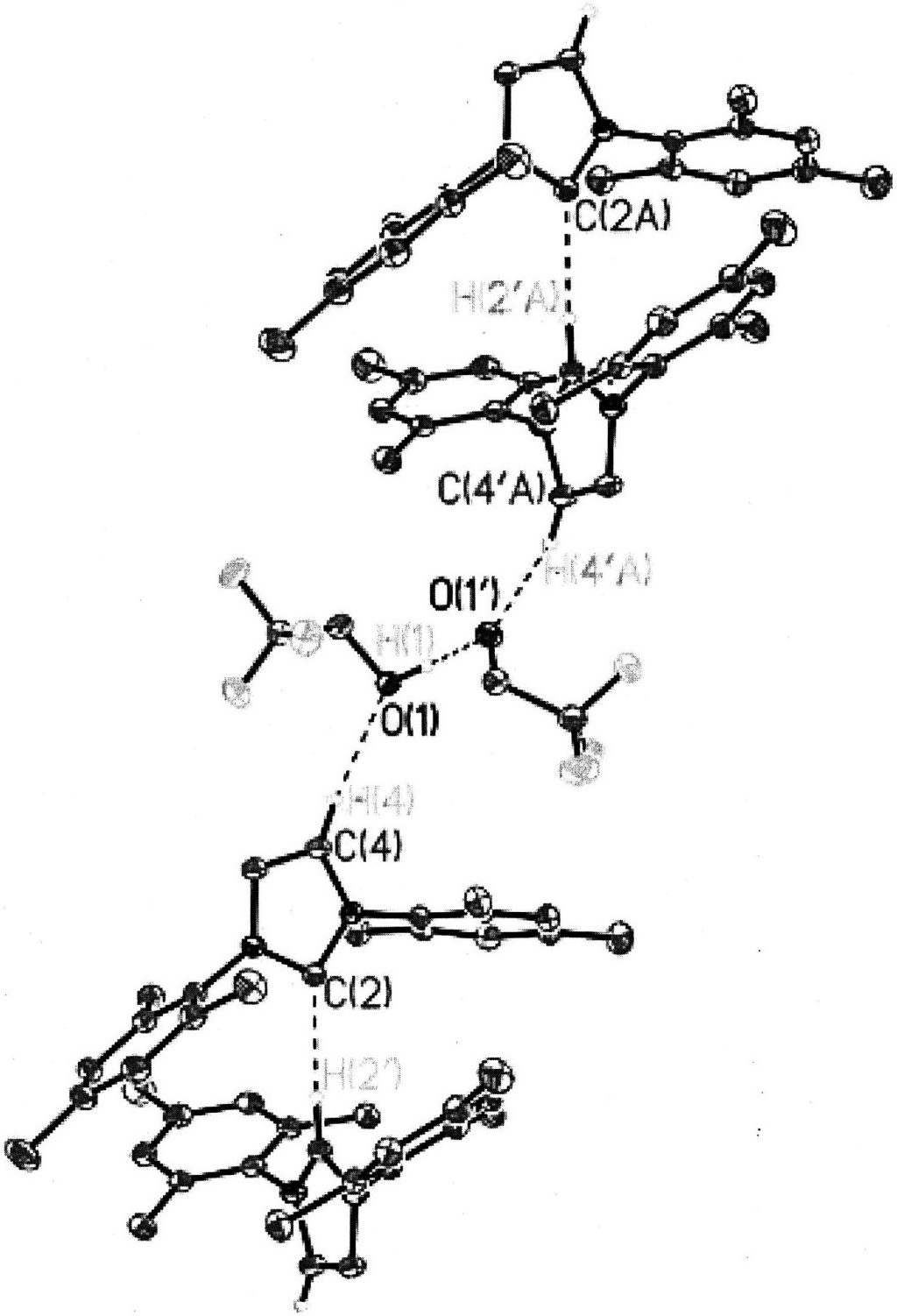


Table 12. Crystal data and structure refinement for 05015.

Identification code	05015	
Empirical formula	C23 H27 F3 N2 O	
Formula weight	404.47	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 14.9225(5) Å	α= 90°.
	b = 18.7163(8) Å	β= 90°.
	c = 30.8310(13) Å	γ = 90°.
Volume	8610.9(6) $Å^3$	
Z	16	
Density (calculated)	1.248 Mg/m^3	
Absorption coefficient	0.094 mm^{-1}	
F(000)	3424	
Crystal size	0.20 x 0.20 x 0.20 mm^3	
Theta range for data collection	1.87 to 30.03°.	
Index ranges	0<=h<=21, 0<=k<=26, 0<=l<=43	
Reflections collected	199412	
Independent reflections	12591 [R(int) = 0.0531]	
Completeness to theta = 30.03°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9814 and 0.9814	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12591 / 2 / 542	
Goodness-of-fit on F^2	1.050	
Final R indices [I>2sigma(I)]	R1 = 0.0521, wR2 = 0.1278	
R indices (all data)	R1 = 0.0686, wR2 = 0.1424	
Largest diff. peak and hole	0.634 and -0.273 $e.Å^{-3}$	

Table 13. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 05015. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1')	6784(1)	3275(1)	1484(1)	21(1)
F(1')	5858(1)	4753(1)	908(1)	41(1)
F(2')	7064(1)	4752(1)	1292(1)	36(1)
F(3')	5792(1)	4530(1)	1593(1)	36(1)
C(30')	6406(1)	3626(1)	1138(1)	21(1)
C(31')	6277(1)	4408(1)	1237(1)	25(1)
O(1)	5712(1)	2354(1)	1689(1)	19(1)
F(1)	5141(1)	1161(1)	1161(1)	35(1)
F(2)	6504(1)	779(1)	1157(1)	33(1)
F(3)	6182(1)	1800(1)	875(1)	30(1)
C(30)	6174(1)	1718(1)	1645(1)	20(1)
C(31)	5998(1)	1370(1)	1212(1)	21(1)
N(1)	2354(1)	2181(1)	1015(1)	17(1)
C(2)	2151(1)	2717(1)	1298(1)	18(1)
N(3)	2932(1)	2794(1)	1521(1)	17(1)
C(4)	3602(1)	2328(1)	1383(1)	20(1)
C(5)	3231(1)	1935(1)	1061(1)	21(1)
C(11)	1696(1)	1911(1)	718(1)	18(1)
C(12)	1056(1)	1429(1)	874(1)	19(1)
C(13)	390(1)	1202(1)	588(1)	24(1)
C(14)	343(1)	1451(1)	163(1)	26(1)
C(15)	991(1)	1932(1)	21(1)	25(1)
C(16)	1680(1)	2168(1)	293(1)	21(1)
C(17)	1072(1)	1182(1)	1338(1)	24(1)
C(18)	-399(1)	1207(1)	-135(1)	39(1)
C(19)	2372(1)	2694(1)	133(1)	30(1)
C(21)	3044(1)	3341(1)	1844(1)	16(1)
C(22)	2701(1)	3231(1)	2262(1)	18(1)
C(23)	2768(1)	3793(1)	2558(1)	22(1)
C(24)	3186(1)	4433(1)	2448(1)	22(1)
C(25)	3534(1)	4515(1)	2030(1)	21(1)
C(26)	3455(1)	3978(1)	1721(1)	18(1)
C(27)	2284(1)	2530(1)	2392(1)	24(1)
C(28)	3282(1)	5029(1)	2774(1)	31(1)
C(29)	3774(1)	4080(1)	1261(1)	23(1)
N(1')	-14(1)	3932(1)	985(1)	18(1)
C(2')	163(1)	3356(1)	1226(1)	17(1)
N(3')	-595(1)	3160(1)	1423(1)	17(1)
C(4')	-1282(1)	3622(1)	1306(1)	20(1)
C(5')	-914(1)	4107(1)	1033(1)	21(1)
C(11')	636(1)	4287(1)	713(1)	18(1)
C(12')	1292(1)	4707(1)	912(1)	20(1)
C(13')	1929(1)	5022(1)	642(1)	22(1)
C(14')	1918(1)	4925(1)	193(1)	22(1)
C(15')	1244(1)	4503(1)	12(1)	22(1)
C(16')	592(1)	4175(1)	266(1)	19(1)
C(17')	1327(1)	4806(1)	1396(1)	27(1)
C(18')	2616(1)	5275(1)	-89(1)	32(1)
C(19')	-114(1)	3705(1)	64(1)	25(1)
C(21')	-674(1)	2552(1)	1709(1)	17(1)
C(22')	-295(1)	2599(1)	2122(1)	19(1)
C(23')	-358(1)	1996(1)	2386(1)	22(1)
C(24')	-791(1)	1377(1)	2247(1)	23(1)
C(25')	-1173(1)	1362(1)	1834(1)	21(1)

C(26')	-1123(1)	1948(1)	1556(1)	18(1)
C(27')	147(1)	3273(1)	2283(1)	25(1)
C(28')	-861(1)	736(1)	2542(1)	34(1)
C(29')	-1537(1)	1930(1)	1110(1)	23(1)

Table 14. Bond lengths [Å] and angles [°] for 05015.

O(1')-C(30')	1.3726(16)
F(1')-C(31')	1.3550(17)
F(2')-C(31')	1.3493(16)
F(3')-C(31')	1.3344(17)
C(30')-C(31')	1.508(2)
O(1)-C(30)	1.3811(15)
F(1)-C(31)	1.3461(16)
F(2)-C(31)	1.3507(15)
F(3)-C(31)	1.3428(16)
C(30)-C(31)	1.5082(18)
N(1)-C(2)	1.3648(16)
N(1)-C(5)	1.3941(16)
N(1)-C(11)	1.4347(16)
C(2)-N(3)	1.3609(16)
N(3)-C(4)	1.3941(16)
N(3)-C(21)	1.4389(16)
C(4)-C(5)	1.3539(18)
C(11)-C(16)	1.3958(18)
C(11)-C(12)	1.3984(18)
C(12)-C(13)	1.3959(18)
C(12)-C(17)	1.5038(19)
C(13)-C(14)	1.391(2)
C(14)-C(15)	1.391(2)
C(14)-C(18)	1.511(2)
C(15)-C(16)	1.3976(19)
C(16)-C(19)	1.509(2)
C(21)-C(26)	1.3944(17)
C(21)-C(22)	1.3988(17)
C(22)-C(23)	1.3965(18)
C(22)-C(27)	1.5069(19)
C(23)-C(24)	1.392(2)
C(24)-C(25)	1.3966(18)
C(24)-C(28)	1.5096(19)
C(25)-C(26)	1.3921(18)
C(26)-C(29)	1.5064(17)
N(1')-C(2')	1.3360(16)
N(1')-C(5')	1.3902(16)
N(1')-C(11')	1.4442(16)
C(2')-N(3')	1.3351(16)
N(3')-C(4')	1.3891(16)
N(3')-C(21')	1.4444(16)
C(4')-C(5')	1.3539(18)
C(11')-C(16')	1.3969(18)
C(11')-C(12')	1.3977(18)
C(12')-C(13')	1.3941(18)
C(12')-C(17')	1.5071(19)
C(13')-C(14')	1.395(2)
C(14')-C(15')	1.3952(19)
C(14')-C(18')	1.5073(19)
C(15')-C(16')	1.3905(18)
C(16')-C(19')	1.5070(18)
C(21')-C(26')	1.3962(18)
C(21')-C(22')	1.3971(18)
C(22')-C(23')	1.3956(19)
C(22')-C(27')	1.5069(19)
C(23')-C(24')	1.394(2)
C(24')-C(25')	1.3940(19)
C(24')-C(28')	1.511(2)
C(25')-C(26')	1.3929(18)
C(26')-C(29')	1.5082(18)
O(1')-C(30')-C(31')	111.16(11)
F(3')-C(31')-F(2')	106.72(12)
F(3')-C(31')-F(1')	106.50(12)
F(2')-C(31')-F(1')	105.57(12)
F(3')-C(31')-C(30')	113.62(12)
F(2')-C(31')-C(30')	112.13(11)
F(1')-C(31')-C(30')	111.77(12)
O(1)-C(30)-C(31)	111.90(11)
F(3)-C(31)-F(1)	106.20(11)
F(3)-C(31)-F(2)	106.25(11)
F(1)-C(31)-F(2)	106.17(11)
F(3)-C(31)-C(30)	112.99(11)
F(1)-C(31)-C(30)	113.15(11)
F(2)-C(31)-C(30)	111.55(11)
C(2)-N(1)-C(5)	112.72(10)
C(2)-N(1)-C(11)	120.98(10)
C(5)-N(1)-C(11)	126.28(11)
N(3)-C(2)-N(1)	102.14(10)
C(2)-N(3)-C(4)	113.24(10)
C(2)-N(3)-C(21)	121.64(10)
C(4)-N(3)-C(21)	125.00(10)
C(5)-C(4)-N(3)	105.65(11)
C(4)-C(5)-N(1)	106.26(11)
C(16)-C(11)-C(12)	122.19(12)
C(16)-C(11)-N(1)	119.34(11)
C(12)-C(11)-N(1)	118.35(11)
C(13)-C(12)-C(11)	117.80(12)
C(13)-C(12)-C(17)	121.18(12)
C(11)-C(12)-C(17)	120.99(12)
C(14)-C(13)-C(12)	121.81(13)
C(15)-C(14)-C(13)	118.58(12)
C(15)-C(14)-C(18)	120.90(14)
C(13)-C(14)-C(18)	120.52(14)
C(14)-C(15)-C(16)	121.80(13)
C(11)-C(16)-C(15)	117.79(12)
C(11)-C(16)-C(19)	121.22(12)
C(15)-C(16)-C(19)	120.97(12)
C(26)-C(21)-C(22)	122.56(11)
C(26)-C(21)-N(3)	117.97(11)
C(22)-C(21)-N(3)	119.40(11)
C(23)-C(22)-C(21)	117.63(12)
C(23)-C(22)-C(27)	120.75(12)

C(21)-C(22)-C(27)	121.61(12)
C(24)-C(23)-C(22)	121.46(12)
C(23)-C(24)-C(25)	119.01(12)
C(23)-C(24)-C(28)	121.09(13)
C(25)-C(24)-C(28)	119.89(13)
C(26)-C(25)-C(24)	121.41(12)
C(25)-C(26)-C(21)	117.88(11)
C(25)-C(26)-C(29)	121.73(12)
C(21)-C(26)-C(29)	120.37(11)
C(2')-N(1')-C(5')	108.85(11)
C(2')-N(1')-C(11')	124.09(10)
C(5')-N(1')-C(11')	127.03(11)
N(3')-C(2')-N(1')	107.81(11)
C(2')-N(3')-C(4')	109.70(11)
C(2')-N(3')-C(21')	124.29(10)
C(4')-N(3')-C(21')	126.01(10)
C(5')-C(4')-N(3')	106.22(11)
C(4')-C(5')-N(1')	107.43(11)
C(16')-C(11')-C(12')	123.36(12)
C(16')-C(11')-N(1')	118.27(11)
C(12')-C(11')-N(1')	118.34(11)
C(13')-C(12')-C(11')	117.04(12)
C(13')-C(12')-C(17')	121.10(12)
C(11')-C(12')-C(17')	121.85(12)
C(12')-C(13')-C(14')	121.87(12)
C(13')-C(14')-C(15')	118.65(12)
C(13')-C(14')-C(18')	120.52(13)
C(15')-C(14')-C(18')	120.83(13)
C(16')-C(15')-C(14')	121.98(13)
C(15')-C(16')-C(11')	117.11(12)
C(15')-C(16')-C(19')	120.98(12)
C(11')-C(16')-C(19')	121.90(12)
C(26')-C(21')-C(22')	123.56(12)
C(26')-C(21')-N(3')	118.12(11)
C(22')-C(21')-N(3')	118.31(11)
C(23')-C(22')-C(21')	116.96(12)
C(23')-C(22')-C(27')	120.98(12)
C(21')-C(22')-C(27')	122.05(12)
C(24')-C(23')-C(22')	121.62(12)
C(25')-C(24')-C(23')	119.11(12)
C(25')-C(24')-C(28')	120.46(13)
C(23')-C(24')-C(28')	120.41(13)
C(26')-C(25')-C(24')	121.62(12)
C(25')-C(26')-C(21')	117.11(12)
C(25')-C(26')-C(29')	121.45(12)
C(21')-C(26')-C(29')	121.44(12)

Symmetry transformations used to generate equivalent atoms:

Table 15. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 05015. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1')	18(1)	22(1)	24(1)	4(1)	-3(1)	-1(1)
F(1')	33(1)	35(1)	54(1)	20(1)	-6(1)	5(1)
F(2')	25(1)	24(1)	60(1)	1(1)	-2(1)	-5(1)
F(3')	33(1)	32(1)	44(1)	-9(1)	8(1)	5(1)
C(30')	22(1)	21(1)	21(1)	1(1)	0(1)	-1(1)
C(31')	20(1)	23(1)	33(1)	4(1)	-1(1)	1(1)
O(1)	18(1)	17(1)	22(1)	0(1)	3(1)	0(1)
F(1)	24(1)	34(1)	47(1)	-10(1)	-5(1)	-6(1)
F(2)	37(1)	24(1)	37(1)	-8(1)	-2(1)	9(1)
F(3)	40(1)	33(1)	17(1)	1(1)	-1(1)	0(1)
C(30)	22(1)	20(1)	17(1)	2(1)	0(1)	2(1)
C(31)	20(1)	19(1)	24(1)	-2(1)	-1(1)	0(1)
N(1)	14(1)	19(1)	19(1)	-2(1)	-2(1)	1(1)
C(2)	16(1)	19(1)	18(1)	0(1)	0(1)	0(1)
N(3)	15(1)	18(1)	18(1)	-2(1)	0(1)	2(1)
C(4)	15(1)	22(1)	24(1)	-3(1)	-2(1)	4(1)
C(5)	16(1)	22(1)	25(1)	-4(1)	-1(1)	4(1)
C(11)	16(1)	18(1)	19(1)	-3(1)	-2(1)	2(1)
C(12)	18(1)	18(1)	21(1)	-2(1)	1(1)	2(1)
C(13)	18(1)	23(1)	31(1)	-6(1)	0(1)	-2(1)
C(14)	20(1)	30(1)	27(1)	-10(1)	-6(1)	3(1)
C(15)	26(1)	30(1)	18(1)	-2(1)	-4(1)	5(1)
C(16)	21(1)	22(1)	20(1)	0(1)	0(1)	1(1)
C(17)	24(1)	24(1)	24(1)	3(1)	2(1)	-1(1)
C(18)	27(1)	55(1)	36(1)	-16(1)	-11(1)	0(1)
C(19)	32(1)	33(1)	27(1)	7(1)	1(1)	-5(1)
C(21)	15(1)	18(1)	17(1)	-2(1)	-1(1)	1(1)
C(22)	15(1)	22(1)	18(1)	2(1)	-1(1)	1(1)
C(23)	22(1)	28(1)	16(1)	-1(1)	1(1)	1(1)
C(24)	22(1)	25(1)	20(1)	-5(1)	-2(1)	3(1)
C(25)	22(1)	20(1)	21(1)	-1(1)	-1(1)	-2(1)
C(26)	16(1)	21(1)	17(1)	0(1)	1(1)	0(1)
C(27)	25(1)	25(1)	24(1)	6(1)	2(1)	-2(1)
C(28)	38(1)	31(1)	25(1)	-10(1)	-2(1)	0(1)
C(29)	25(1)	27(1)	17(1)	0(1)	4(1)	-5(1)
N(1')	15(1)	18(1)	20(1)	1(1)	2(1)	1(1)
C(2')	15(1)	18(1)	19(1)	0(1)	0(1)	1(1)
N(3')	14(1)	19(1)	19(1)	2(1)	0(1)	2(1)
C(4')	15(1)	22(1)	23(1)	2(1)	1(1)	4(1)
C(5')	16(1)	21(1)	25(1)	3(1)	1(1)	4(1)
C(11')	17(1)	17(1)	19(1)	2(1)	2(1)	1(1)
C(12')	20(1)	20(1)	20(1)	0(1)	-1(1)	1(1)
C(13')	19(1)	20(1)	27(1)	1(1)	-2(1)	-3(1)
C(14')	20(1)	21(1)	26(1)	4(1)	4(1)	-1(1)
C(15')	24(1)	23(1)	20(1)	0(1)	2(1)	0(1)
C(16')	19(1)	18(1)	21(1)	-1(1)	0(1)	0(1)
C(17')	26(1)	34(1)	21(1)	-3(1)	-2(1)	-4(1)
C(18')	27(1)	35(1)	34(1)	7(1)	8(1)	-8(1)
C(19')	25(1)	26(1)	24(1)	-4(1)	1(1)	-6(1)
C(21')	14(1)	18(1)	18(1)	3(1)	1(1)	2(1)
C(22')	15(1)	22(1)	20(1)	0(1)	-1(1)	2(1)
C(23')	20(1)	28(1)	18(1)	4(1)	-2(1)	3(1)
C(24')	20(1)	24(1)	24(1)	7(1)	1(1)	1(1)
C(25')	19(1)	20(1)	25(1)	2(1)	1(1)	0(1)

C(26')	15(1)	21(1)	19(1)	0(1)	1(1)	2(1)
C(27')	23(1)	24(1)	27(1)	-2(1)	-6(1)	0(1)
C(28')	37(1)	33(1)	34(1)	16(1)	-4(1)	-4(1)
C(29')	22(1)	26(1)	20(1)	-1(1)	-2(1)	-1(1)

Table 16. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 05015.

	x	y	z	U(eq)
H(30C)	5819	3407	1070	25
H(30D)	6797	3574	881	25
H(1)	6113(11)	2707(8)	1621(5)	23
H(30A)	5992	1388	1879	24
H(30B)	6824	1810	1675	24
H(4)	4196	2292	1493	25
H(5)	3512	1567	898	25
H(13)	-45	867	686	29
H(15)	964	2105	-268	30
H(17A)	596	829	1383	36
H(17B)	974	1592	1530	36
H(17C)	1654	965	1402	36
H(18A)	-501	1569	-359	59
H(18B)	-950	1137	32	59
H(18C)	-227	755	-273	59
H(19A)	2375	3115	322	46
H(19B)	2226	2839	-164	46
H(19C)	2965	2469	138	46
H(23)	2523	3738	2840	26
H(25)	3831	4947	1956	25
H(27A)	2751	2165	2417	37
H(27B)	1847	2384	2172	37
H(27C)	1981	2586	2672	37
H(28A)	2770	5022	2974	46
H(28B)	3300	5489	2623	46
H(28C)	3838	4964	2939	46
H(29A)	4249	3735	1197	35
H(29B)	4008	4567	1227	35
H(29C)	3272	4007	1061	35
H(2')	736(10)	3144(9)	1256(5)	21
H(4')	-1889	3602	1399	24
H(5')	-1216	4495	898	25
H(13')	2384	5311	767	27
H(15')	1231	4437	-293	27
H(17D)	720	4891	1507	41
H(17E)	1709	5216	1466	41
H(17F)	1574	4375	1531	41
H(18D)	2410	5752	-174	48
H(18E)	2711	4984	-350	48
H(18F)	3180	5315	72	48
H(19D)	-702	3934	92	38
H(19E)	-123	3242	211	38
H(19F)	23	3634	-244	38
H(23')	-100	2007	2668	26
H(25')	-1474	943	1740	25
H(27D)	293	3221	2591	37
H(27E)	-262	3678	2244	37

H(27F)	698	3359	2118	37
H(28D)	-1492	643	2609	52
H(28E)	-533	830	2812	52
H(28F)	-603	317	2398	52
H(29D)	-2053	2254	1101	35
H(29E)	-1736	1443	1044	35
H(29F)	-1093	2082	895	35

Table 17. Torsion angles [°] for 05015.

N(1)-C(2)-C(2')-N(3')	89.52(14)

Symmetry transformations used to generate equivalent atoms:

Table 18. Hydrogen bonds for 05015 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(1')	0.916(14)	1.520(14)	2.4354(13)	176.9(18)

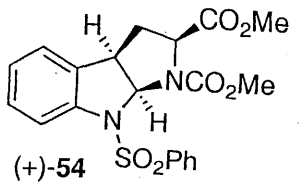
Symmetry transformations used to generate equivalent atoms:

Appendix A

Spectra for Chapter I

exp2 s2pul

SAMPLE		DEC. & VT	
date	Oct 15 2006	dfrq	125.795
solvent	CDCl3	dn	C13
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	500.235	dm	nnn
tn	H1	dmm	c
at	3.200	dmf	10000
np	64000	dseq	
sw	10000.0	dres	1.0
fb	not used	homo	n
bs	1	temp	50.0
ss	1	PROCESSING	
tpwr	59	wtfile	
pw	9.8	proc	ft
d1	7.000	fn	131072
tof	1498.2	math	f
nt	16		
ct	16	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.2		
wp	6252.8		
vs	151		
sc	0		
wc	250		
hzmm	40.00		
is	283.67		
rfl	4632.2		
rfp	3636.7		
th	7		
ins	1.000		
nm	ph		



(+)-**54**

```
exp1  s2pul

      SAMPLE
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solvent       CDCl3
file            exp
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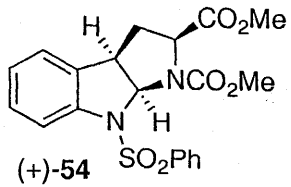
tn              C13
at              1.736
np            131010
sw           37735.8
fb         not used
bs                8
ss                1
tpwr             53
pw              6.9
d1            0.763
tof           631.4
nt           100000
ct             2040
alock             n
gain       not used
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp          -2516.4
wp          30189.8
vs              151
sc                0
wc              250
hzmm         150.94
is           500.00
rfl         15994.3
rfp          9715.0
th               20
ins           1.000
nm     ph

      DEC. & VT
dfrq        500.233
dn               H1
dpwr             37
dof          -500.0
dm                y
dmm               w
dmf           10000
dseq
dres            1.0
homo              n
     PROCESSING..
lb              0.30
wtfile
proc              ft
fn           131072
math              f

werr
wexp
wbs
wnt
```



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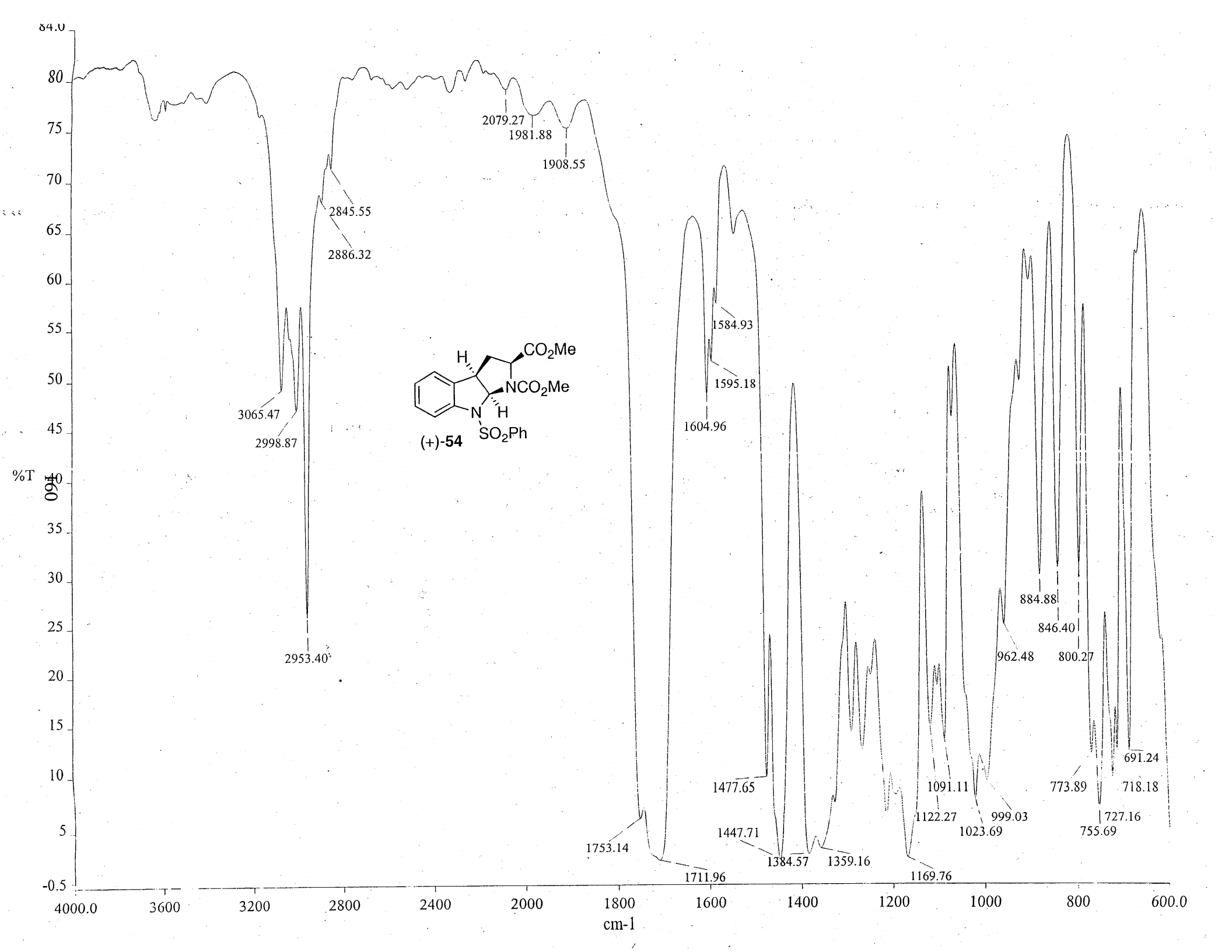
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80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
-0.5
%T
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1
3065.47
2998.87
2953.40
2886.32
2845.55
2079.27
1981.88
1908.55
1604.96
1584.93
1595.18
1477.65
1447.71
1384.57
1359.16
1753.14
1711.96
1169.76
1122.27
1091.11
1023.69
999.03
962.48
884.88
846.40
800.27
773.89
755.69
727.16
718.18
691.24
H
CO2Me
NCO2Me
N
H
SO2Ph
(+)-54

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		Inj Volume	: 1 µl
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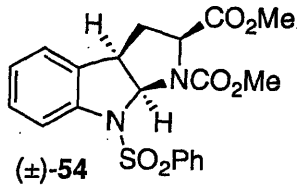

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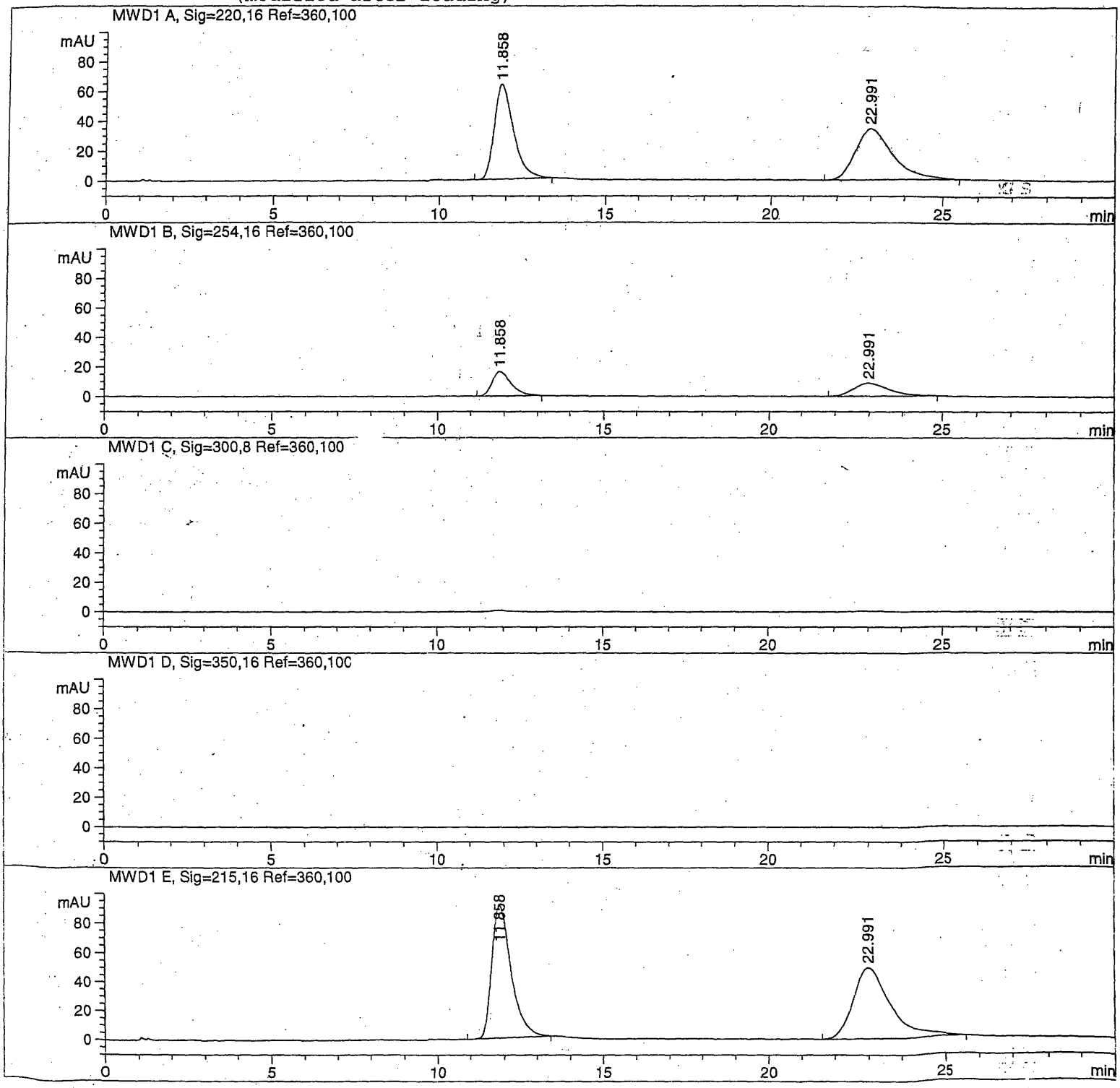

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.858	PB	0.6182	2585.91675	63.62169	50.0545
2	22.991	PB	1.0919	2580.28857	34.28851	49.9455
Totals :				5166.20532	97.91020	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.858	BB	0.6104	663.39410	16.52487	51.1690
2	22.991	BB	0.9137	633.08154	8.77511	48.8310
Totals :				1296.47565	25.29999	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.858	PB	0.6178	3665.81055	90.27012	49.6775
2	22.991	PB	1.1018	3713.41357	48.90760	50.3225
Totals :				7379.22412	139.17772	

Results obtained with enhanced integrator!

*** End of Report ***

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Acq. Operator   :                                  Inj :   1
                                               Inj Volume : 1 µl

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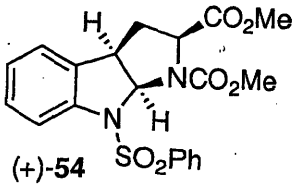

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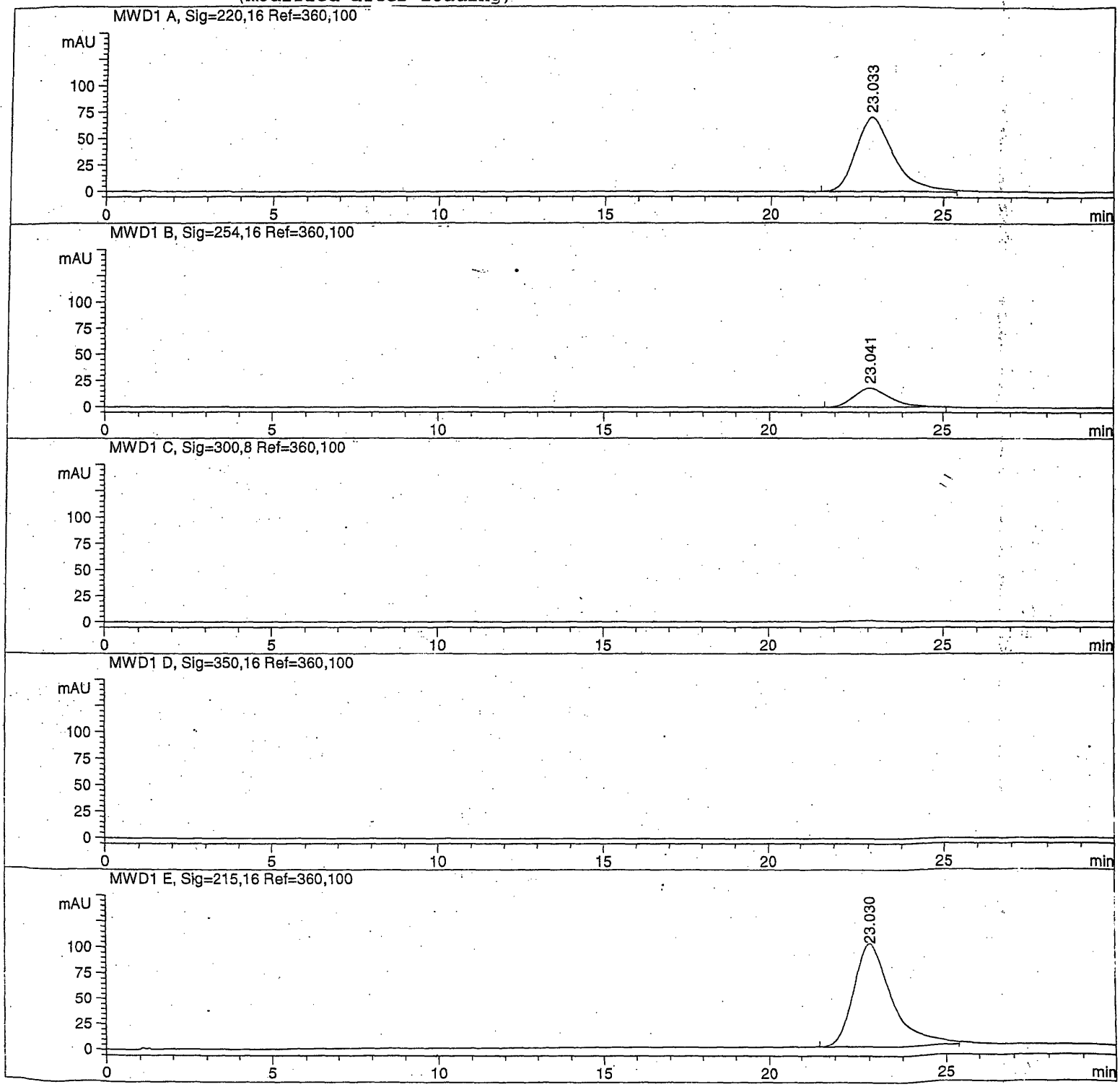


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.033	VV	0.9641	5360.91748	70.42066	100.0000
Totals :				5360.91748	70.42066	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.041	VB	0.8716	1318.07544	18.05686	100.0000
Totals :				1318.07544	18.05686	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

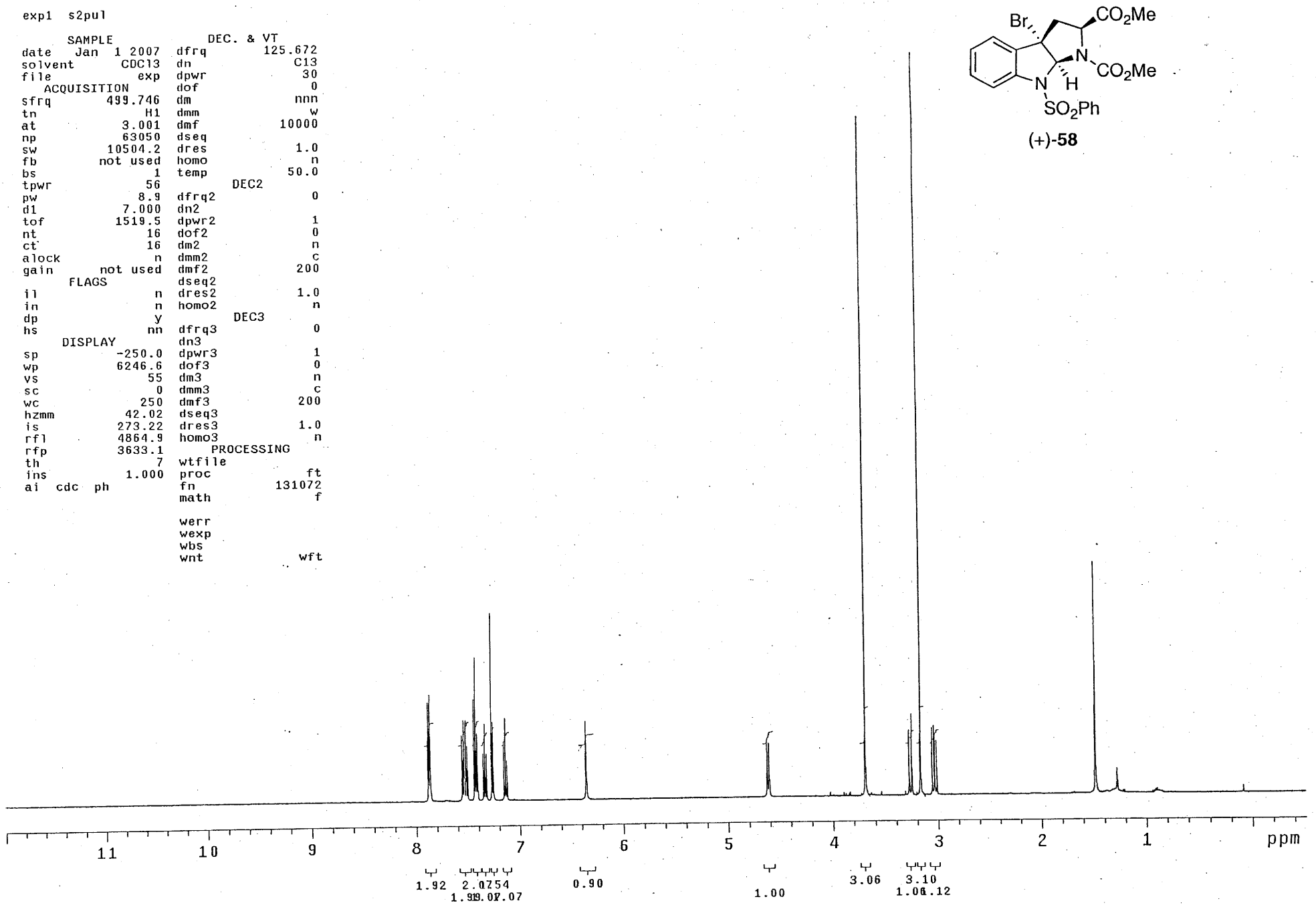
Signal 4: MWD1 D, Sig=350,16 Ref=360,100

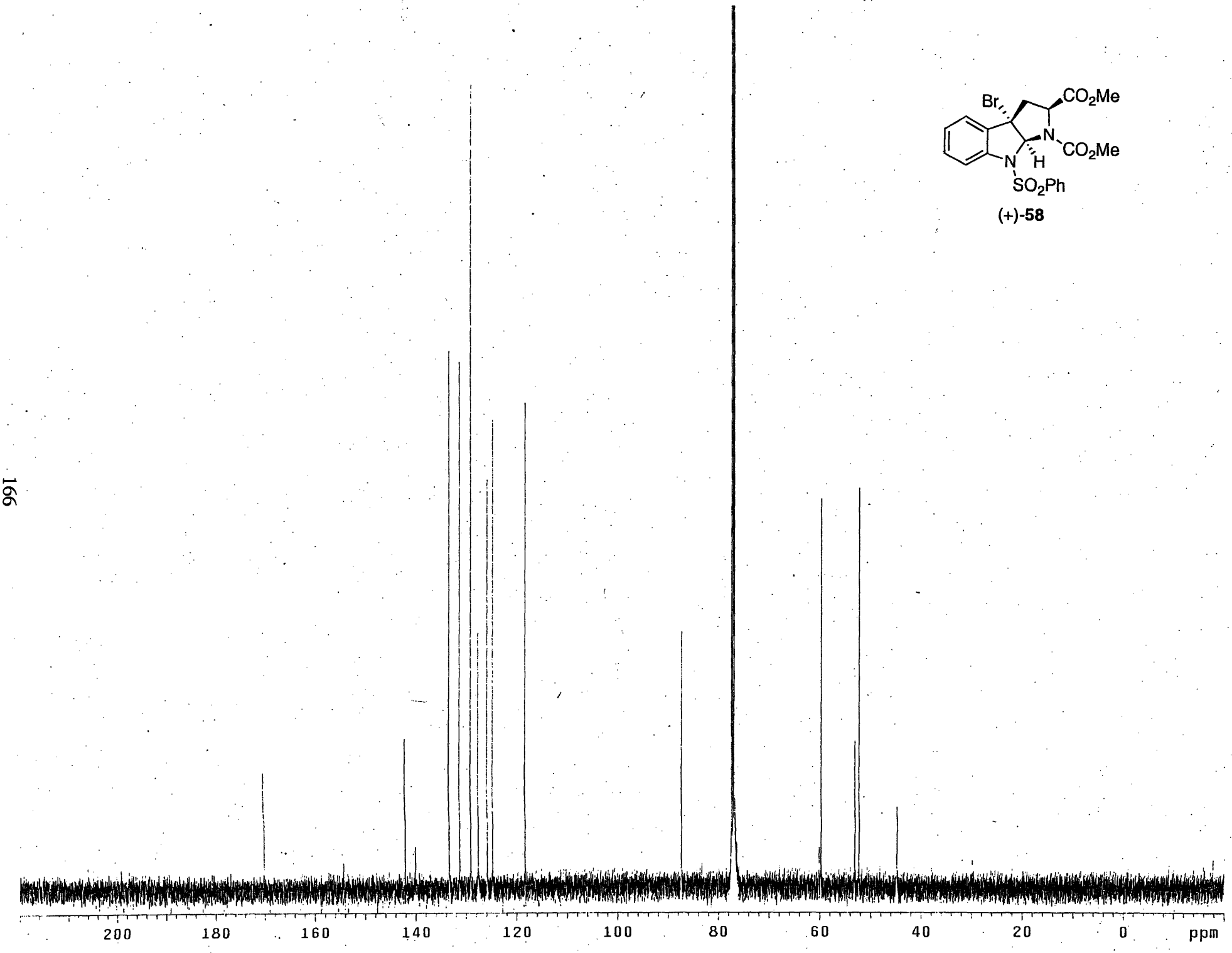
Signal 5: MWD1 E, Sig=215,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.030	VV	1.0140	7638.75244	100.13385	100.0000
Totals :				7638.75244	100.13385	

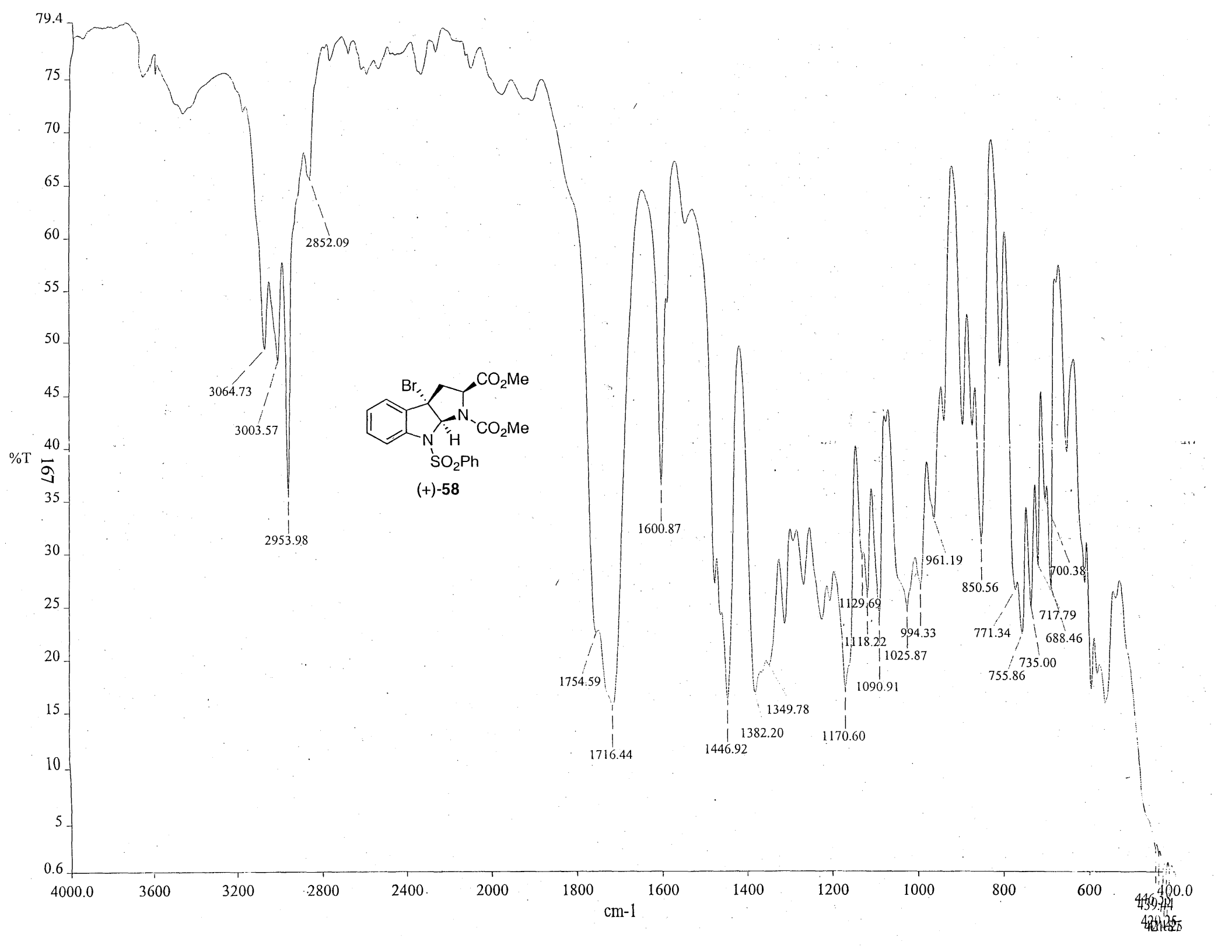
Results obtained with enhanced integrator!

*** End of Report ***


exp1 s2pul
SAMPLE
date Jan 1 2007
solvent CDCl3
file exp
ACQUISITION
sfrq 499.746
tn H1
at 3.001
np 63050
sw 10504.2
fb not used
bs 1
tpwr 56
pw 8.9
d1 7.000
tof 1519.5
nt 16
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.0
wp 6246.6
vs 55
sc 0
wc 250
hzmm 42.02
is 273.22
rfl 4864.9
rfp 3633.1
th 7
ins 1.000
ai cdc ph
DEC. & VT
dfrq 125.672
dn C13
dpwr 30
dof 0
dm nnn
dmm w
dmf 10000
dseq
dres 1.0
homo n
temp 50.0
DEC2
dfrq2 0
dn2
dpwr2 1
dof2 0
dm2 n
dmm2 c
dmf2 200
dseq2
dres2 1.0
homo2 n
DEC3
dfrq3 0
dn3
dpwr3 1
dof3 0
dm3 n
dmm3 c
dmf3 200
dseq3
dres3 1.0
homo3 n
PROCESSING
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt wft
Br
CO2Me
N
CO2Me
N
H
SO2Ph
(+)-58
11
10
9
8
7
6
5
4
3
2
1
ppm
1.92
2.07
0.90
1.00
3.06
3.10


Br
CO2Me
N
CO2Me
N
H
SO2Ph
200
180
160
140
120
100
80
60
40
20
0
ppm

(+)-**58**


79.4
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.6
%T
167
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400.0
cm-1
3064.73
3003.57
2953.98
2852.09
1754.59
1716.44
1600.87
1446.92
1382.20
1349.78
1170.60
1129.69
1118.22
1090.91
1025.87
994.33
961.19
850.56
771.34
755.86
735.00
717.79
700.38
688.46
Br
CO2Me
N
CO2Me
N
H
SO2Ph
(+)-58

```
Injection Date   : 8/25/2006 4:36:58 PM          Seq. Line :   1
Sample Name      :                               Location : Vial 1
Acq. Operator    :                                  Inj :   1
                                                 Inj. Volume : 1 µl

Acq. Method      : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed     : 8/10/2006 9:12:26 AM
Analysis Method  : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed     : 11/3/2006 9:53:11 AM
                   (modified after loading)
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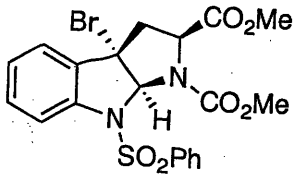
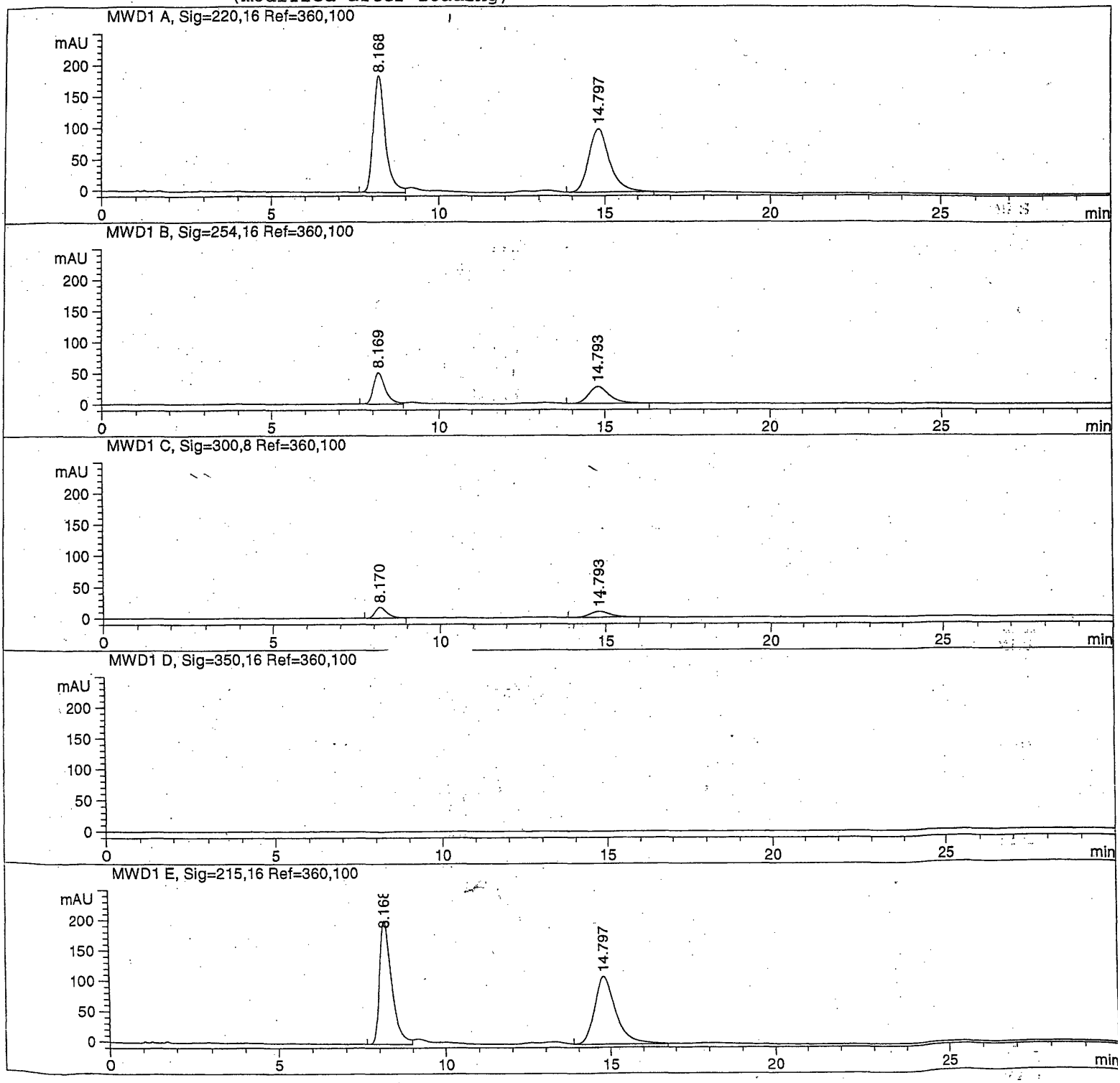


(±)-58



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.168	VV	0.3799	4729.16699	186.43048	51.1452
2	14.797	VB	0.6735	4517.38184	101.44996	48.8548
Totals :				9246.54883	287.88044	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.169	VV	0.3825	1285.78845	50.59615	50.8871
2	14.793	VV	0.6615	1240.95898	27.54830	49.1129
Totals :				2526.74744	78.14444	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.170	BB	0.3812	441.07721	17.42985	52.1192
2	14.793	VB	0.5962	405.20792	9.37651	47.8808
Totals :				846.28513	26.80636	

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

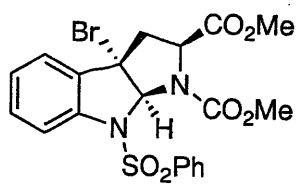
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.168	VV	0.3797	5157.93701	203.47020	50.0545
2	14.797	VB	0.6910	5146.70264	111.82165	49.9455
Totals :				1.03046e4	315.29185	

Results obtained with enhanced integrator!

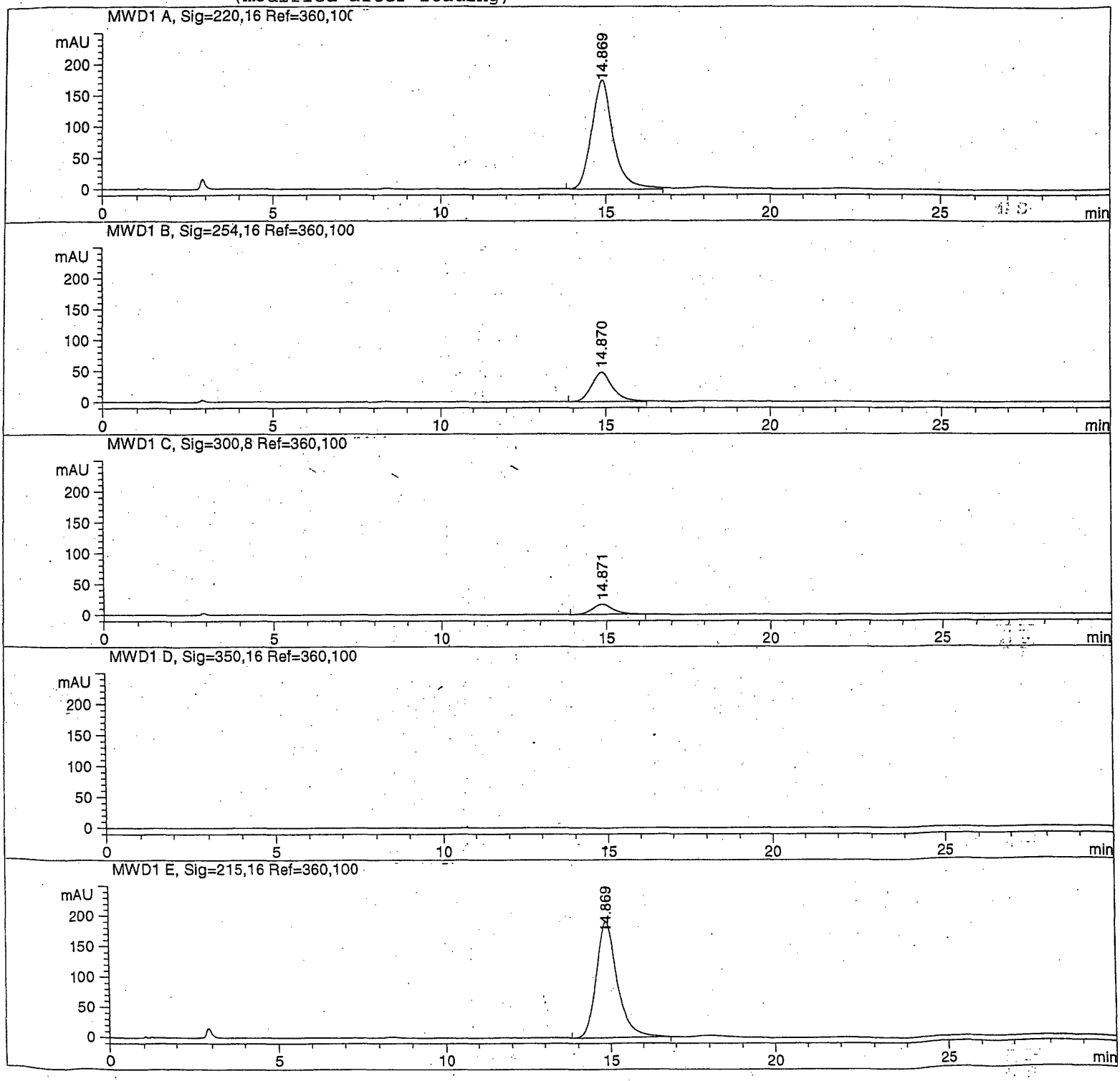
*** End of Report ***

```
==========================================================================
Injection Date  : 8/25/2006 5:09:48 PM          Seq. Line :   1
Sample Name     :                               Location : Vial 1
Acq. Operator   :                                  Inj :   1
                                                Inj Volume : 1 µl

Acq. Method     : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 8/10/2006 9:12:26 AM
Analysis Method : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 11/3/2006 9:53:11 AM
                  (modified after loading)
```



(+)-**58**



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.869	VV	0.6733	7974.86328	175.11238	100.0000
Totals :				7974.86328	175.11238	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.870	VV	0.6657	2145.04810	47.42588	100.0000
Totals :				2145.04810	47.42588	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.871	PB	0.6027	704.74915	16.16243	100.0000
Totals :				704.74915	16.16243	

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

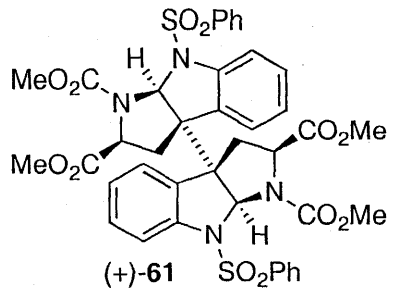
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.869	VB	0.6633	8502.20898	190.29601	100.0000
Totals :				8502.20898	190.29601	

Results obtained with enhanced integrator!

*** End of Report ***

exp2 s2pul

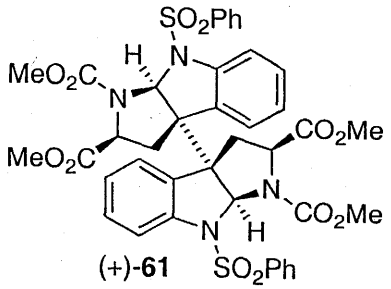
SAMPLE		DEC. & VT	
date	Jan 6 2007	dfrq	125.796
solvent	DMSO	dn	C13
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	500.238	dm	nnn
tn	H1	dmm	c
at	3.200	dmf	10000
np	64000	dseq	
sw	10000.0	dres	1.0
fb	not used	homo	n
bs	1	temp	100.0
ss	1	PROCESSING	
tpwr	59	wtfile	
pw	9.8	proc	ft
d1	7.000	fn	131072
tof	1498.2	math	f
nt	16		
ct	0	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.1		
wp	6252.8		
vs	151		
sc	0		
wc	250		
hzmm	40.00		
is	870.01		
rfl	2243.2		
rfp	1250.6		
th	44		
ins	2.000		
nm ph			



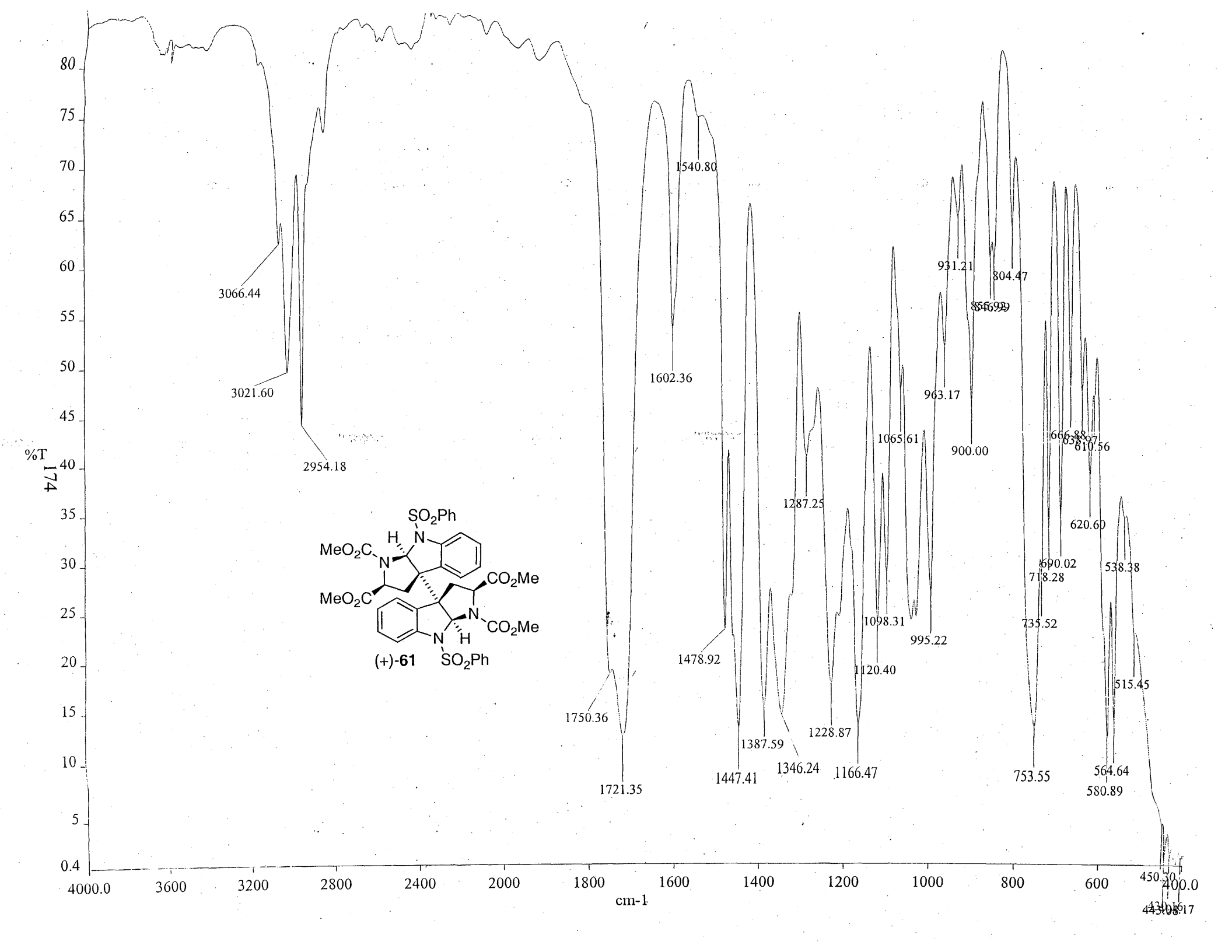
(+)-**61**

exp4 s2pul

SAMPLE		DEC. & VT	
date	Jan 6 2007	dfrq	500.236
solvent	DMSO	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	temp	not used
ss	1	PROCESSING	
tpwr	53	lb	0.30
pw	6.9	wtfile	
d1	0.763	proc	ft
tof	631.4	fn	131072
nt	1e+06	math	f
ct	0		
alock	n	werr	
gain	not used	wexp	
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.2		
wp	30189.3		
vs	151		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	11405.7		
rfp	4969.9		
th	15		
ins	1.000		
nm	ph		



(+)-**61**


%T
cm-1
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
450.30
400.0
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.4
3066.44
3021.60
2954.18
1750.36
1721.35
1602.36
1540.80
1478.92
1447.41
1387.59
1346.24
1287.25
1228.87
1166.47
1120.40
1098.31
1065.61
995.22
963.17
931.21
900.00
804.47
753.55
735.52
718.28
690.02
620.60
610.56
580.89
564.64
538.38
515.45
SO2Ph
MeO2C
CO2Me
(+)-61

```
Injection Date   : 2/4/2007 2:02:53 PM          Seq. Line :   1
Sample Name      :                              Location : Vial 1
Acq. Operator    :                                  Inj :   1
                                                Inj Volume : 10 µl
Acq. Method      : C:\HPCHEM\2\METHODS\
Last changed     : 2/4/2007 2:18:18 PM
                   (modified after loading)
Analysis Method  : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed     : 4/20/2008 10:58:06 AM
                   (modified after loading)
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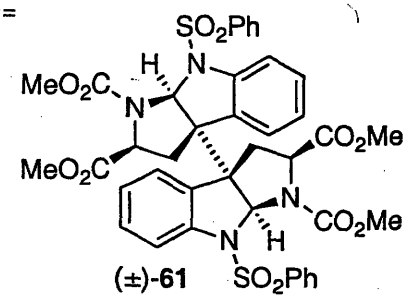
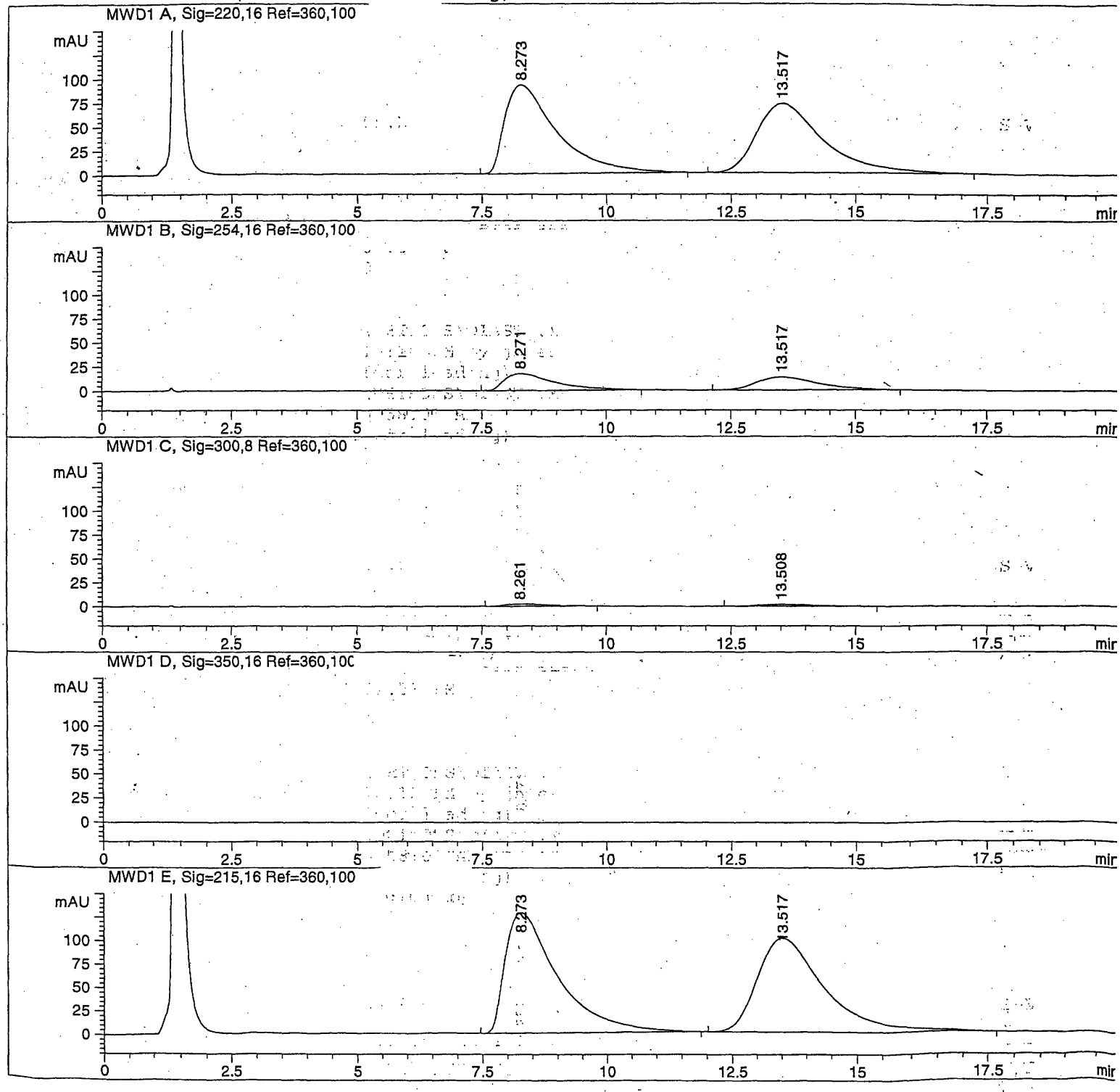


(±)-61



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.273	PB	1.0746	6723.83008	92.22232	50.2531
2	13.517	BB	1.3247	6656.10840	71.72623	49.7469
Totals :				1.33799e4	163.94855	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.271	PB	0.9890	1210.04333	17.32205	50.9955
2	13.517	BB	1.1372	1162.79785	13.31084	49.0045
Totals :				2372.84119	30.63289	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.261	PB	0.7330	150.77000	2.41303	49.2840
2	13.508	BB	0.9804	155.15099	1.87301	50.7160
Totals :				305.92099	4.28603	

Results obtained with enhanced integrator!

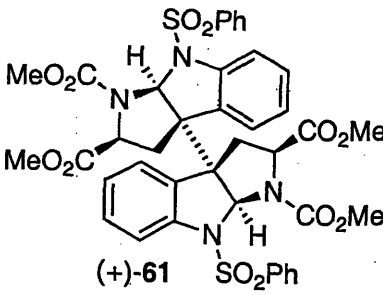
Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.273	PB	1.0785	9358.08594	127.77487	50.1776
2	13.517	BB	1.3478	9291.83203	99.46951	49.8224
Totals :				1.86499e4	227.24438	

Results obtained with enhanced integrator!

*** End of Report ***



(+)-61

```
==========================================================================
Injection Date  : 2/4/2007 2:44:38 PM          Seq. Line :   1
Sample Name     :                              Location : Vial 2
Acq. Operator   :                                  Inj :   1
                                               Inj Volume : 1 µl
Acq. Method     : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 2/4/2007 2:24:09 PM
Analysis Method : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 4/20/2008 10:58:37 AM
                  (modified after loading)
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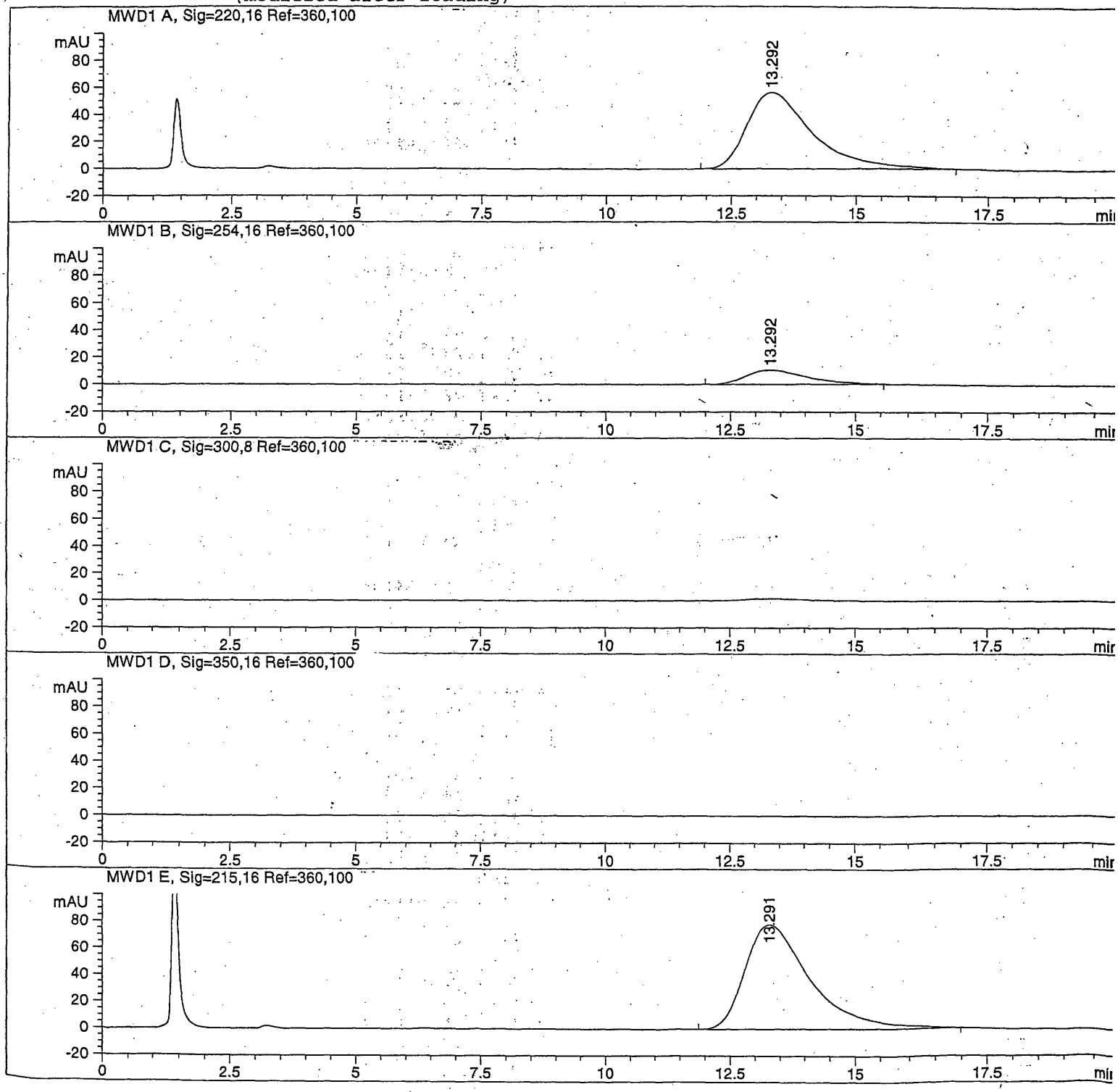


```
================================================================================
                            Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
   #   [min]       [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
    1  13.292 BB    1.3205 5109.18359   56.41901 100.0000

Totals :                  5109.18359   56.41901

 Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
   #   [min]       [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
    1  13.292 BB    1.0247  884.91693   10.46322 100.0000

Totals :                   884.91693   10.46322

 Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100


Signal 4: MWD1 D, Sig=350,16 Ref=360,100


Signal 5: MWD1 E, Sig=215,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
   #   [min]       [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
    1  13.291 BB    1.3380 7069.39355   78.10255 100.0000

Totals :                  7069.39355   78.10255

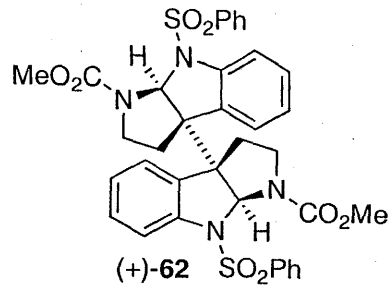
 Results obtained with enhanced integrator!
================================================================================
                            *** End of Report ***
```

```
expl  s2pul

      SAMPLE
date    Jan 18 2007
solvent        DMSO
file            exp
   ACQUISITION
sfrq         500.238
tn                H1
at             3.200
np             64000
sw           10000.0
fb         not used
bs                1
ss                1
tpwr             59
pw              9.8
d1            7.000
tof          1498.2
nt               16
ct               16
alock             n
gain       not used
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp           -250.1
wp           6252.8
vs              151
sc                0
wc              250
hzmm          40.00
is          1033.84
rfl           2243.2
rfp           1250.6
th                7
ins           2.000
nm     ph

      DEC. & VT
dfrq         125.796
dn               C13
dpwr              38
dof                0
dm               nnn
dmm                c
dmf            10000
dseq
dres             1.0
homo               n
temp           100.0
     PROCESSING
wtfile
proc              ft
fn            131072
math               f

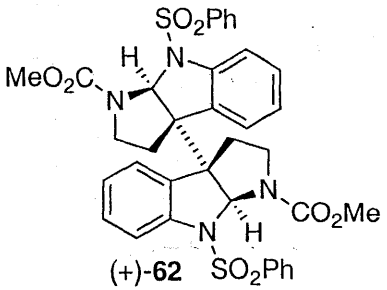
werr
wexp
wbs
wnt
```



(+)-**62**

expl s2pul

SAMPLE		DEC. & VT	
date	Jan 18 2007	dfrq	500.236
solvent	DMSO	dn	H1
file	exp	dpwr	38
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	temp	not used
ss	1	PROCESSING	
tpwr	53	lb	0.30
pw	6.9	wtfile	
d1	0.763	proc	ft
tof	631.4	fn	131072
nt	1e+06	math	f
ct	17772		
alock	n	werr	
gain	not used	wexp	
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.2		
wp	30189.3		
vs	878		
sc	0		
wc	250		
hzmm	4.60		
is	500.00		
rfl	11409.1		
rfp	4969.9		
th	12		
ins	1.000		
ai	ph		



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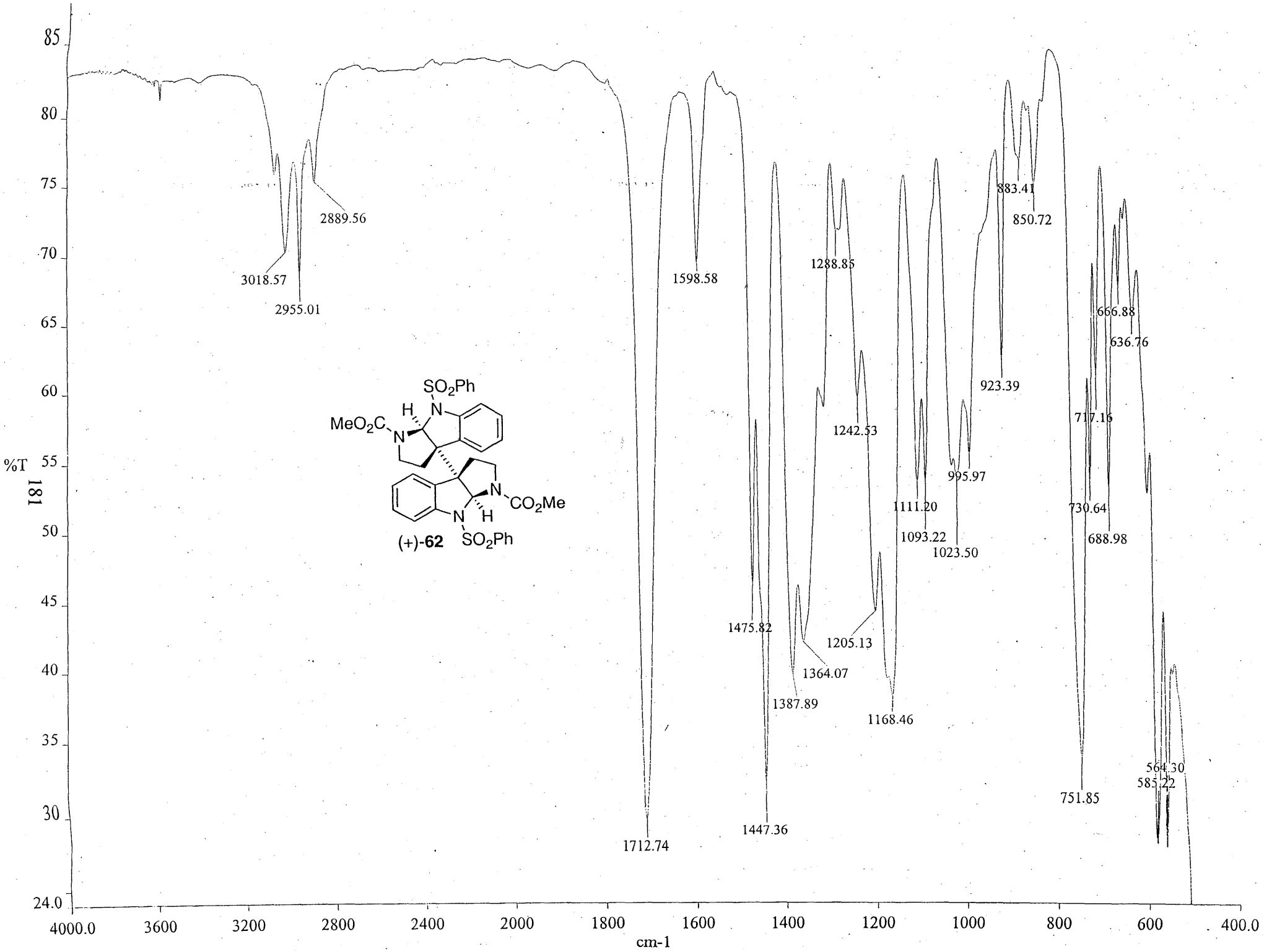
%T
cm-1
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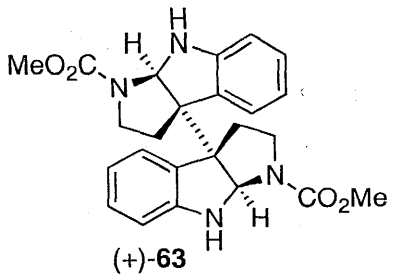
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400.0
85
80
75
70
65
60
55
50
45
40
35
30
24.0
3018.57
2955.01
2889.56
1598.58
1712.74
1475.82
1447.36
1387.89
1364.07
1288.85
1242.53
1205.13
1168.46
1111.20
1093.22
1023.50
995.97
923.39
883.41
850.72
751.85
730.64
717.16
688.98
666.88
636.76
585.22
564.30
181
(+)-62

exp2 s2pul

SAMPLE		DEC. & VT	
date	Jan 22 2007	dfrq	125.796
solvent	DMSO	dn	C13
file	exp	dpwr	38
ACQUISITION		dof	0
sfrq	500.238	dm	nnn
tn	H1	dmm	c
at	3.200	dmf	10000
np	64000	dseq	
sw	10000.0	dres	1.0
fb	not used	homo	n
bs	1	temp	100.0
ss	1	PROCESSING	
tpwr	59	wtfile	
pw	9.8	proc	ft
d1	7.000	fn	131072
tof	1498.2	math	f
nt	16		
ct	16	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.1		
wp	6252.8		
vs	151		
sc	0		
wc	250		
hzmm	40.00		
is	1480.22		
rfl	2242.9		
rfp	1250.6		
th	7		
ins	2.000		
nm	ph		



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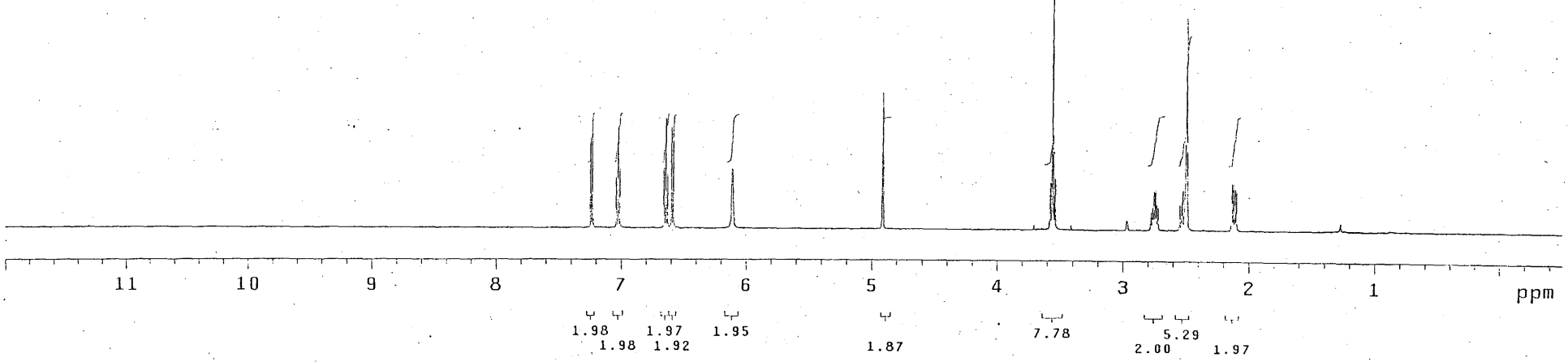
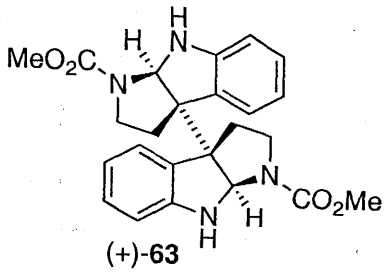
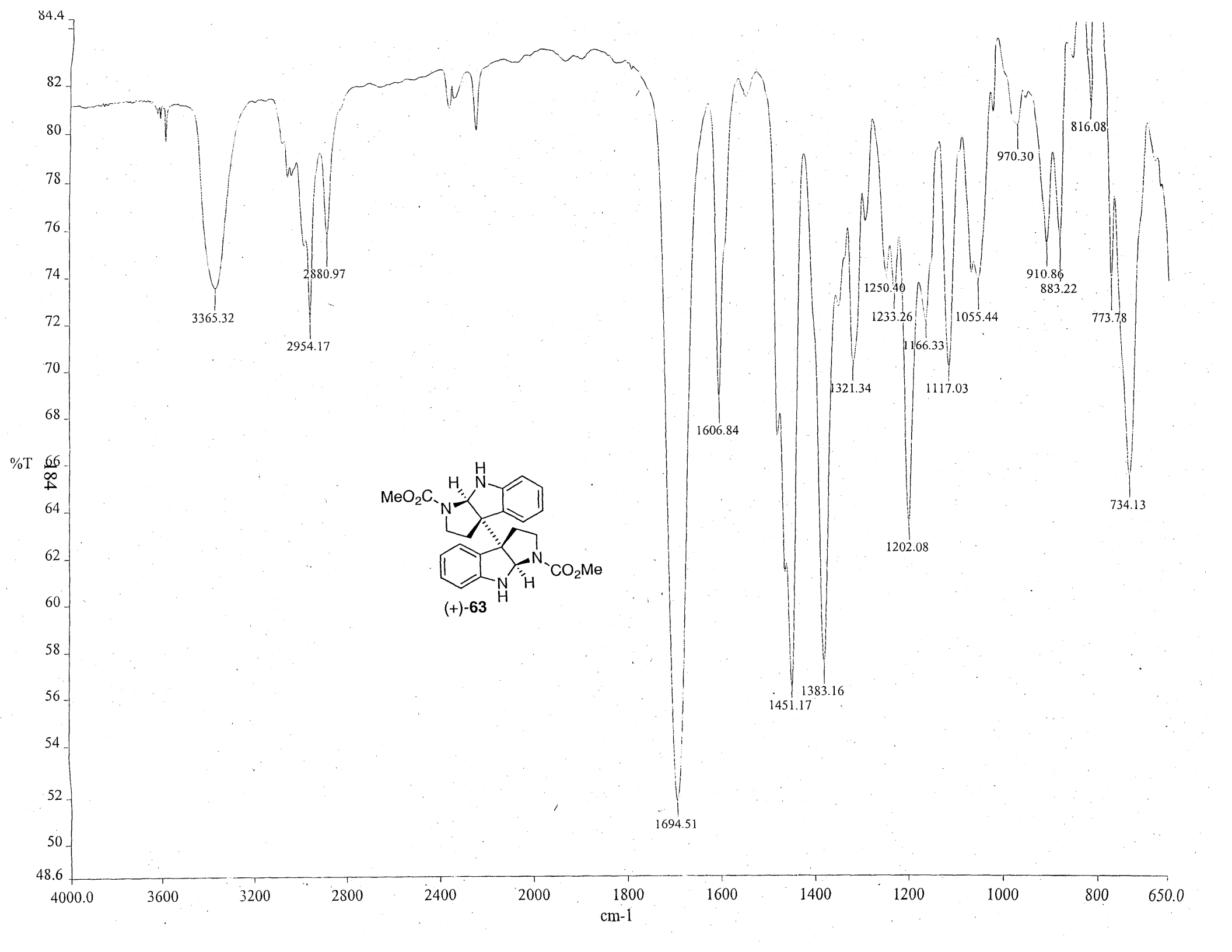


exp2 s2pul

SAMPLE		DEC. & VT	
date	Jan 22 2007	dfrq	500.236
solvent	DMSO	dn	H1
file	exp	dpwr	38
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	temp	100.0
ss	1	PROCESSING	
tpwr	53	lb	0.30
pw	6.9	wtfile	
d1	0.763	proc	ft
tof	631.4	fn	131072
nt	1e+06	math	f
ct	18327		
alock	n	werr	
gain	not used	wexp	
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.2		
wp	30189.3		
vs	151		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	11410.3		
rfp	4969.9		
th	20		
ins	1.000		
nm	ph		



(+)-**63**


84.4
82
80
78
76
74
72
70
68
66
64
62
60
58
56
54
52
50
48.6
%T
3365.32
2954.17
2880.97
1694.51
1606.84
1451.17
1383.16
1321.34
1250.40
1233.26
1202.08
1166.33
1117.03
1055.44
970.30
910.86
883.22
816.08
773.78
734.13
MeO2C
CO2Me
(+)-63
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
650.0
cm-1

```
Injection Date  : 10/8/2006 11:14:12 AM          Seq. Line :   1
Sample Name     :                               Location : Vial 1
Acq. Operator   :                                  Inj :   1
                                                Inj Volume : 1 µl

Acq. Method     : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 10/5/2006 8:02:15 PM
Analysis Method : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 4/21/2008 7:35:37 AM
                  (modified after loading)
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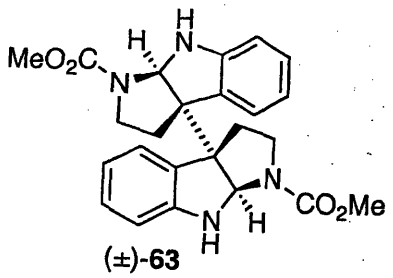
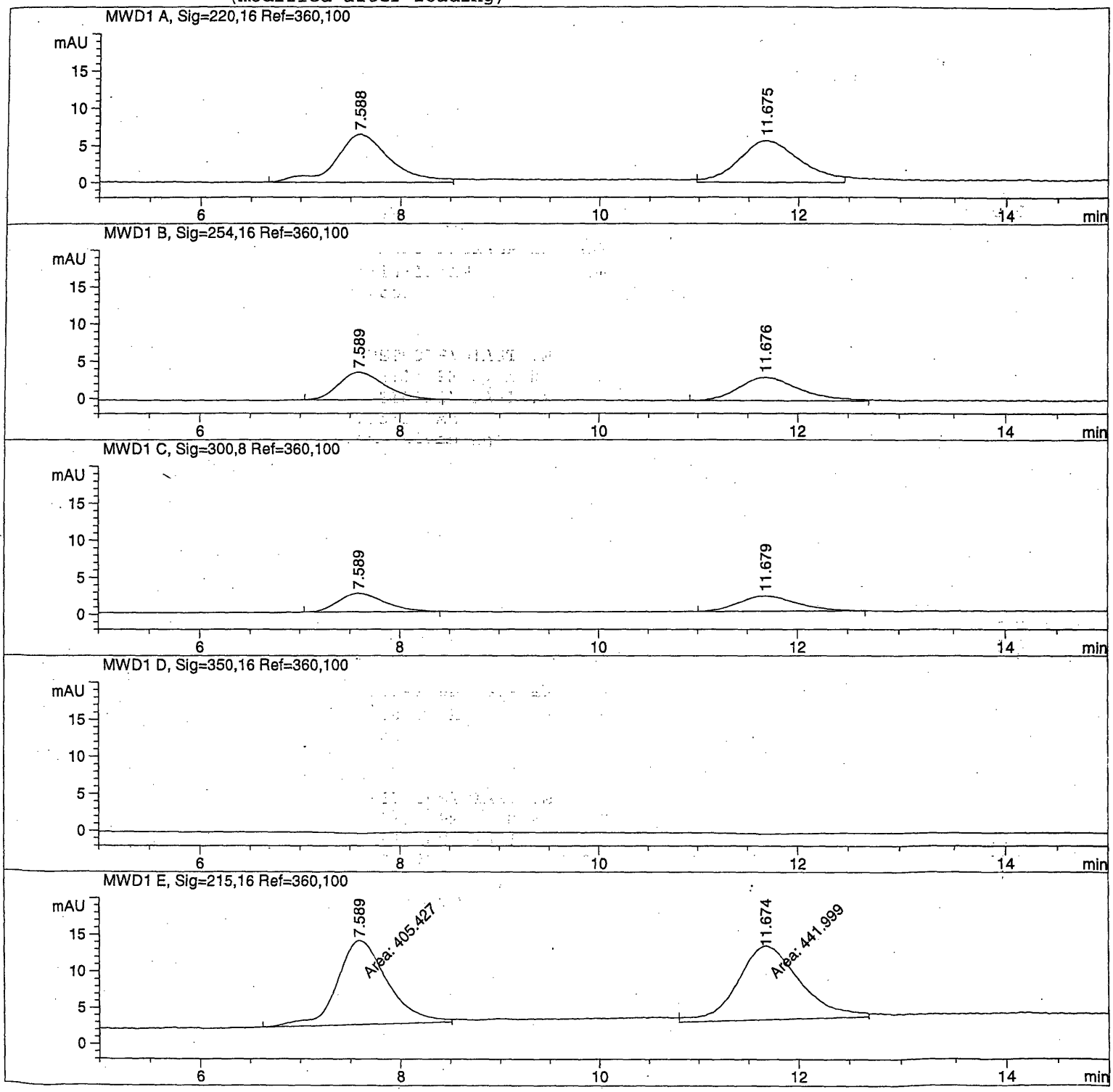


(±)-63



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.588	BV	0.4916	245.93385	6.46734	50.4826
2	11.675	VV	0.5146	241.23187	5.64461	49.5174
Totals :				487.16573	12.11195	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.589	BB	0.4437	118.53646	3.68065	47.6941
2	11.676	BV	0.4996	129.99820	3.13637	52.3059
Totals :				248.53466	6.81702	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.589	BB	0.4477	81.09453	2.51831	49.1445
2	11.679	BB	0.4839	83.91788	2.09222	50.8555
Totals :				165.01241	4.61052	

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.589	MM	0.5859	405.42715	11.53222	47.8422
2	11.674	MM	0.7279	441.99927	10.12015	52.1578
Totals :				847.42642	21.65237	

Results obtained with enhanced integrator!

*** End of Report ***

```
Injection Date  : 10/5/2006 8:03:13 PM          Seq. Line :   1
Sample Name     :                              Location : Vial 1
Acq. Operator   :                                  Inj :   1
                                               Inj Volume : 1 µl

Acq. Method     : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 10/5/2006 8:02:15 PM
Analysis Method : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 4/21/2008 7:37:23 AM
                  (modified after loading)
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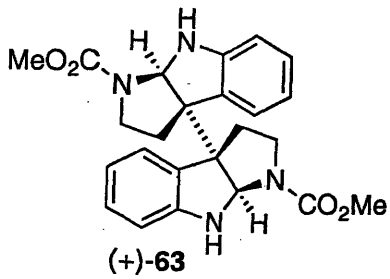
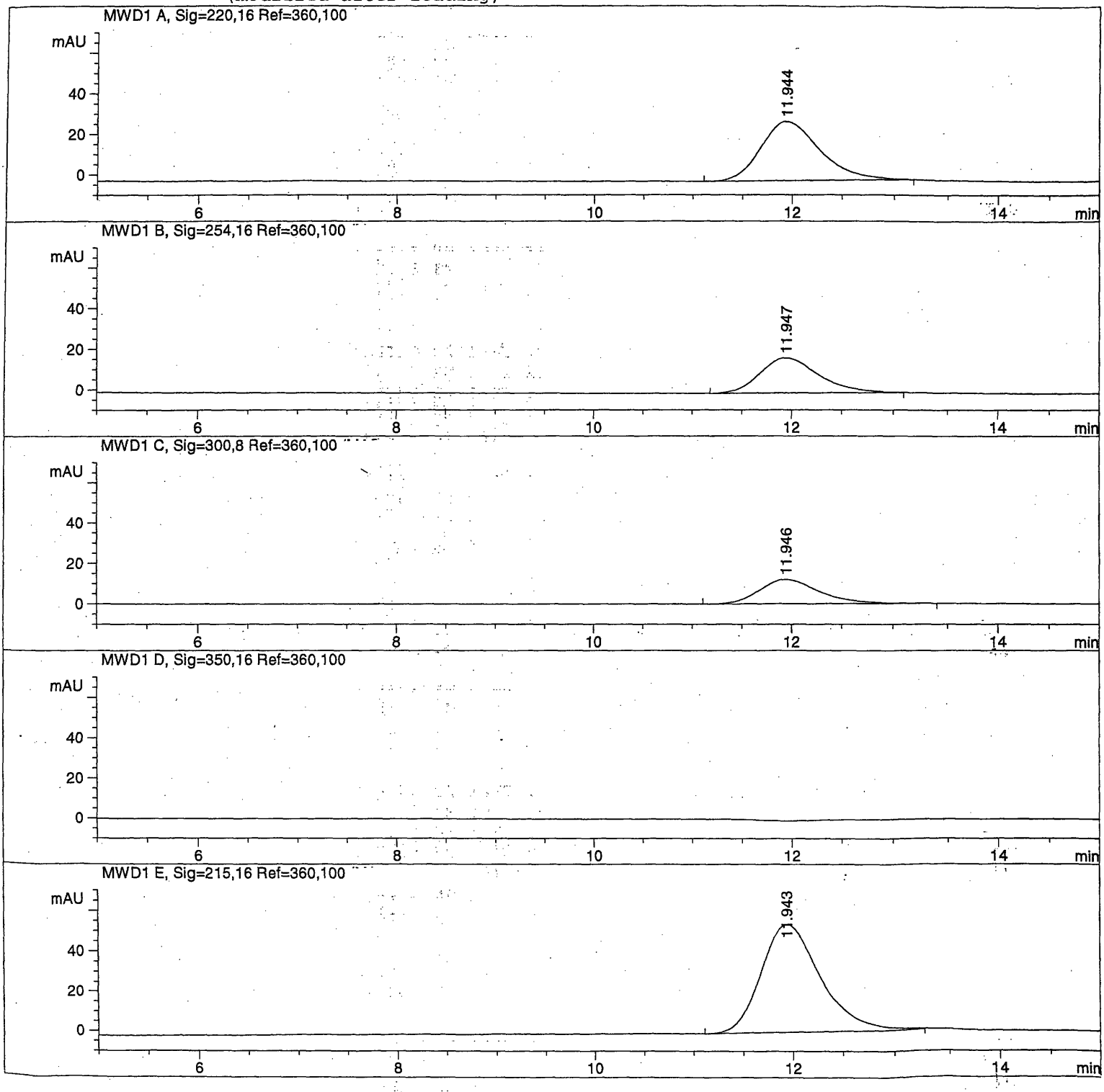


(+)-63



```
================================================================================
                              Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.944 VB    0.6221 1205.06702   29.16266 100.0000

Totals :                  1205.06702   29.16266

 Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.947 VB    0.5942  712.70563   17.31634 100.0000

Totals :                   712.70563   17.31634

 Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.946 VV    0.6064  502.43103   11.95302 100.0000

Totals :                   502.43103   11.95302

 Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=350,16 Ref=360,100


Signal 5: MWD1 E, Sig=215,16 Ref=360,100

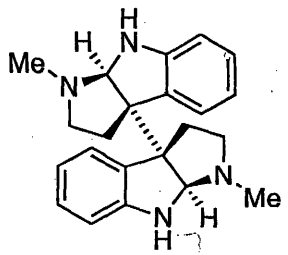
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.943 VB    0.6284 2234.56982   53.59673 100.0000

Totals :                  2234.56982   53.59673

 Results obtained with enhanced integrator!
================================================================================
                            *** End of Report ***
```

exp2 s2pul

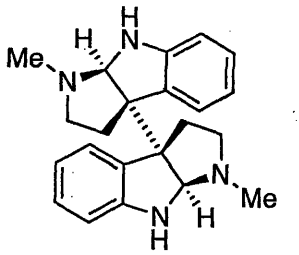
SAMPLE		DEC. & VT	
date	Jan 26 2007	dfrq	125.795
solvent	CDCl3	dn	C13
file	exp	dpwr	38
ACQUISITION		dof	0
sfrq	500.235	dm	nnn
tn	H1	dmm	c
at	3.200	dmf	10000
np	64000	dseq	
sw	10000.0	dres	1.0
fb	not used	homo	n
bs	1	temp	50.0
ss	1	PROCESSING	
tpwr	59	wtfile	
pw	9.8	proc	ft
d1	7.000	fn	131072
tof	1498.2	math	f
nt	16		
ct	16	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.7		
wp	6252.8		
vs	151		
sc	0		
wc	250		
hzmm	40.00		
is	616.67		
rfl	4633.2		
rfp	3636.7		
th	7		
ins	2.000		
nm	ph		



(+)-Chimonanthine (2)

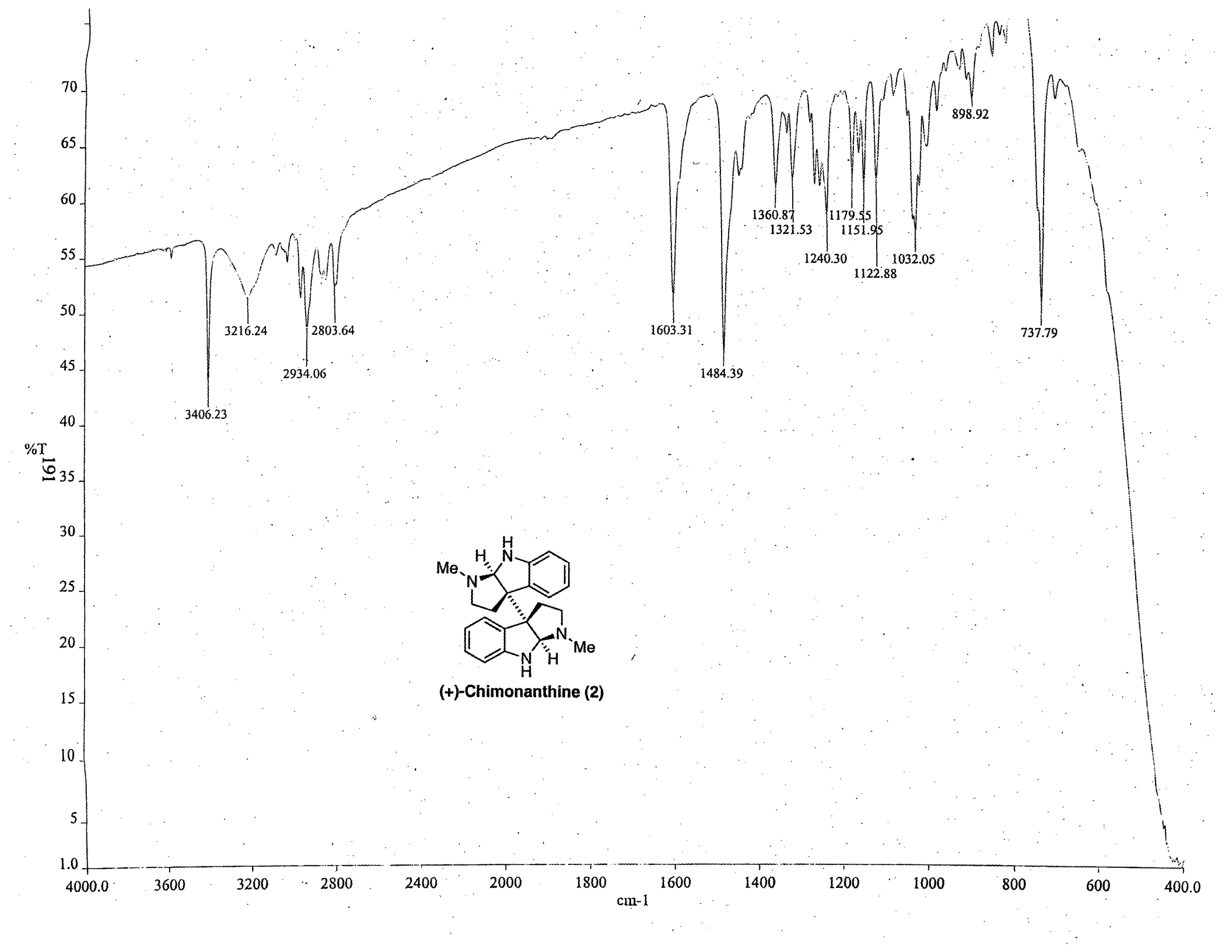
exp2 s2pul

SAMPLE		DEC. & VT	
date	Jan 26 2007	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	38
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	temp	50.0
ss	1	PROCESSING	
tpwr	53	lb	0.30
pw	6.9	wtfile	
d1	0.763	proc	ft
tof	631.4	fn	131072
nt	1e+06	math	f
ct	1478		
alock	n	werr	
gain	not used	wexp	
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	30189.8		
vs	796		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	15993.2		
rfp	9715.0		
th	20		
ins	1.000		
ai	ph		



(+)-Chimonanthine (2)

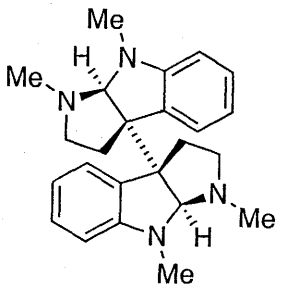
200 180 160 140 120 100 80 60 40 20 0 ppm



(+)-Chimonanthine (2)

exp2 s2pul

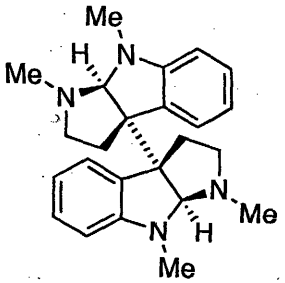
SAMPLE		DEC. & VT	
date	Jan 27 2007	dfrq	125.795
solvent	CDCl3	dn	C13
file	exp	dpwr	38
ACQUISITION		dof	0
sfrq	500.235	dm	nnn
tn	H1	dmm	c
at	3.200	dmf	10000
np	64000	dseq	
sw	10000.0	dres	1.0
fb	not used	homo	n
bs	1	temp	50.0
ss	1	PROCESSING	
tpwr	59	wtfile	
pw	9.8	proc	ft
d1	7.000	fn	131072
tof	1498.2	math	f
nt	16		
ct	16	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.2		
wp	6252.8		
vs	38		
sc	0		
wc	250		
hzmm	2.14		
is	200.77		
rfl	4633.1		
rfp	3636.7		
th	44		
ins	2.000		
ai	ph		



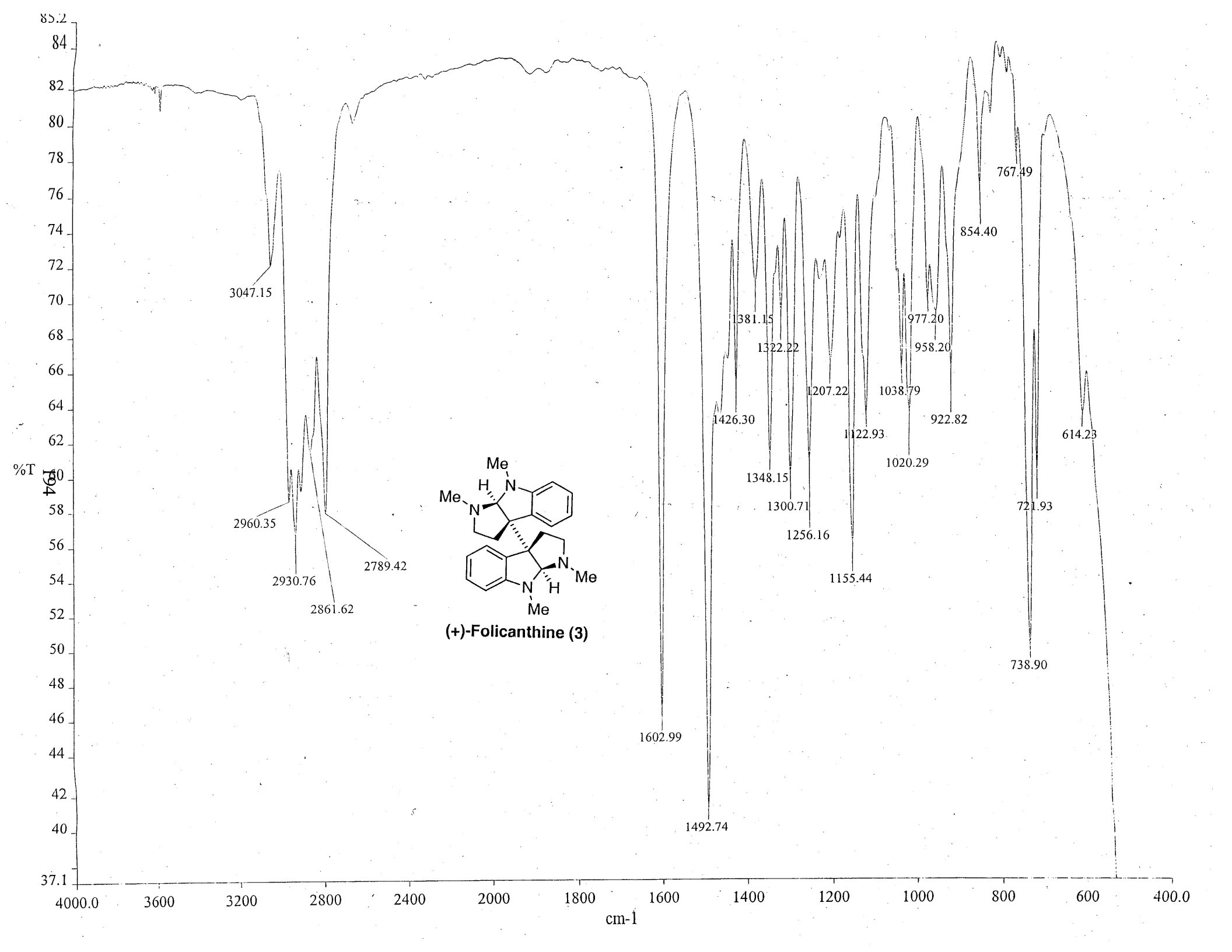
(+)-Folicanthine (3)

exp3 s2pul

SAMPLE		DEC. & VT	
date	Jan 27 2007	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	38
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	**PROCESSING**	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	552	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	30189.8		
vs	915		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	15991.5		
rfp	9715.0		
th	20		
ins	1.000		
ai	ph		



(+)-Folicanthine (3)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cm-1
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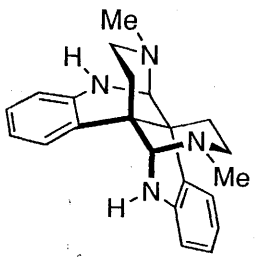
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400.0
3047.15
2960.35
2930.76
2861.62
2789.42
1602.99
1492.74
1426.30
1381.15
1322.22
1348.15
1300.71
1256.16
1207.22
1155.44
1122.93
1038.79
1020.29
977.20
958.20
922.82
854.40
767.49
738.90
721.93
614.23
Me
N
H
Me
N
N
Me
N
H
Me
(+)-Folicanthine (3)

exp2 s2pul

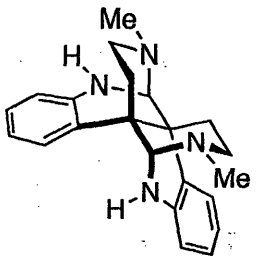
SAMPLE		DEC. & VT	
date	Jan 21 2007	dfrq	125.672
solvent	CDCl3	dn	C13
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.746	dm	nnn
tn	H1	dmm	w
at	3.001	dmf	10000
np	63050	dseq	
sw	10504.2	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.9	dn2	
d1	7.000	dpwr2	1
tof	1519.5	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.0	dof3	0
wp	6246.6	dm3	n
vs	52	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	42.02	dres3	1.0
is	256.75	homo3	n
rfl	4864.7	PROCESSING	
rfp	3633.1	wtfile	
th	7	proc	ft
ins	2.000	fn	131072
ai cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	wft



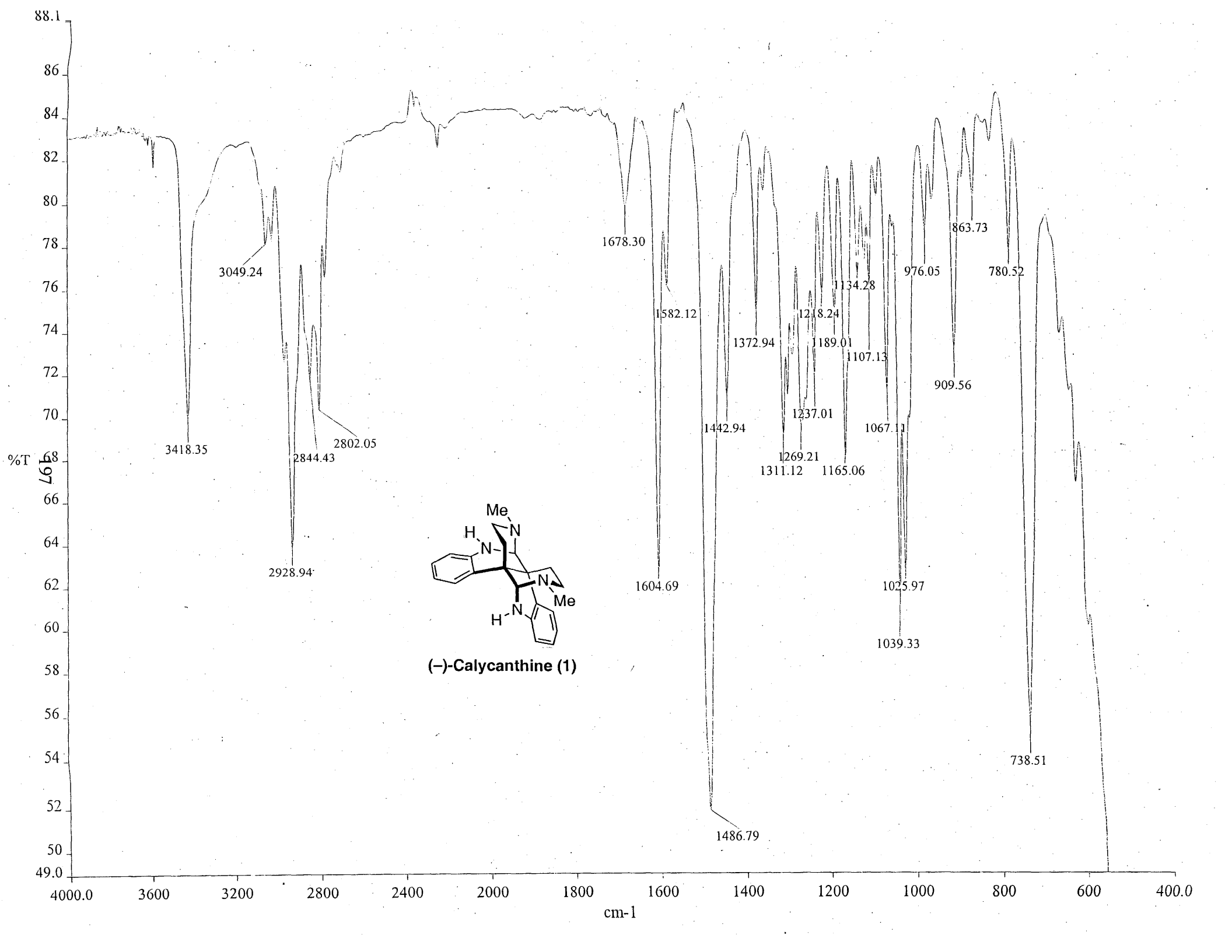
(–)-Calycanthine (1)

exp2 s2pul

SAMPLE		DEC. & VT	
date	Jan 21 2007	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	38
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	0	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	30189.8		
vs	1386		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	16003.0		
rfp	9715.0		
th	20		
ins	1.000		
ai	ph		



(–)-Calycanthine (1)

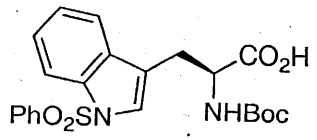


(–)-Calycanthine (1)

Appendix B

Spectra for Chapter II

Pulse Sequence: s2pul
Solvent: DMSO
Ambient temperature
File:
INOVA-500 zippy
PULSE SEQUENCE
Pulse 88.0 degrees
Acq. time 3.200 sec
Width 10000.0 Hz
16 repetitions
OBSERVE H1, 500.2336478 MHz
DATA PROCESSING
FT size 131072
Total time 0 min, 54 sec

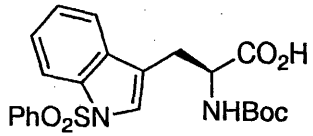


(–)-**15**

Solvent: DMSO
Ambient temperature
User: 1-14-87
INOVA-500 "rocky"

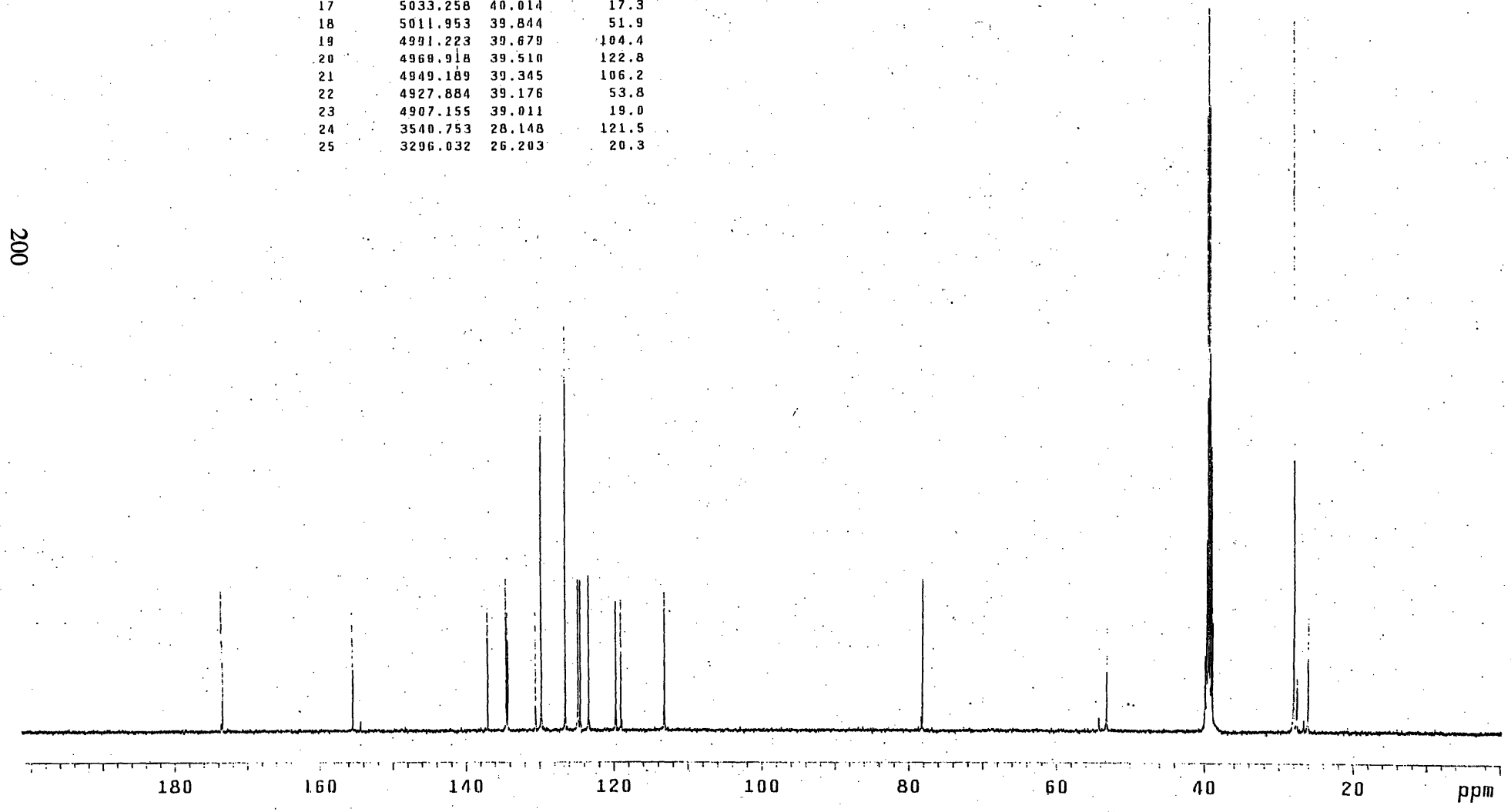
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
1580 repetitions
OBSERVE C13, 125.7839031 MHz
DECOUPLE H1, 500.2356514 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 65 minutes

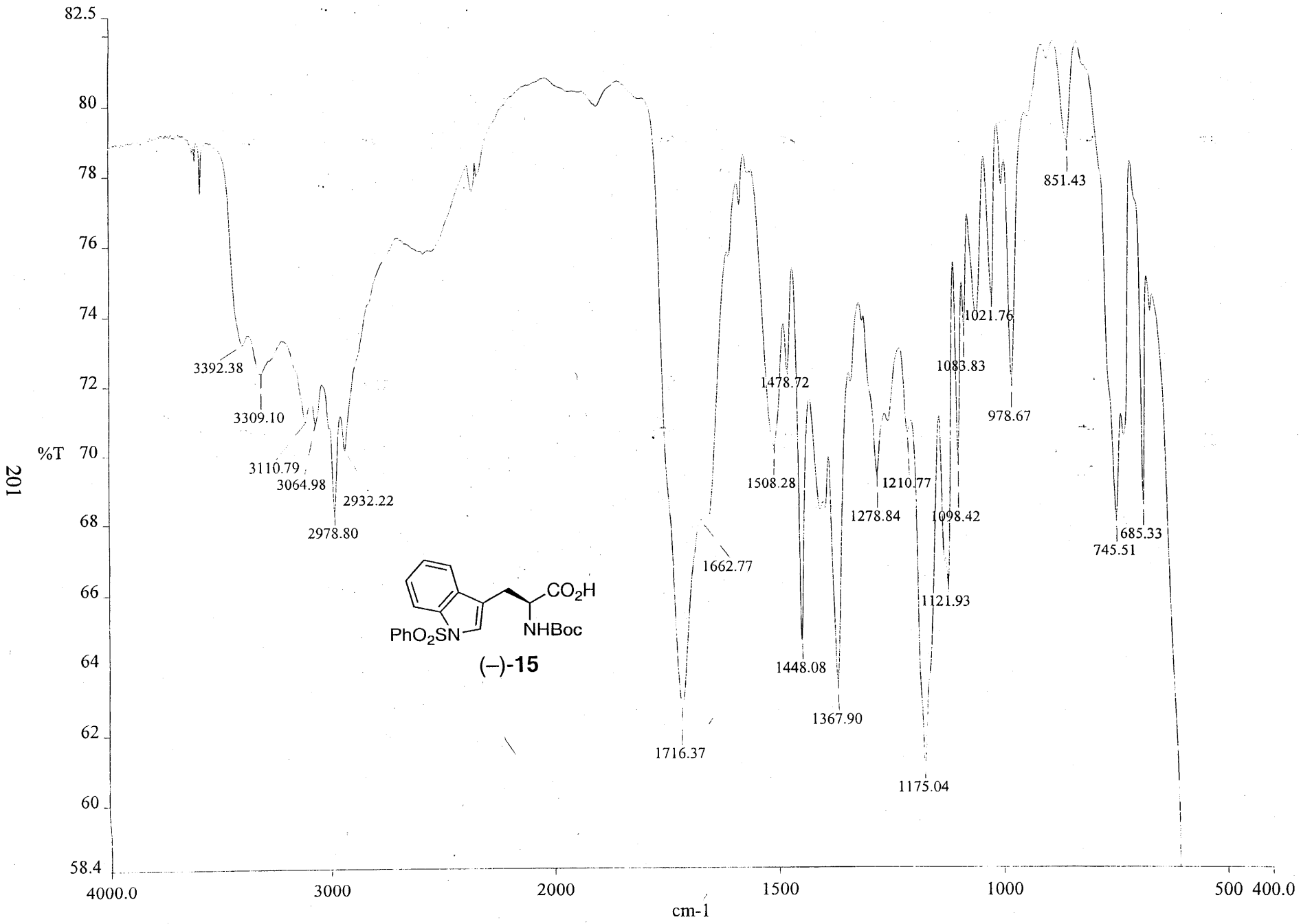
INDEX	FREQUENCY	PPM	HEIGHT
1	21812.424	173.405	23.4
2	19551.209	155.429	20.7
3	17237.596	137.036	20.4
4	16920.899	134.518	25.4
5	16894.988	134.312	20.2
6	16423.974	130.568	19.6
7	16326.681	129.794	63.1
8	15920.138	126.562	68.8
9	15705.360	124.855	27.9
10	15666.205	124.544	26.3
11	15525.131	123.422	26.5
12	15065.633	119.769	21.3
13	14978.685	119.078	21.9
14	14237.039	113.182	23.1
15	9836.107	78.195	25.6
16	6700.810	53.270	24.0
17	5033.258	40.014	17.3
18	5011.953	39.844	51.9
19	4991.223	39.679	104.4
20	4969.918	39.510	122.8
21	4949.189	39.345	106.2
22	4927.884	39.176	53.8
23	4907.155	39.011	19.0
24	3540.753	28.148	121.5
25	3296.032	26.203	20.3



(–)-15

200




82.5
80
78
76
74
72
70
68
66
64
62
60
58.4
%T
201
3392.38
3309.10
3110.79
3064.98
2978.80
2932.22
1716.37
1662.77
1508.28
1478.72
1448.08
1367.90
1278.84
1210.77
1175.04
1121.93
1098.42
1083.83
1021.76
978.67
851.43
745.51
685.33
PhO2SN
CO2H
NHBoc
(–)-15
4000.0
3000
2000
1500
1000
500
400.0
cm-1

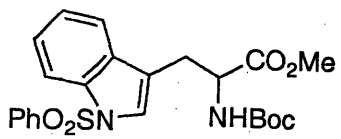
chiralcell ad
10% iprox/hx

==========

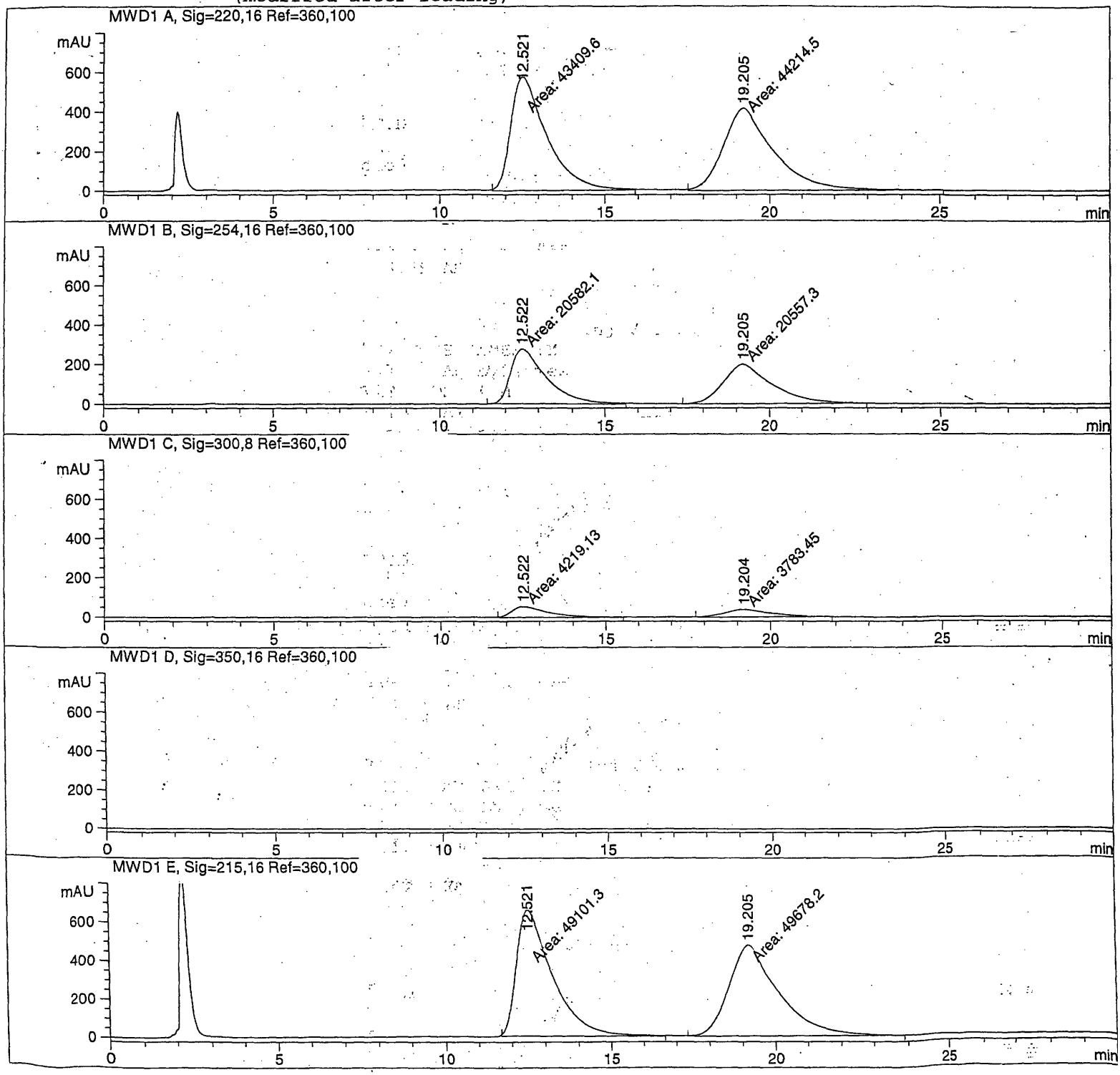
Injection Date : 2/13/2007 8:58:29 AM
Sample Name :
Acq. Operator :

Seq. Line : 1
Location : Vial 61
Inj : 1
Inj Volume : 10 µl

Acq. Method : C:\HPCHEM\2\METHODS\JAMES1.M
Last changed : 2/10/2007 9:47:40 AM
Analysis Method : C:\HPCHEM\2\METHODS\OA.M
Last changed : 6/1/2007 10:14:20 AM
(modified after loading)



(±)-**15** methyl ester



```
================================================================
                      Area Percent Report
================================================================

orted By             :      Signal
ultiplier            :      1.0000
ilution              :      1.0000
se Multiplier & Dilution Factor with ISTDs


ignal 1: MWD1 A, Sig=220,16 Ref=360,100

eak RetTime Type  Width     Area      Height     Area
 #    [min]       [min]   [mAU*s]     [mAU]       %
---|-------|----|-------|----------|----------|--------|
   1  12.521 MM    1.2608 4.34096e4   573.83820  49.5407
   2  19.205 MM    1.7759 4.42145e4   414.94598  50.4593

otals :                  8.76241e4   988.78418

Results obtained with enhanced integrator!

ignal 2: MWD1 B, Sig=254,16 Ref=360,100

eak RetTime Type  Width     Area      Height     Area
 #    [min]       [min]   [mAU*s]     [mAU]       %
---|-------|----|-------|----------|----------|--------|
   1  12.522 MM    1.2447 2.05821e4   275.60135  50.0302
   2  19.205 MM    1.7217 2.05573e4   198.99901  49.9698

otals :                  4.11395e4   474.60036

Results obtained with enhanced integrator!

ignal 3: MWD1 C, Sig=300,8 Ref=360,100

eak RetTime Type  Width     Area      Height     Area
 #    [min]       [min]   [mAU*s]     [mAU]       %
---|-------|----|-------|----------|----------|--------|
   1  12.522 MM    1.2932 4219.13281   54.37683  52.7221
   2  19.204 MM    1.6471 3783.45142   38.28338  47.2779

otals :                  8002.58423   92.66021

Results obtained with enhanced integrator!

ignal 4: MWD1 D, Sig=350,16 Ref=360,100


ignal 5: MWD1 E, Sig=215,16 Ref=360,100

eak RetTime Type  Width     Area      Height     Area
 #    [min]       [min]   [mAU*s]     [mAU]       %
---|-------|----|-------|----------|----------|--------|
   1  12.521 MM    1.2510 4.91013e4   654.13672  49.7080
   2  19.205 MM    1.7468 4.96782e4   473.99106  50.2920

otals :                  9.87796e4  1128.12778

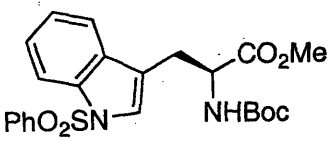
Results obtained with enhanced integrator!
================================================================
                      *** End of Report ***
```

==========

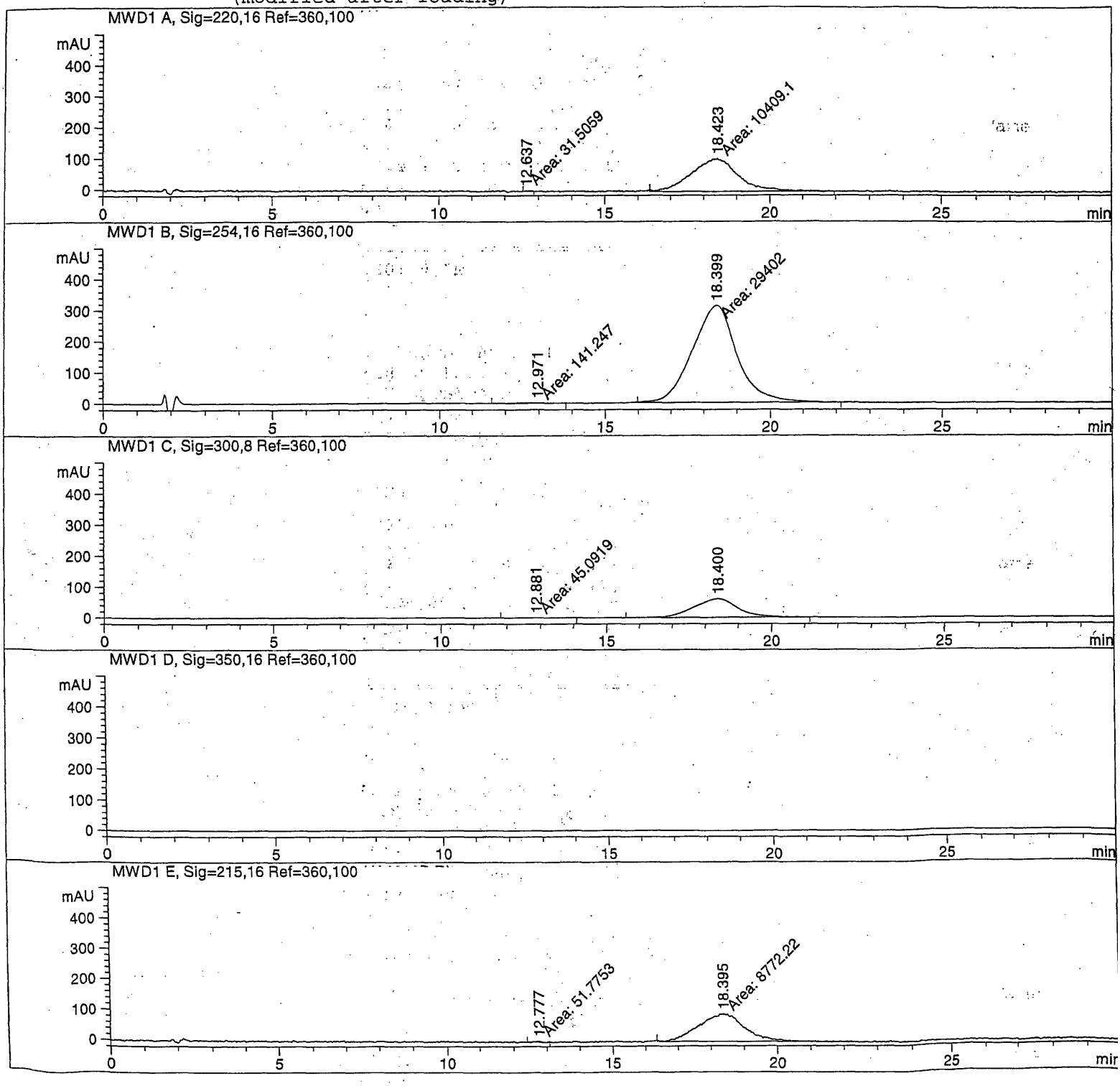
Injection Date : 5/19/2007 6:20:19 PM
Sample Name :
Acq. Operator :

Seq. Line : 1
Location : Vial 51
Inj : 1
Inj Volume : 30 µl

Acq. Method : C:\HPCHEM\2\METHODS\JAMES1.M
Last changed : 5/19/2007 6:18:55 PM
Analysis Method : C:\HPCHEM\2\METHODS\OA.M
Last changed : 6/1/2007 10:09:08 AM
(modified after loading)



(–)-**15** methyl ester



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.637	MM	0.1826	31.50595	2.87612	0.3018
2	18.423	MM	1.6360	1.04091e4	106.04495	99.6982
Totals :				1.04406e4	108.92107	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.971	MM	1.2766	141.24713	1.84410	0.4781
2	18.399	MM	1.5671	2.94020e4	312.70255	99.5219
Totals :				2.95432e4	314.54665	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.881	MM	1.7989	45.09192	4.17762e-1	0.8037
2	18.400	BB	1.3271	5565.57471	59.84031	99.1963
Totals :				5610.66663	60.25807	

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

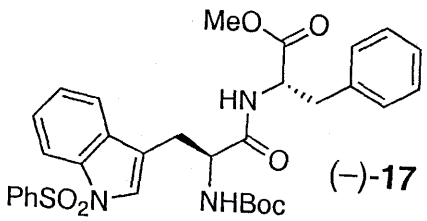
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.777	MM	0.2445	51.77533	3.52983	0.5868
2	18.395	MM	1.6219	8772.22266	90.14417	99.4132
Totals :				8823.99799	93.67401	

Results obtained with enhanced integrator!

*** End of Report ***

exp2 s2pul

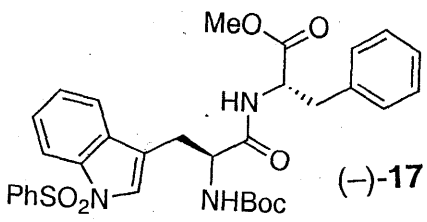
SAMPLE		DEC. & VT	
date	Mar 25 2007	dfrq	125.672
solvent	CDCl3	dn	C13
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.746	dm	nnn
tn	H1	dmm	w
at	3.001	dmf	10000
np	63050	dseq	
sw	10504.2	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.6	dn2	
d1	7.000	dpwr2	1
tof	1519.5	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	6246.7	dm3	n
vs	26	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	2.48	dres3	1.0
is	259.20	homo3	n
rfl	1233.3	PROCESSING	
rfp	0	wtfile	
th	5	proc	ft
ins	3.000	fn	262144
ai cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	wft



(−)-17

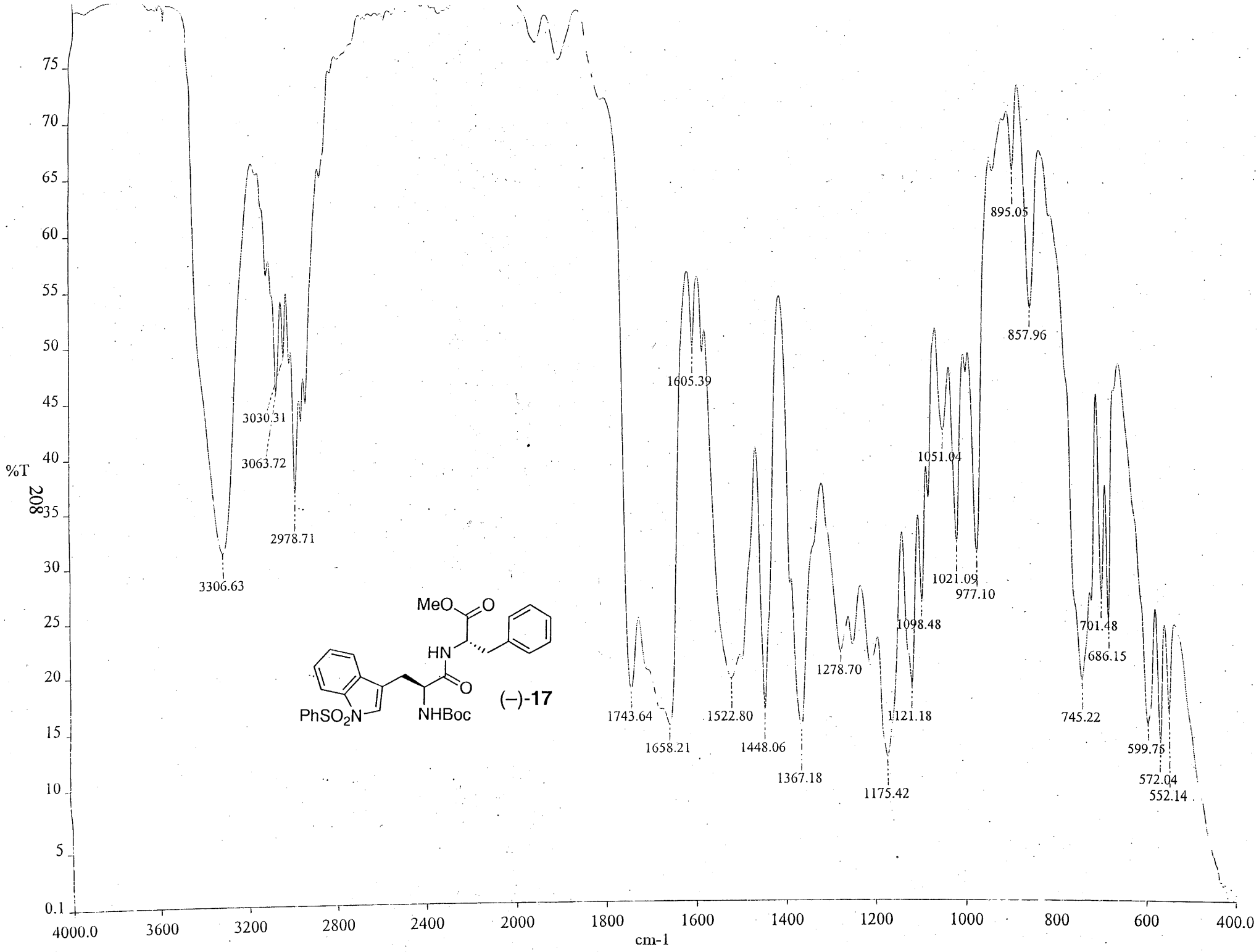
exp6 s2pul

SAMPLE		DEC. & VT	
date	Mar 28 2007	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	0	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	30189.8		
vs	124		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	16021.4		
rfp	9715.0		
th	8		
ins	1.000		
ai	ph		



(–)-17

200 180 160 140 120 100 80 60 40 20 0 ppm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cm-1
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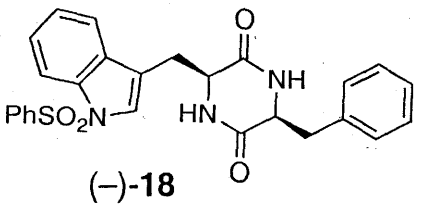
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400.0
3306.63
3030.31
3063.72
2978.71
1605.39
1743.64
1658.21
1522.80
1448.06
1367.18
1278.70
1175.42
1121.18
1098.48
1051.04
1021.09
977.10
895.05
857.96
745.22
701.48
686.15
599.75
572.04
552.14
MeO
O
HN
O
NHBoc
PhSO2N
(–)-17

exp1 s2pul

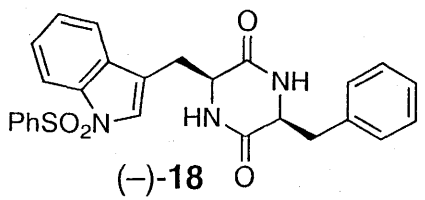
SAMPLE		DEC. & VT	
date	Mar 2 2007	dfrq	125.673
solvent	DMSO	dn	C13
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.748	dm	nnn
tn	H1	dmm	w
at	3.001	dmf	10000
np	63050	dseq	
sw	10504.2	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.9	dn2	
d1	7.000	dpwr2	1
tof	1519.5	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	6246.6	dm3	n
vs	116	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	1.61	dres3	1.0
is	206.25	homo3	n
rfl	2478.9	PROCESSING	
rfp	1249.4	wtfile	
th	7	proc	ft
ins	2.000	fn	131072
ai cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	wft



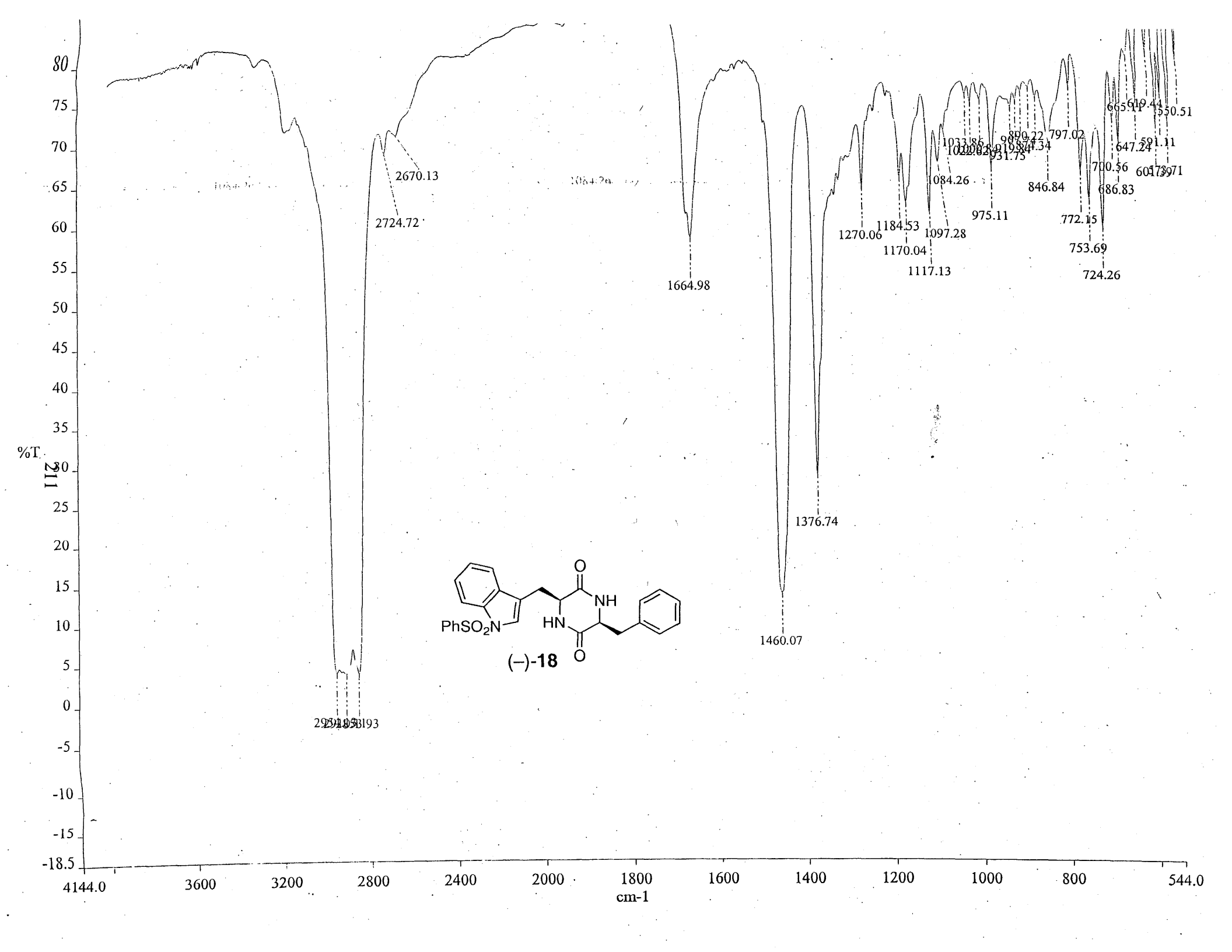
(–)-18

exp2 s2pul

SAMPLE		DEC. & VT	
date	Mar 9 2007	dfrq	500.236
solvent	DMSO	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	2540	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.2		
wp	30189.3		
vs	248		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	11338.3		
rfp	4969.9		
th	9		
ins	1.000		
ai	ph		



(–)-**18**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cm-1
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3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
544.0
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-18.5
2670.13
2724.72
1664.98
1376.74
1460.07
1270.06
1184.53
1170.04
1117.13
1097.28
1084.26
975.11
931.75
846.84
797.02
772.15
753.69
724.26
700.56
686.83
665.11
647.24
619.44
591.11
550.51
PhSO2N
NH
HN
O
(–)-18

```
==================================================================
Injection Date  : 1/27/2007 1:39:21 PM          Seq. Line :   1
Sample Name     :                               Location : Vial 59
Acq. Operator   :                                   Inj :   1
                                                Inj Volume : 10 µl

Acq. Method     : C:\HPCHEM\2\METHODS\JAMES1.M
Last changed    : 1/23/2007 5:10:06 PM
Analysis Method : C:\HPCHEM\2\METHODS\OA.M
Last changed    : 5/21/2007 1:04:56 PM
                  (modified after loading)
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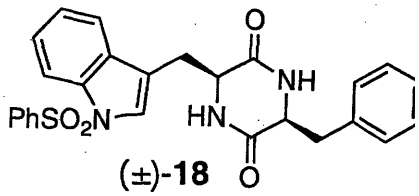
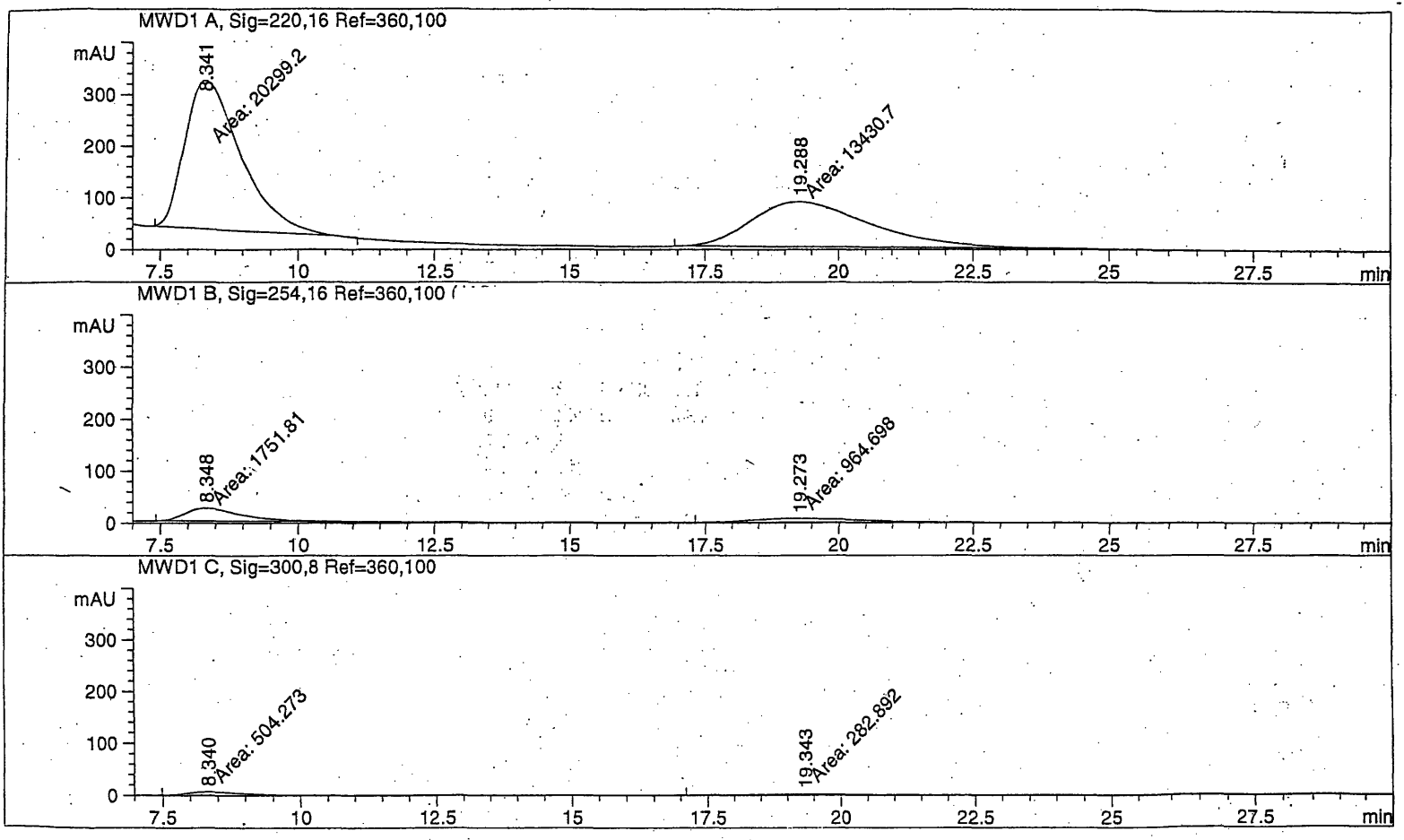
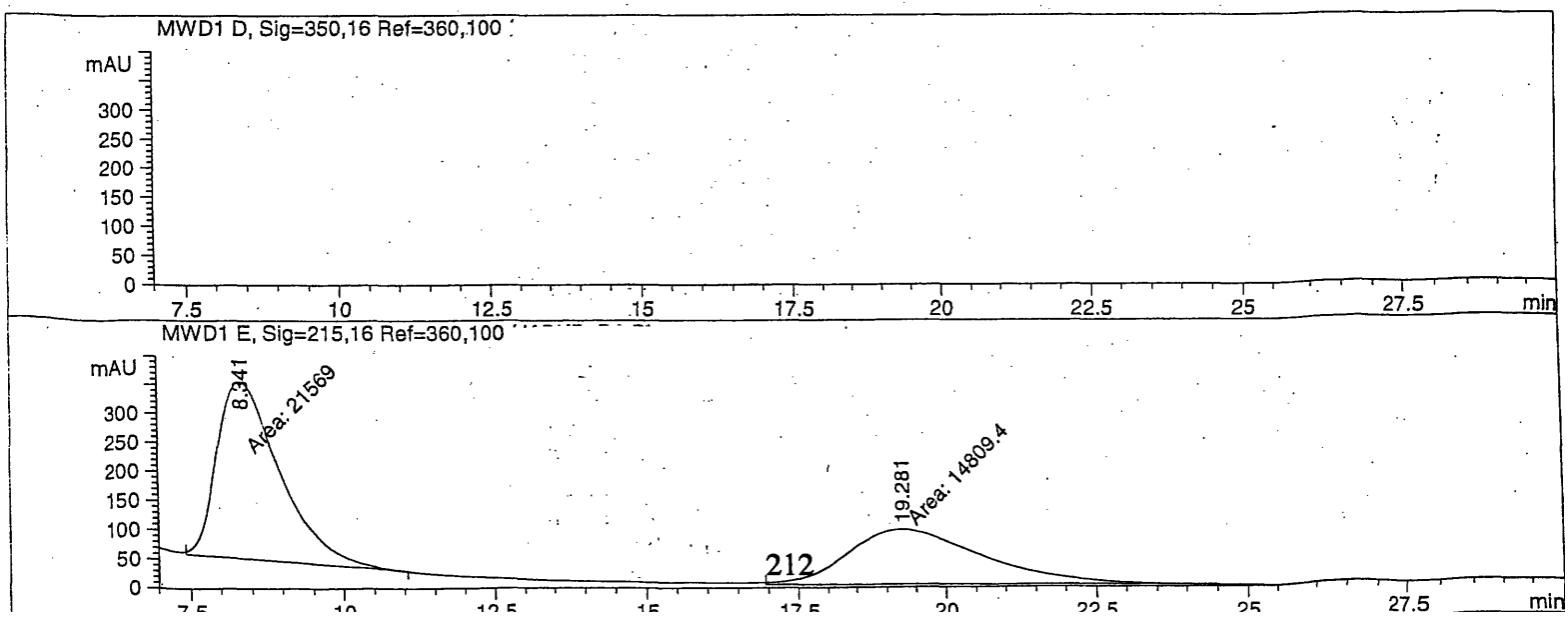


(±)-18





Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.341	MM	1.1761	2.02992e4	287.65393	60.1816
2	19.288	MM	2.5754	1.34307e4	86.91595	39.8184
Totals :				3.37299e4	374.56989	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.348	MM	1.1882	1751.81079	24.57288	64.4876
2	19.273	MM	2.2994	964.69812	6.99241	35.5124
Totals :				2716.50891	31.56529	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.340	MM	1.2739	504.27307	6.59755	64.0619
2	19.343	MM	2.5752	282.89249	1.83089	35.9381
Totals :				787.16556	8.42844	

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.341	MM	1.1824	2.15690e4	304.03726	59.2907
2	19.281	MM	2.6255	1.48094e4	94.00824	40.7093
Totals :				3.63784e4	398.04550	

Results obtained with enhanced integrator!

*** End of Report ***

```
==========================================================================
Injection Date  : 5/23/2007 9:43:56 AM          Seq. Line :   1
Sample Name     :                               Location : Vial 51
Acq. Operator   :                                   Inj :   1
                                              Inj Volume : 1 µl

Acq. Method     : C:\HPCHEM\2\METHODS\JAMES1.M
Last changed    : 5/22/2007 7:26:42 PM
Analysis Method : C:\HPCHEM\2\METHODS\OA.M
Last changed    : 5/23/2007 10:54:19 AM
                  (modified after loading)
==========================================================================
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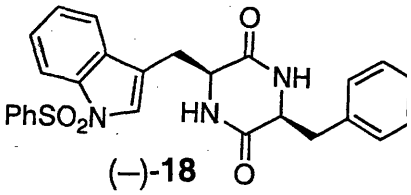
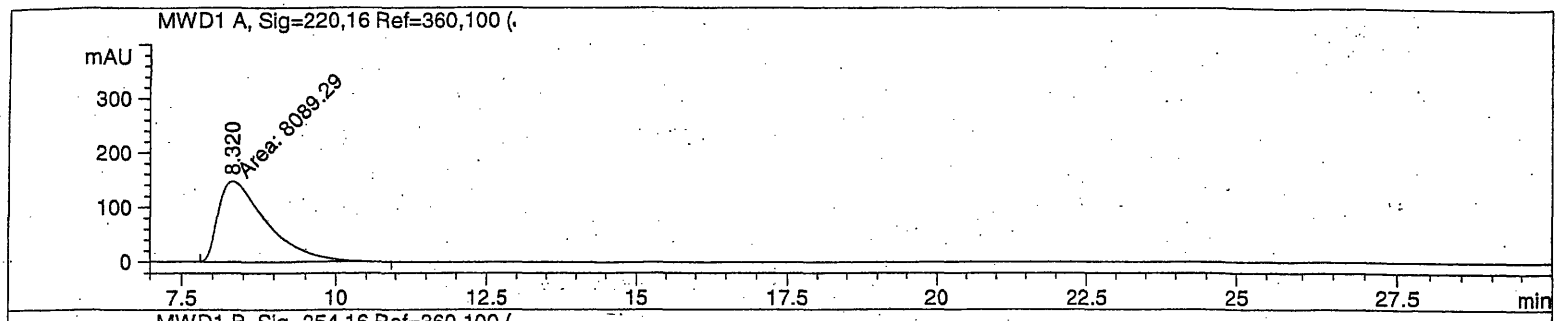
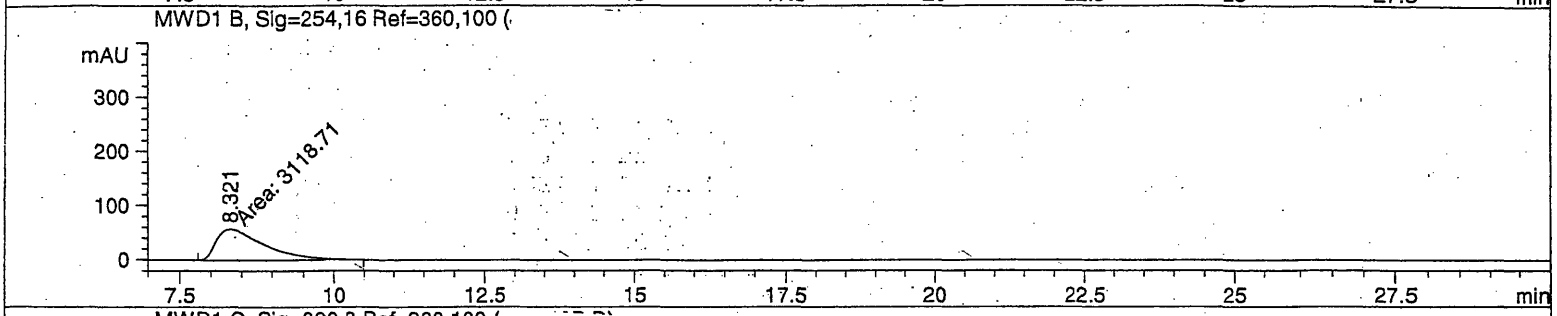
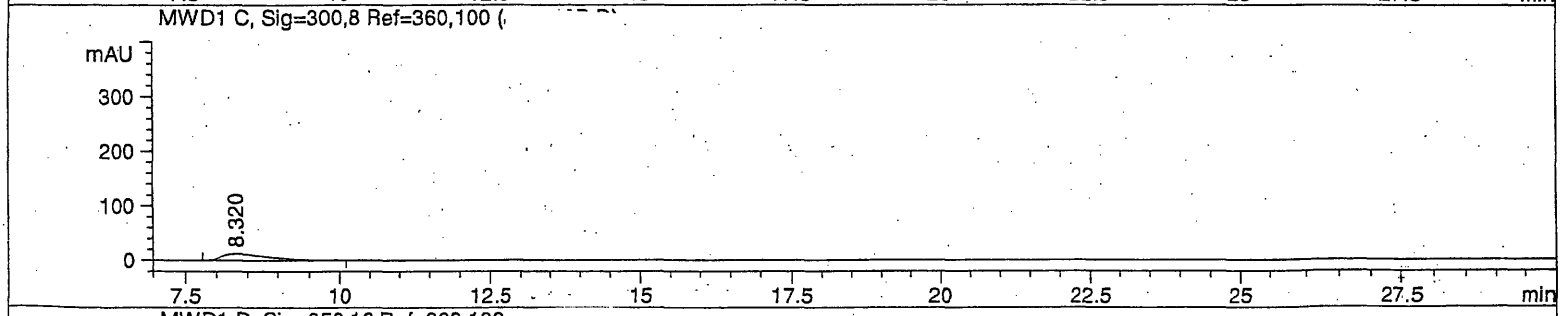
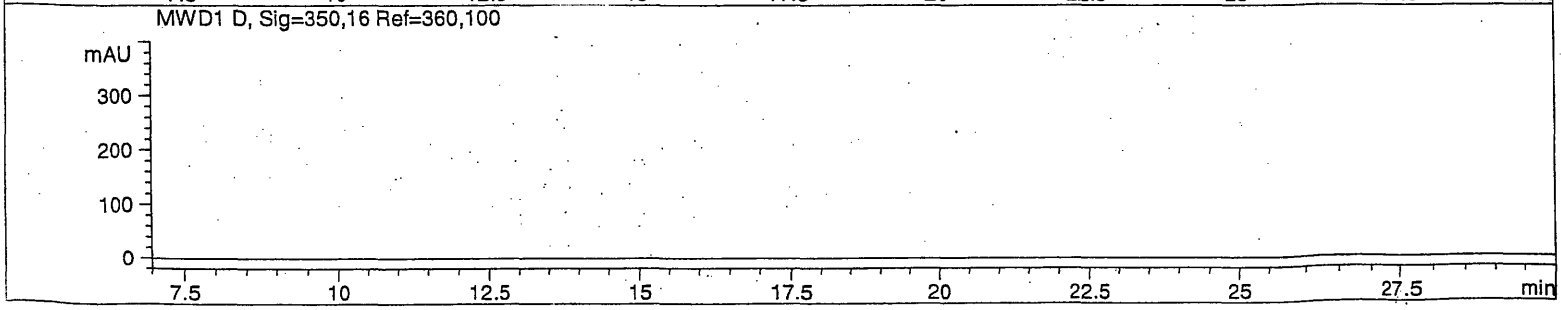


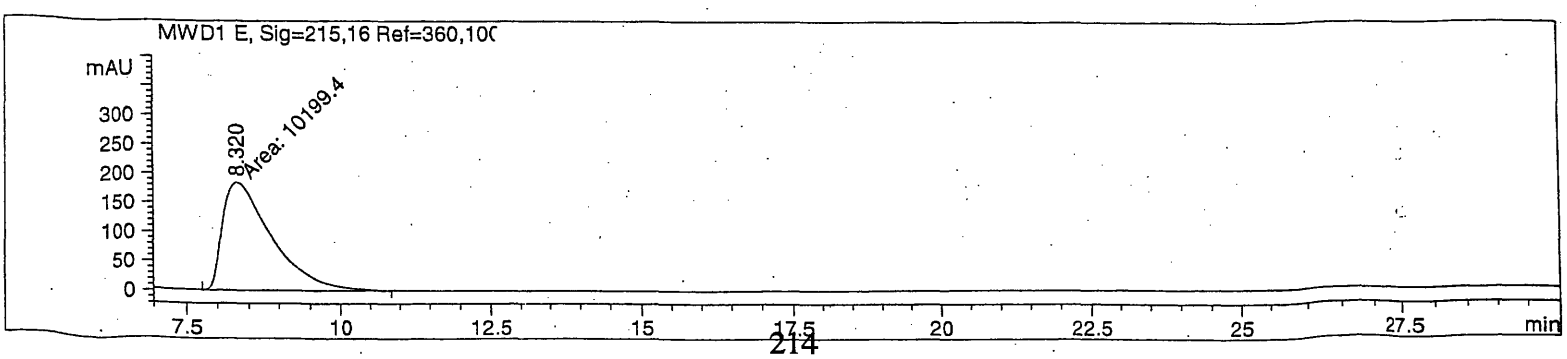
(–)-18











Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.320	MM	0.9147	8089.29248	147.40128	100.0000
Totals :				8089.29248	147.40128	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.321	MM	0.9107	3118.70630	57.07457	100.0000
Totals :				3118.70630	57.07457	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.320	BB	0.7424	671.77313	12.55270	100.0000
Totals :				671.77313	12.55270	

Results obtained with enhanced integrator!

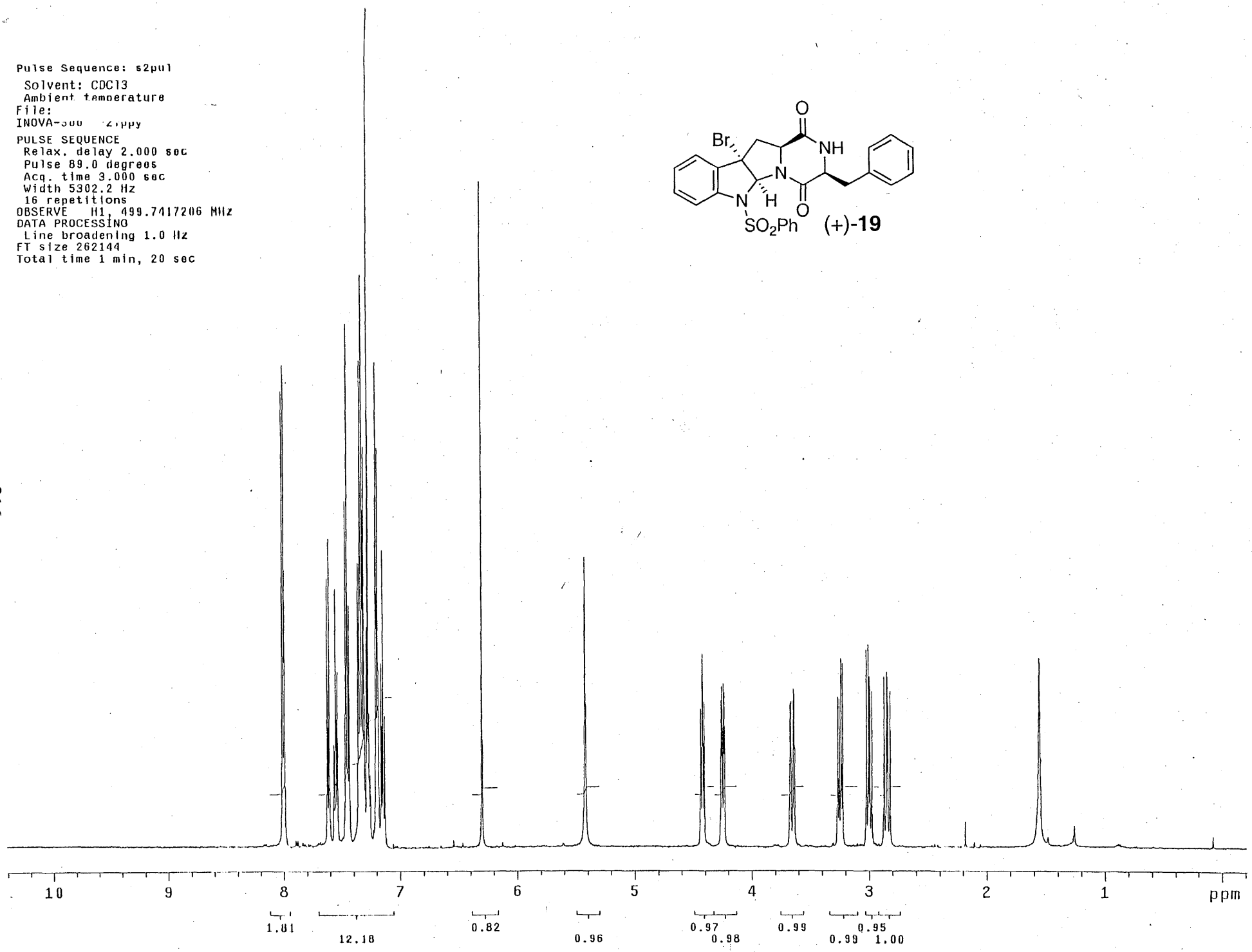
Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.320	MM	0.9256	1.01994e4	183.65283	100.0000
Totals :				1.01994e4	183.65283	

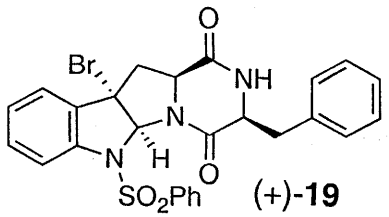
Results obtained with enhanced integrator!

*** End of Report ***

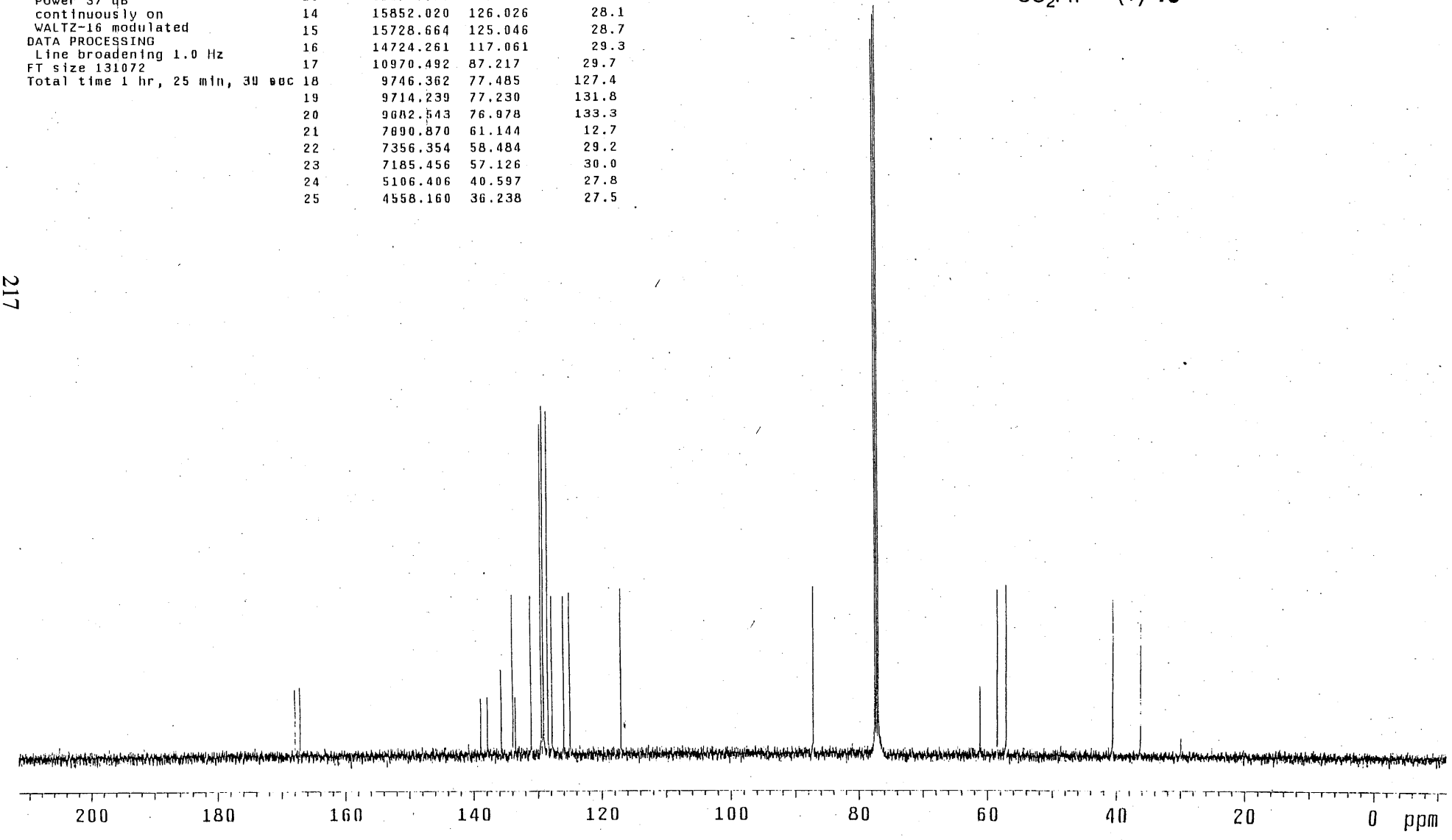

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File:
INOVA-500 Zippy
PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.000 sec
Width 5302.2 Hz
16 repetitions
OBSERVE H1, 499.7417206 MHz
DATA PROCESSING
Line broadening 1.0 Hz
FT size 262144
Total time 1 min, 20 sec
Br
NH
N
N
H
O
O
O
SO2Ph
(+)-19
10
9
8
7
6
5
4
3
2
1
ppm
1.81
12.18
0.82
0.96
0.97
0.98
0.99
0.99
0.95
1.00

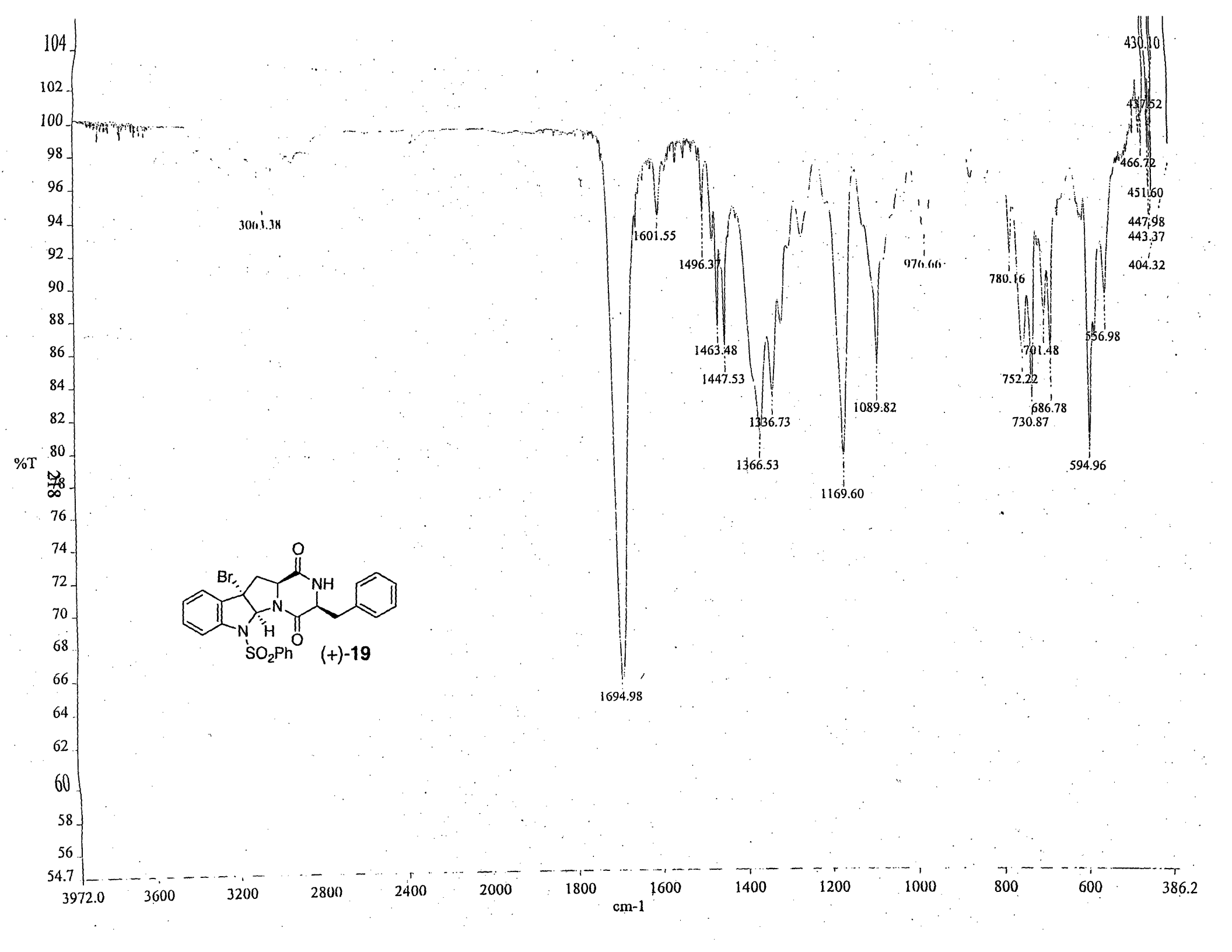
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File:
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 28070.2 Hz
2048 repetitions
OBSERVE C13, 125.7832275 MHz
DECOUPLE H1, 500.2332763 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 1 hr, 25 min, 39 sec

INDEX	FREQUENCY	PPM	HEIGHT
1	21123.744	167.938	12.4
2	21023.946	167.144	12.8
3	17476.626	138.942	10.8
4	17345.561	137.900	11.0
5	17074.008	135.742	15.7
6	16847.428	133.940	28.3
7	16798.600	133.552	11.1
8	16490.640	131.104	28.1
9	16291.473	129.520	58.6
10	16249.498	129.187	61.9
11	16243.073	129.135	60.8
12	16159.123	128.468	60.9
13	16078.171	127.824	28.2
14	15852.020	126.026	28.1
15	15728.664	125.046	28.7
16	14724.261	117.061	29.3
17	10970.492	87.217	29.7
18	9746.362	77.485	127.4
19	9714.239	77.230	131.8
20	9682.543	76.978	133.3
21	7690.870	61.144	12.7
22	7356.354	58.484	29.2
23	7185.456	57.126	30.0
24	5106.406	40.597	27.8
25	4558.160	36.238	27.5



(+)-19

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cm-1
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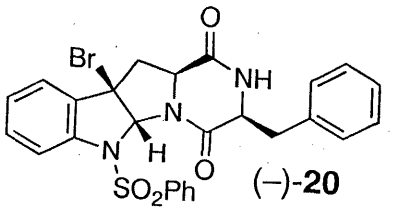
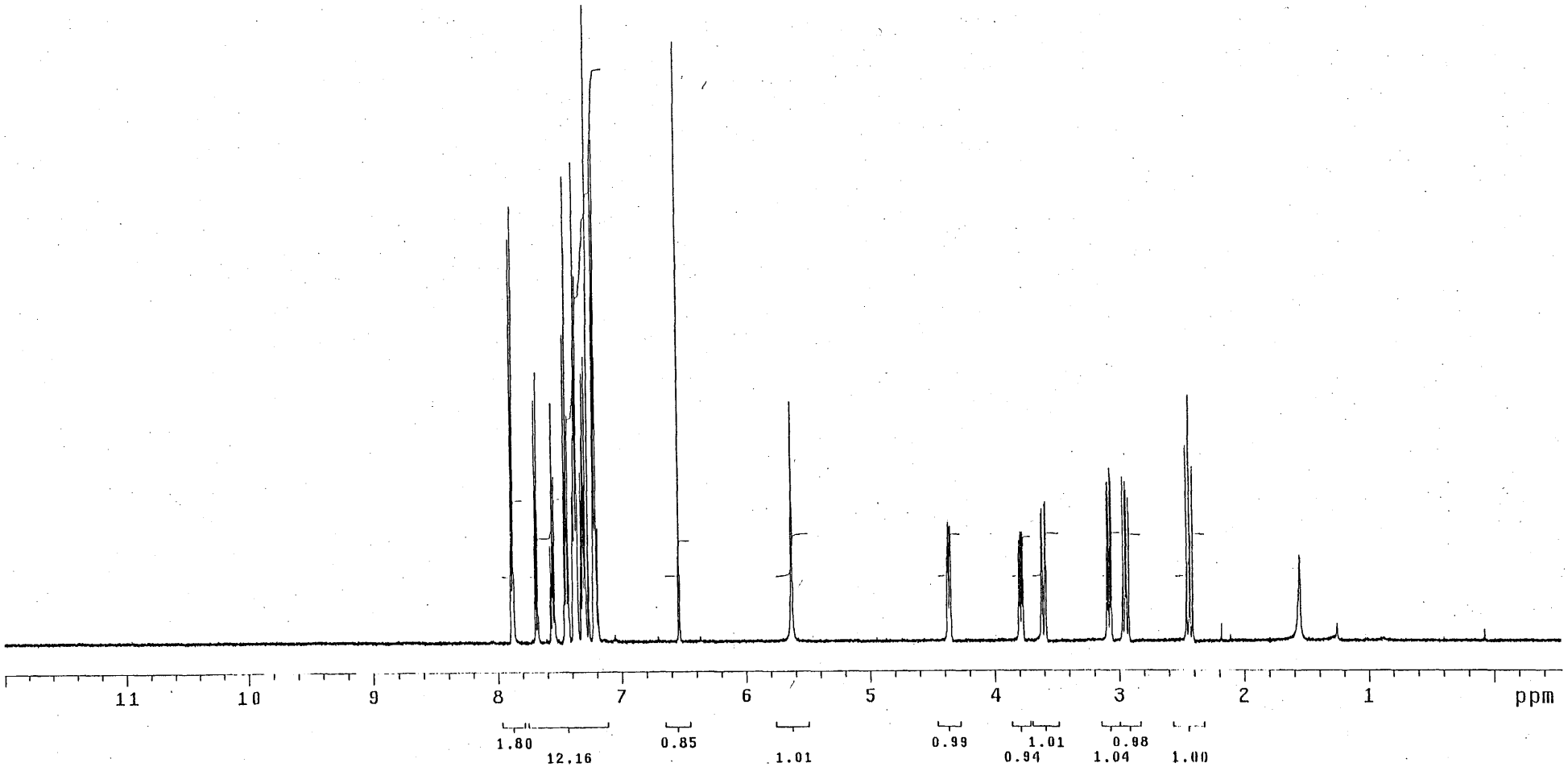
1601.55
1496.37
1463.48
1447.53
1366.53
1336.73
1694.98
1169.60
1089.82
976.66
780.16
752.22
730.87
701.48
686.78
594.96
556.98
466.72
451.60
447.98
443.37
430.10
404.32
Br
NH
N
H
O
SO2Ph
(+)-19

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: ;
INOVA-500 zippy

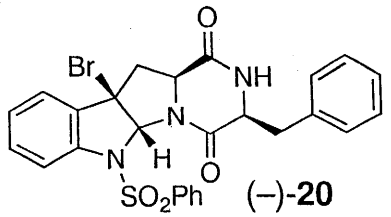
PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
13 repetitions
OBSERVE H1, 499.7417200 MHz
DATA PROCESSING
FT size 262144
Total time 1 min, 20 sec



(−)-**20**

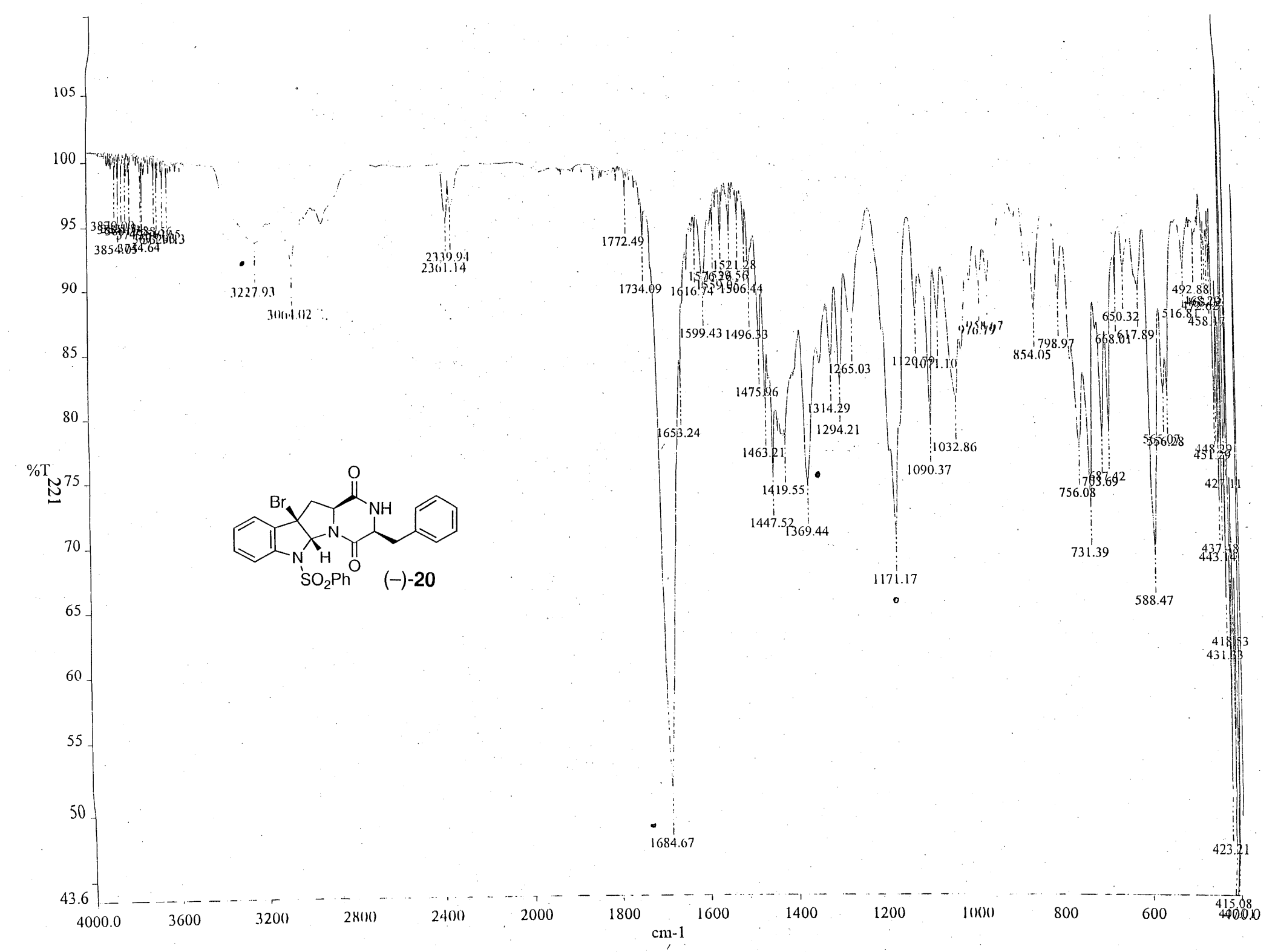


Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: 1-14-87
File:
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 28070.2 Hz
2048 repetitions
OBSERVE C13, 125.7832275 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 1 hr, 25 min, 30 sec



(–)-**20**

220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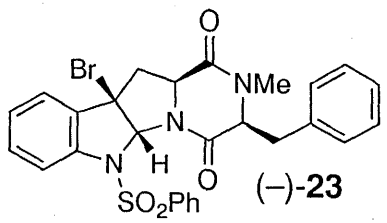
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400.0
105
100
95
90
85
80
75
70
65
60
55
50
43.6
3227.93
3064.02
2339.94
2361.14
1772.49
1734.09
1653.24
1684.67
1616.74
1599.43
1576.20
1550.95
1521.28
1506.44
1496.33
1475.96
1463.21
1447.52
1419.55
1369.44
1314.29
1294.21
1265.03
1171.17
1120.79
1090.37
1071.10
1032.86
976.97
854.05
798.97
756.08
731.39
668.01
650.32
617.89
588.47
556.28
516.81
492.88
458.17
437.58
431.29
427.11
423.21
418.53
415.08
443.11
Br
NH
N
H
O
SO2Ph
(–)-20

exp2 s2pul

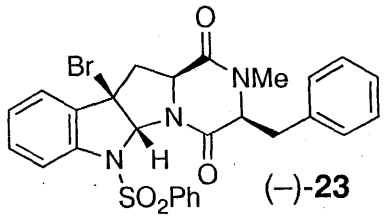
SAMPLE		DEC. & VT	
date	Mar 11 2007	dfrq	125.672
solvent	CDCl3	dn	C13
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.746	dm	nnn
tn	H1	dmm	w
at	3.001	dmf	10000
np	63050	dseq	
sw	10504.2	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.6	dn2	
d1	7.000	dpwr2	1
tof	1519.5	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	6246.7	dm3	n
vs	38	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	42.02	dres3	1.0
is	229.86	homo3	n
rfl	4865.2	PROCESSING	
rfp	3633.1	wtfile	
th	7	proc	ft
ins	1.000	fn	262144
ai cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	wft



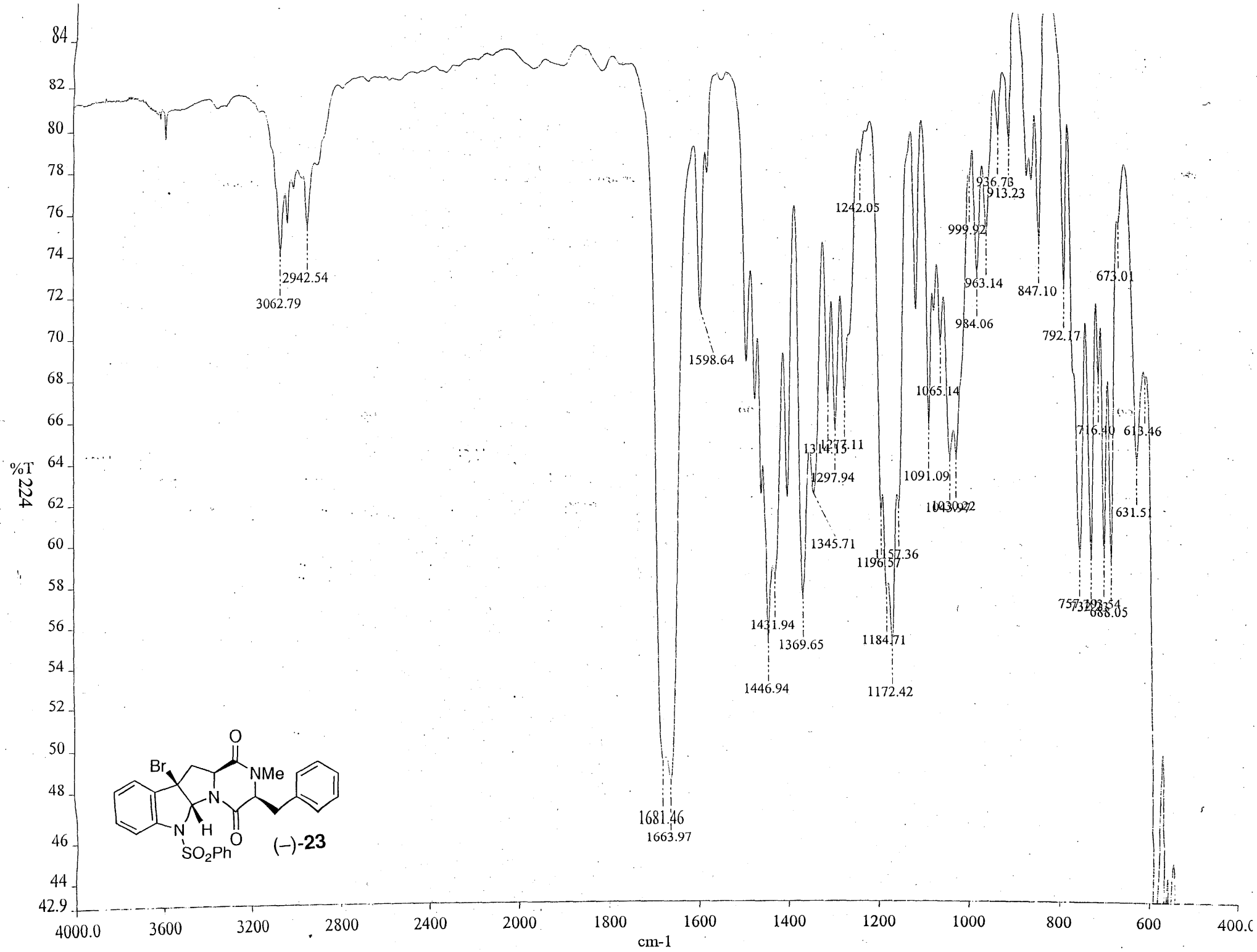
(–)-**23**

exp3 s2pul

SAMPLE		DEC. & VT	
date	Mar 14 2007	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	256	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	30189.8		
vs	253		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	16007.6		
rfp	9715.0		
th	14		
ins	1.000		
ai	ph		



(–)-**23**


%T
cm-1
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400.0
84
82
80
78
76
74
72
70
68
66
64
62
60
58
56
54
52
50
48
46
44
42.9
3062.79
2942.54
1598.64
1681.46
1663.97
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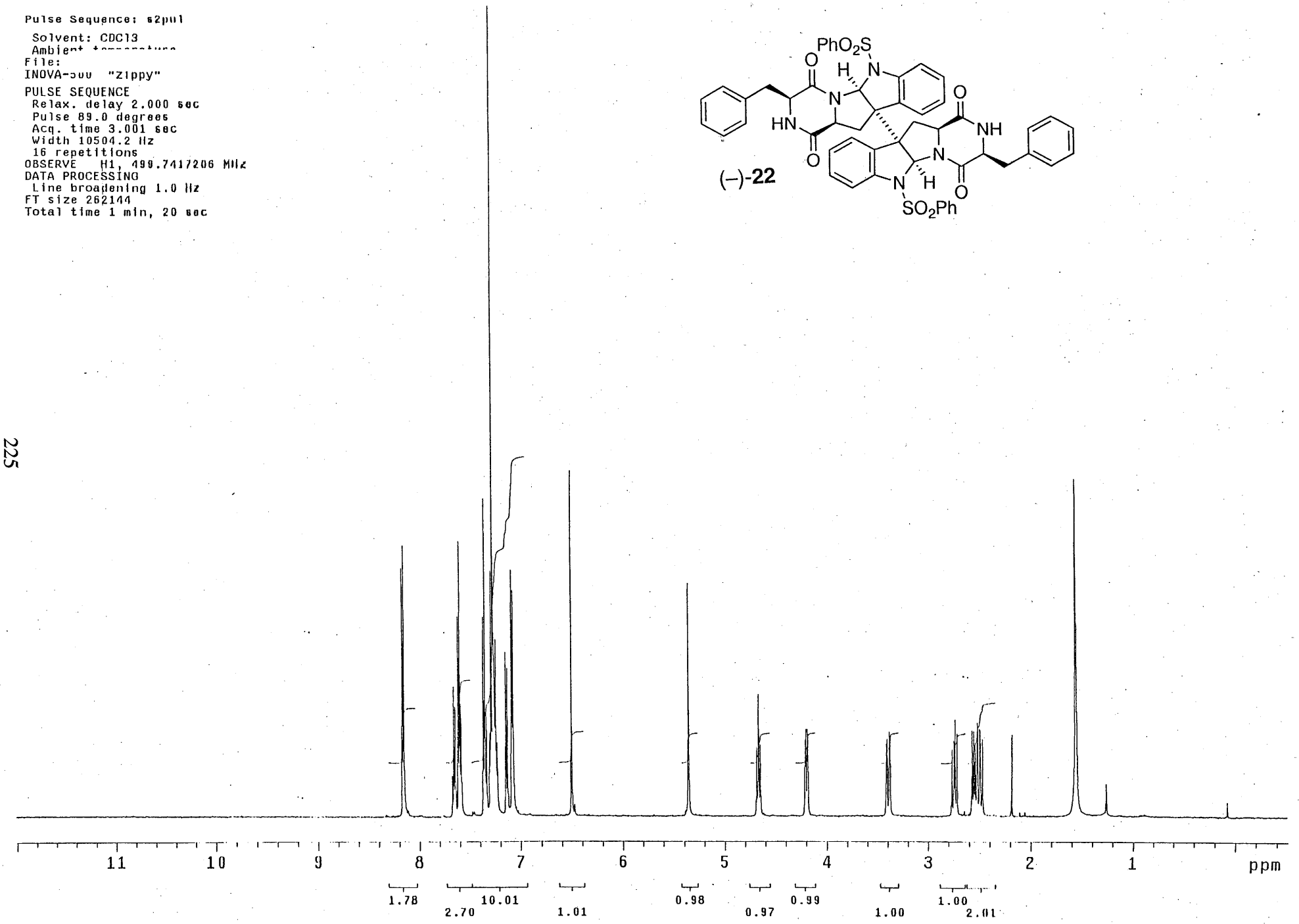
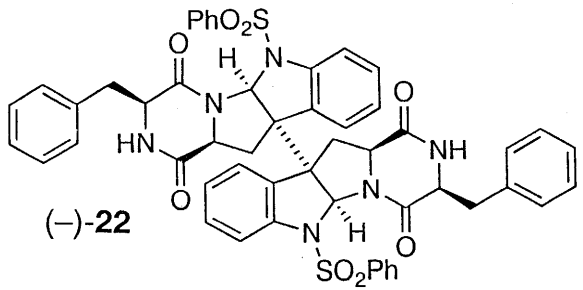
1431.94
1369.65
1345.71
1314.15
1297.94
1277.11
1242.05
1196.57
1184.71
1172.42
1157.36
1091.09
1065.14
1043.72
999.92
984.06
963.14
936.78
913.23
847.10
792.17
757.32
716.40
688.05
673.01
631.51
613.46
Br
O
NMe
N
N
H
O
SO2Ph
(–)-23


Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File:
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.001 sec
Width 10504.2 Hz
16 repetitions
OBSERVE H1, 499.7417206 MHz
DATA PROCESSING
Line broadening 1.0 Hz
FT size 262144
Total time 1 min, 20 sec
PhO2S
H
N
O
N
HN
O
O
NH
N
N
H
O
SO2Ph
(–)-22
11
10
9
8
7
6
5
4
3
2
1
ppm
1.78
2.70
10.01
1.01
0.98
0.97
0.99
1.00
1.00
2.01

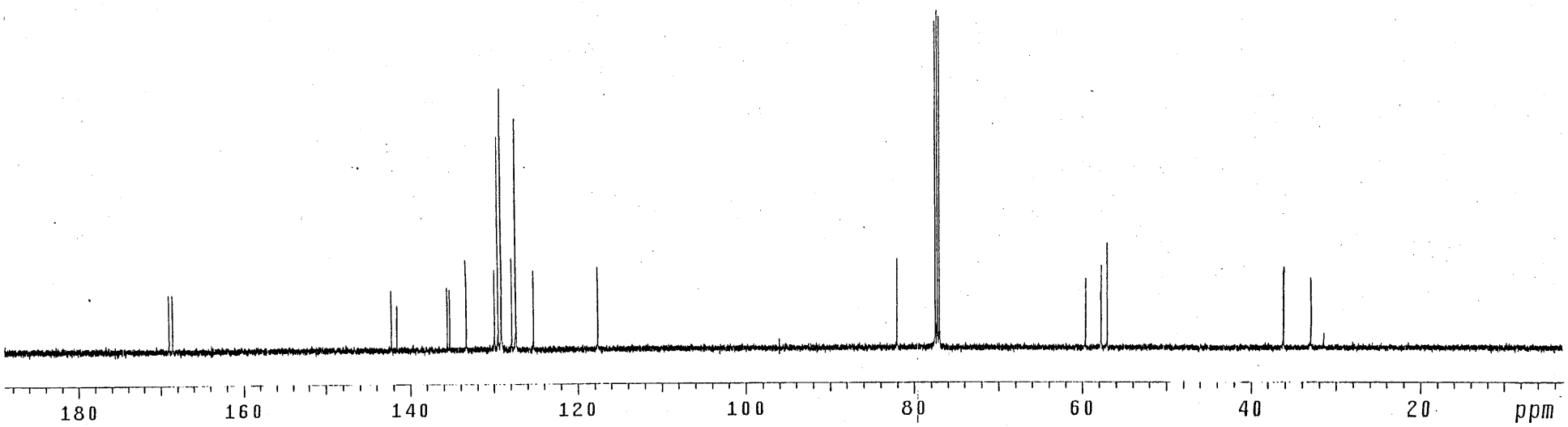
Pulse Sequence: s2pul

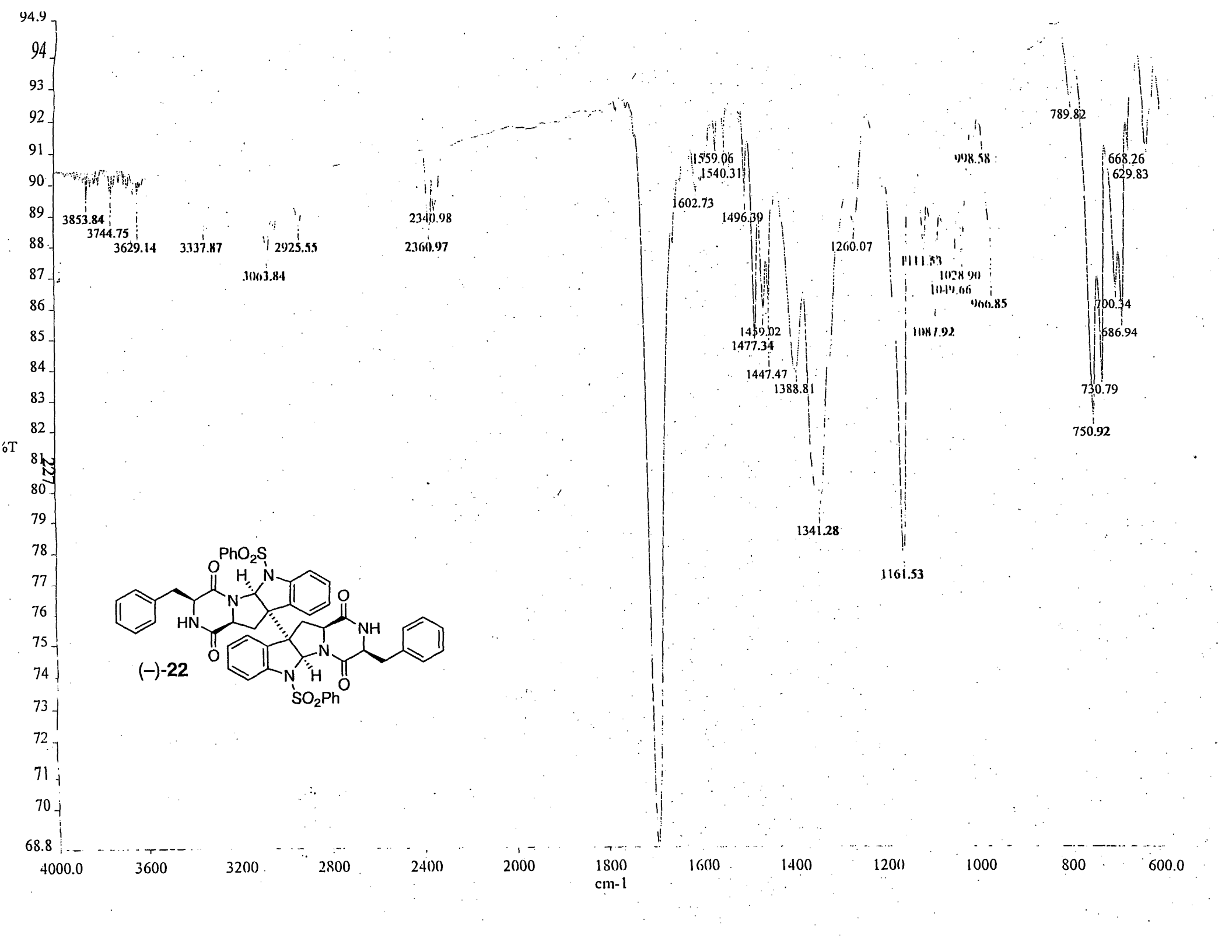
Solvent: CDCl3
Ambient temperature
User: 1-14-R7
File:
INOVA-500 "zippy"

PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.737 sec
Width 23391.8 Hz
1656 repetitions
OBSERVE C13, 125.7832583 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 2 hr, 51 min, 10 sec



(–)-22




94.9
94
93
92
91
90
89
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87
86
85
84
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82
81
80
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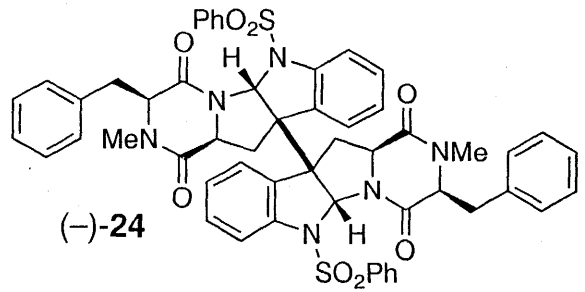
78
77
76
75
74
73
72
71
70
68.8
%T
3853.84
3744.75
3629.14
3337.87
3063.84
2925.55
2360.97
2340.98
1602.73
1559.06
1540.31
1496.39
1459.02
1477.34
1447.47
1388.81
1341.28
1260.07
1161.53
1111.53
1087.92
1049.66
1028.90
998.58
966.85
789.82
750.92
730.79
700.34
686.94
668.26
629.83
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1
(–)-22

exp2 s2pul

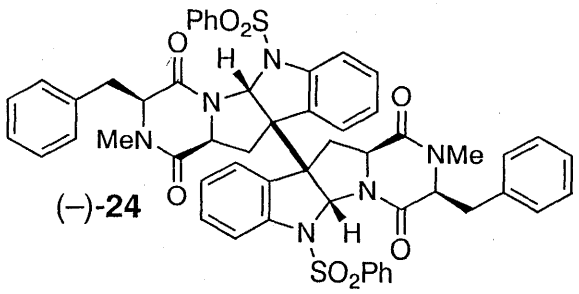
SAMPLE		DEC. & VT	
date	Mar 14 2007	dfrq	125.672
solvent	CDCl3	dn	C13
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.746	dm	nnn
tn	H1	dmm	w
at	3.001	dmf	10000
np	63050	dseq	
sw	10504.2	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.6	dn2	
d1	7.000	dpwr2	1
tof	1519.5	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	6246.7	dm3	n
vs	53	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	42.02	dres3	1.0
is	207.18	homo3	n
rfl	4864.9	PROCESSING	
rfp	3633.1	wtfile	
th	7	proc	ft
ins	2.000	fn	262144
ai cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	wft



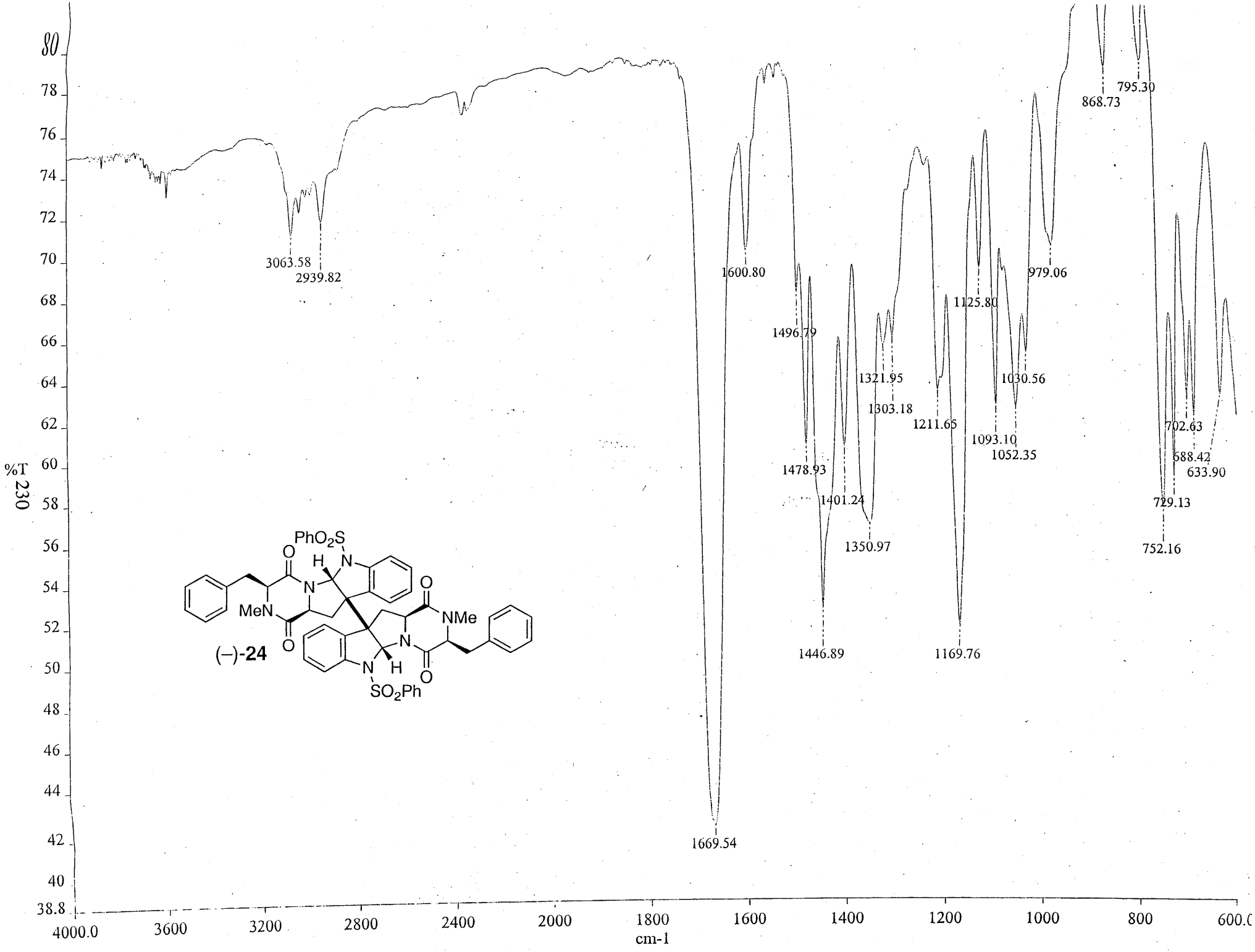
(–)-**24**

exp3 s2pul

SAMPLE		DEC. & VT	
date	Mar 14 2007	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	580	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	30189.8		
vs	229		
sc	0		
wc	250		
hzmm	31.73		
is	500.00		
rfl	16007.6		
rfp	9715.0		
th	14		
ins	1.000		
ai	ph		



(–)-24


80
78
76
74
72
70
68
66
64
62
60
58
56
54
52
50
48
46
44
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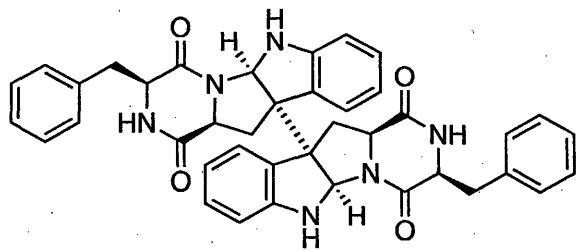
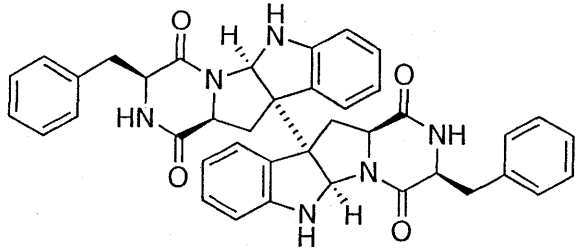
38.8
%T
230
3063.58
2939.82
1600.80
1496.79
1478.93
1446.89
1401.24
1350.97
1321.95
1303.18
1211.65
1169.76
1125.80
1093.10
1052.35
1030.56
979.06
868.73
795.30
752.16
729.13
702.63
688.42
633.90
1669.54
PhO2S
MeN
NMe
SO2Ph
(–)-24
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1

Pulse Sequence: s2pul
Solvent: CD3CN
Ambient temperature
File:
INOVA-[illegible]
PULSE SEQUENCE
Relax. delay 2.000 sec
Pulse 89.0 degrees
Acq. time 3.003 sec
Width 6305.2 Hz
4 repetitions
OBSERVE H1, 499.7443801 MHz
DATA PROCESSING
FT size 262144
Total time 0 min, 20 sec



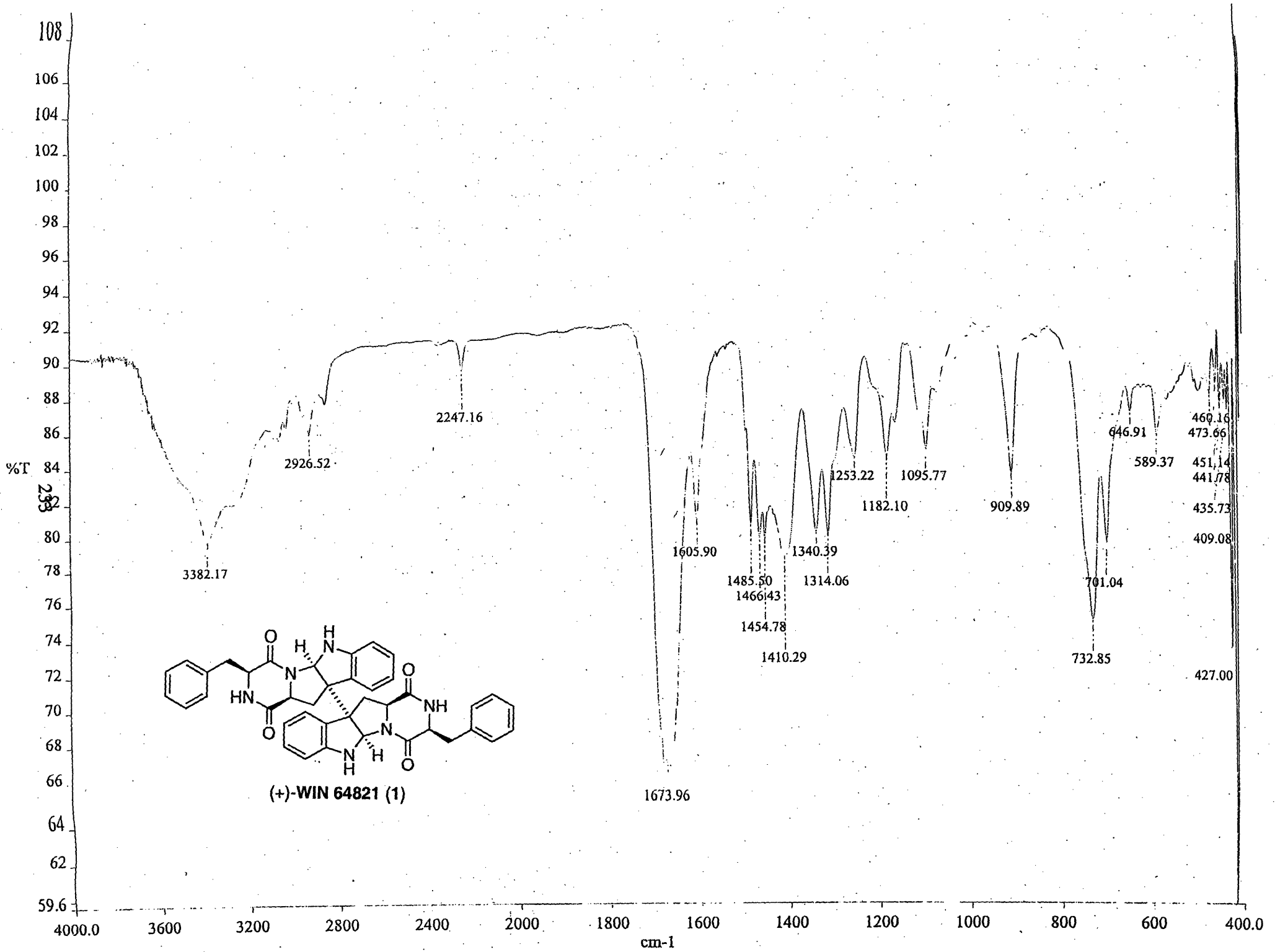
(+)-WIN 64821 (1)

Pulse Sequence: s2pul
Solvent: CD3CN
Ambient temperature
User: 1-14-87
File:
INOVA-500 "zippy"
PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 69.0 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
256 repetitions
OBSERVE C13, 125.7837511 MHz
DECOUPLE H1, 500.2359266 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 10 min, 44 sec



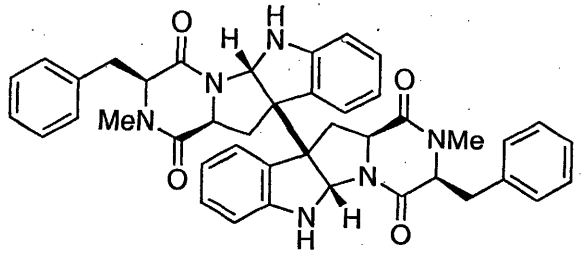
(+)-**WIN 64821 (1)**

200 180 160 140 120 100 80 60 40 20 0 ppm


%T
cm-1
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400.0
3382.17
2926.52
2247.16
1673.96
1605.90
1485.50
1466.43
1454.78
1410.29
1340.39
1314.06
1253.22
1182.10
1095.77
909.89
732.85
701.04
646.91
589.37
460.16
473.66
451.14
441.78
435.73
409.08
427.00
(+)-WIN 64821 (1)

exp2 s2pul

SAMPLE		DEC. & VT	
date	Mar 30 2007	dfrq	125.672
solvent	CDCl3	dn	C13
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.746	dm	nnn
tn	H1	dmm	w
at	3.001	dmf	10000
np	63050	dseq	
sw	10504.2	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.6	dn2	
d1	7.000	dpwr2	1
tof	1519.5	dof2	0
nt	16	dm2	n
ct	0	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	6246.7	dm3	n
vs	68	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	1.44	dres3	1.0
is	457.70	homo3	n
rfl	4864.9	PROCESSING	
rfp	3633.1	wtfile	
th	7	proc	ft
ins	2.000	fn	262144
ai cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	wft



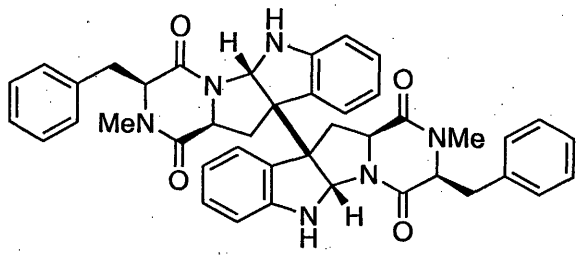
(−)-Ditryptophenaline (2)

```
exp3  s2pul

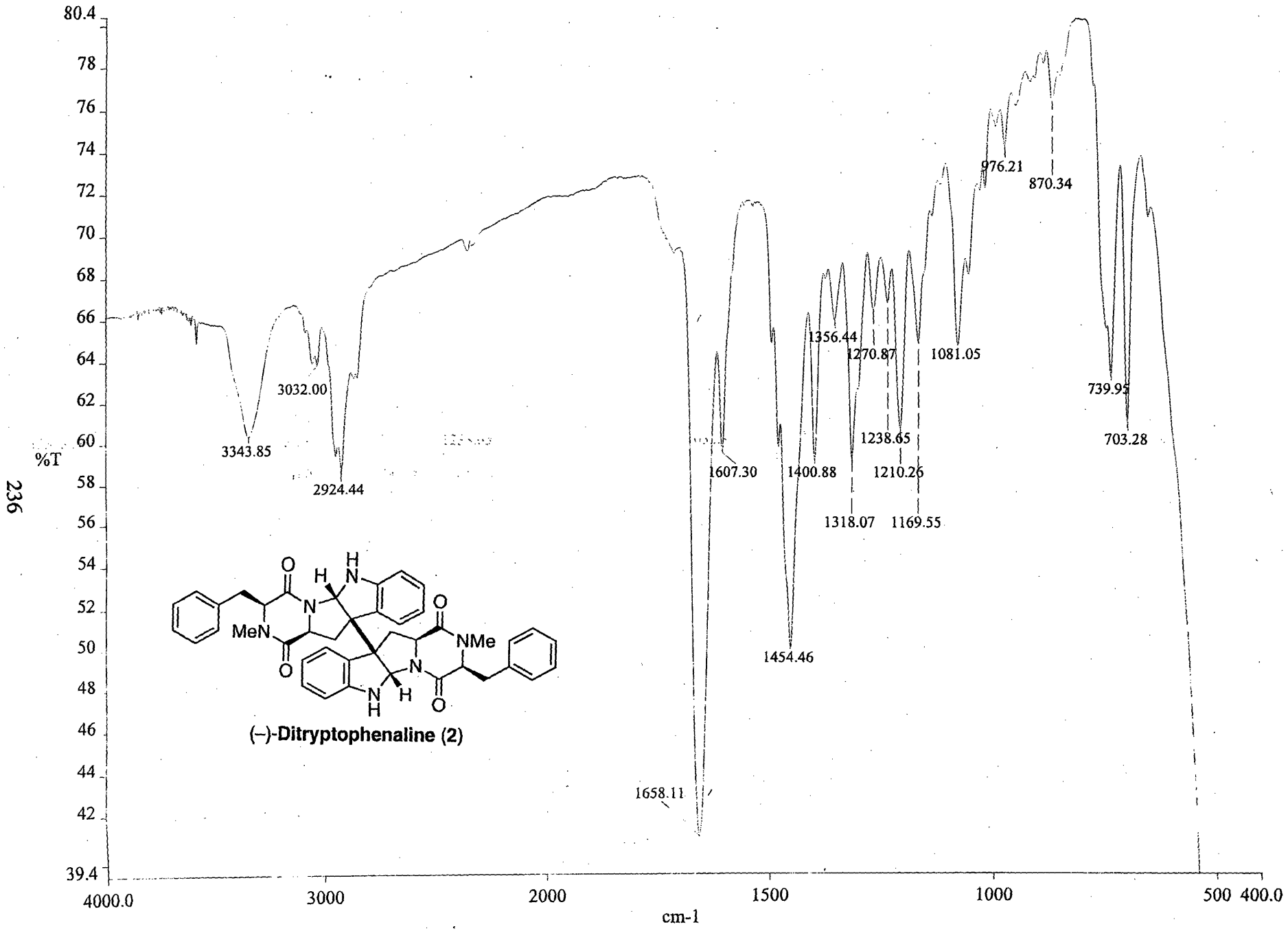
      SAMPLE
date    Apr  6 2007
solvent      CDCl3
file            exp
   ACQUISITION
sfrq        125.796
tn              C13
at              1.736
np            131010
sw           37735.8
fb       not used
bs                8
ss                1
tpwr             53
pw              6.9
d1            0.763
tof           631.4
nt            1e+06
ct             1696
alock             n
gain             60
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp          -2516.4
wp          30189.8
vs             1111
sc                0
wc              250
hzmm         120.76
is           500.00
rfl         16003.5
rfp          9715.0
th                9
ins           1.000
ai     ph

      DEC. & VT
dfrq        500.233
dn               H1
dpwr             37
dof          -500.0
dm               y
dmm              w
dmf          10000
dseq
dres           1.0
homo             n
     PROCESSING
lb             1.00
wtfile
proc             ft
fn          131072
math             f

werr
wexp
wbs
wnt
```



(–)-Ditryptophenaline (2)

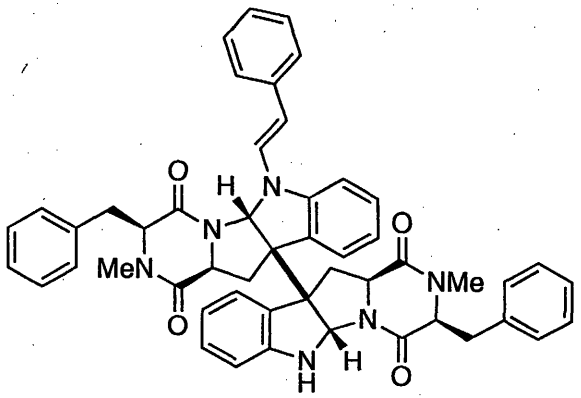

80.4
78
76
74
72
70
68
66
64
62
60
58
56
54
52
50
48
46
44
42
39.4
%T
4000.0
3000
2000
1500
1000
500 400.0
cm-1
3343.85
3032.00
2924.44
1658.11
1607.30
1454.46
1400.88
1356.44
1318.07
1270.87
1238.65
1210.26
1169.55
1081.05
976.21
870.34
739.95
703.28
MeN
NMe
(–)-Ditryptophenaline (2)

```
exp11  s2pul

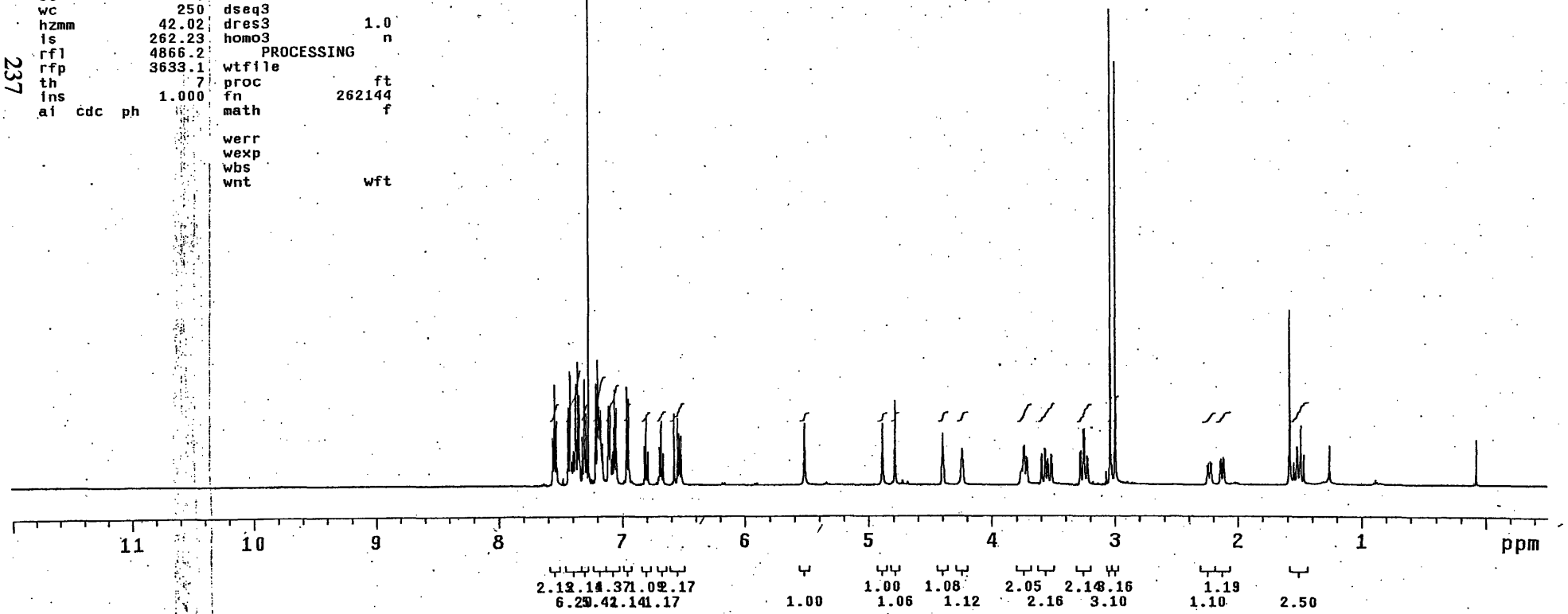
      SAMPLE
date    May 12 2007
solvent       CDCl3
file             exp
   ACQUISITION
sfrq         499.746
tn                H1
at            3.001
np            63050
sw          10504.2
fb        not used
bs                8
tpwr             56
pw              8.6
d1            7.000
tof          1519.5
nt               16
ct               16
alock             n
gain      not used
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp           -249.9
wp           6246.7
vs               64
sc                0
wc              250
hzmm          42.02
is            262.23
rfl           4866.2
rfp           3633.1
th                7
ins           1.000
ai  cdc  ph

     DEC. & VT
dfrq         125.672
dn               C13
dpwr              30
dof                0
dm               nnn
dmm                w
dmf            10000
dseq
dres             1.0
homo               n
     DEC2
dfrq2              0
dn2
dpwr2              1
dof2               0
dm2                n
dmm2               c
dmf2             200
dseq2
dres2            1.0
homo2              n
     DEC3
dfrq3              0
dn3
dpwr3              1
dof3               0
dm3                n
dmm3               c
dmf3             200
dseq3
dres3            1.0
homo3              n
     PROCESSING
wtfile
proc              ft
fn            262144
math               f

werr
wexp
wbs
wnt             wft
```

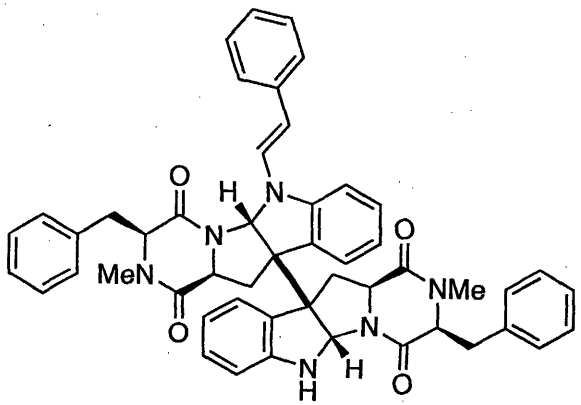


(–)-1'-(2-Phenylethylene)-ditryptophenaline (3)



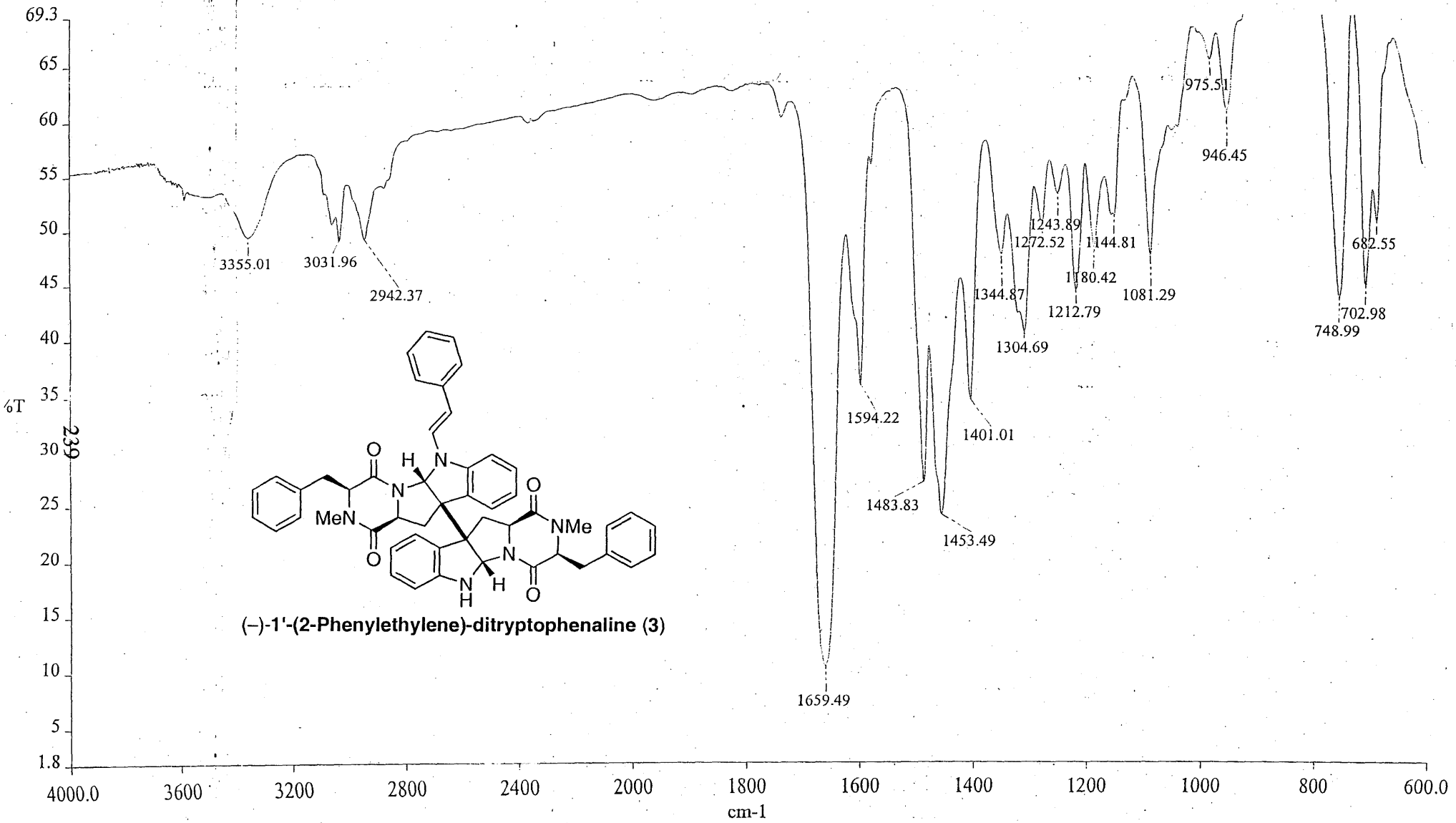
exp2 s2pul

SAMPLE		DEC. & VT	
date	May 11 2007	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f.
nt	1e+06		
ct	0	werr	
alock	n	wexp	
gain	60	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	30189.8		
vs	1356		
sc	0		
wc	250		
hzmm	120.76		
is	500.00		
rfl	16003.5		
rfp	9715.0		
th	20		
ins	1.000		
ai ph			



(–)-1'-(2-Phenylethylene)-ditryptophenaline (3)

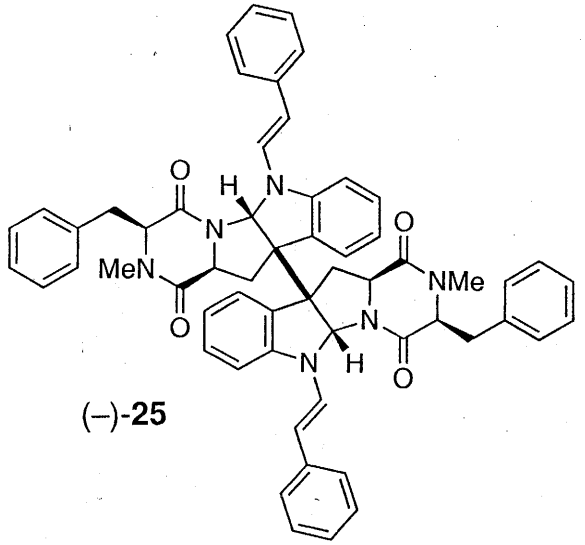
200 180 160 140 120 100 80 60 40 20 0 ppm



(–)-1'-(2-Phenylethylene)-ditryptophenaline (3)

exp2 s2pul

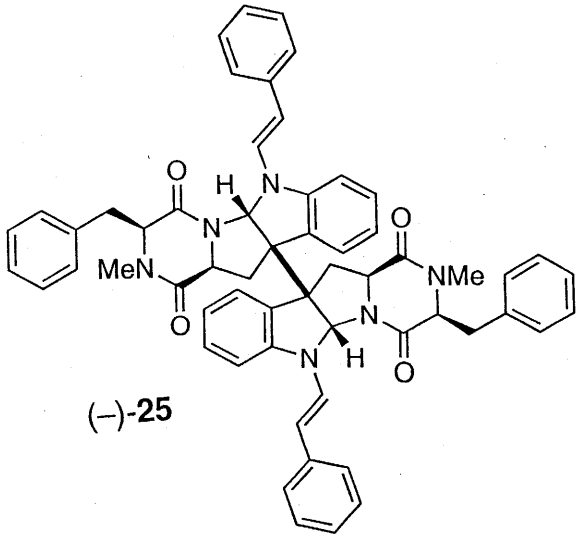
SAMPLE		DEC. & VT	
date	May 5 2007	dfrq	125.672
solvent	Benzene	dn	C13
file	exp	dpwr	30
ACQUISITION		dof	0
sfrq	499.746	dm	nnn
tn	H1	dmm	w
at	3.001	dmf	10000
np	63050	dseq	
sw	10504.2	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.6	dn2	
d1	7.000	dpwr2	1
tof	1519.5	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-249.9	dof3	0
wp	6246.7	dm3	n
vs	114	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	1.27	dres3	1.0
is	225.07	homo3	n
rfl	4794.0	PROCESSING	
rfp	3593.1	wtfile	
th	7	proc	ft
ins	2.000	fn	262144
ai cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	wft



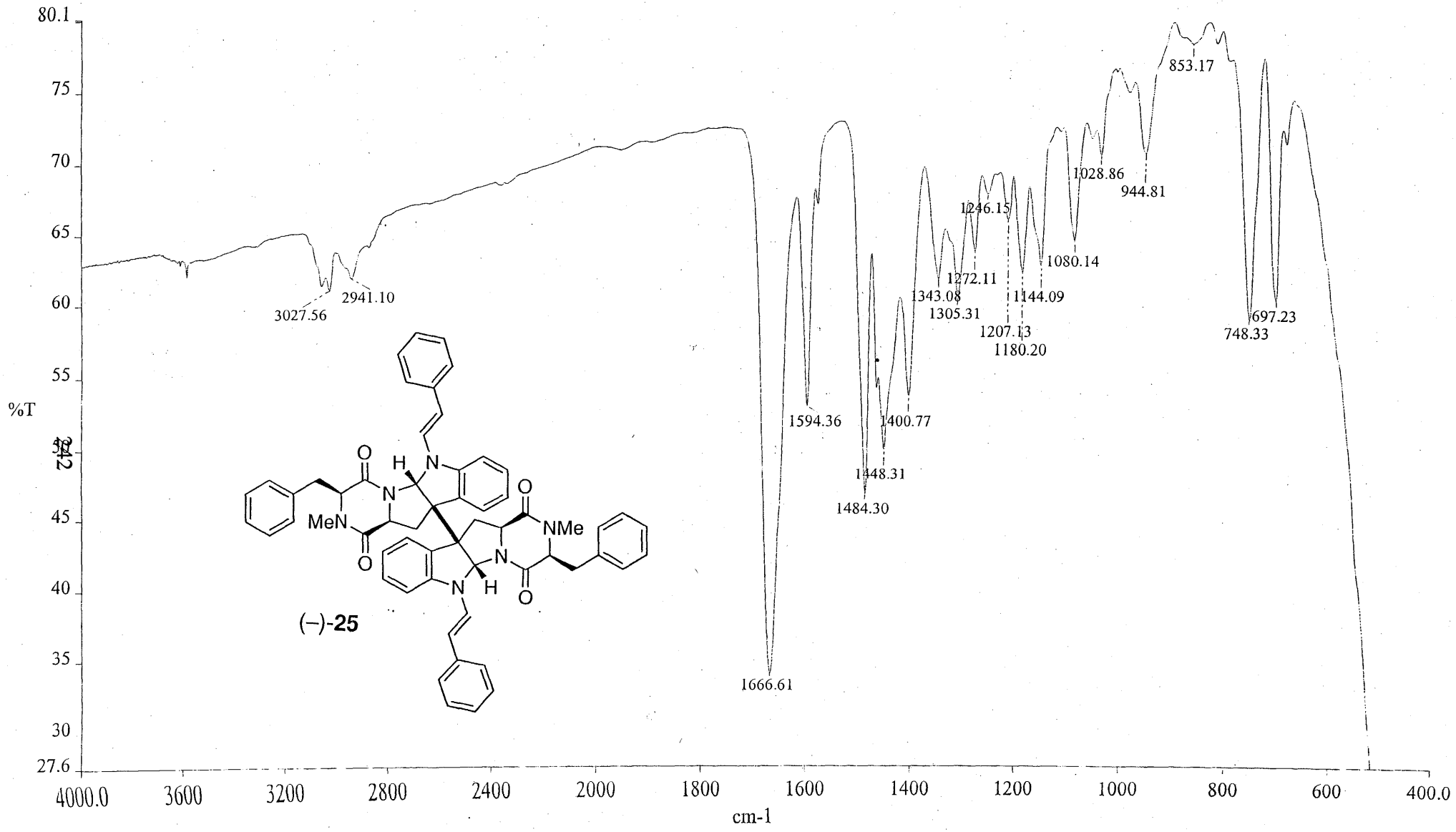
(–)-25

exp3 s2pul

SAMPLE		DEC. & VT	
date	May 5 2007	dfrq	500.233
solvent	Benzene	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	1749	werr	
alock	n	wexp	
gain	60	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.5		
wp	30191.6		
vs	143		
sc	0		
wc	250		
hzmm	0.92		
is	500.00		
rfl	22374.3		
rfp	16151.4		
th	20		
ins	1.000		
ai	ph		



(–)-25

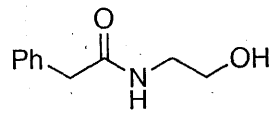

80.1
75
70
65
60
55
%T
50
45
40
35
30
27.6
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400.0
cm-1
3027.56
2941.10
1666.61
1594.36
1484.30
1448.31
1400.77
1343.08
1305.31
1272.11
1246.15
1207.13
1180.20
1144.09
1080.14
1028.86
944.81
853.17
748.33
697.23
MeN
NMe
O
H
N
(–)-25

Appendix C

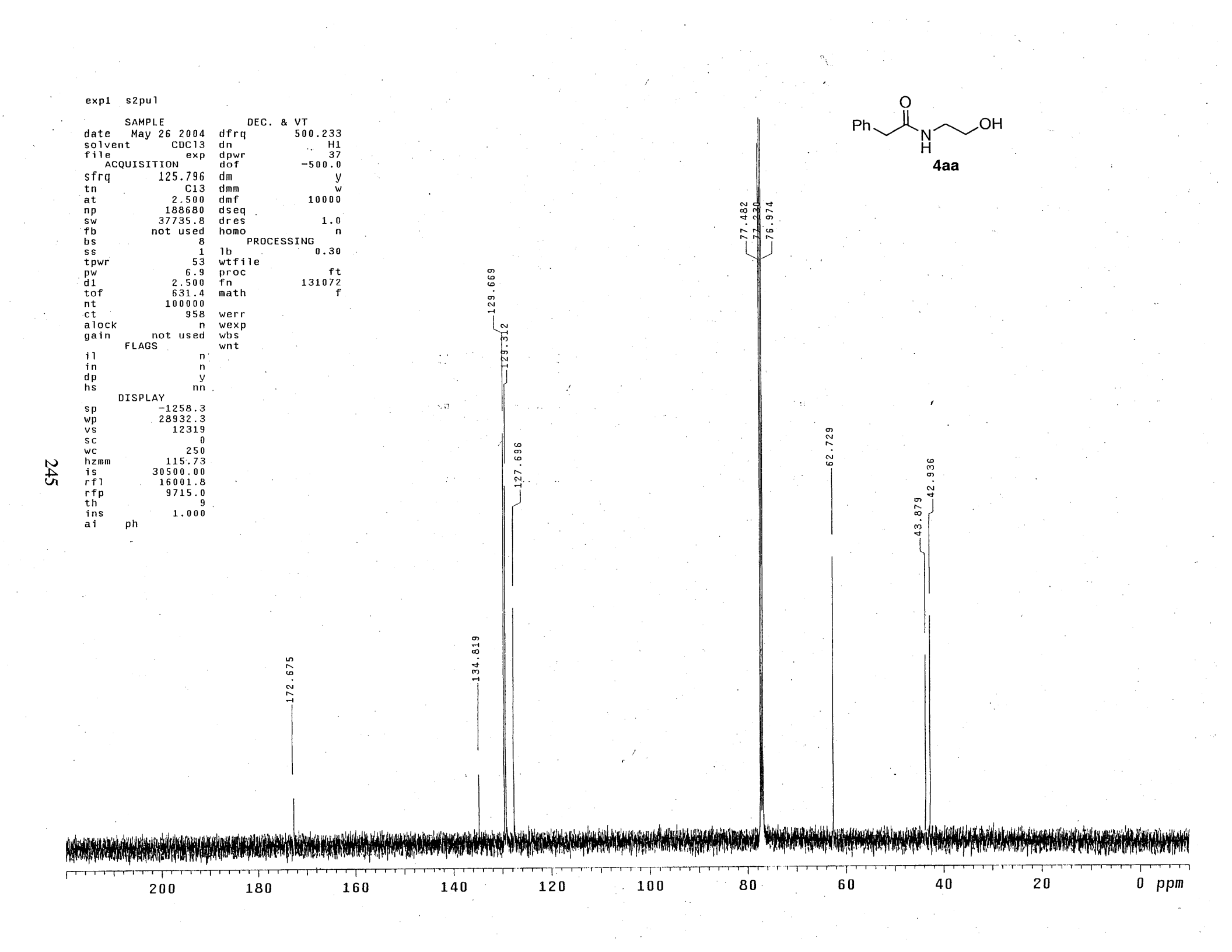
Spectra for Chapter III

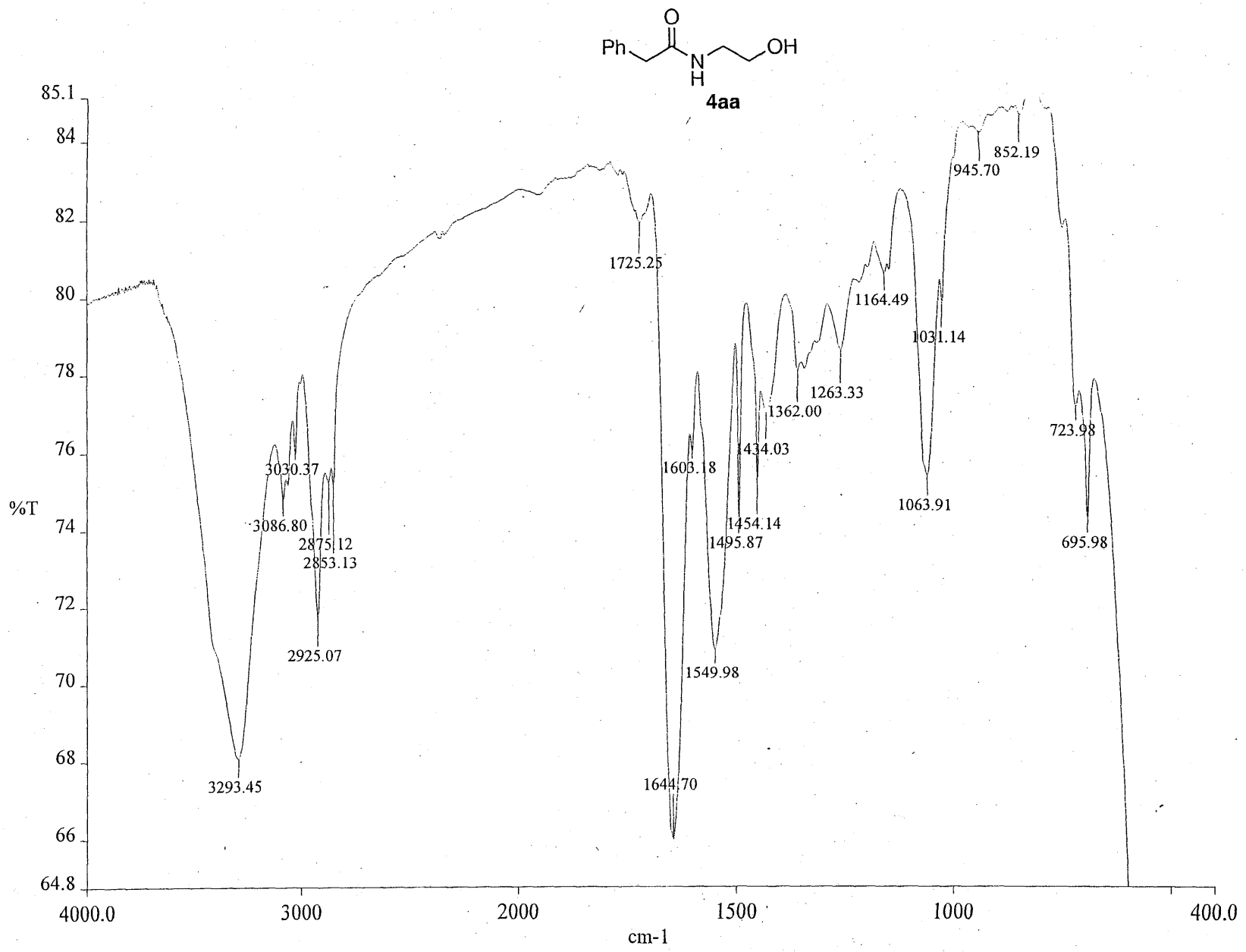
exp2 s2pul

SAMPLE		DEC. & VT	
date	Jan 13 2005	dfrq	125.677
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
SW	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	190.18	homo3	n
rfl	4635.5	PROCESSING	
rfp	3633.2	wtfile	
th	5	proc	ft
ins	2.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



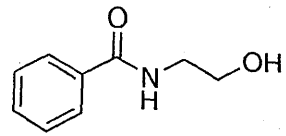
4aa


exp1 s2pul
SAMPLE
date May 26 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 125.796
tn C13
at 2.500
np 188680
sw 37735.8
fb not used
bs 8
ss 1
tpwr 53
pw 6.9
d1 2.500
tof 631.4
nt 100000
ct 958
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -1258.3
wp 28932.3
vs 12319
sc 0
wc 250
hzmm 115.73
is 30500.00
rfl 16001.8
rfp 9715.0
th 9
ins 1.000
ai ph
DEC. & VT
dfrq 500.233
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
Ph
O
N
H
OH
4aa
172.675
134.819
129.669
129.312
127.696
77.482
77.230
76.974
62.729
43.879
42.936
200
180
160
140
120
100
80
60
40
20
0 ppm

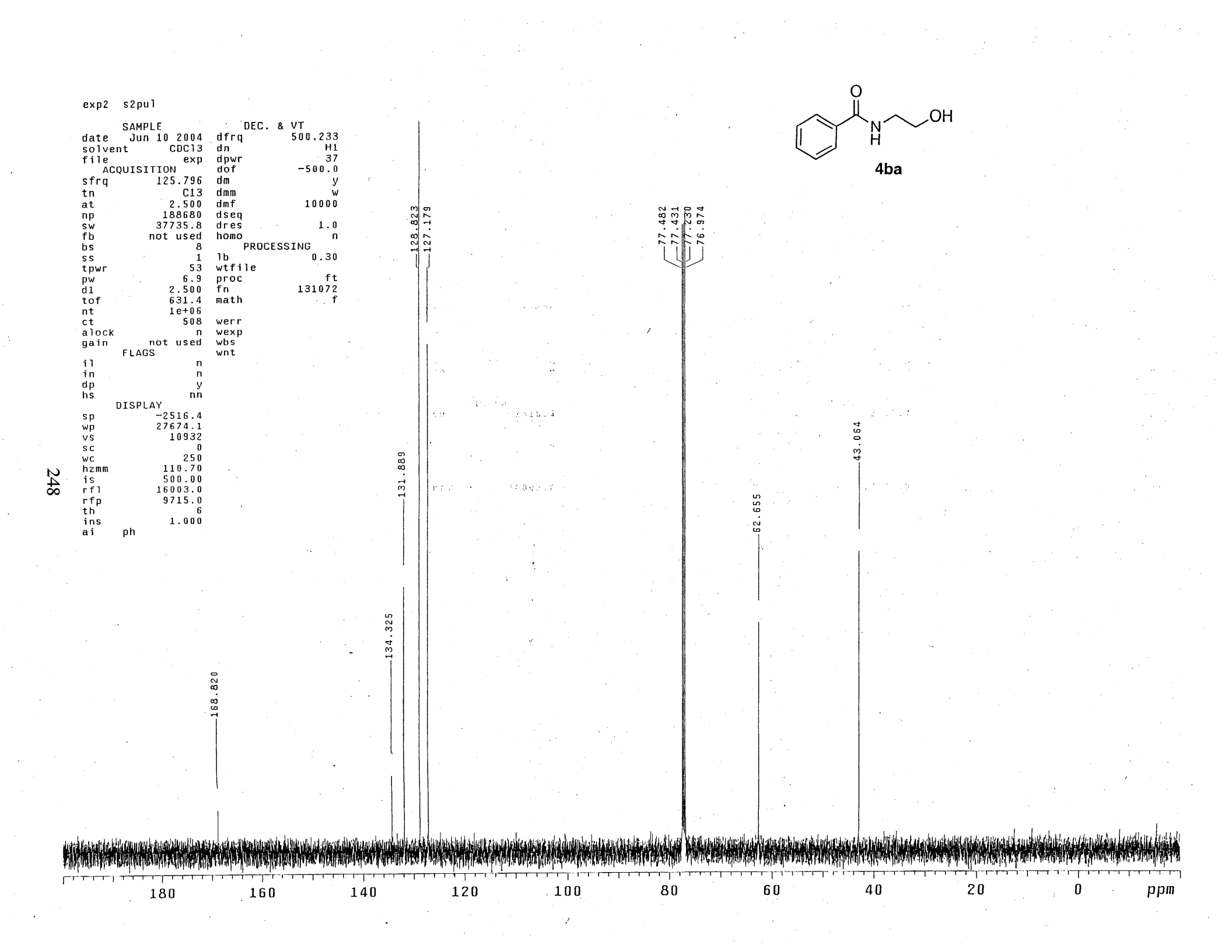

O
Ph
N
H
OH
4aa
85.1
84
82
80
78
76
74
72
70
68
66
64.8
%T
3293.45
3086.80
3030.37
2925.07
2875.12
2853.13
1725.25
1644.70
1603.18
1549.98
1495.87
1454.14
1434.03
1362.00
1263.33
1164.49
1063.91
1031.14
945.70
852.19
723.98
695.98
4000.0
3000
2000
1500
1000
400.0
cm-1

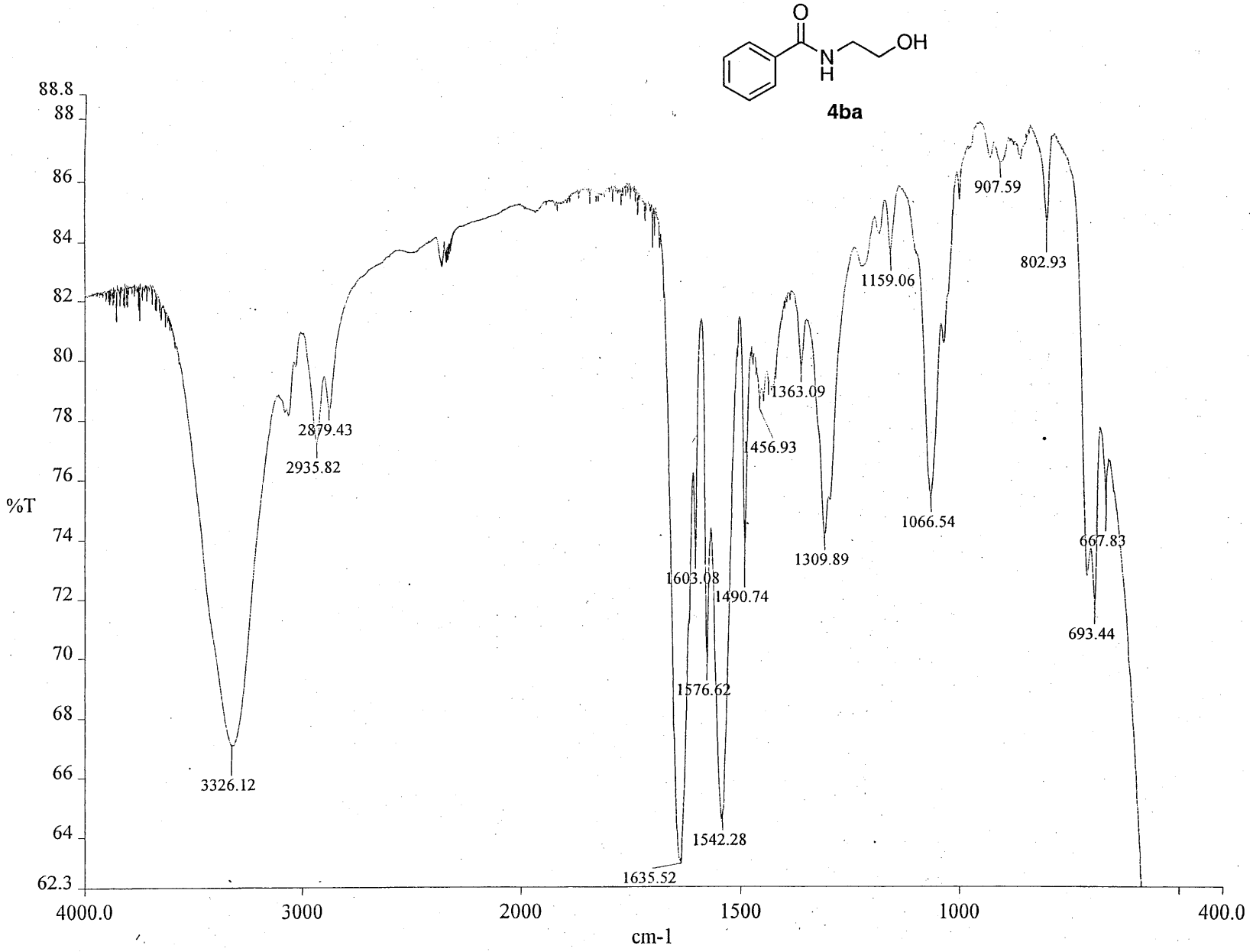
exp1 s2pul

SAMPLE		DEC. & VT	
date	Jun 10 2004	dfrq	125.677
solvent	CDCl3	dn	C13
		dpwr	34
		dof	1498.1
		dm	nnn
		dmm	w
ACQUISITION		dmf	10000
sfrq	499.758	dseq	
tn	H1	dres	1.0
at	3.277	homo	n
np	65536	PROCESSING	
sw	9998.8	wtfile	
fb	not used	proc	ft
bs	16	fn	65536
tpwr	56	math	f
pw	8.2		
d1	0	werr	
tof	1498.1	wexp	
nt	16	wbs	
ct	16	wnt	
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.1		
wp	6246.8		
vs	151		
sc	0		
wc	250		
hzmm	24.99		
is	226.04		
rfl	1002.5		
rfp	0		
th	7		
ins	2.000		
nm cdc ph			



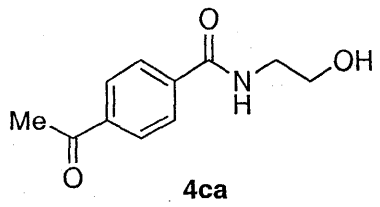
4ba


exp2 s2pul
SAMPLE
date Jun 10 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 125.796
tn C13
at 2.500
np 188680
sw 37735.8
fb not used
bs 8
ss 1
tpwr 53
pw 6.9
d1 2.500
tof 631.4
nt 1e+06
ct 508
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -2516.4
wp 27674.1
vs 10932
sc 0
wc 250
hzmm 110.70
is 500.00
rfl 16003.0
rfp 9715.0
th 6
ins 1.000
ai ph
DEC. & VT
dfrq 500.233
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
O
N
H
OH
4ba
168.820
134.325
131.889
128.823
127.179
77.482
77.431
77.230
76.974
62.655
43.064
180
160
140
120
100
80
60
40
20
0
ppm


O
N
H
OH
4ba
88.8
88
86
84
82
80
78
76
74
72
70
68
66
64
62.3
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3326.12
2879.43
2935.82
1635.52
1603.08
1576.62
1542.28
1490.74
1456.93
1363.09
1309.89
1159.06
1066.54
907.59
802.93
693.44
667.83

exp2 s2pul

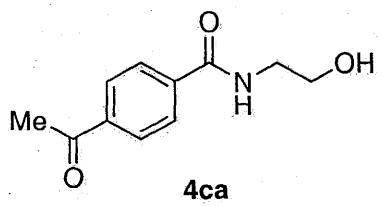
SAMPLE		DEC. & VT	
date	Nov 29 2004	dfrq	125.677
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	232.97	homo3	n
rfl	4636.1	PROCESSING	
rfp	3633.2	wtfile	
th	12	proc	ft
ins	2.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



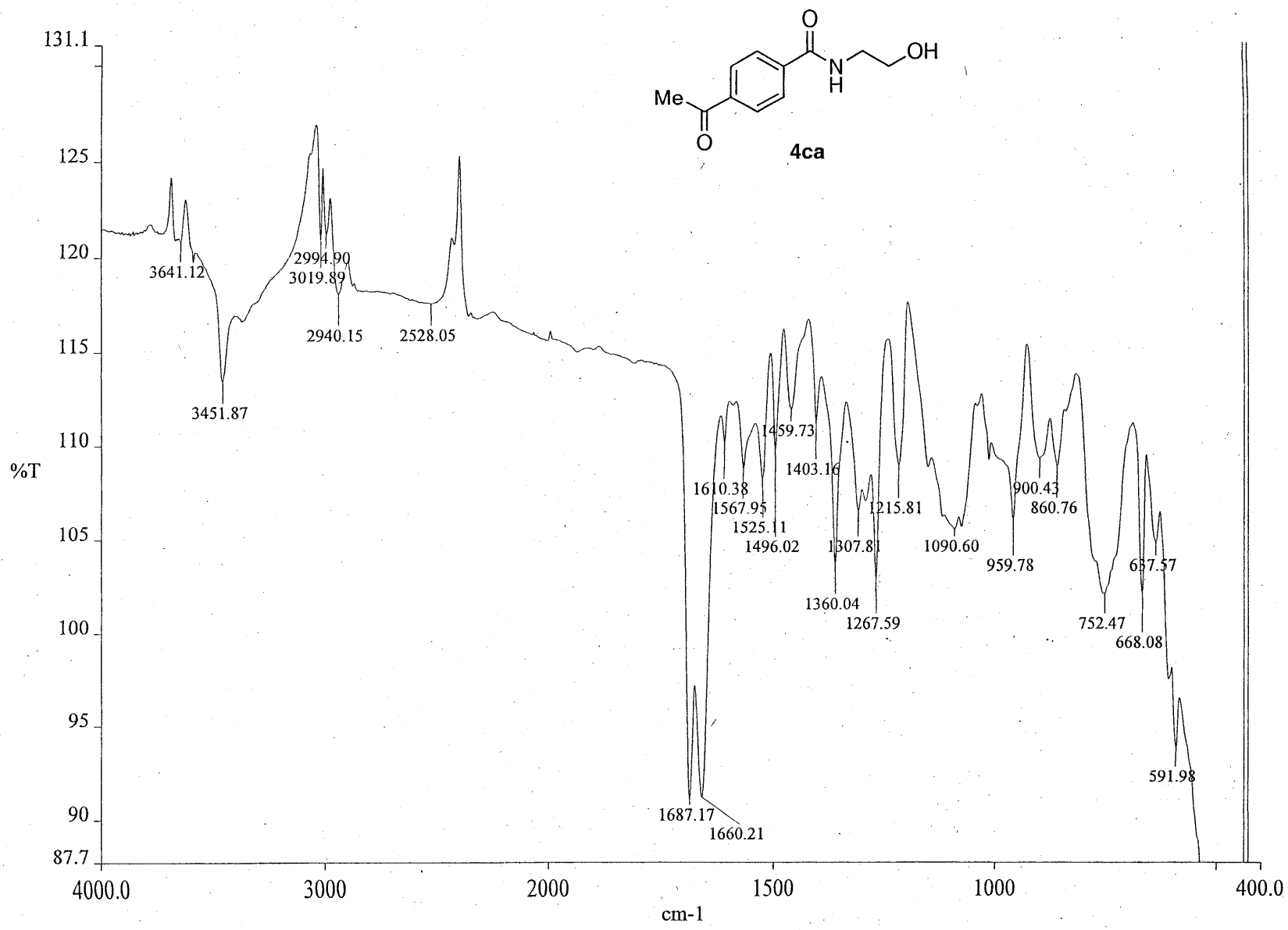
4ca

exp2 s2pul

SAMPLE		DEC. & VT	
date	Dec 1 2004	dfrq	500.235
solvent	CD3OD	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	2	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	2.500	fn	131072
tof	631.4	math	f
nt	10000		
ct	546	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.2		
wp	30189.3		
vs	1371		
sc	0		
wc	250		
hzmm	120.76		
is	500.00		
rfl	12301.1		
rfp	6182.6		
th	2		
ins	1.000		
ai	ph		

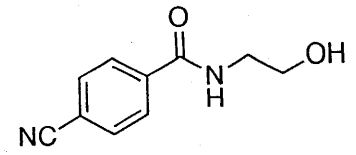


4ca

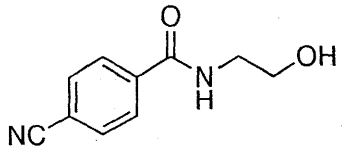

4ca
%T
cm-1
131.1
125
120
115
110
105
100
95
90
87.7
4000.0
3000
2000
1500
1000
400.0
3641.12
3451.87
2994.90
3019.89
2940.15
2528.05
1687.17
1660.21
1610.38
1567.95
1525.11
1496.02
1459.73
1403.16
1360.04
1307.81
1267.59
1215.81
1090.60
959.78
900.43
860.76
752.47
668.08
591.98

exp1 s2pul

SAMPLE		DEC. & VT	
date	Nov 10 2004	dfrq	125.677
solvent	CDCl3	dn	C13
		dpwr	34
		dof	1498.1
		dm	nnn
ACQUISITION		dmm	W
sfrq	499.758	dmf	10000
tn	H1	dseq	
at	3.277	dres	1.0
np	65536	homo	n
sw	9998.8	DEC2	
fb	not used	dfrq2	0
bs	1	dn2	
tpwr	56	dpwr2	1
pw	8.2	dof2	0
d1	10.000	dm2	n
tof	1498.1	dmm2	c
nt	16	dmf2	200
ct	16	dseq2	
alock	n	dres2	1.0
gain	not used	homo2	n
FLAGS		DEC3	
il	n	dfrq3	0
in	n	dn3	
dp	y	dpwr3	1
hs	nn	dof3	0
DISPLAY		dm3	n
sp	-250.1	dmm3	c
wp	6246.7	dmf3	200
vs	151	dseq3	
sc	0	dres3	1.0
wc	250	homo3	n
hzmm	40.00	PROCESSING	
is	287.75	wtfile	
rfl	4635.2	proc	ft
rfp	3633.2	fn	65536
th	10	math	f
ins	2.000		
nm cdc ph		werr	
		wexp	
		wbs	
		wnt	



4da

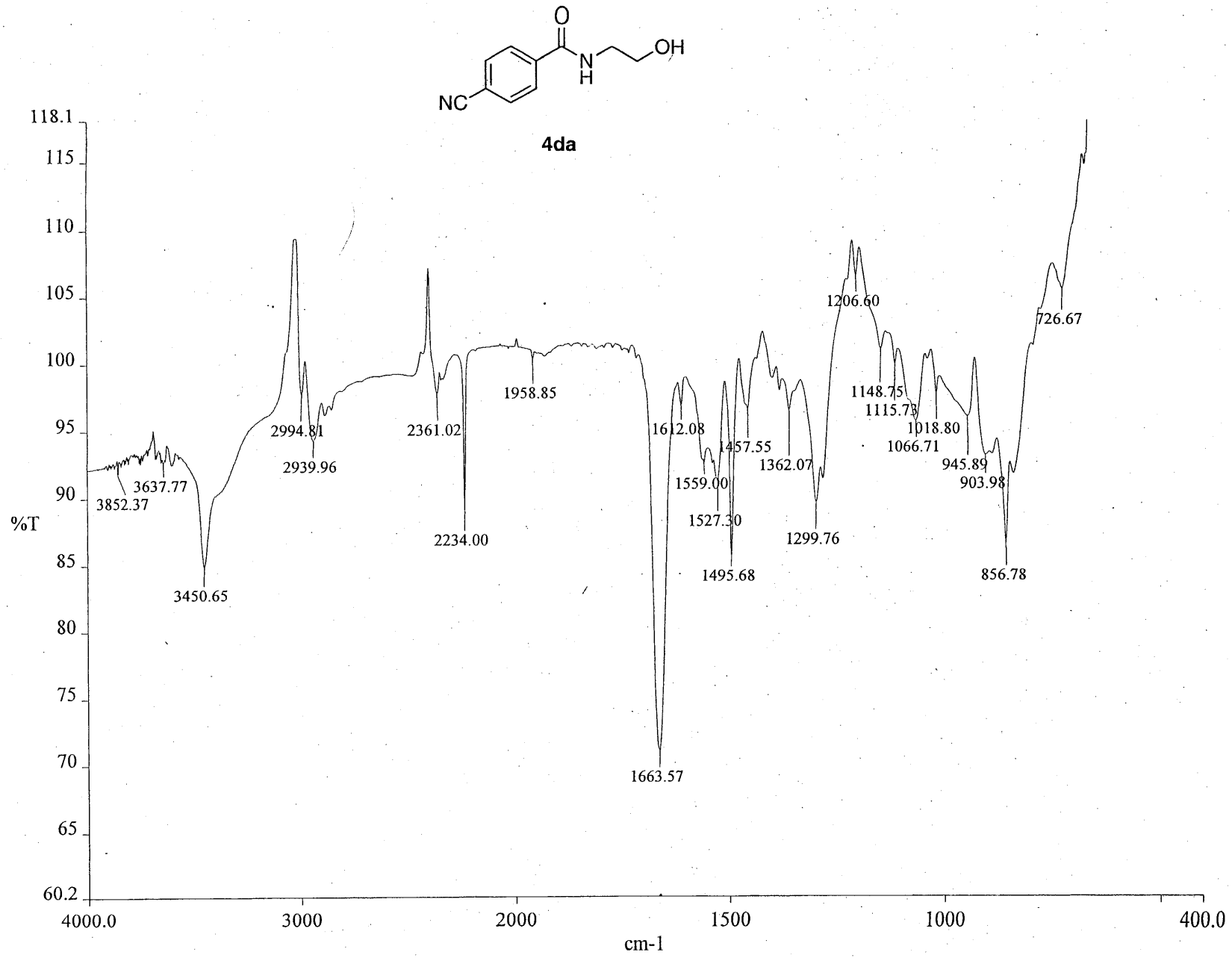


4da

```
exp2  s2pul

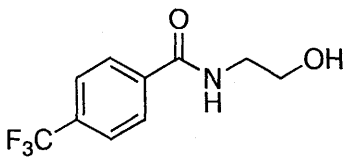
      SAMPLE
date   Nov 17 2004
solvent       DMSO
file           exp
   ACQUISITION
sfrq       125.796
tn             C13
at             1.736
np            131010
sw          37735.8
fb        not used
bs                1
ss                1
tpwr             53
pw              6.9
d1            2.000
tof           631.4
nt            1e+06
ct              553
alock             n
gain      not used
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp          -2516.2
wp          30189.3
vs              151
sc                0
wc              250
hzmm         150.94
is           500.00
rfl         11332.6
rfp          4969.9
th               18
ins           1.000
nm    ph

      DEC. & VT
dfrq       500.236
dn              H1
dpwr            37
dof         -500.0
dm                y
dmm               w
dmf           10000
dseq
dres            1.0
homo              n
     PROCESSING
lb             0.30
wtfile
proc            ft
fn          131072
math               f
werr
wexp
wbs
wnt
```

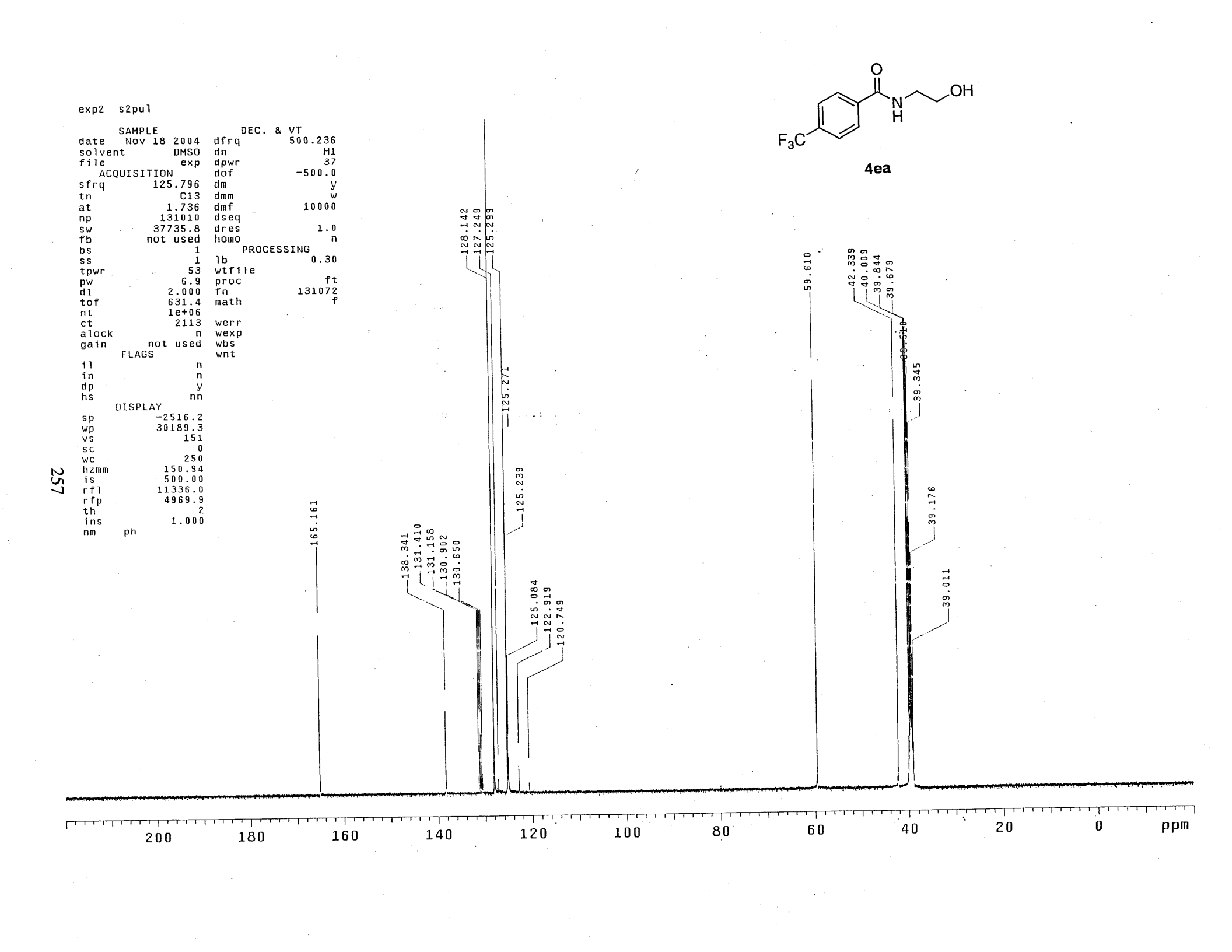

O
N
H
OH
NC
4da
118.1
115
110
105
100
95
90
85
80
75
70
65
60.2
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3852.37
3637.77
3450.65
2994.81
2939.96
2361.02
2234.00
1958.85
1663.57
1612.08
1559.00
1527.30
1495.68
1457.55
1362.07
1299.76
1206.60
1148.75
1115.73
1066.71
1018.80
945.89
903.98
856.78
726.67

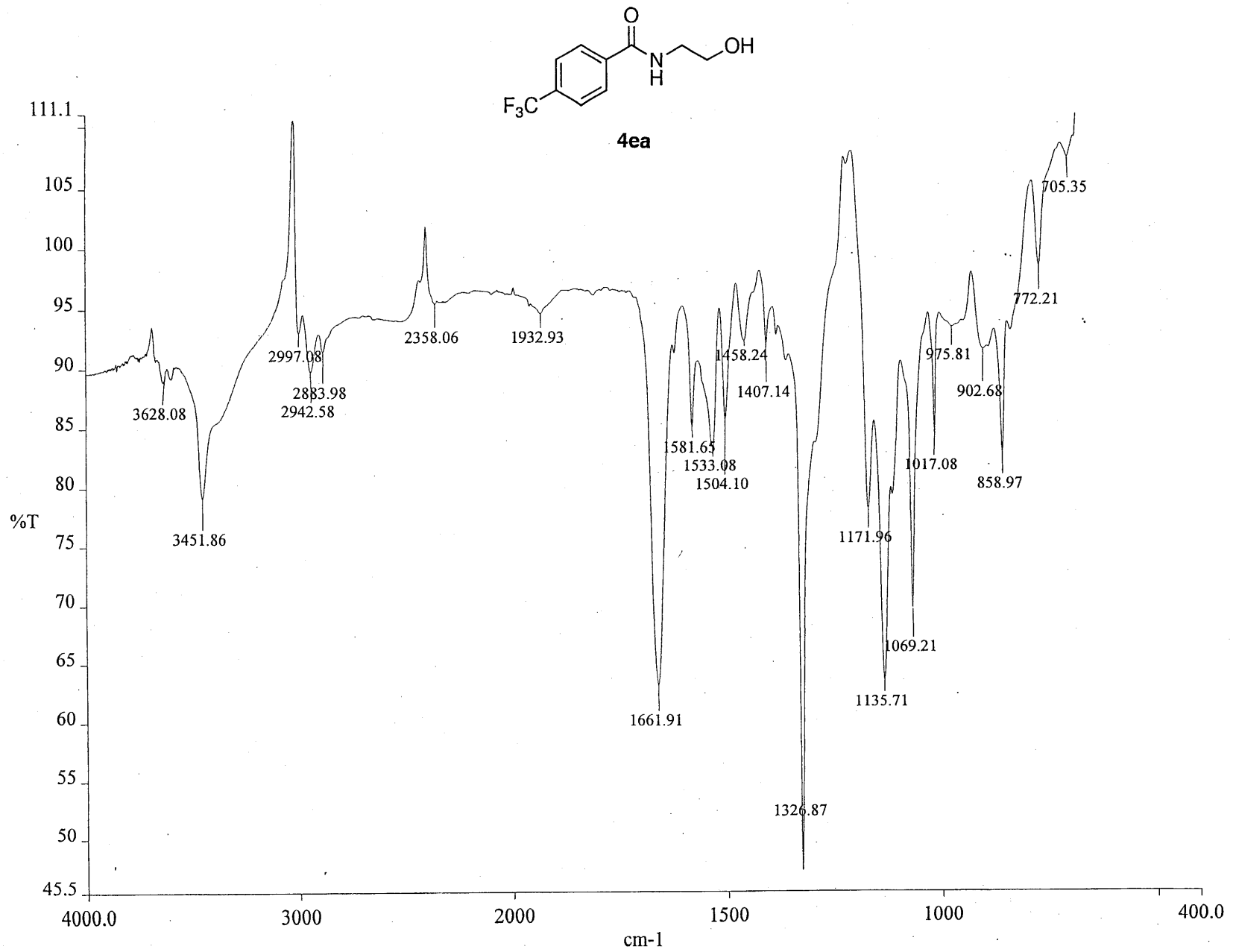
exp1 s2pul

SAMPLE		DEC. & VT	
date	Nov 29 2004	dfrq	125.677
solvent	CDCl3	dn	C13
		dpwr	34
		dof	1498.1
		dm	nnn
		dmm	w
ACQUISITION		dmf	10000
sfrq	499.758	dseq	
tn	H1	dres	1.0
at	3.277	homo	n
np	65536	PROCESSING	
sw	9998.8	wtfile	
fb	not used	proc	ft
bs	1	fn	65536
tpwr	56	math	f
pw	8.2		
d1	7.000	werr	
tof	1498.1	wexp	
nt	16	wbs	
ct	16	wnt	
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.1		
wp	6246.8		
vs	151		
sc	0		
wc	250		
hzmm	24.99		
is	117.53		
rfl	4635.8		
rfp	3633.2		
th	39		
ins	2.000		
nm cdc ph			



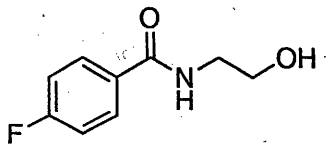
4ea


exp2 s2pul
SAMPLE
date Nov 18 2004
solvent DMSO
file exp
ACQUISITION
sfrq 125.796
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 1
ss 1
tpwr 53
pw 6.9
d1 2.000
tof 631.4
nt 1e+06
ct 2113
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -2516.2
wp 30189.3
vs 151
sc 0
wc 250
hzmm 150.94
is 500.00
rfl 11336.0
rfp 4969.9
th 2
ins 1.000
nm ph
DEC. & VT
dfrq 500.236
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
O
N
H
OH
F3C
4ea
165.161
138.341
131.410
131.158
130.902
130.650
128.142
127.249
125.299
125.271
125.239
125.084
122.919
120.749
59.610
42.339
40.009
39.844
39.679
39.510
39.345
39.176
39.011
200
180
160
140
120
100
80
60
40
20
0
ppm


O
N
H
OH
F3C
4ea
111.1
105
100
95
90
85
80
75
70
65
60
55
50
45.5
%T
3628.08
3451.86
2997.08
2883.98
2942.58
2358.06
1932.93
1661.91
1581.65
1533.08
1504.10
1458.24
1407.14
1326.87
1171.96
1135.71
1069.21
1017.08
975.81
902.68
858.97
772.21
705.35
4000.0
3000
2000
1500
1000
400.0
cm-1

exp1 s2pul

SAMPLE		DEC. & VT	
date	Nov 10 2004	dfrq	125.677
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	W
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	10.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	2.21	dres3	1.0
is	192.61	homo3	n
rfl	4635.2	PROCESSING	
rfp	3633.2	wtfile	
th	10	proc	ft
ins	2.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



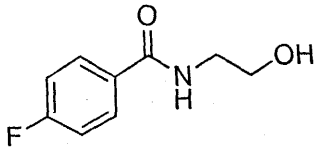
4fa

11 10 9 8 7 6 5 4 3 2 1 ppm

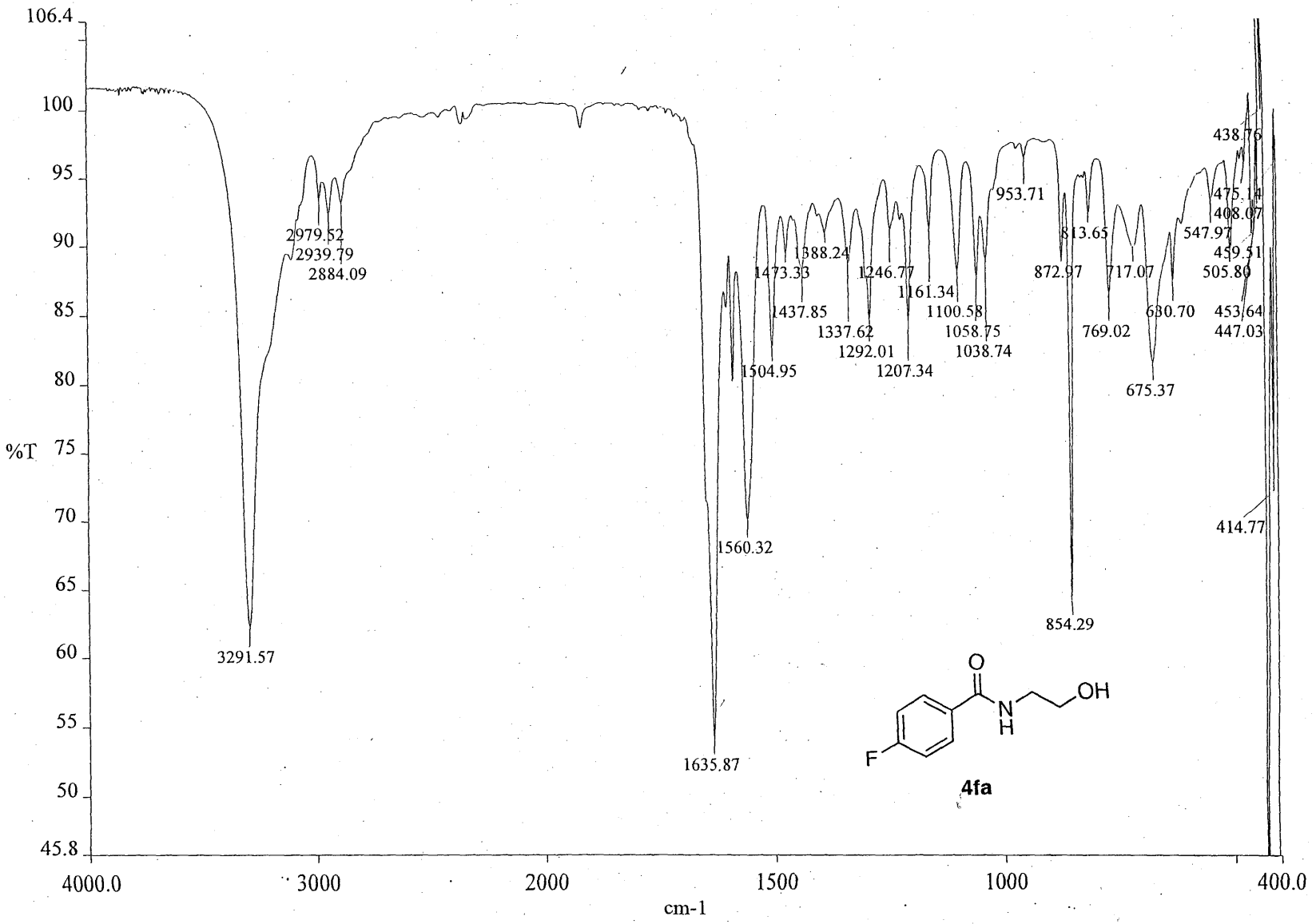
1.94 1.91 1.02 2.00 2.01 0.96

exp4 s2pul

SAMPLE		DEC. & VT	
date	Nov 11 2004	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	1	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	2.000	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	1361	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	30189.8		
vs	151		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	16003.5		
rfp	9715.0		
th	7		
ins	1.000		
nm	ph		



4fa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100
95
90
85
80
75
70
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60
55
50
45.8
%T
4000.0
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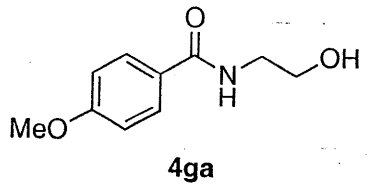
2000
1500
1000
400.0
cm-1
3291.57
2979.52
2939.79
2884.09
1635.87
1560.32
1504.95
1473.33
1437.85
1388.24
1337.62
1292.01
1246.77
1207.34
1161.34
1100.58
1058.75
1038.74
953.71
872.97
854.29
813.65
769.02
717.07
675.37
630.70
547.97
505.80
475.14
459.51
453.64
447.03
438.76
414.77
408.07
O
N
H
OH
F
4fa

```
exp1  s2pul

      SAMPLE
date    Nov 10 2004
solvent      CDCl3
file            exp
   ACQUISITION
sfrq       499.758
tn              H1
at          3.277
np          65536
sw         9998.8
fb       not used
bs              1
tpwr           56
pw            8.2
d1         10.000
tof        1498.1
nt             16
ct             16
alock           n
gain     not used
      FLAGS
il              n
in              n
dp              y
hs             nn
     DISPLAY
sp         -250.1
wp         6246.7
vs            151
sc              0
wc            250
hzmm        40.00
is         192.61
rfl        4634.9
rfp        3633.2
th            142
ins         2.000
nm  cdc  ph

      DEC. & VT
dfrq       125.677
dn             C13
dpwr            34
dof        1498.1
dm             nnn
dmm              w
dmf          10000
dseq
dres           1.0
homo             n
      DEC2
dfrq2            0
dn2
dpwr2            1
dof2             0
dm2              n
dmm2             c
dmf2           200
dseq2
dres2          1.0
homo2            n
      DEC3
dfrq3            0
dn3
dpwr3            1
dof3             0
dm3              n
dmm3             c
dmf3           200
dseq3
dres3          1.0
homo3            n
     PROCESSING
wtfile
proc            ft
fn          65536
math             f

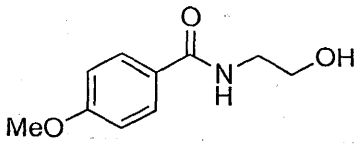
werr
wexp
wbs
wnt
```



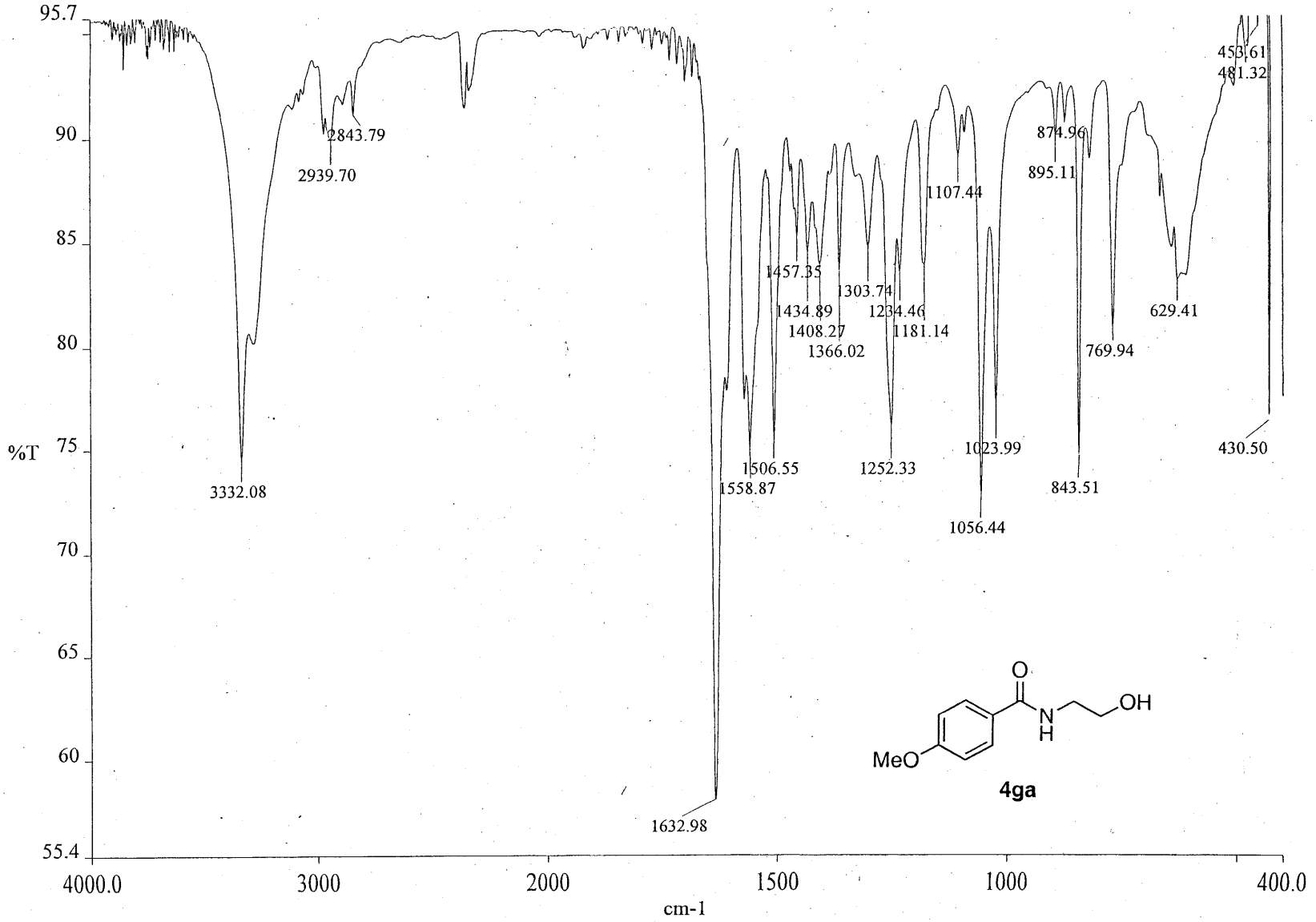
4ga

exp4 s2pul

SAMPLE		DEC. & VT	
date	Nov 13 2004	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	1	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	2.000	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	670	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	30189.3		
vs	151		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	16004.1		
rfp	9715.0		
th	14		
ins	1.000		
nm	ph		



4ga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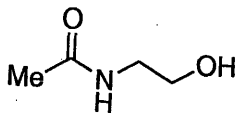
90
85
80
75
70
65
60
55.4
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3332.08
2939.70
2843.79
1632.98
1558.87
1506.55
1457.35
1434.89
1408.27
1366.02
1303.74
1252.33
1234.46
1181.14
1107.44
1056.44
1023.99
895.11
874.96
843.51
769.94
629.41
481.32
453.61
430.50
O
N
H
OH
MeO
4ga

exp3 s2pul

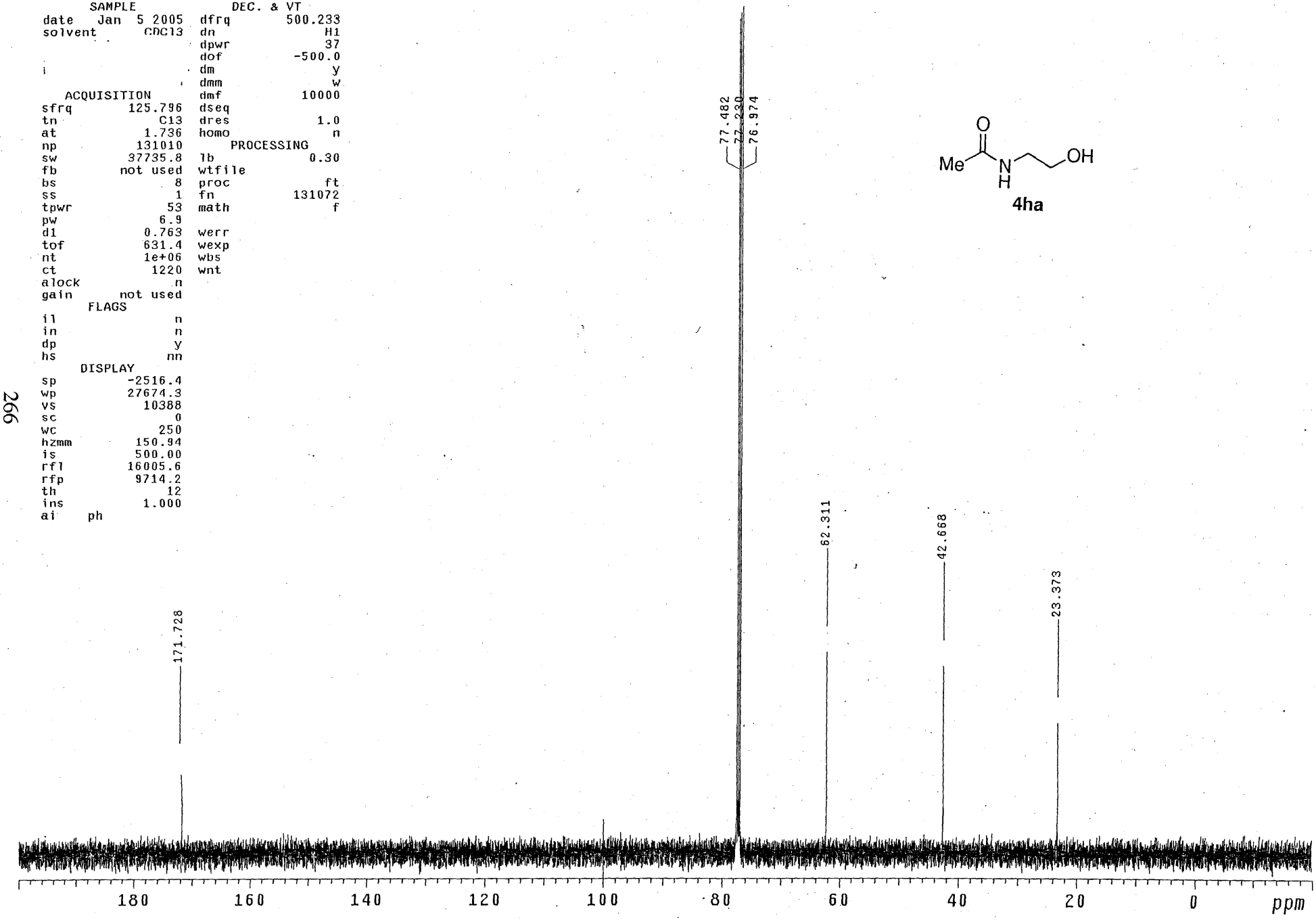
SAMPLE		DEC. & VT	
date	Jan 5 2005	dfrq	125.677
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	206.27	homo3	n
rfl	4635.5	PROCESSING	
rfp	3633.2	wtfile	
th	7	proc	ft
ins	2.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



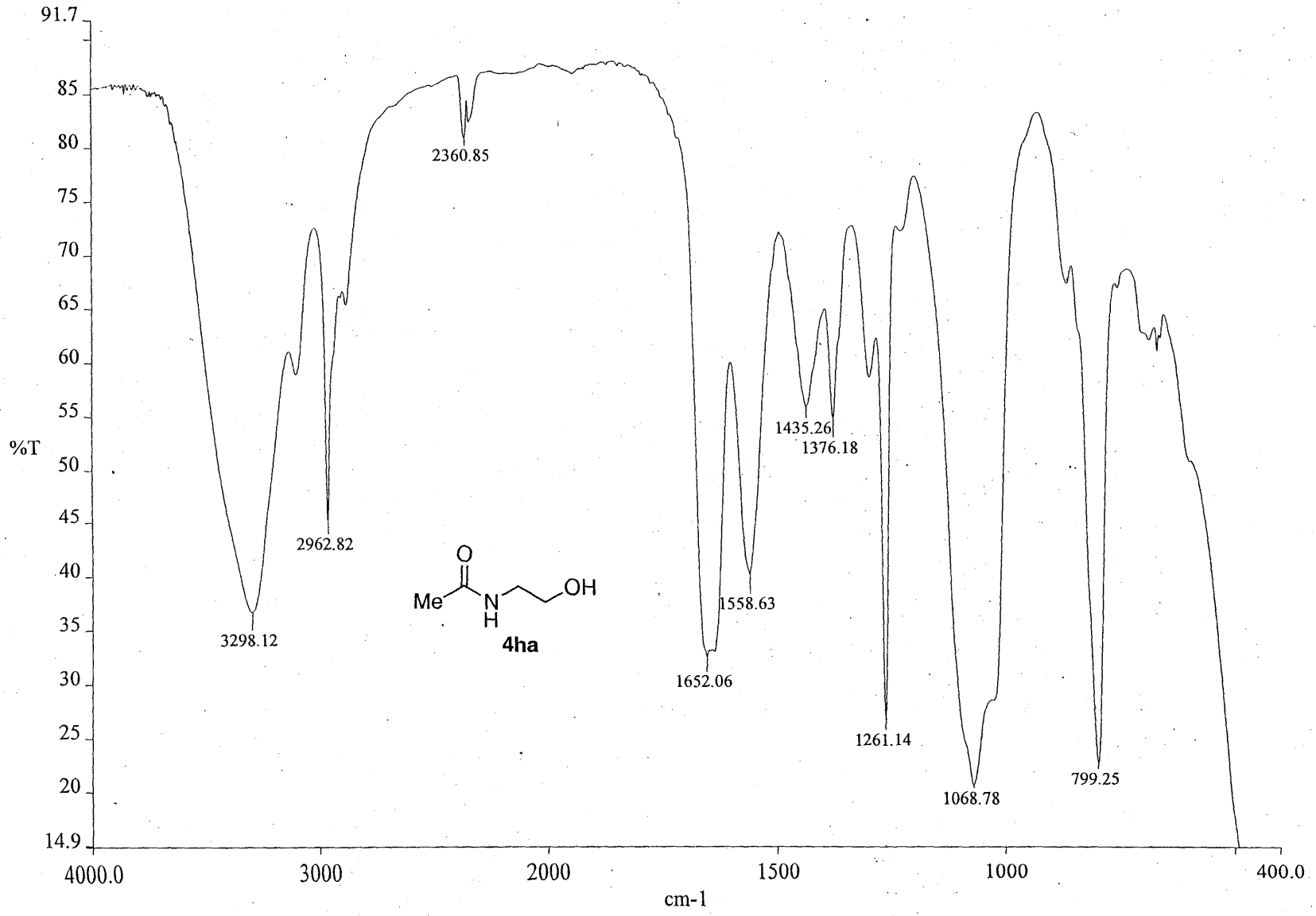
4ha

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jan 5 2005	dfrq	500.233
solvent	CDCl3	dn	H1
		dpwr	37
		dof	-500.0
		dm	y
		dmm	w
ACQUISITION		dmf	10000
sfrq	125.796	dseq	
tn	C13	dres	1.0
at	1.736	homo	n
np	131010	PROCESSING	
sw	37735.8	lb	0.30
fb	not used	wtfile	
bs	8	proc	ft
ss	1	fn	131072
tpwr	53	math	f
pw	6.9		
d1	0.763	werr	
tof	631.4	wexp	
nt	1e+06	wbs	
ct	1220	wnt	
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	27674.3		
vs	10388		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	16005.6		
rfp	9714.2		
th	12		
ins	1.000		
ai	ph		



4ha


91.7
85
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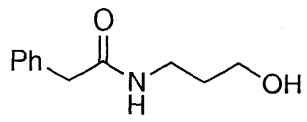
75
70
65
60
55
50
45
40
35
30
25
20
14.9
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3298.12
2962.82
2360.85
1652.06
1558.63
1435.26
1376.18
1261.14
1068.78
799.25
Me
N
H
O
OH
4ha

exp2 s2pul

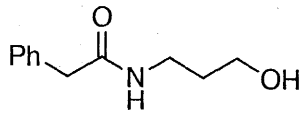
SAMPLE		DEC. & VT	
date	Jan 10 2005	dfrq	125.677
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	151.14	homo3	n
rfl	4636.4	PROCESSING	
rfp	3633.2	wtfile	
th	7	proc	ft
ins	2.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



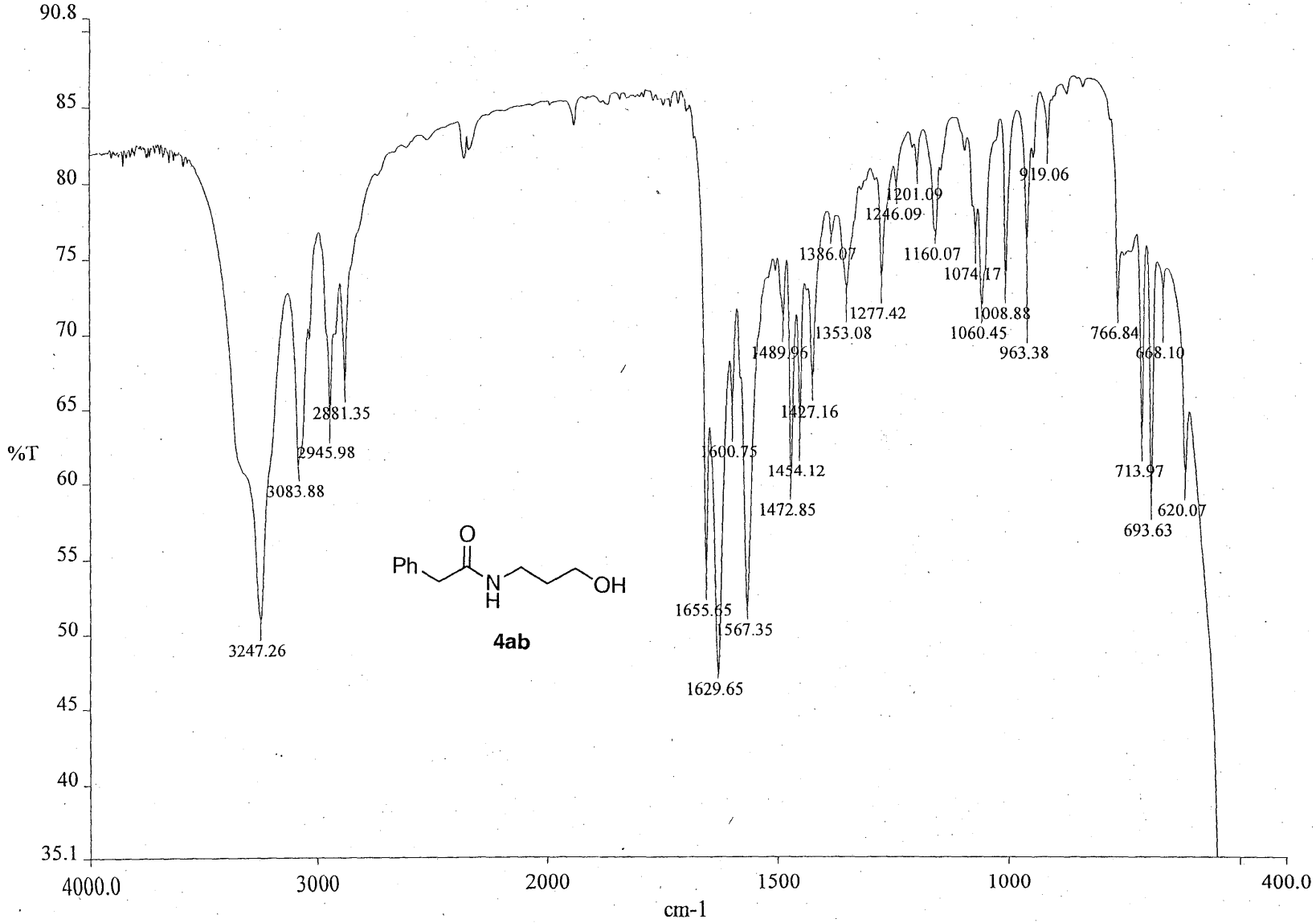
4ab

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jan 10 2005	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	1501	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	27674.1		
vs	8851		
sc	0		
wc	250		
hzmm	110.70		
is	500.00		
rfl	16008.2		
rfp	9715.0		
th	11		
ins	1.000		
ai	ph		



4ab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80
75
70
65
60
55
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45
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35.1
%T
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3000
2000
1500
1000
400.0
cm-1
3247.26
3083.88
2945.98
2881.35
1655.65
1629.65
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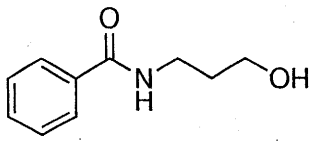
1567.35
1489.96
1472.85
1454.12
1427.16
1386.07
1353.08
1277.42
1246.09
1201.09
1160.07
1074.17
1060.45
1008.88
963.38
919.06
766.84
713.97
693.63
668.10
620.07
Ph
O
N
H
OH
4ab

exp2 s2pul

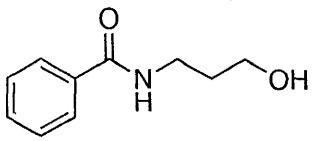
SAMPLE		DEC. & VT	
date	Jan 11 2005	dfrq	125.677
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	211.61	homo3	n
rfl	4635.8	PROCESSING	
rfp	3633.2	wtfile	
th	7	proc	ft
ins	2.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



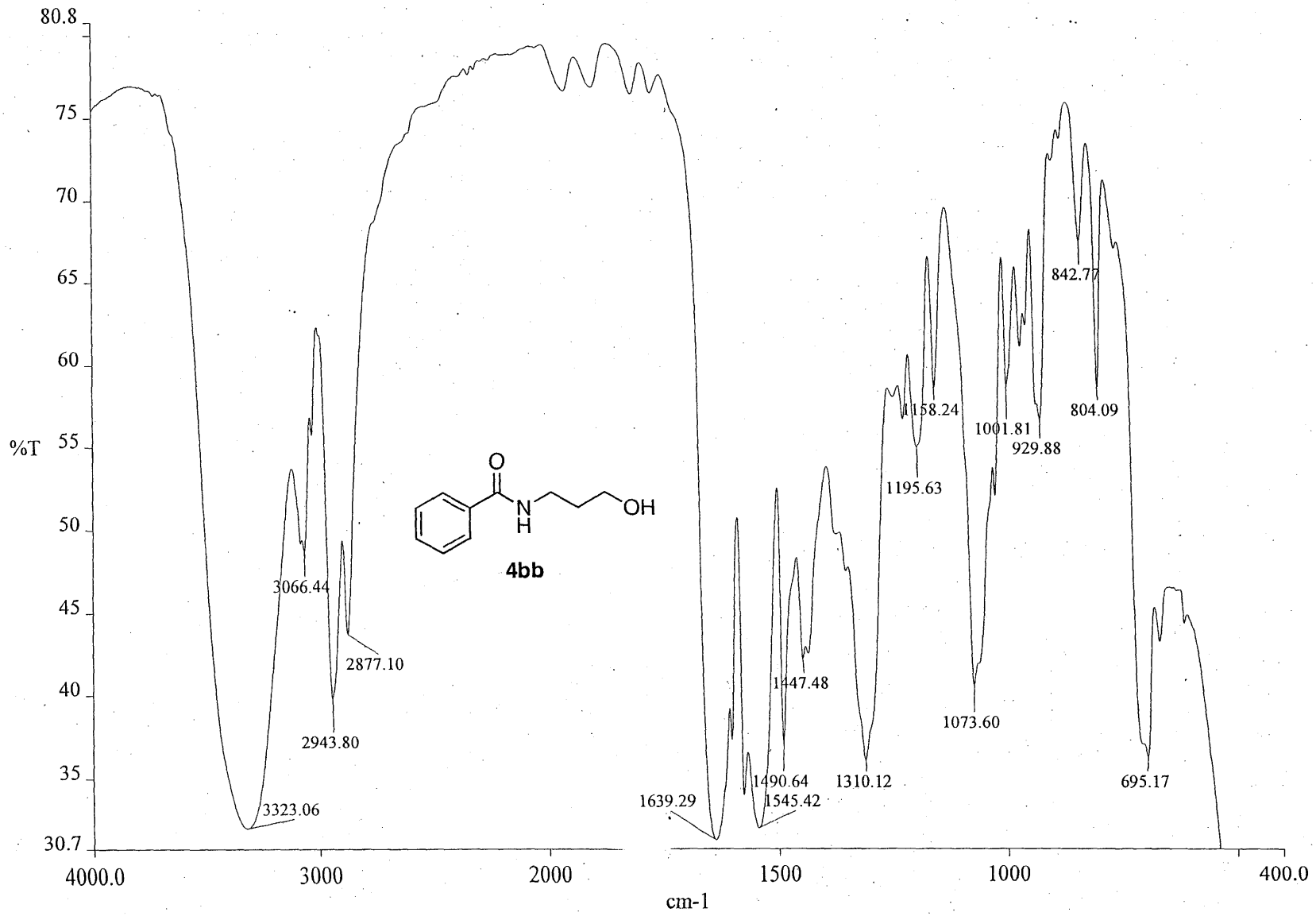
4bb

Solvent: CDCl3
Ambient temperature
User: 1-14-87
INOVA-500 "rocky"

PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
32 repetitions
OBSERVE C13, 125.7832458 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 1 minute

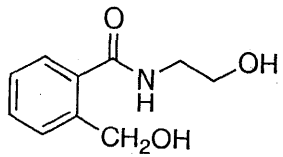


4bb


80.8
75
70
65
60
55
50
45
40
35
30.7
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3323.06
3066.44
2943.80
2877.10
1639.29
1545.42
1490.64
1447.48
1310.12
1195.63
1158.24
1073.60
1001.81
929.88
842.77
804.09
695.17
O
N
H
OH
4bb

exp4 s2pul

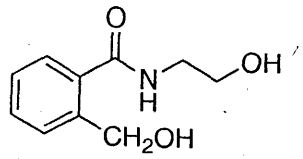
SAMPLE		DEC. & VT	
date	Jan 12 2005	dfrq	125.677
solvent	DMSO	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.760	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	0	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	284.09	homo3	n
rfl	2248.3	PROCESSING	
rfp	1249.4	wtfile	
th	7	proc	ft
ins	2.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



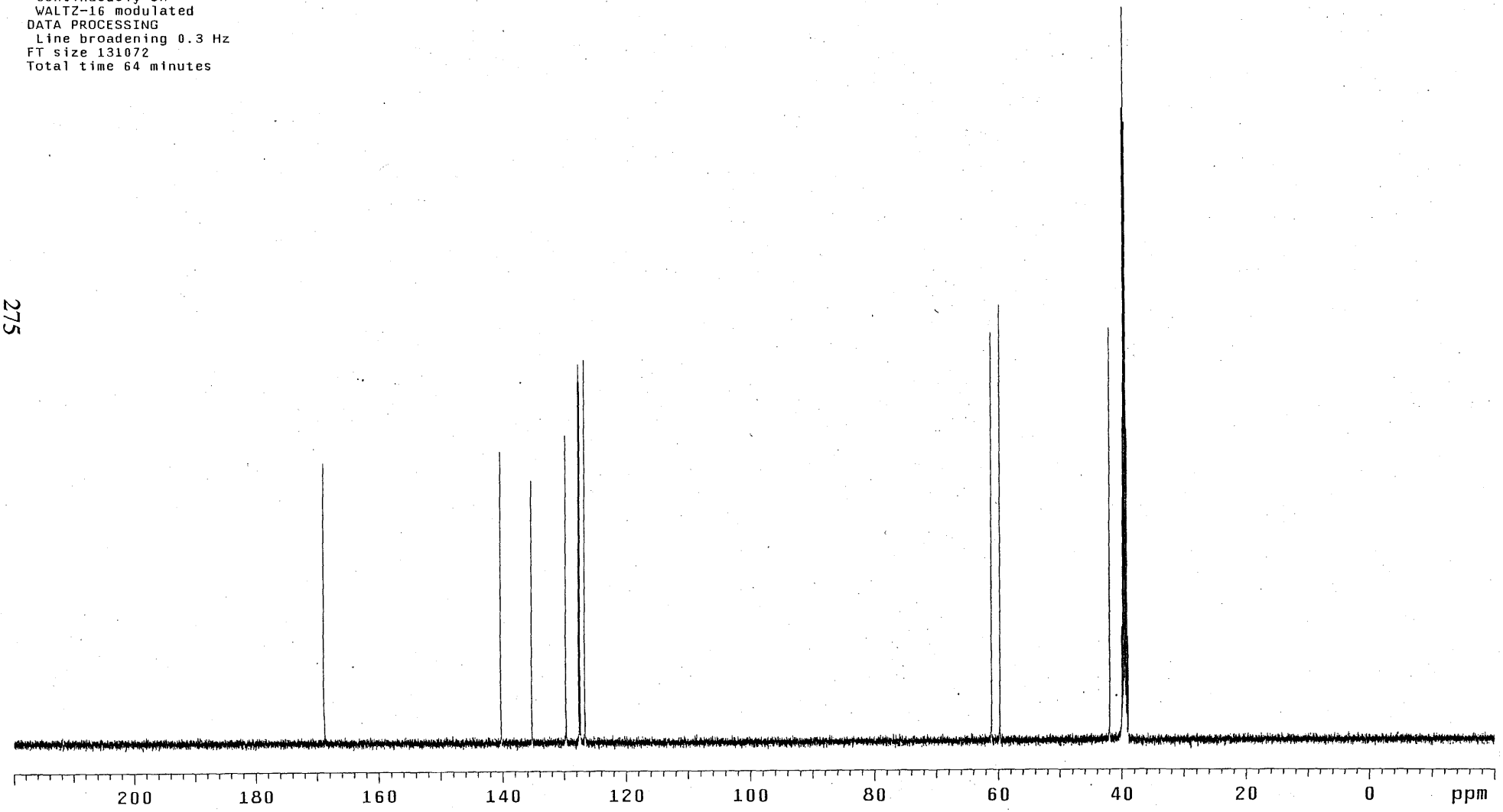
4la

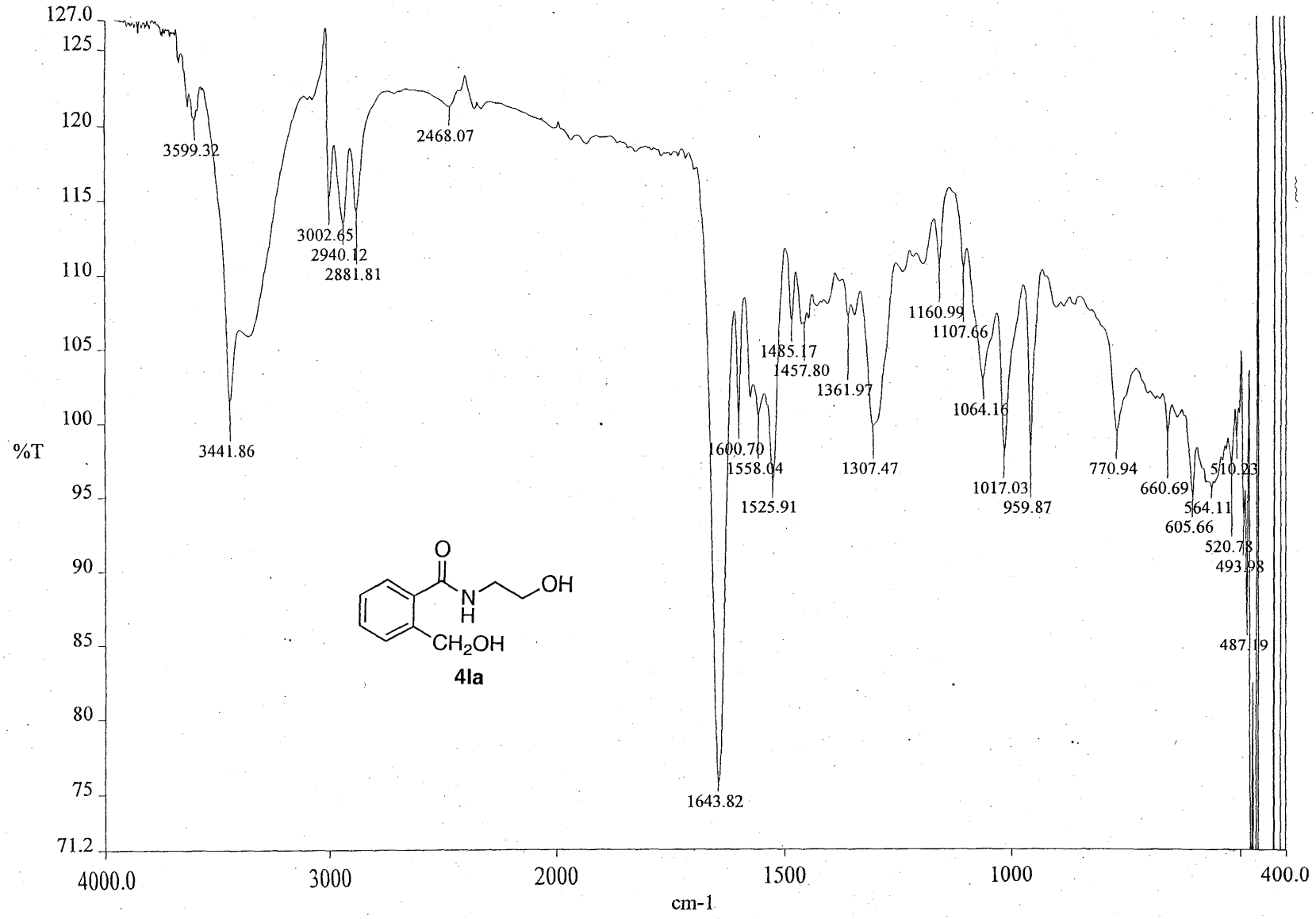
Solvent: DMSO
Ambient temperature
User: 1-14-87
INOVA-500 "rocky"

PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
1544 repetitions
OBSERVE C13, 125.7839025 MHz
DECOUPLE H1, 500.2356514 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 64 minutes



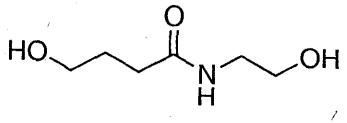
4la




127.0
125
120
115
110
105
100
95
90
85
80
75
71.2
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3599.32
3441.86
3002.65
2940.12
2881.81
2468.07
1643.82
1600.70
1558.04
1525.91
1485.17
1457.80
1361.97
1307.47
1160.99
1107.66
1064.16
1017.03
959.87
770.94
660.69
605.66
564.11
520.78
493.98
487.19
O
N
H
OH
CH2OH
4la

exp2 s2pul

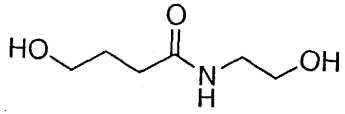
SAMPLE		DEC. & VT	
date	Jan 4 2005	dfrq	125.677
solvent	DMSO	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.760	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	195.18	homo3	n
rfl	2248.9	PROCESSING	
rfp	1249.4	wtfile	
th	6	proc	ft
ins	2.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



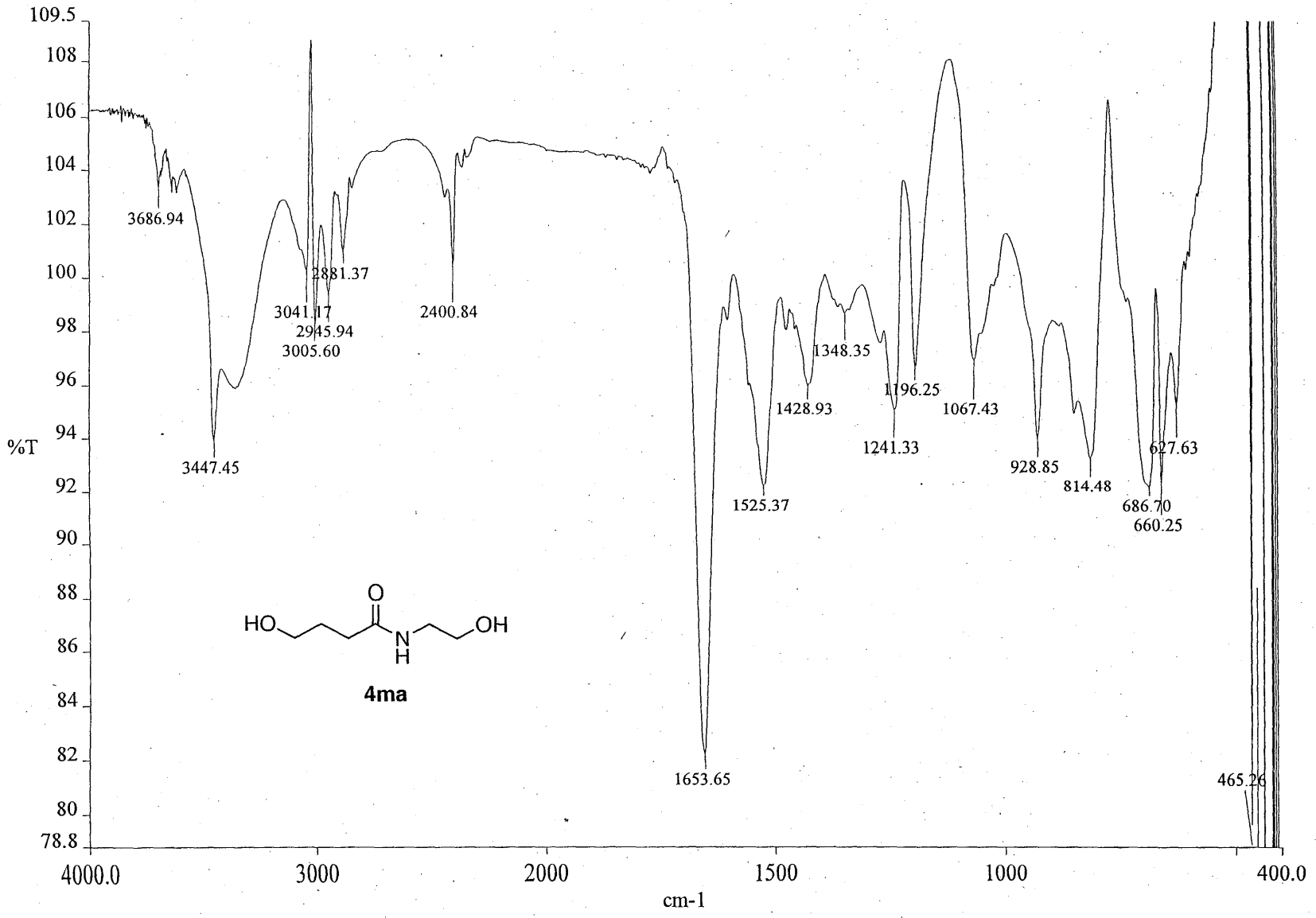
4ma

exp1 s2pul

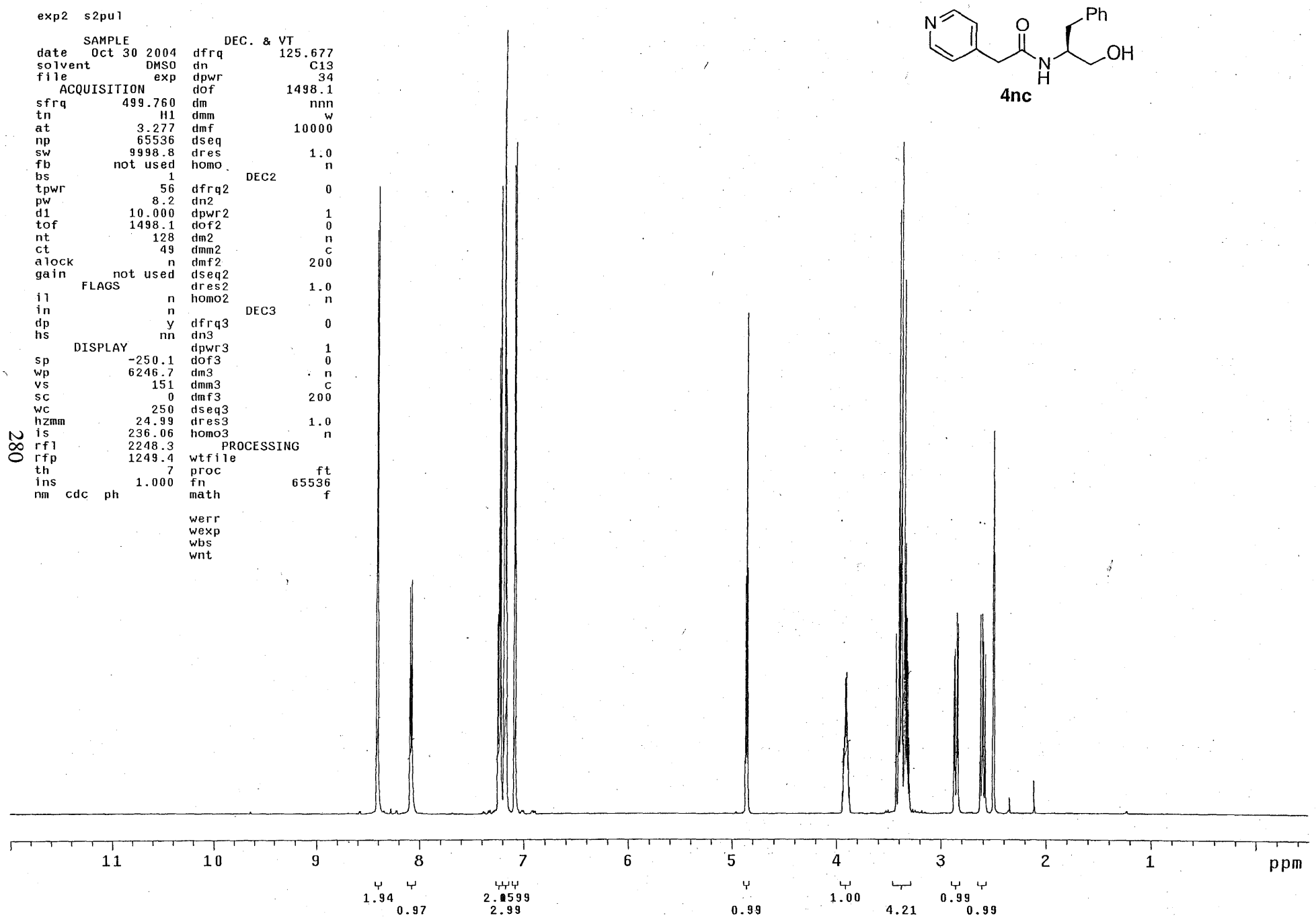
SAMPLE		DEC. & VT	
date	Jan 4 2005	dfrq	500.236
solvent	DMSO	dn	H1
		dpwr	37
		dof	-500.0
		dm	y
		dmm	w
ACQUISITION		dmf	10000
sfrq	125.796	dseq	
tn	C13	dres	1.0
at	1.736	homo	n
np	131010	PROCESSING	
sw	37735.8	lb	0.30
fb	not used	wtfile	
bs	4	proc	ft
ss	1	fn	131072
tpwr	53	math	f
pw	6.9		
d1	0.763	werr	
tof	631.4	wexp	
nt	1e+06	wbs	
ct	624	wnt	
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.3		
wp	27673.1		
vs	5812		
sc	0		
wc	250		
hzmm	110.69		
is	500.00		
rfl	11336.0		
rfp	4969.9		
th	20		
ins	1.000		
ai	ph		



4ma

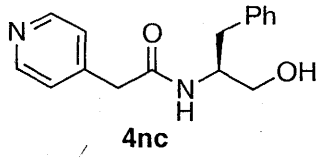

109.5
108
106
104
102
100
98
96
94
92
90
88
86
84
82
80
78.8
%T
3686.94
3447.45
3041.17
2945.94
3005.60
2881.37
2400.84
1653.65
1525.37
1428.93
1348.35
1241.33
1196.25
1067.43
928.85
814.48
686.70
660.25
627.63
465.26
4000.0
3000
2000
1500
1000
400.0
cm-1
HO
O
N
H
OH

4ma

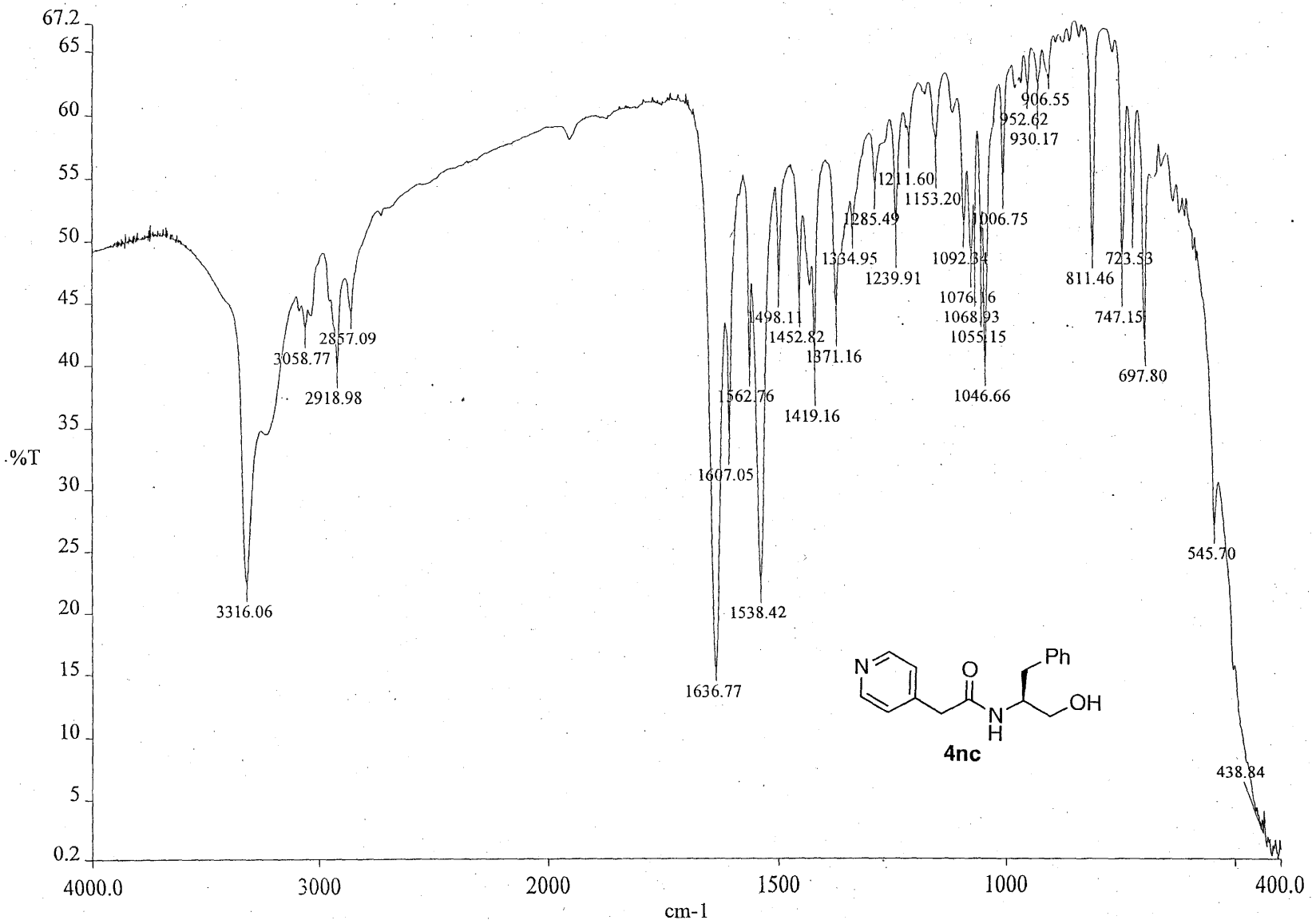

exp2 s2pul
SAMPLE
date Oct 30 2004
solvent DMSO
file exp
ACQUISITION
sfrq 499.760
tn H1
at 3.277
np 65536
sw 9998.8
fb not used
bs 1
tpwr 56
pw 8.2
d1 10.000
tof 1498.1
nt 128
ct 49
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.1
wp 6246.7
vs 151
sc 0
wc 250
hzmm 24.99
is 236.06
rfl 2248.3
rfp 1249.4
th 7
ins 1.000
nm cdc ph
DEC. & VT
dfrq 125.677
dn C13
dpwr 34
dof 1498.1
dm nnn
dmm w
dmf 10000
dseq
dres 1.0
homo n
DEC2
dfrq2 0
dn2
dpwr2 1
dof2 0
dm2 n
dmm2 c
dmf2 200
dseq2
dres2 1.0
homo2 n
DEC3
dfrq3 0
dn3
dpwr3 1
dof3 0
dm3 n
dmm3 c
dmf3 200
dseq3
dres3 1.0
homo3 n
PROCESSING
wtfile
proc ft
fn 65536
math f
werr
wexp
wbs
wnt
N
O
Ph
OH
N
H
4nc
11
10
9
8
7
6
5
4
3
2
1
ppm
1.94
0.97
2.0599
2.99
0.99
1.00
4.21
0.99
0.99

exp5 s2pul

SAMPLE		DEC. & VT	
date	Oct 30 2004	dfrq	500.236
solvent	DMSO	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	1	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	2.000	fn	131072
tof	631.4	math	f
nt	1e+07		
ct	1000	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1258.1		
wp	28931.1		
vs	151		
sc	0		
wc	250		
hzmm	115.73		
is	500.00		
rfl	11341.8		
rfp	4969.9		
th	10		
ins	1.000		
nm	ph		



4nc


67.2
65
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55
50
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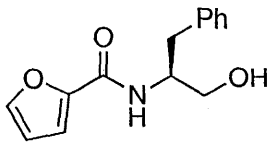
40
35
30
25
20
15
10
5
0.2
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3316.06
3058.77
2918.98
2857.09
1636.77
1607.05
1562.76
1538.42
1498.11
1452.82
1419.16
1371.16
1334.95
1285.49
1239.91
1211.60
1153.20
1092.34
1076.16
1068.93
1055.15
1046.66
1006.75
952.62
930.17
906.55
811.46
747.15
723.53
697.80
545.70
438.84
N
O
Ph
OH
N
H
4nc

exp2 s2pul

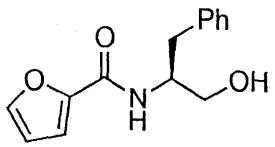
SAMPLE		DEC. & VT	
date	Nov 29 2004	dfrq	125.677
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	235.05	homo3	n
rfl	4635.8	PROCESSING	
rfp	3633.2	wtfile	
th	40	proc	ft
ins	1.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



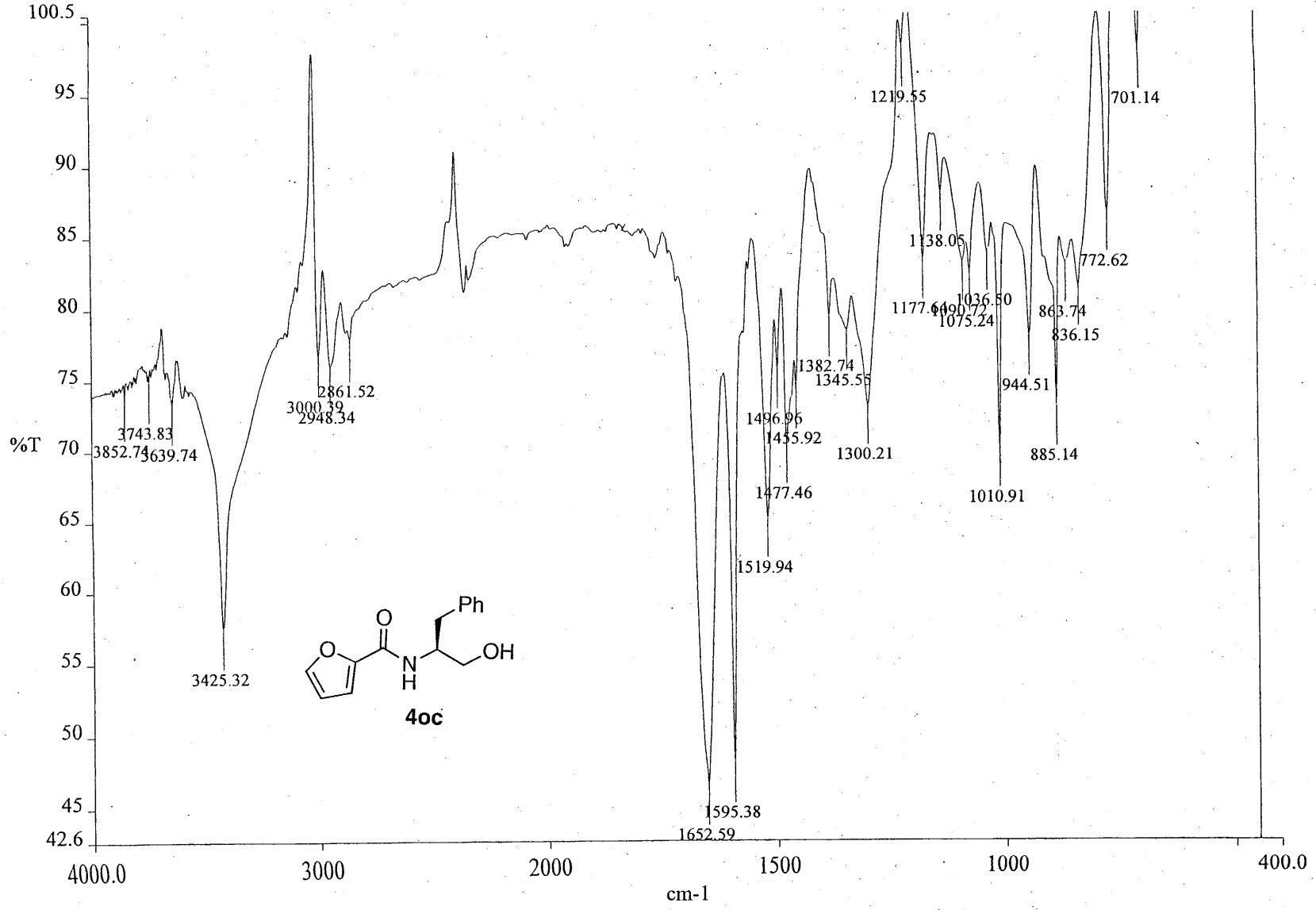
4oc

exp2 s2pul

SAMPLE		DEC. & VT	
date	Nov 30 2004	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	4	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	2.500	fn	131072
tof	631.4	math	f
nt	10000		
ct	300	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	30189.8		
vs	3352		
sc	0		
wc	250		
hzmm	120.76		
is	500.00		
rfl	16014.5		
rfp	9715.0		
th	20		
ins	1.000		
ai	ph		



4oc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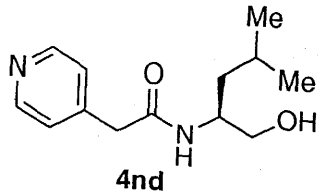
85
80
75
70
65
60
55
50
45
42.6
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3852.74
3743.83
3639.74
3425.32
3000.39
2948.34
2861.52
1652.59
1595.38
1519.94
1496.96
1477.46
1455.92
1382.74
1345.55
1300.21
1219.55
1177.64
1138.05
1090.77
1075.24
1036.50
1010.91
944.51
885.14
863.74
836.15
772.62
701.14
Ph
O
O
N
H
OH
4oc

exp1 s2pul

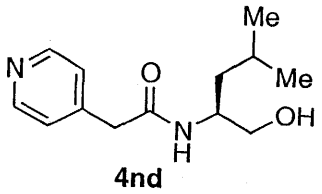
SAMPLE		DEC. & VT	
date	Dec 11 2004	dfrq	125.796
solvent	DMSO	dn	C13
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	500.238	dm	nnn
tn	H1	dmm	c
at	3.200	dmf	10000
np	64000	dseq	
sw	10000.0	dres	1.0
fb	not used	homo	n
bs	1	PROCESSING	
ss	1	wtfile	
tpwr	59	proc	ft
pw	9.8	fn	131072
d1	7.000	math	f
tof	1498.2		
nt	16	werr	
ct	16	wexp	
alock	n	wbs	
gain	not used	wnt	
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.3		
wp	6252.8		
vs	151		
sc	0		
wc	250		
hzmm	40.00		
is	263.27		
rfl	2243.2		
rfp	1250.6		
th	7		
ins	1.000		
nm	ph		



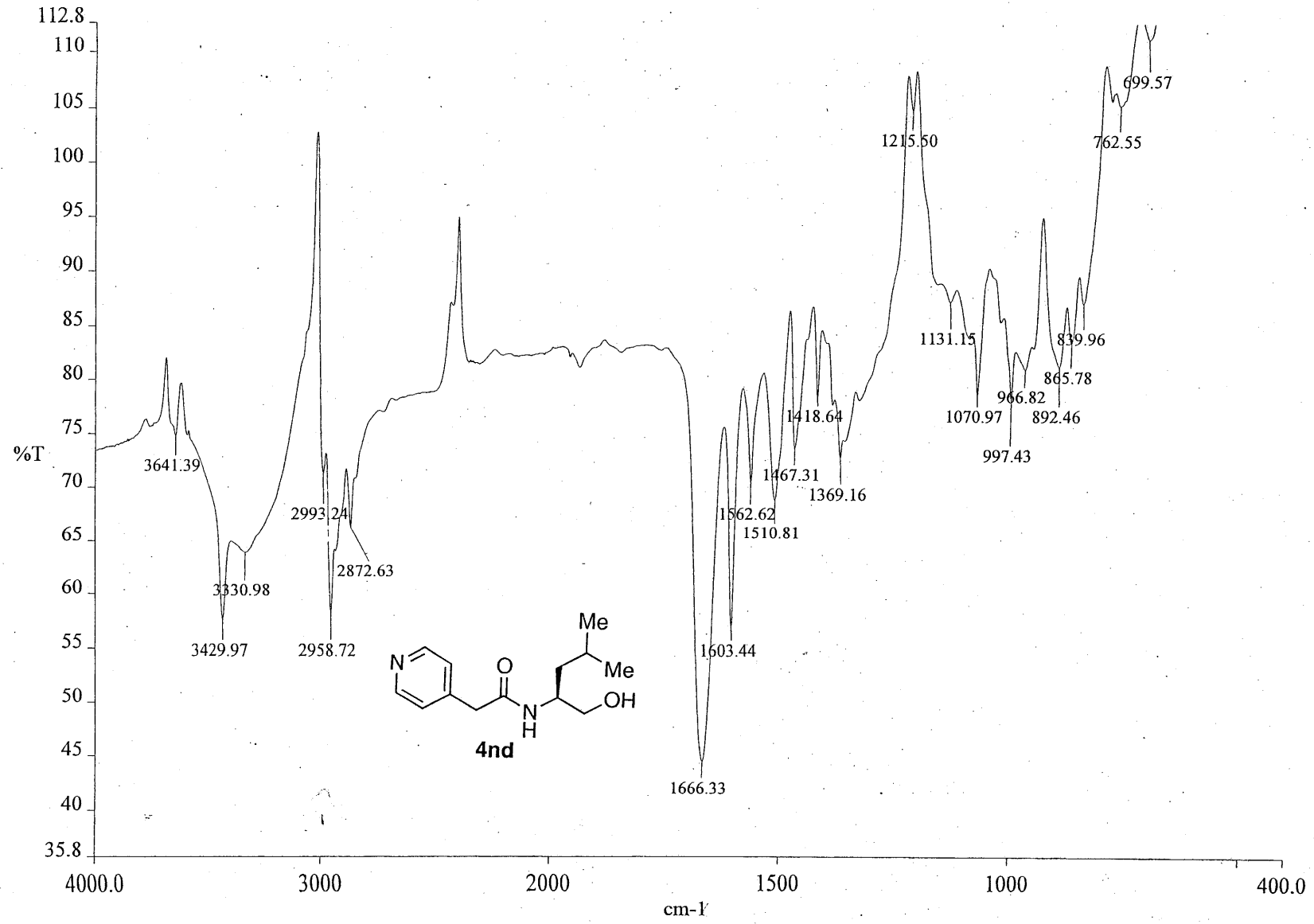
4nd

exp1 s2pul

SAMPLE		DEC. & VT	
date	Dec 11 2004	dfrq	500.236
solvent	DMSO	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	2.500	dmf	10000
np	188680	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	16	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	2.500	fn	131072
tof	631.4	math	f
nt	100000		
ct	748	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2594.5		
wp	33962.6		
vs	151		
sc	0		
wc	250		
hzmm	135.85		
is	500.00		
rfl	11337.7		
rfp	4969.9		
th	13		
ins	1.000		
nm	ph		



4nd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80
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40
35.8
%T
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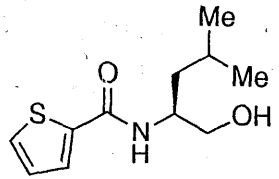
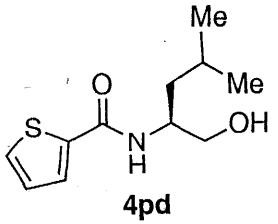
3000
2000
1500
1000
400.0
cm-1
3641.39
3429.97
3330.98
2993.24
2958.72
2872.63
1666.33
1603.44
1562.62
1510.81
1467.31
1418.64
1369.16
1215.50
1131.15
1070.97
997.43
966.82
892.46
865.78
839.96
762.55
699.57
N
O
N
H
Me
Me
OH
4nd

exp2 s2pul

SAMPLE		DEC. & VT	
date	Nov 29 2004	dfrq	125.677
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	..
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	487.45	homo3	n
rfl	4636.1	PROCESSING	
rfp	3633.2	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



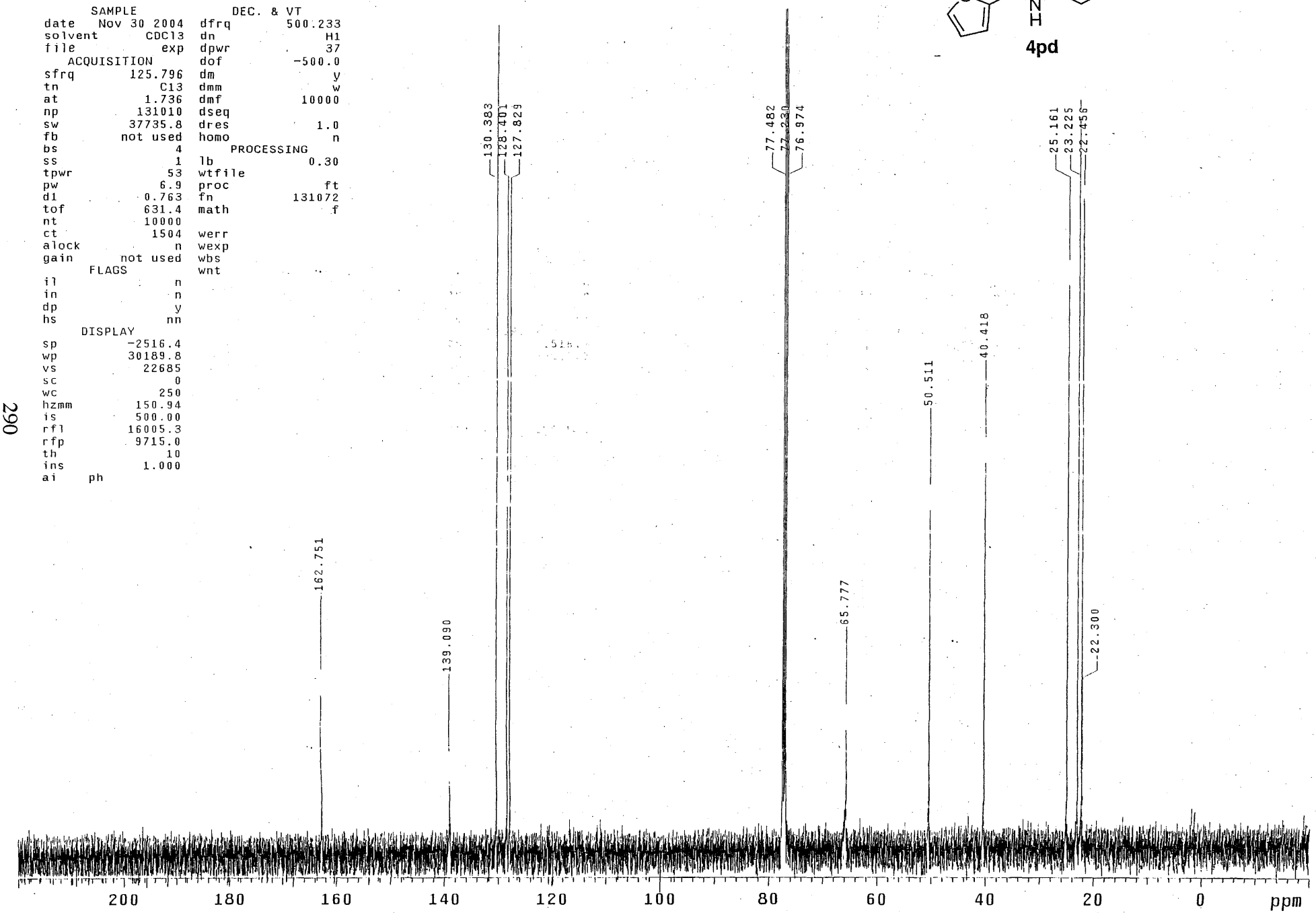
4pd

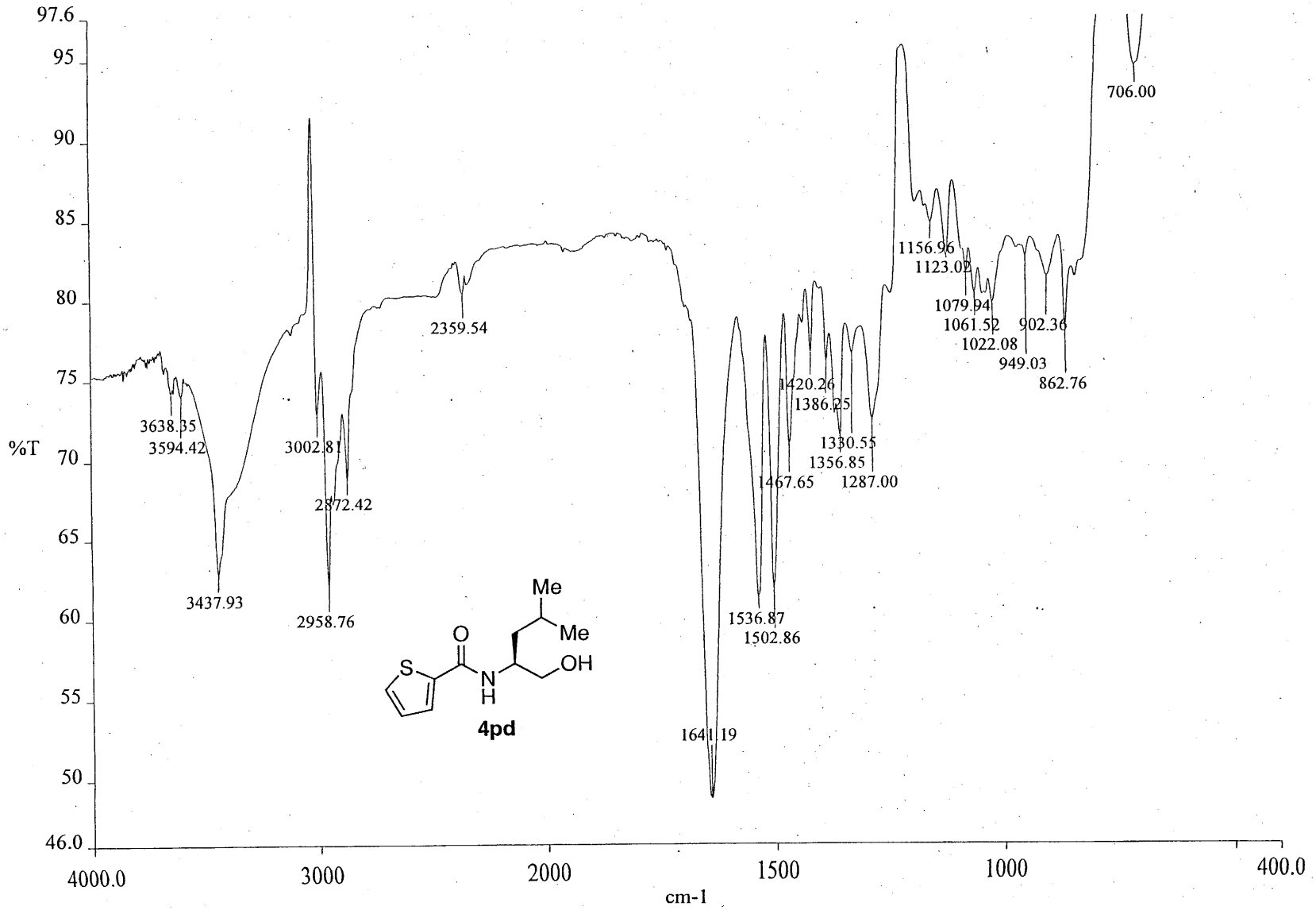


4pd

exp2 s2pul

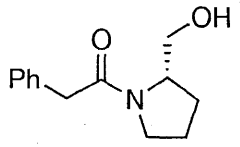
SAMPLE		DEC. & VT	
date	Nov 30 2004	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	4	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	10000		
ct	1504	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	30189.8		
vs	22685		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	16005.3		
rfp	9715.0		
th	10		
ins	1.000		
ai	ph		




97.6
95
90
85
80
75
70
65
60
55
50
46.0
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3638.35
3594.42
3437.93
3002.81
2872.42
2958.76
2359.54
1641.19
1536.87
1502.86
1467.65
1420.26
1386.25
1330.55
1356.85
1287.00
1156.96
1123.02
1079.94
1061.52
1022.08
949.03
902.36
862.76
706.00
Me
Me
OH
O
N
H
S
4pd

exp1 s2pul

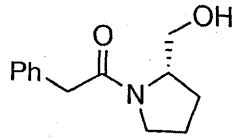
SAMPLE		DEC. & VT	
date	Jan 7 2005	dfrq	125.677
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	172.75	homo3	n
rfl	4635.5	PROCESSING	
rfp	3633.2	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



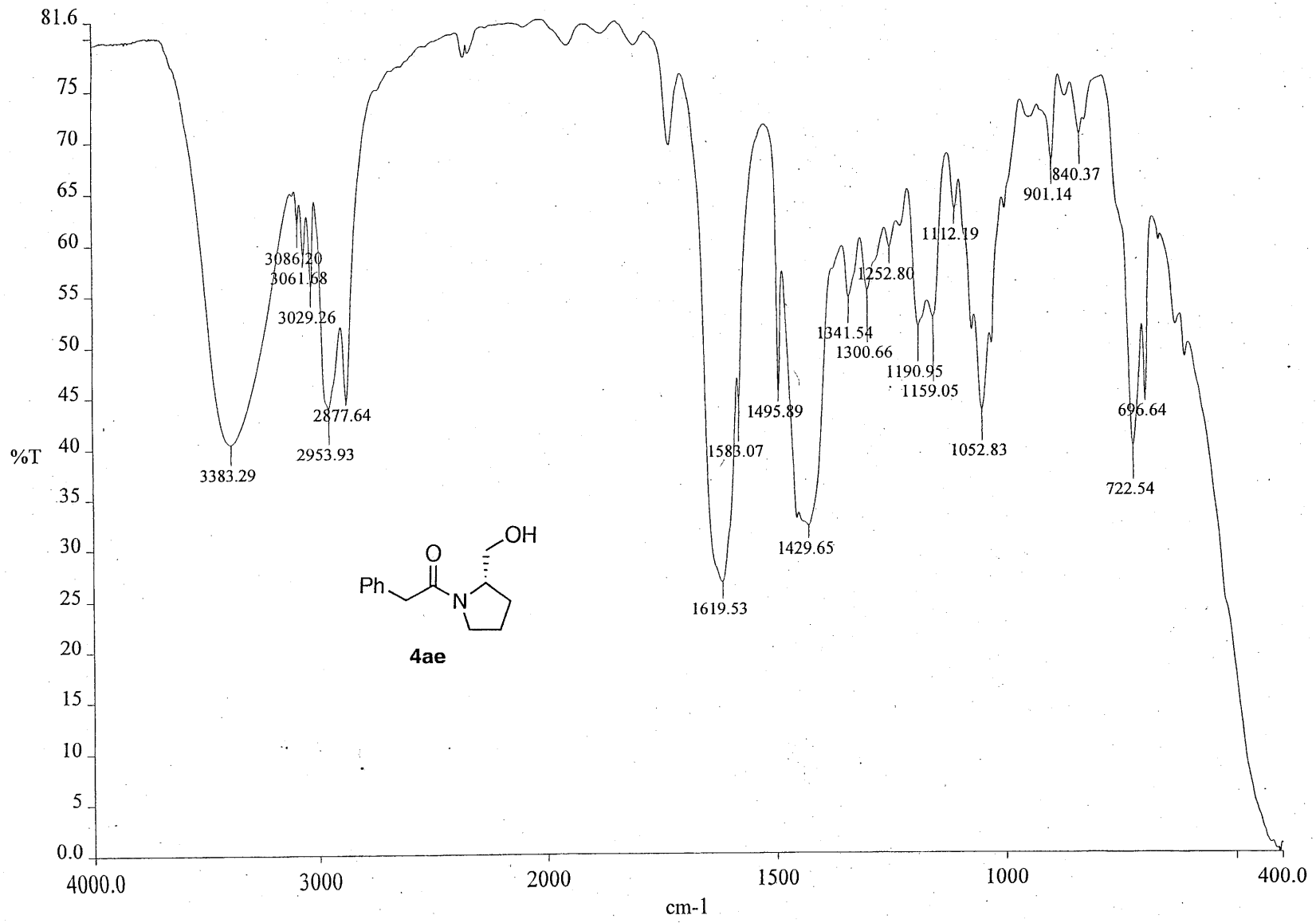
4ae

exp2 s2pul

SAMPLE		DEC. & VT	
date	Jan 8 2005	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	2500	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	27674.1		
vs	14169		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	16003.5		
rfp	9715.0		
th	10		
ins	1.000		
ai	ph		



4ae


81.6
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.0
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3383.29
3086.20
3061.68
3029.26
2953.93
2877.64
1619.53
1583.07
1495.89
1429.65
1341.54
1300.66
1252.80
1190.95
1159.05
1112.19
1052.83
901.14
840.37
722.54
696.64
Ph
O
N
OH

4ae

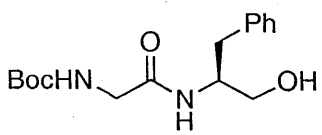
```
exp1  s2pul

      SAMPLE
date    Nov 13 2004
solvent       CDCl3

   ACQUISITION
sfrq        499.758
tn               H1
at           3.277
np           65536
sw          9998.8
fb        not used
bs                1
tpwr             56
pw              8.2
d1            7.000
tof          1498.1
nt               16
ct               16
alock             n
gain      not used
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp           -250.1
wp           6246.8
vs              151
sc                0
wc              250
hzmm          40.00
is           132.90
rfl          4635.5
rfp          3633.2
th                7
ins           1.000
nm  cdc  ph

     DEC. & VT
dfrq        125.677
dn              C13
dpwr             34
dof          1498.1
dm              nnn
dmm               w
dmf           10000
dseq
dres            1.0
homo              n
     PROCESSING
wtfile
proc             ft
fn            65536
math              f

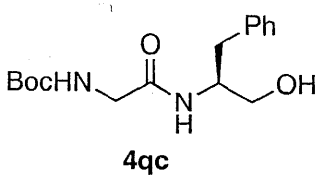
werr
wexp
wbs
wnt
```



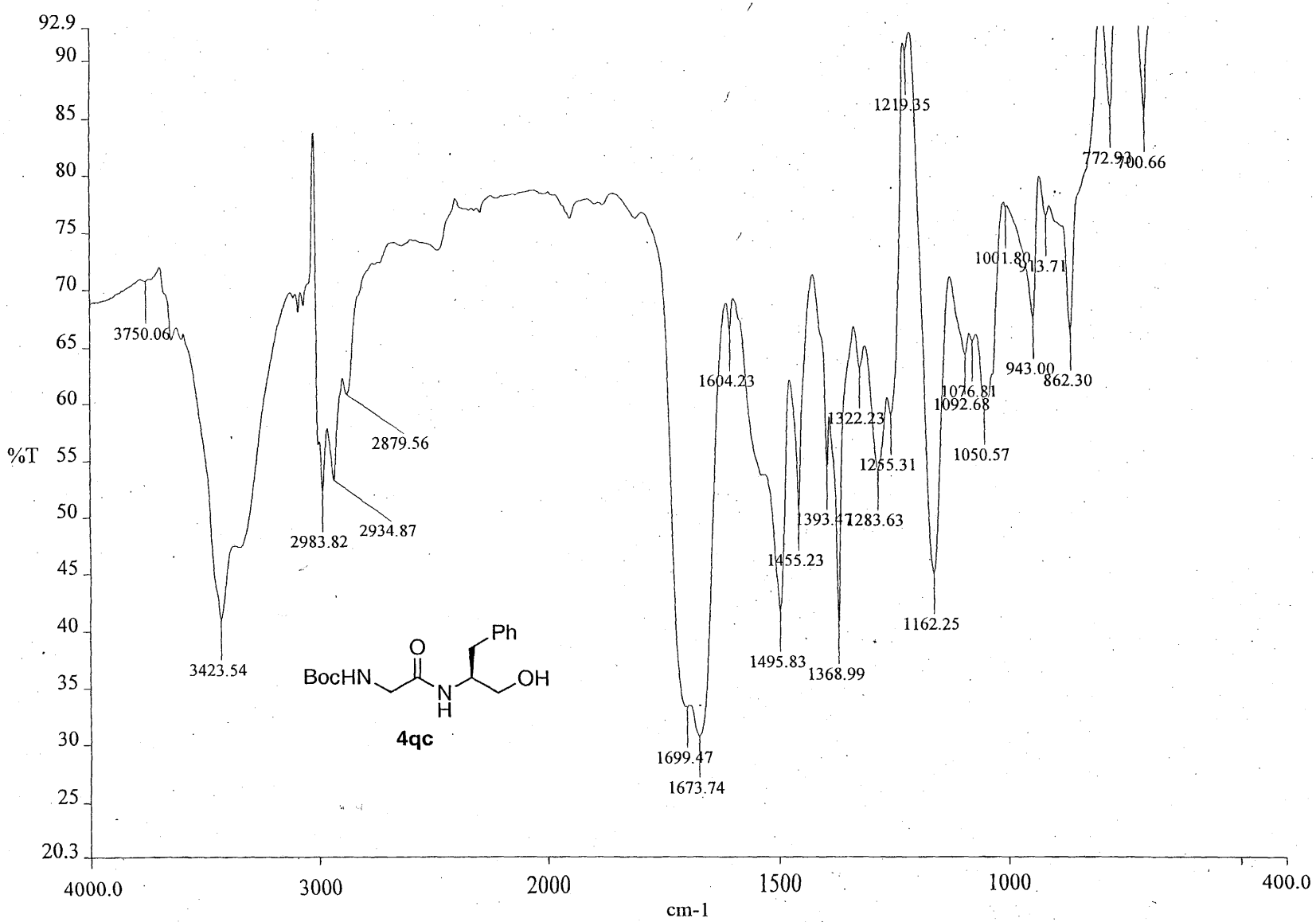
4qc

exp2 s2pul

SAMPLE		DEC. & VT	
date	Jan 8 2005	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	1651	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	27674.1		
vs	5424		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	16005.3		
rfp	9715.0		
th	3		
ins	1.000		
ai	ph		



4qc


92.9
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20.3
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3750.06
3423.54
2983.82
2934.87
2879.56
1699.47
1673.74
1604.23
1495.83
1455.23
1393.47
1368.99
1322.23
1283.63
1255.31
1219.35
1162.25
1092.68
1076.81
1050.57
1001.80
943.00
913.71
862.30
772.92
700.66
BocHN
O
N
H
Ph
OH
4qc

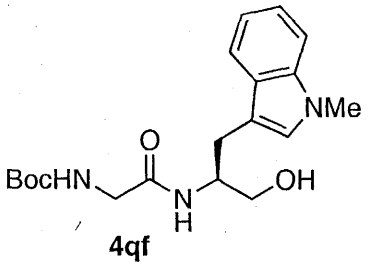
```
exp1  s2pul

      SAMPLE
date    Nov 20 2004
solvent        DMSO

   ACQUISITION
sfrq        500.238
tn               H1
at             3.200
np             64000
sw           10000.0
fb         not used
bs                1
ss                1
tpwr             59
pw              9.8
d1            7.000
tof          1498.2
nt              256
ct               32
alock             n
gain       not used
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp           -250.1
wp           6252.9
vs              151
sc                0
wc              250
hzmm          25.01
is           339.58
rfl          2242.9
rfp          1250.6
th               127
ins            3.000
nm    ph

      DEC. & VT
dfrq        125.796
dn              C13
dpwr             37
dof               0
dm              nnn
dmm               c
dmf           10000
dseq
dres            1.0
homo              n
     PROCESSING
wtfile
proc             ft
fn           131072
math              f

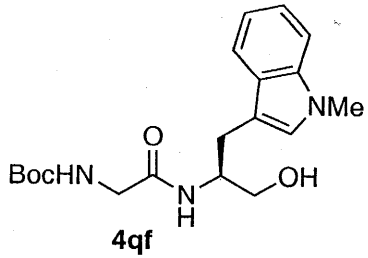
werr
wexp
wbs
wnt
```



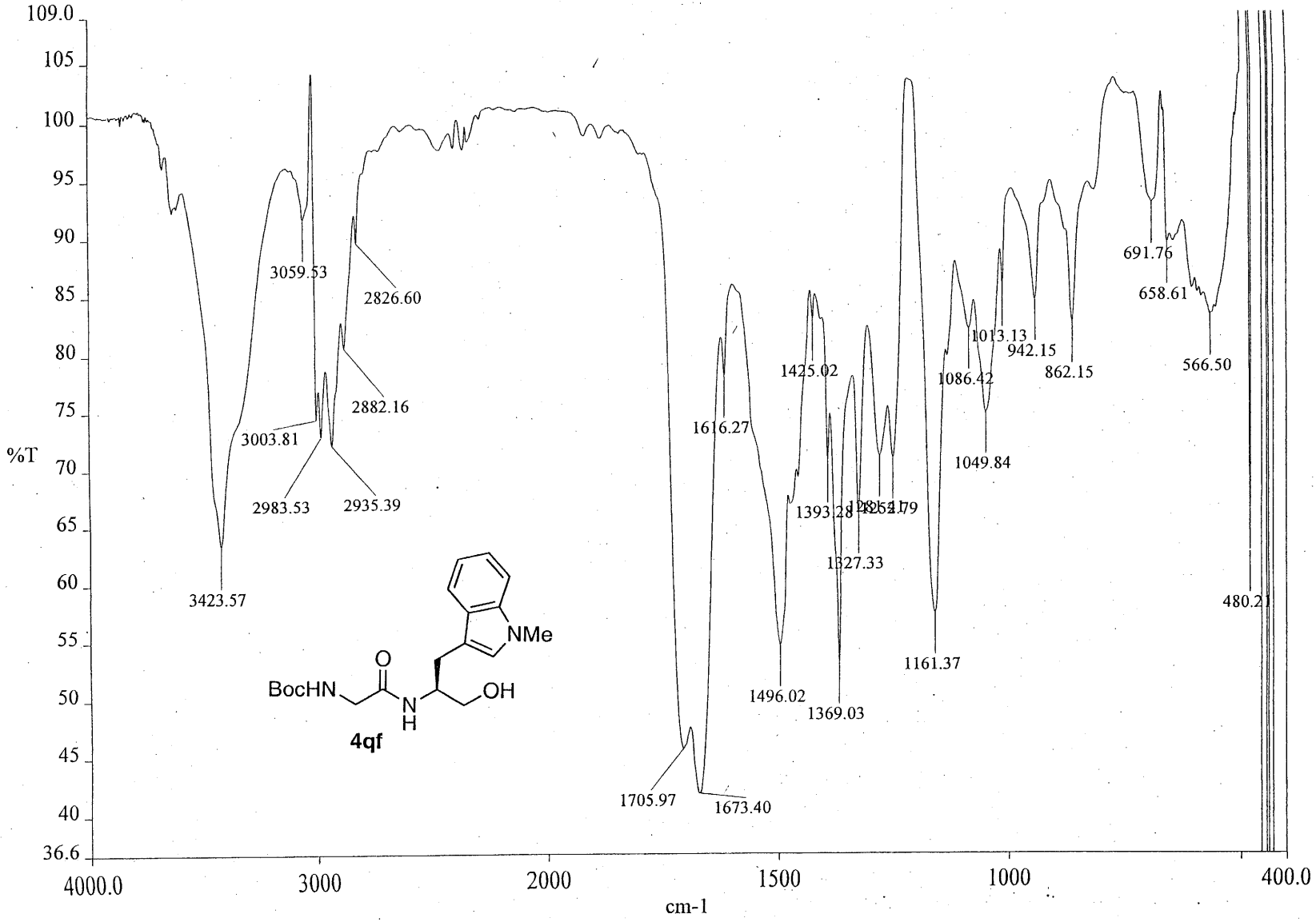
4qf

exp2 s2pul

SAMPLE		DEC. & VT	
date	Jan 8 2005	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	1.736	dmf	10000
np	131010	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	0.763	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	2368	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.4		
wp	27674.1		
vs	7919		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	16007.0		
rfp	9715.0		
th	4		
ins	1.000		
ai	ph		



4qf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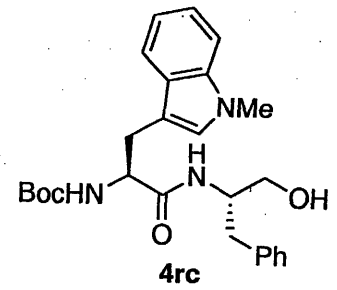
85
80
75
70
65
60
55
50
45
40
36.6
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3423.57
3059.53
3003.81
2983.53
2935.39
2882.16
2826.60
1705.97
1673.40
1616.27
1496.02
1425.02
1393.28
1369.03
1327.33
1161.37
1086.42
1049.84
1013.13
942.15
862.15
691.76
658.61
566.50
480.21
BocHN
O
N
H
OH
NMe
4qf

exp2 s2pul

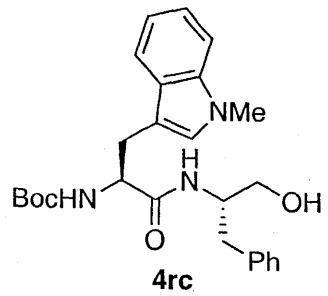
SAMPLE		DEC. & VT	
date	Jan 15 2005	dfrq	125.677
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	213.50	homo3	n
rfl	4634.0	PROCESSING	
rfp	3633.2	wtfile	
th	7	proc	ft
ins	2.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



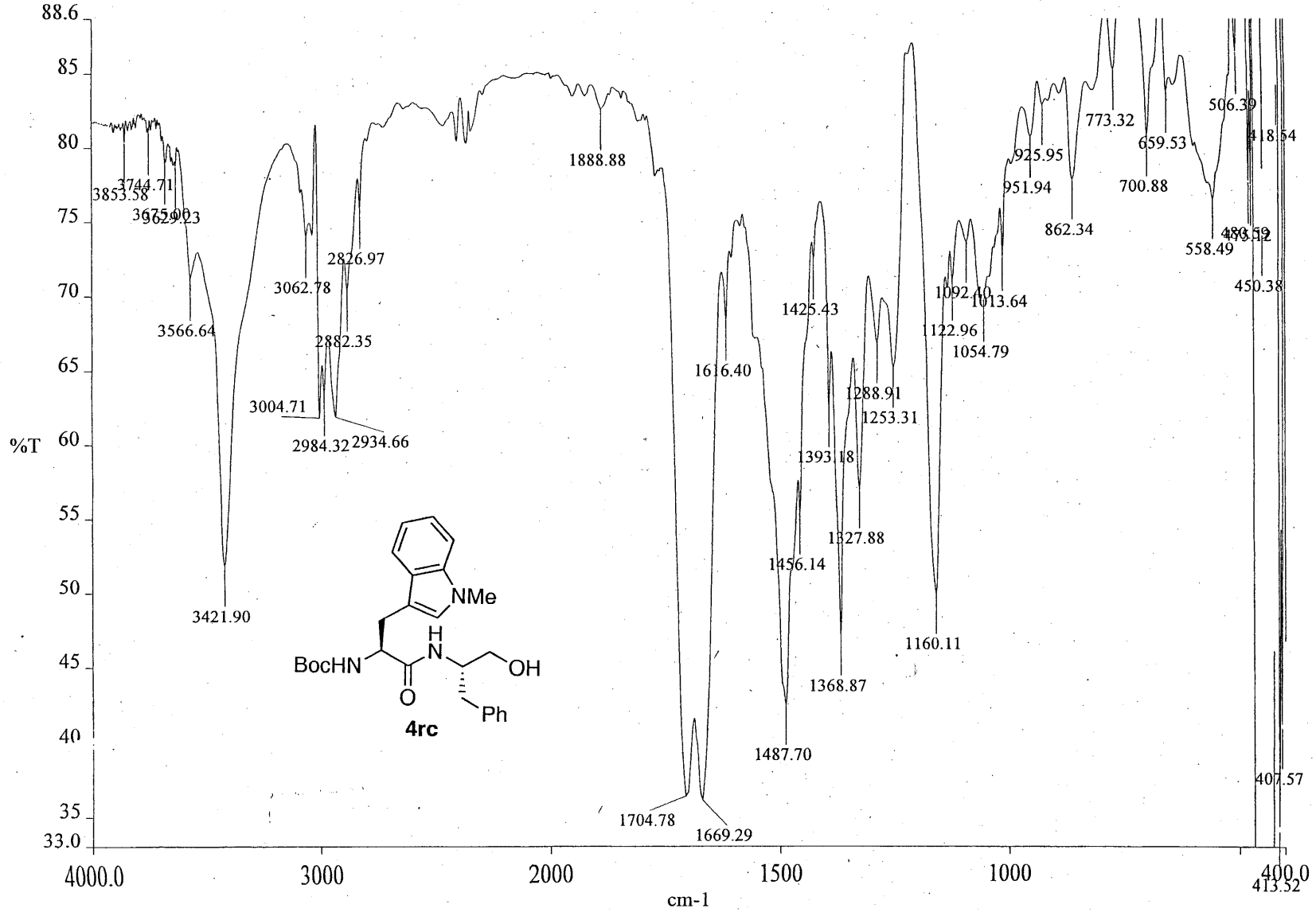
4rc

Solvent: CDCl3
Ambient temperature
User: 1-14-87
INOVA-500 "rocky"

PULSE SEQUENCE
Relax. delay 0.763 sec
Pulse 65.4 degrees
Acq. time 1.736 sec
Width 37735.8 Hz
1520 repetitions
OBSERVE C13, 125.7832360 MHz
DECOUPLE H1, 500.2332753 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 131072
Total time 63 minutes



4rc


88.6
85
80
75
70
65
60
55
50
45
40
35
33.0
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3853.58
3744.71
3675.00
3629.23
3566.64
3421.90
3062.78
2826.97
2882.35
3004.71
2984.32
2934.66
1888.88
1616.40
1425.43
1456.14
1487.70
1704.78
1669.29
1393.18
1327.88
1368.87
1288.91
1253.31
1160.11
1122.96
1092.40
1054.79
1013.64
951.94
925.95
862.34
773.32
700.88
659.53
558.49
506.39
450.38
418.54
413.52
407.57
NMe
H
N
BocHN
OH
O
Ph
4rc

```
==========================================================================
Injection Date  : 3/5/2005 6:18:41 PM          Seq. Line :   1
Sample Name     :                             Location : Vial 5
Acq. Operator   :                                 Inj :   1
                                              Inj Volume : 1 µl

Acq. Method     : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 3/5/2005 6:17:57 PM
Analysis Method : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 4/21/2008 2:58:23 PM
                  (modified after loading)
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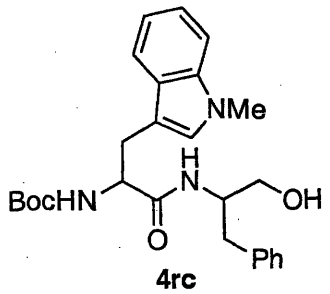
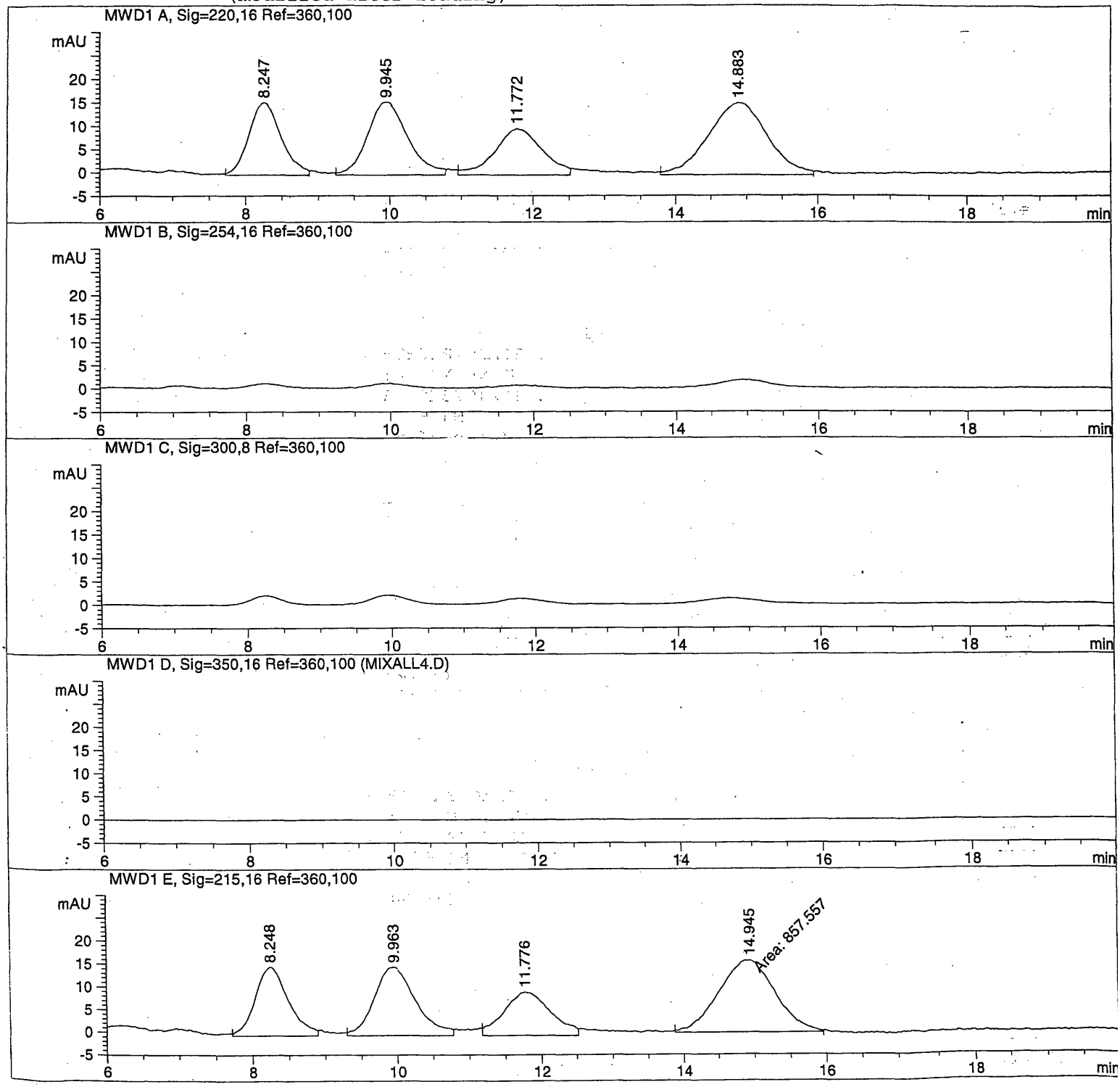


4rc



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.247	VV	0.3799	481.76340	15.52990	19.7389
2	9.945	VV	0.4650	614.19940	15.61203	25.1651
3	11.772	VV	0.5422	456.89044	9.97821	18.7198
4	14.883	VV	0.6835	887.82440	15.42557	36.3761
Totals :				2440.67764	56.54571	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.248	VV	0.4055	477.61615	15.08105	20.2034
2	9.963	VV	0.4773	599.29999	15.02562	25.3507
3	11.776	VV	0.5342	429.56683	9.52479	18.1709
4	14.945	MM	0.9093	857.55713	15.71803	36.2751
Totals :				2364.04010	55.34949	

Results obtained with enhanced integrator!

*** End of Report ***

```
==========================================================================
Injection Date  : 3/4/2005 4:26:54 PM          Seq. Line :   1
Sample Name     :                             Location : Vial 3
Acq. Operator   :                                 Inj :   1
                                              Inj Volume : 1 µl

Acq. Method     : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 3/4/2005 4:26:00 PM
Analysis Method : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 3/4/2005 5:55:09 PM
                  (modified after loading)
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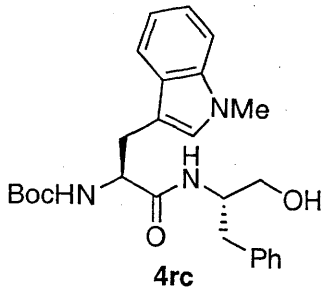
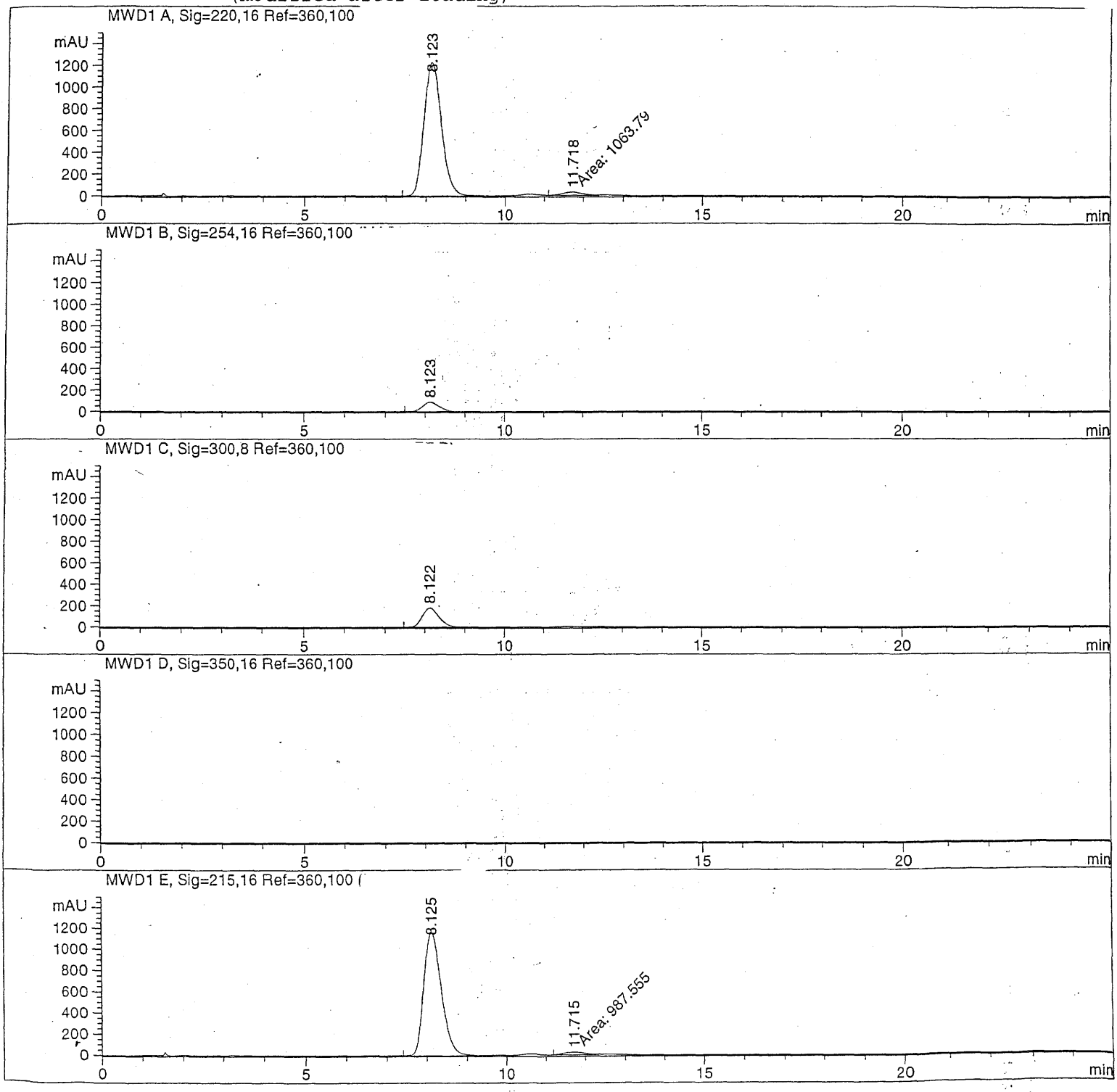


4rc



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.123	VV	0.4846	3.76649e4	1225.48999	97.2532
2	11.718	MM	0.6233	1063.79309	28.44707	2.7468
Totals :				3.87286e4	1253.93707	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.123	VV	0.4515	2570.82812	87.82916	100.0000
Totals :				2570.82812	87.82916	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.122	BB	0.4502	5233.93945	179.49063	100.0000
Totals :				5233.93945	179.49063	

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

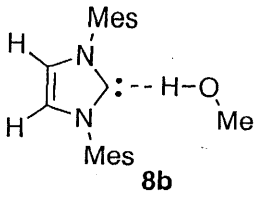
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.125	VV	0.4804	3.55983e4	1158.75781	97.3007
2	11.715	MM	0.6095	987.55511	27.00609	2.6993
Totals :				3.65859e4	1185.76390	

Results obtained with enhanced integrator!

*** End of Report ***

exp4 s2pul

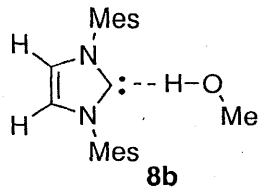
SAMPLE		DEC. & VT	
date	Aug 14 2004	dfrq	125.677
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	26.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	247.07	homo3	n
rfl	4564.4	PROCESSING	
rfp	3578.2	wtfile	
th	4	proc	ft
ins	18.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



8b

expl s2pul

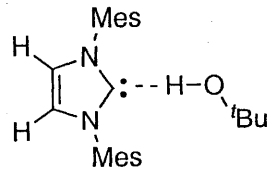
SAMPLE		DEC. & VT	
date	Dec 11 2004	dfrq	500.233
solvent	Benzene	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	2.500	dmf	10000
np	188680	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	16	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	2.500	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	1197	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.5		
wp	33965.4		
vs	151		
sc	0		
wc	250		
hzmm	135.86		
is	500.00		
rfl	22373.8		
rfp	16151.4		
th	9		
ins	1.000		
nm	ph		



8b

exp5 s2pul

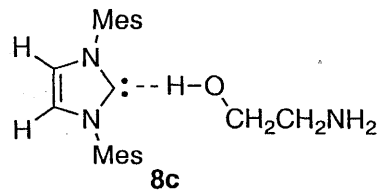
SAMPLE		DEC. & VT	
date	Jan 28 2005	dfrq	125.677
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	26.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	194.25	homo3	n
rfl	4563.8	PROCESSING	
rfp	3578.2	wtfile	
th	109	proc	ft
ins	18.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



8a

exp4 s2pul

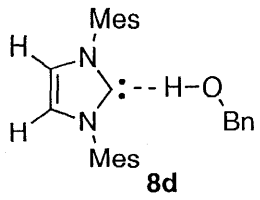
SAMPLE		DEC. & VT	
date	Aug 14 2004	dfrq	125.677
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	26.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	322.55	homo3	n
rfl	4564.4	PROCESSING	
rfp	3578.2	wtfile	
th	2	proc	ft
ins	18.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



8c

exp4 s2pul

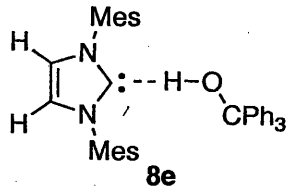
SAMPLE		DEC. & VT	
date	Aug 13 2004	dfrq	125.677
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.758	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	4	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	26.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.1	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	307.49	homo3	n
rfl	4564.7	PROCESSING	
rfp	3578.2	wtfile	
th	3	proc	ft
ins	6.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



8d

exp4 s2pul

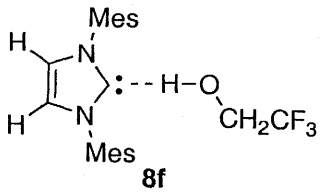
SAMPLE		DEC. & VT	
date	Oct 9 2005	dfrq	125.674
solvent	Benzene	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.749	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	26.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	38	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.2	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	128.97	homo3	n
rfl	4567.4	PROCESSING	
rfp	3578.2	wtfile	
th	32	proc	ft
ins	9.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



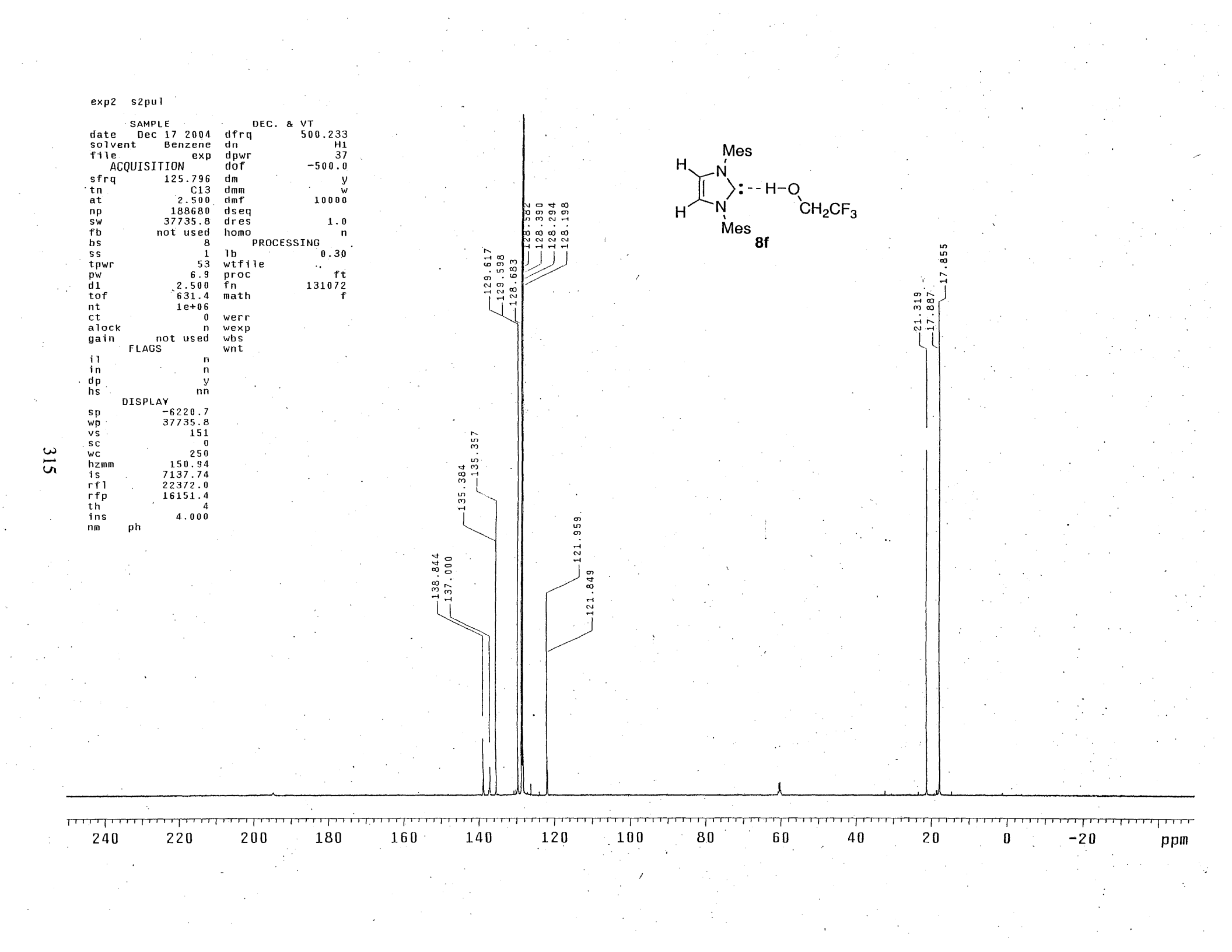
8e

exp2 s2pul

SAMPLE		DEC. & VT	
date	Dec 17 2004	dfrq	125.795
solvent	Benzene	dn	C13
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	500.235	dm	nnn
tn	H1	dmm	c
at	3.200	dmf	10000
np	64000	dseq	
sw	10000.0	dres	1.0
fb	not used	homo	n
bs	1	PROCESSING	
ss	1	wtfile	
tpwr	59	proc	ft
pw	9.8	fn	131072
d1	26.000	math	f
tof	1498.2		
nt	16	werr	
ct	0	wexp	
alock	n	wbs	
gain	not used	wnt	
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.2		
wp	6252.8		
vs	151		
sc	0		
wc	250		
hzmm	40.00		
is	100.00		
rfl	4562.1		
rfp	3581.7		
th	2		
ins	6.000		
nm	ph		



8f

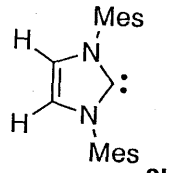

exp2 s2pul
SAMPLE
date Dec 17 2004
solvent Benzene
file exp
ACQUISITION
sfrq 125.796
tn C13
at 2.500
np 188680
sw 37735.8
fb not used
bs 8
ss 1
tpwr 53
pw 6.9
d1 2.500
tof 631.4
nt 1e+06
ct 0
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6220.7
wp 37735.8
vs 151
sc 0
wc 250
hzmm 150.94
is 7137.74
rfl 22372.0
rfp 16151.4
th 4
ins 4.000
nm ph
DEC. & VT
dfrq 500.233
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
Mes
H
N
H
N
Mes
H–O
CH2CF3
8f
138.844
137.000
135.384
135.357
129.617
129.598
128.683
128.582
128.390
128.294
128.198
121.959
121.849
21.319
17.887
17.855
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

```
exp1  s2pul

      SAMPLE
date    Dec 10 2004
solvent     Benzene

   ACQUISITION
sfrq        500.235
tn               H1
at              3.200
np              64000
sw          10000.0
fb          not used
bs                 1
ss                 1
tpwr              59
pw               9.8
d1            26.000
tof           1498.2
nt                16
ct                 7
alock              n
gain        not used
      FLAGS
il                 n
in                 n
dp                 y
hs                nn
     DISPLAY
sp            -250.2
wp            6252.9
vs               151
sc                 0
wc               250
hzmm           25.01
is            399.50
rfl           4561.4
rfp           3581.7
th                 7
ins           18.000
nm    ph

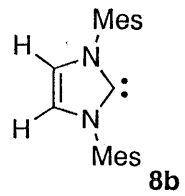
      DEC. & VT
dfrq        125.795
dn              C13
dpwr             37
dof               0
dm              nnn
dmm               c
dmf           10000
dseq
dres            1.0
homo              n
     PROCESSING
wtfile
proc             ft
fn           131072
math              f
werr
wexp
wbs
wnt
```



8b

exp2 s2pul

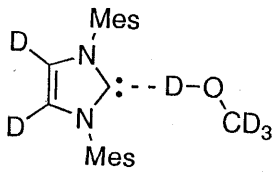
SAMPLE		DEC. & VT	
date	Dec 10 2004	dfrq	500.233
solvent	Benzene	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.804	dm	y
tn	C13	dmm	w
at	2.500	dmf	10000
np	238950	dseq	
sw	47789.7	dres	1.0
fb	not used	homo	n
bs	16	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	2.500	fn	131072
tof	9005.5	math	f
nt	1e+06		
ct	4329	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.0		
wp	46545.7		
vs	151		
sc	0		
wc	250		
hzmm	191.16		
is	500.00		
rfl	19026.9		
rfp	16151.4		
th	3		
ins	1.000		
nm	ph		



8b

exp2 s2pul

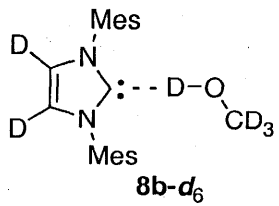
SAMPLE		DEC. & VT	
date	Dec 6 2004	dfrq	125.795
solvent	Benzene	dn	C13
file	exp	dpwr	37
ACQUISITION		dof	0
sfrq	500.235	dm	nnn
tn	H1	dmm	c
at	3.200	dmf	10000
np	64000	dseq	
sw	10000.0	dres	1.0
fb	not used	homo	n
bs	1	PROCESSING	
ss	1	wtfile	
tpwr	59	proc	ft
pw	9.8	fn	131072
d1	26.000	math	f
tof	1498.2		
nt	64	werr	
ct	16	wexp	
alock	n	wbs	
gain	not used	wnt	
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.2		
wp	6252.8		
vs	151		
sc	0		
wc	250		
hzmm	40.00		
is	356.52		
rfl	4561.8		
rfp	3581.7		
th	13		
ins	18.000		
nm	ph		



8b-d_6

exp2 s2pul

SAMPLE		DEC. & VT	
date	Dec 6 2004	dfrq	500.233
solvent	Benzene	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.805	dm	y
tn	C13	dmm	w
at	2.500	dmf	10000
np	235988	dseq	
sw	47197.6	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	2.500	fn	131072
tof	9565.6	math	f
nt	1e+06		
ct	10662	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2018.3		
wp	46545.1		
vs	151		
sc	0		
wc	250		
hzmm	186.18		
is	500.00		
rfl	18169.7		
rfp	16151.4		
th	16		
ins	1.000		
nm	ph		



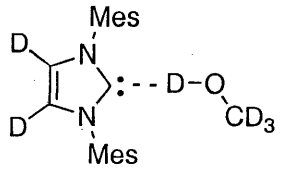
8b-d_6

```
exp1  s2pul

      SAMPLE
date    Dec 11 2004
solvent         THF
file            exp
   ACQUISITION
sfrq        500.238
tn               H1
at           3.200
np           64000
sw         10000.0
fb        not used
bs                1
ss                1
tpwr             59
pw              9.8
d1           26.000
tof          1498.2
nt               16
ct                4
alock             n
gain             10
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp            -77.9
wp           6252.8
vs              151
sc                0
wc              250
hzmm          40.00
is          4925.19
rfl           1868.8
rfp           1790.8
th                7
ins            6.000
nm    ph

      DEC. & VT
dfrq        125.796
dn              C13
dpwr             37
dof               0
dm              nnn
dmm               c
dmf           10000
dseq
dres            1.0
homo              n
     PROCESSING
wtfile
proc             ft
fn           131072
math              f

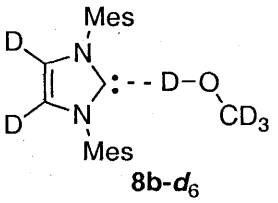
werr
wexp
wbs
wnt
```



8b-d_6

exp1 s2pul

SAMPLE		DEC. & VT	
date	Dec 11 2004	dfrq	500.236
solvent	THF	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	2.500	dmf	10000
np	188680	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	16	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	2.500	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	12203	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-2516.1		
wp	33963.7		
vs	151		
sc	0		
wc	250		
hzmm	150.94		
is	500.00		
rfl	14671.7		
rfp	8499.8		
th	6		
ins	1.000		
nm	ph		



8b-d_6

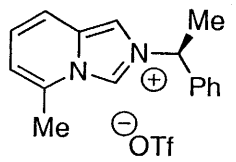
```
exp3  s2pul

      SAMPLE
date   Aug 10 2005
solvent      CDCl3

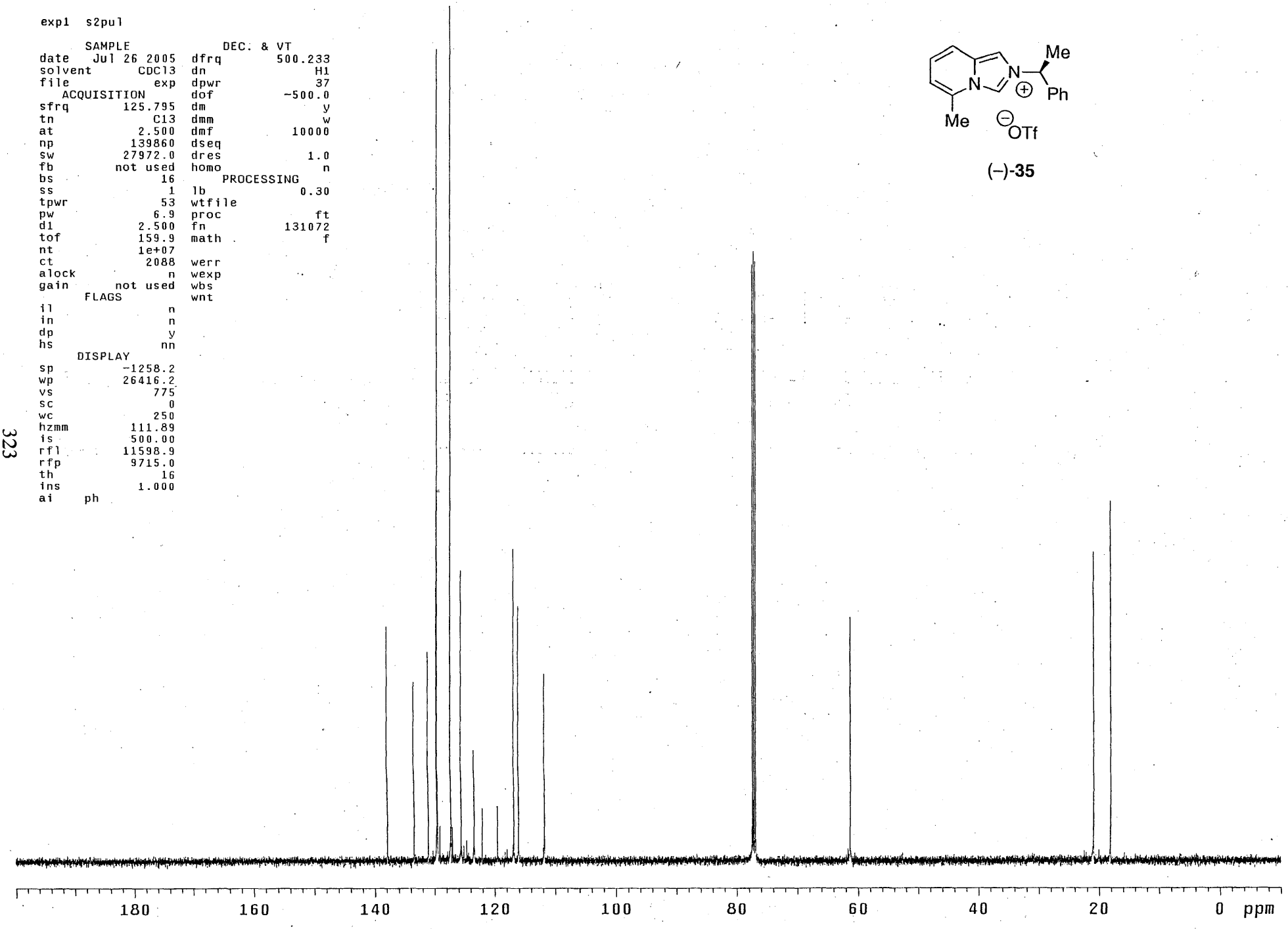
   ACQUISITION
sfrq       499.749
tn              H1
at            3.277
np            65536
sw           9998.8
fb         not used
bs                1
tpwr             56
pw              8.2
d1            7.000
tof          1498.1
nt               16
ct               16
alock             n
gain       not used
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp          -250.2
wp          6246.5
vs             151
sc               0
wc             250
hzmm         40.00
is           200.59
rfl         4638.2
rfp         3633.1
th               7
ins          1.000
nm  cdc  ph

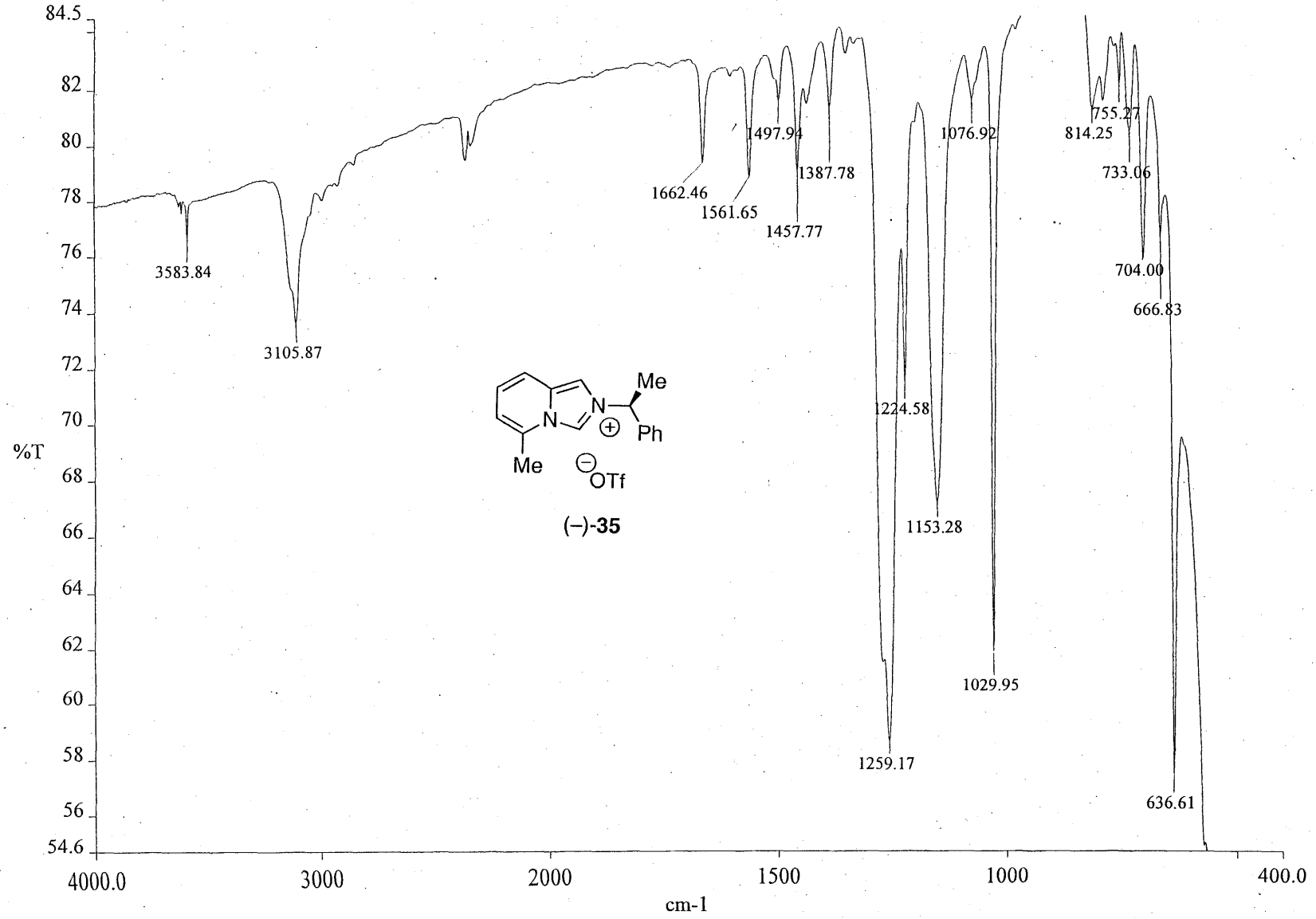
      DEC. & VT
dfrq       125.674
dn             C13
dpwr            34
dof         1498.1
dm               nnn
dmm                w
dmf            10400
dseq
dres             1.0
homo               n
     PROCESSING
wtfile
proc              ft
fn             65536
math               f

werr
wexp
wbs
wnt
```



(–)-**35**

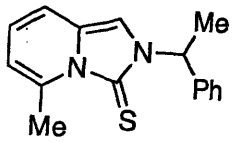

exp1 s2pul
SAMPLE
date Jul 26 2005
solvent CDCl3
file exp
ACQUISITION
sfrq 125.795
tn C13
at 2.500
np 139860
sw 27972.0
fb not used
bs 16
ss 1
tpwr 53
pw 6.9
d1 2.500
tof 159.9
nt 1e+07
ct 2088
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -1258.2
wp 26416.2
vs 775
sc 0
wc 250
hzmm 111.89
is 500.00
rfl 11598.9
rfp 9715.0
th 16
ins 1.000
ai ph
DEC. & VT
dfrq 500.233
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
Me
N
N
Ph
Me
OTf
(–)-35
180
160
140
120
100
80
60
40
20
0
ppm


84.5
82
80
78
76
74
72
70
68
66
64
62
60
58
56
54.6
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
3583.84
3105.87
1662.46
1561.65
1497.94
1457.77
1387.78
1259.17
1224.58
1153.28
1076.92
1029.95
814.25
755.27
733.06
704.00
666.83
636.61
Me
N
N
Ph
Me
OTf

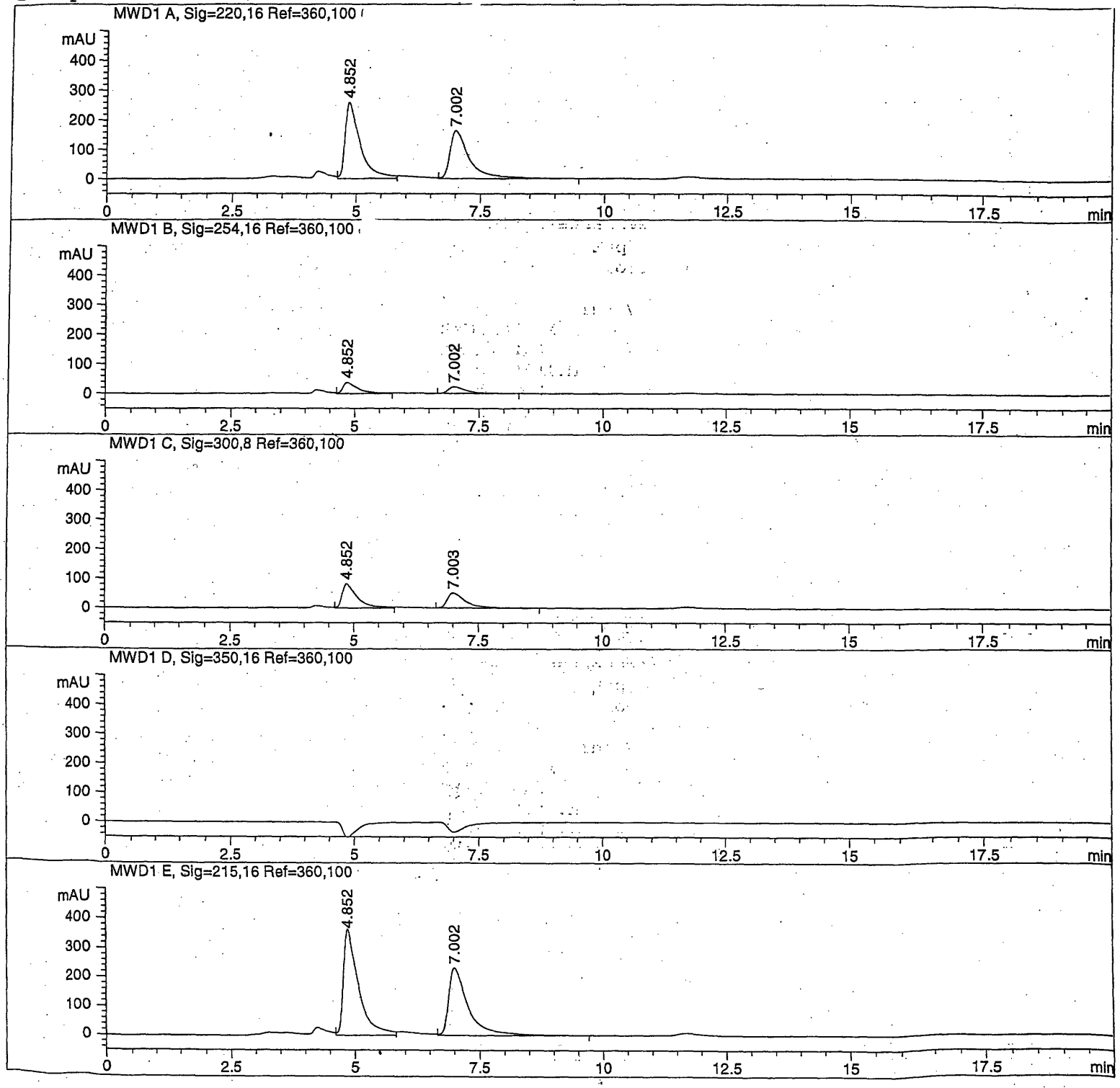
(–)-**35**

```
==========================================================================
Injection Date  : 5/20/2005 7:25:32 PM          Seq. Line :   2
Sample Name     :                               Location : Vial 21
Acq. Operator   :                                   Inj :   1
                                              Inj Volume : 1 µl

Acq. Method     : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 5/19/2005 9:09:28 AM
Analysis Method : C:\HPCHEM\2\METHODS\AOII0691.M
Last changed    : 5/20/2005 7:46:20 PM 1
                  (modified after loading)
5% ipa-hexanes 3 mL/min
```



(±)-39



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.852	VV	0.2906	5453.06396	257.99884	55.1631
2	7.002	VB	0.4051	4432.29150	163.06731	44.8369
Totals :				9885.35547	421.06615	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.852	VB	0.2905	784.26221	37.11151	57.2456
2	7.002	VB	0.3875	585.73376	22.81642	42.7544
Totals :				1369.99597	59.92793	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.852	VV	0.2872	1698.74036	81.49438	55.7989
2	7.003	VB	0.3942	1345.65759	51.26698	44.2011
Totals :				3044.39795	132.76136	

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

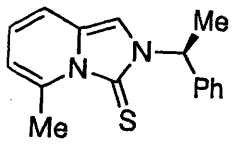
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.852	VV	0.2911	7716.72705	364.28534	54.9170
2	7.002	VB	0.4053	6334.89844	231.49046	45.0830
Totals :				1.40516e4	595.77580	

Results obtained with enhanced integrator!

*** End of Report ***

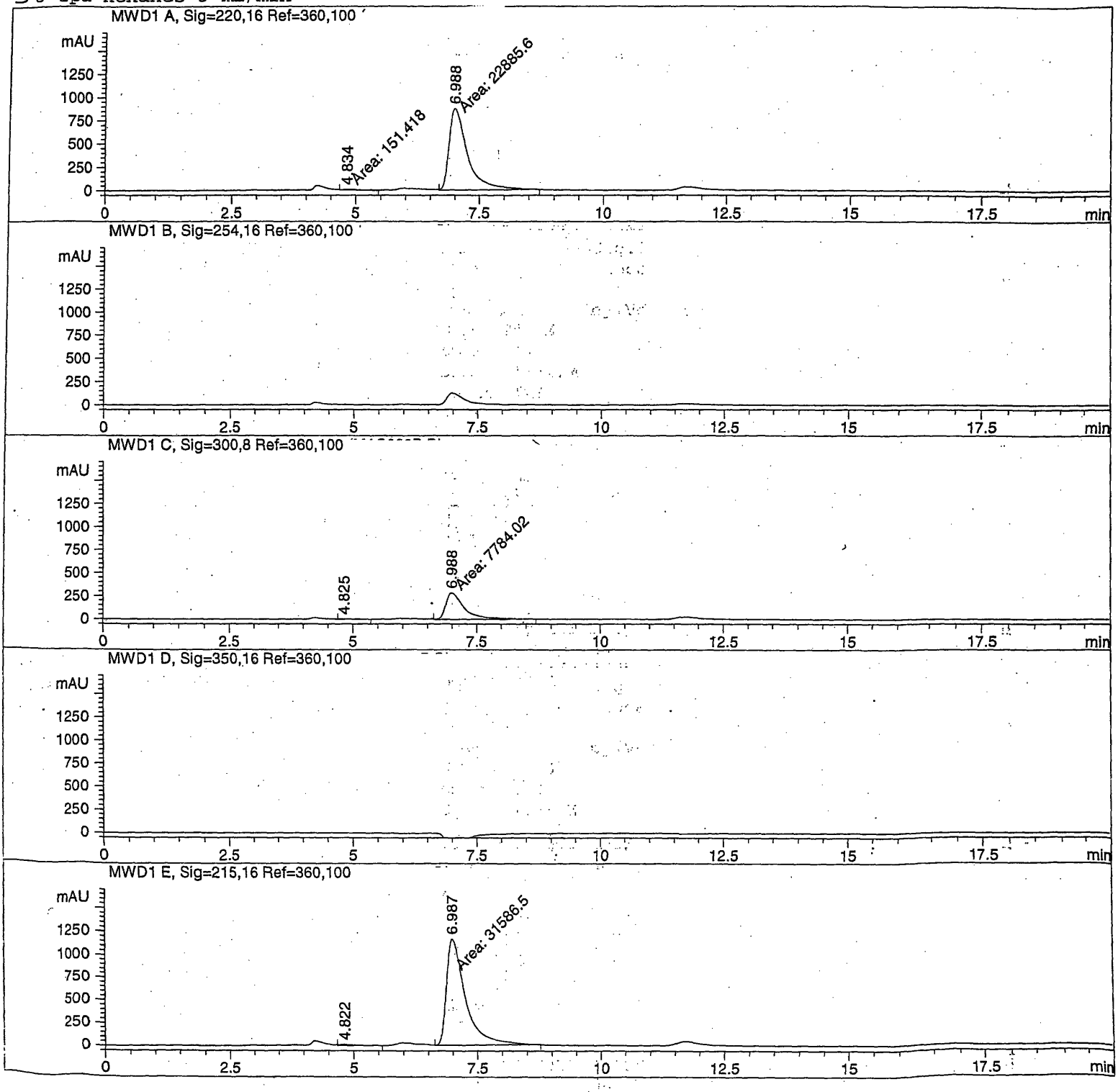
```
Injection Date  : 5/20/2005 7:04:24 PM          Seq. Line :   1
Sample Name     :                              Location : Vial 21
Acq. Operator   :                                  Inj :   1
                                               Inj Volume : 1 µl

Acq. Method     : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 5/19/2005 9:09:28 AM
Analysis Method : C:\HPCHEM\2\METHODS\AOII0691.M
Last changed    : 5/20/2005 6:48:14 PM
                  (modified after loading)
```



39

5% ipa-hexanes 3 mL/min



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.834	MM	0.4688	151.41840	5.38308	0.6573
2	6.988	MM	0.4355	2.28856e4	875.91901	99.3427
Totals :				2.30370e4	881.30209	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.825	VB	0.2675	38.52739	1.95838	0.4925
2	6.988	MM	0.4501	7784.01904	288.25955	99.5075
Totals :				7822.54644	290.21793	

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

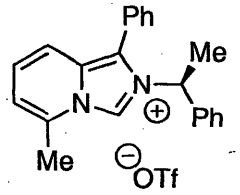
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.822	VV	0.3380	303.83167	12.05777	0.9527
2	6.987	MM	0.4526	3.15865e4	1163.02954	99.0473
Totals :				3.18904e4	1175.08731	

Results obtained with enhanced integrator!

*** End of Report ***

exp1 s2pul

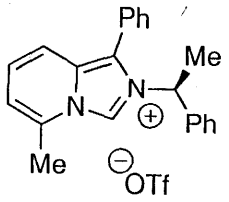
SAMPLE		DEC. & VT	
date	May 6 2005	dfrq	125.674
solvent	CDCl3	dn	C13
file	exp	dpwr	34
ACQUISITION		dof	1498.1
sfrq	499.749	dm	nnn
tn	H1	dmm	w
at	3.277	dmf	10000
np	65536	dseq	
sw	9998.8	dres	1.0
fb	not used	homo	n
bs	1	DEC2	
tpwr	56	dfrq2	0
pw	8.2	dn2	
d1	7.000	dpwr2	1
tof	1498.1	dof2	0
nt	16	dm2	n
ct	16	dmm2	c
alock	n	dmf2	200
gain	not used	dseq2	
FLAGS		dres2	1.0
il	n	homo2	n
in	n	DEC3	
dp	y	dfrq3	0
hs	nn	dn3	
DISPLAY		dpwr3	1
sp	-250.2	dof3	0
wp	6246.7	dm3	n
vs	151	dmm3	c
sc	0	dmf3	200
wc	250	dseq3	
hzmm	40.00	dres3	1.0
is	603.83	homo3	n
rfl	4637.6	PROCESSING	
rfp	3633.1	wtfile	
th	7	proc	ft
ins	1.000	fn	65536
nm cdc ph		math	f
		werr	
		wexp	
		wbs	
		wnt	



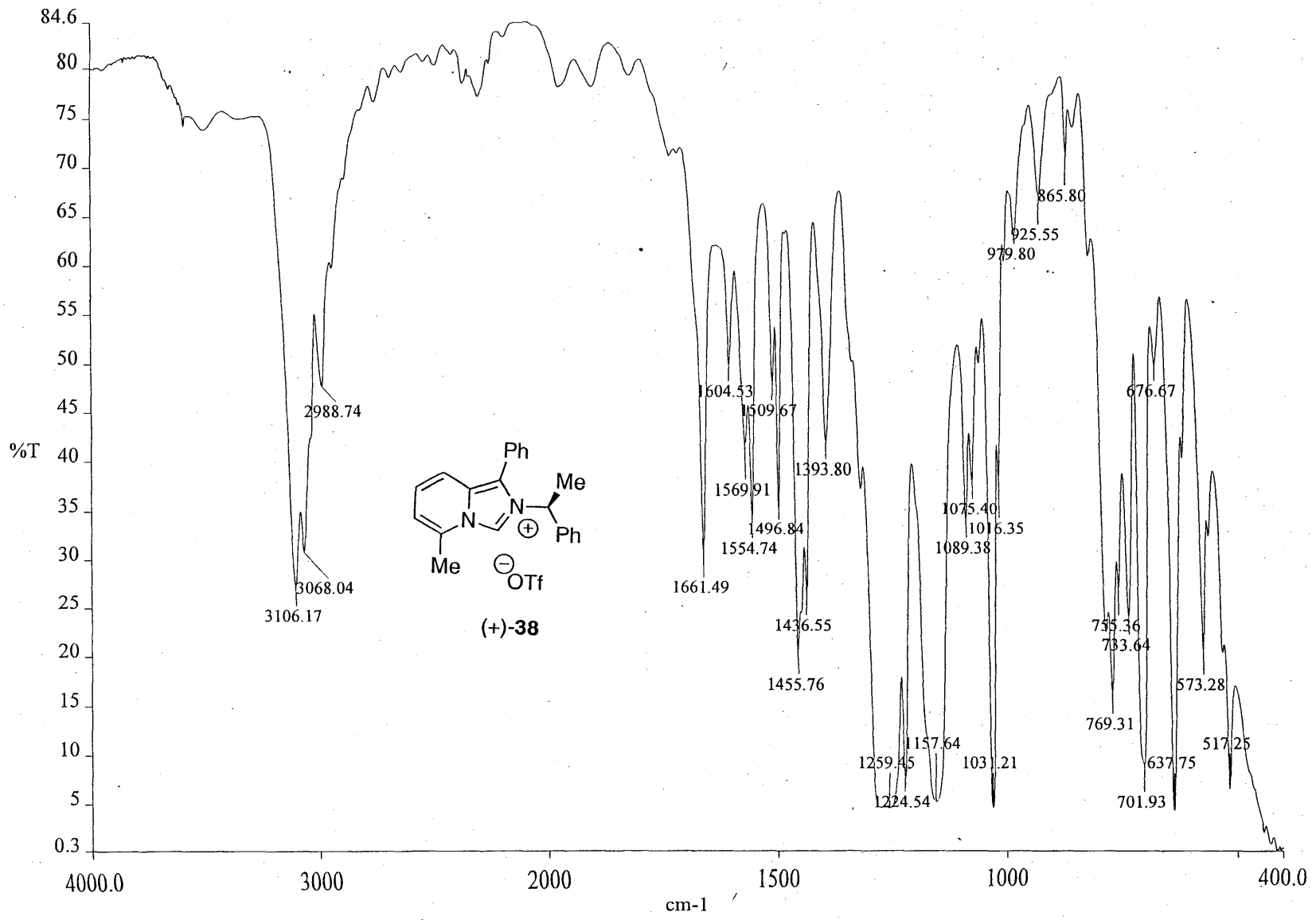
(+)-**38**

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jul 28 2005	dfrq	500.233
solvent	CDCl3	dn	H1
file	exp	dpwr	37
ACQUISITION		dof	-500.0
sfrq	125.796	dm	y
tn	C13	dmm	w
at	2.500	dmf	10000
np	188680	dseq	
sw	37735.8	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	lb	0.30
tpwr	53	wtfile	
pw	6.9	proc	ft
d1	2.500	fn	131072
tof	631.4	math	f
nt	1e+06		
ct	3862	werr	
alock	n	wexp	
gain	not used	wbs	
FLAGS		wnt	
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1258.3		
wp	27674.1		
vs	524		
sc	0		
wc	250		
hzmm	110.70		
is	500.00		
rfl	16004.1		
rfp	9715.0		
th	20		
ins	1.000		
ai	ph		



(+)-**38**


84.6
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.3
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
2988.74
3068.04
3106.17
1604.53
1509.67
1569.91
1496.84
1554.74
1661.49
1393.80
1436.55
1455.76
1259.45
1224.54
1157.64
1075.40
1016.35
1089.38
1031.21
979.80
925.55
865.80
676.67
735.36
733.64
769.31
637.75
701.93
573.28
517.25
Ph
Me
N
Ph
Me
OTf

(+)-**38**

```
==========================================================================
Injection Date  : 5/24/2005 2:58:35 PM          Seq. Line :   1
Sample Name     :                               Location : Vial 45
Acq. Operator   :                                   Inj :   1
                                              Inj Volume : 1 µl

Acq. Method     : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 5/24/2005 2:57:31 PM
Analysis Method : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 5/24/2005 1:35:59 PM
                  (modified after loading)
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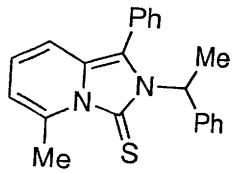
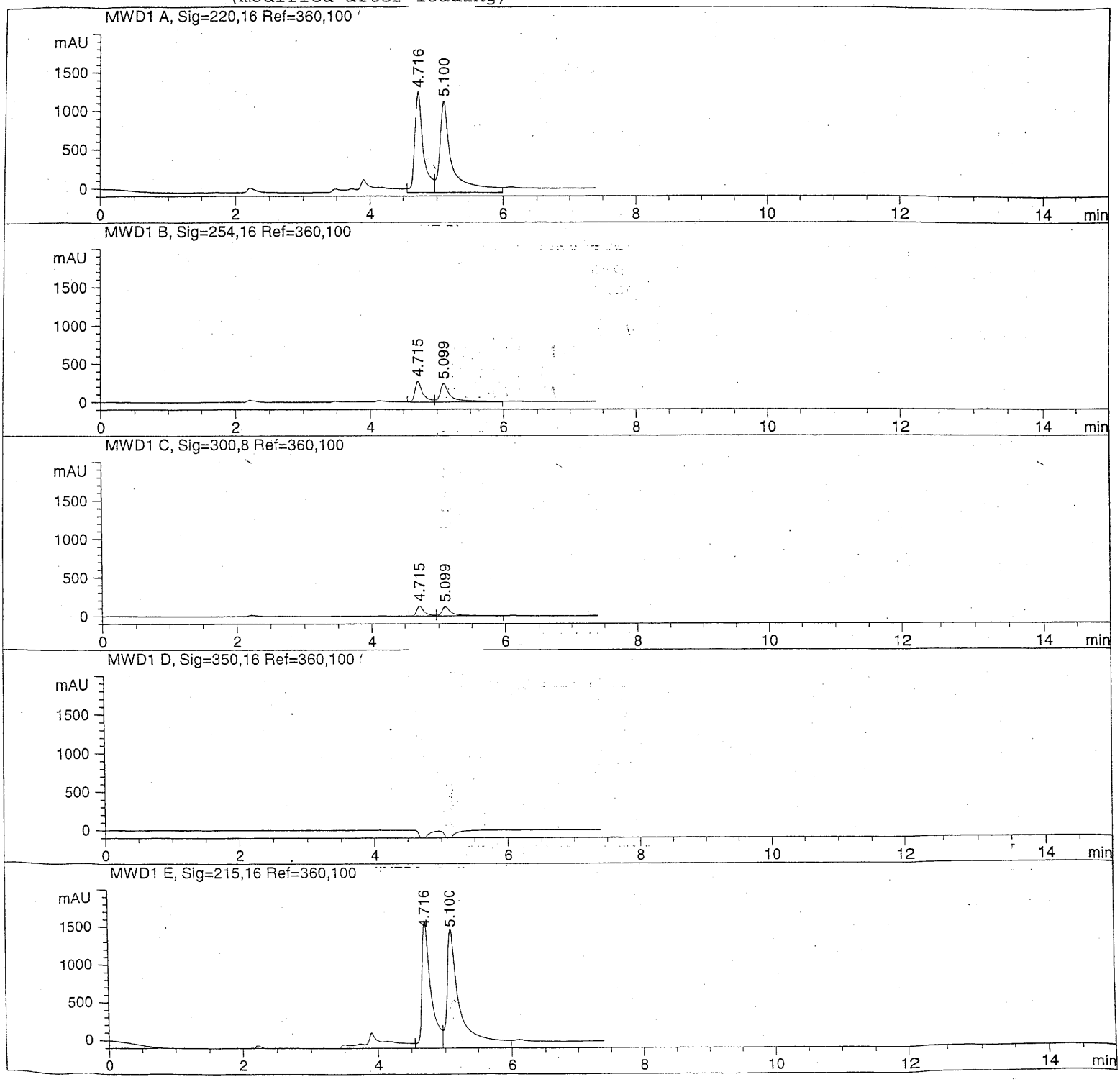


(±)-40



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.716	VV	0.1272	1.14547e4	1294.98450	42.8758
2	5.100	VV	0.1774	1.52613e4	1175.71423	57.1242
Totals :				2.67160e4	2470.69873	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.715	VV	0.1214	2318.43579	277.66431	44.4630
2	5.099	VV	0.1646	2895.86670	243.81204	55.5370
Totals :				5214.30249	521.47635	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.715	VV	0.1190	1061.15454	130.37691	45.2722
2	5.099	VV	0.1529	1282.78870	117.91399	54.7278
Totals :				2343.94324	248.29089	

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.716	VV	0.1382	1.64526e4	1710.07495	41.4615
2	5.100	VV	0.1987	2.32290e4	1587.38013	58.5385
Totals :				3.96816e4	3297.45508	

Results obtained with enhanced integrator!

*** End of Report ***

```
==========================================================================
Injection Date  : 5/24/2005 3:08:12 PM          Seq. Line :   1
Sample Name     :                               Location : Vial 41
Acq. Operator   :                                  Inj :   1
                                                Inj Volume : 1 µl

Acq. Method     : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 5/24/2005 2:57:31 PM
Analysis Method : C:\HPCHEM\2\METHODS\DIAST1.M
Last changed    : 5/24/2005 3:41:07 PM
                  (modified after loading)
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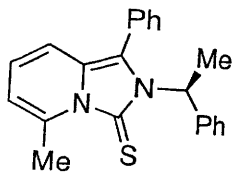
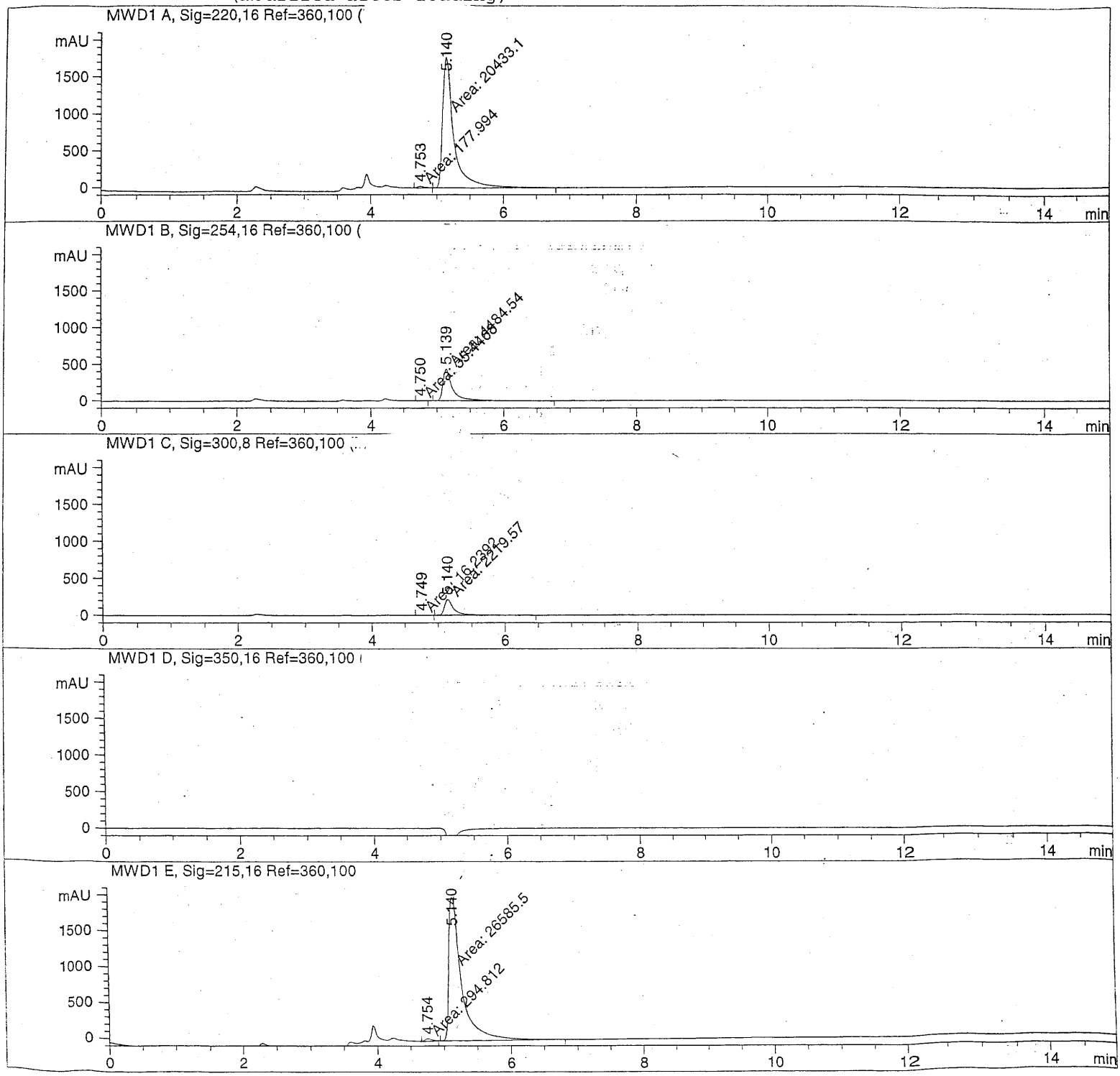


40



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.753	MM	0.1219	177.99432	24.34356	0.8636
2	5.140	MM	0.1930	2.04331e4	1764.48950	99.1364
Totals :				2.06111e4	1788.83306	

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.750	MM	0.1173	35.44678	5.03654	0.7842
2	5.139	MM	0.1725	4484.53613	433.34204	99.2158
Totals :				4519.98291	438.37859	

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=300,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.749	MM	0.1215	16.23923	2.22783	0.7263
2	5.140	MM	0.1712	2219.57397	216.10258	99.2737
Totals :				2235.81320	218.33042	

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=350,16 Ref=360,100

Signal 5: MWD1 E, Sig=215,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.754	MM	0.1253	294.81195	39.21825	1.0968
2	5.140	MM	0.2218	2.65855e4	1997.77417	98.9032
Totals :				2.68803e4	2036.99242	

Results obtained with enhanced integrator!

*** End of Report ***

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Personal:

Born: March 20, 1980

Citizenship:

Citizen of the United States of America

Education:

2003-Present	**Massachusetts Institute of Technology** Graduate studies toward a Ph.D. in Chemistry
2002-2003	**University of California, at Irvine** First year of graduate studies
1999-2002	**Ohio State University** B.S. *with Distinction in Biochemistry*, Biochemistry

Research Experience:

2003-present **Graduate Research**
Massachusetts Institute of Technology
Advisor: Professor Mohammad Movassaghi

- Complex Alkaloid Total Synthesis.
- Development of New Reactions for Organic Synthesis.

2001-2002 **Undergraduate Research**
Ohio State University
Advisor: Professor David J. Hart

- Development of a general route to 1-monoacylglycerols

Honors and Awards:

2007-2008	Bristol-Myers Squibb Graduate Fellowship in Synthetic Organic Chemistry for accomplishments in research
2007	Merck Summer Graduate Fellowship for accomplishments in research
2007	MIT Wyeth Scholar Award for outstanding accomplishments in research
2007	Morse Travel Grant to attend a Gordon Research Conference
2002	Graduated Magna Cum Laude with Distinction in Biochemistry from The Ohio State University.
2002	Awarded for excellence in academics by the Department of Arts and Sciences at The Ohio State University.
1999-2002	A member of: • Alpha Lambda Delta • National Society of Collegiate Scholars • Golden Key National Honor Society • Phi Beta Kappa.

1999-2001	Dean's List at Ohio State University on six occasions.

Teaching Experience:

2006	Teaching assistant for undergraduate introductory organic chemistry at the Massachusetts Institute of Technology (Dr. Kimberly Berkowski and Professor Barbra Imperiali).
2004	Teaching assistant for undergraduate introductory organic chemistry at the Massachusetts Institute of Technology (Dr. Sarah Tabacco and Professor Barbra Imperiali).
2003-2004	Teaching assistant of undergraduate chemistry laboratories at the Massachusetts Institute of Technology. (Professor Richard Schrock and Professor Joseph Sadighi).
2002-2003	Teaching assistant of undergraduate general and organic chemistry laboratories at the University of California, at Irvine. (Dr. Jhong Kim)
2001	Tutor for the Department of Mathematics at The Ohio State University. (Richard Brown)

Scientific Publications:

1. ""On the Interactions of *N,N'*-Bismesitylimidazolin-2-yl and Alcohols" Schmidt, M. A.; Müller, P.; Movassaghi, M. *Tetrahedron Lett.* **2008**, Accepted.

2. "New Strategies for the Synthesis of Hexahydropyrroloindole Alkaloids Inspired by Biosynthetic Hypotheses" Schmidt, M. A.; Movassaghi, M. *Synlett* **2008**, *3*, 313-324.

3. "Concise Total Synthesis of (–)-Ditryptophenaline and (+)-WIN 64821" Movassaghi, M; Schmidt, M. A.; Ashenhurst, J. A. *Angew. Chem., Int. Ed.* **2008**, *47*, 1485–1487. Selected as a "Hot Paper".

4. "Concise Total Synthesis of (–)-Calycanthine, (+)-Chimonanthine, and (+)-Folicanthine" Movassaghi, M.; Schmidt, M. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 3725–3728. Selected as a "Very Important Paper".

5. "Synthesis of Optically Active Imidazopyridium Salts and their NHCs" Schmidt, M. A.; Movassaghi, M.; *Tetrahedron Lett.* **2007**, *48*, 101-104.

6. "N-Heterocyclic Carbene-Catalyzed Amidation of Unactivated Esters with Amino Alcohols." Movassaghi, M.; Schmidt, M. A. *Org. Lett.* **2005**, *7*, 2453-2456.

7. "Modular Approach to the Synthesis of Unsaturated 1-Monoacyl Glycerols." Coleman, B. E.; Cwynar, V.; Hart, D. J.; Havas, F.; Mohan, J. M.; Patterson, S.; Schmidt, M.; Smith, E.; Wells, A. *Synlett*, **2004**, *8*, 1339-1342.

Presentations:

1. "The Development of a General Route to Dimeric Hexahydropyrroloindole Alkaloids." Mohammad Movassaghi and Mike Schmidt. Oral presentation by Mike Schmidt at the Merck Research Laboratories, November, 2007; Boston, MA.

2. "The Development of a General Route to Dimeric Hexahydropyrroloindole Alkaloids." Mohammad Movassaghi and Mike Schmidt. Oral Presentation #707 by Mike Schmidt at the 234th American Chemical Society National Meeting, August 19–23, 2007; Boston, MA.

3. "The Development of a General Route to Dimeric Hexahydropyrroloindole Alkaloids." Mohammad Movassaghi and Mike Schmidt. Poster presented by Mike Schmidt at the Gordon Research Conference on Heterocyclic Chemistry, Salve Regina University, 2007.

4. "Development of a General Route to the Synthesis of 1-Monoacylglycerols." David J. Hart and Mike Schmidt. Poster presented by Mike Schmidt at Ohio State University, Meek Lectures, Columbus OH, 2002.

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