Development of a Copper-catalyzed Amidation-Base-promoted Cyclization Sequence for the Synthesis of 2-Aryl- and 2-Vinyl-4-quinolones

By

Carrie Preston Jones

B.A. Chemistry
Williams College, 2002

SUBMITTED TO THE DEPARTMENT OF CHEMISTRY IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF

MASTER OF SCIENCE IN ORGANIC CHEMISTRY

AT THE

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

SEPTEMBER 2007

Signature of Author:.....
Department of Chemistry
June 26, 2007

Certified by:.....
Stephen L. Buchwald
Camille Dreyfus Professor of Chemistry
Academic Advisor

Accepted by:.....
Robert W. Field
Chairman, Department Committee on Graduate Students

Development of a Copper-catalyzed Amidation-Base-promoted Cyclization Sequence for the Synthesis of 2-Aryl- and 2-Vinyl-4-quinolones

By

Carrie Preston Jones

Submitted to the Department of Chemistry

on June 26, 2007 in Partial Fulfillment of the

Requirements for the Degree of Master of Science in

Chemistry

ABSTRACT

A direct two-step method for the preparation of 2-aryl- and 2-vinyl-4-quinolones that utilizes a copper-catalyzed amidation of *ortho*-halophenones followed by a base-promoted Camps cyclization of the resulting *N*-(2-keto-aryl)amides is described. With CuI, a diamine ligand, and base as the catalyst system, the amidation reactions proceed in good yields for a range of aryl, heteroaryl, and vinyl amides. The subsequent Camps cyclization efficiently provides the desired 4-quinolones using the conditions that are described.

Thesis Supervisor : Stephen L. Buchwald
Title: Camille Dreyfus Professor of Chemistry

Acknowledgments

I would like to thank Stephen Buchwald for giving me the great opportunity to do research in his group and for being so supportive. I would also like to thank the members of the Buchwald group for all your help. I feel very honored to have met such genuine labmates and I greatly value the friendships I have made through MIT. I would like to thank my chemistry mentors both in college (Lee) and at Merck (Ping, Tom, Linus, and James) for their advice and inspiration even now- I am very grateful for the opportunity I had to work with you. I would like to thank my family for supporting me through all my endeavors, especially my brother, Kevin, for emotional support and biweekly lunches, and my friends Karen and Laddie for continual uplifting and because they too love complaining. Lastly, I want to thank Brian for enduring grad school and for wanting me to be happy no matter what- your thoughtfulness, humor, and understanding have been invaluable to me.

Preface

Parts of this thesis have been adapted from the following article co-written by the author.

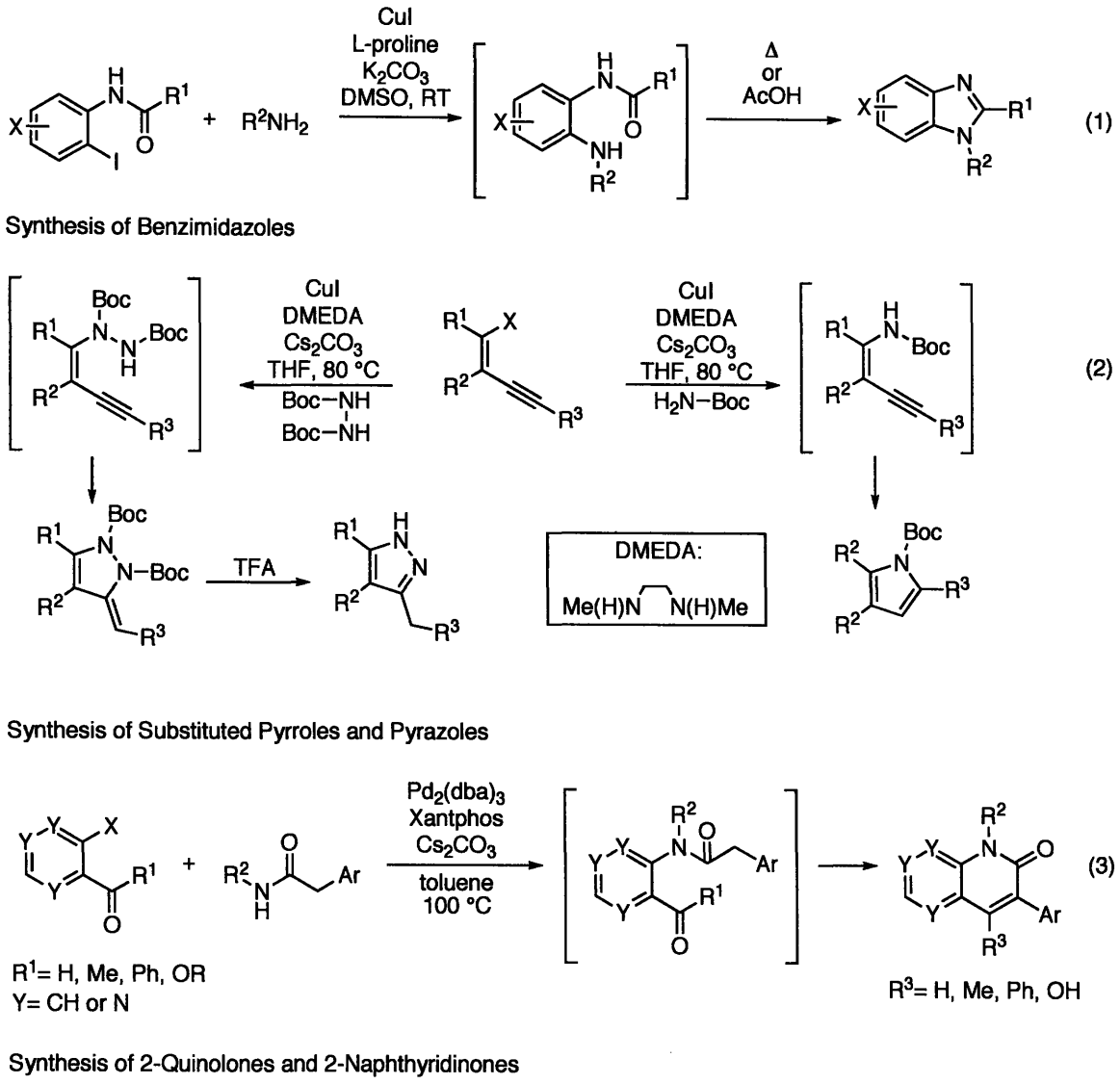
"Sequential Cu-Catalyzed Amidation-Base-mediated Camps Cyclization: A Two-step Synthesis of 2-Aryl-4-quinolones from *ortho*-Halophenones" Jones, C. P.; Anderson, K. W.; Buchwald, S. L. *J. Org. Chem.* **2007**, *submitted.*

Table of Contents

Development of a Copper-catalyzed Amidation-Base-promoted Cyclization Sequence for the Synthesis of 2-Aryl- and 2-Vinyl-4-quinolones

I. Introduction

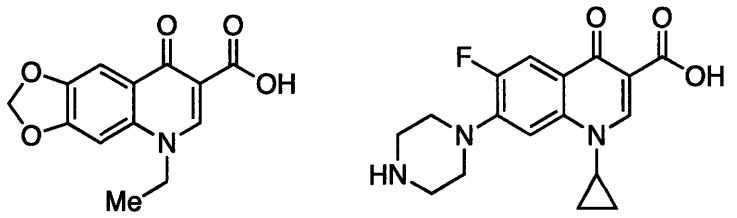
The metal-catalyzed formation of aromatic C-N bonds has become increasingly important in organic synthesis over the past decade.[1] Palladium and copper catalyst systems for cross-coupling aryl halides and nitrogen nucleophiles have recently found application in the synthesis of nitrogen-containing heterocycles. Several efficient methods have been developed in which a sequential metal-catalyzed C-N bond-forming/cyclization process yields a heterocycle. For example, Ma has reported a one-pot procedure for synthesizing benzimidazoles in which a Cu-catalyzed amination of iodoacetanilides provides an *ortho*-aminoanilide that can undergo a thermal or acid-promoted cyclization to the benzimidazole (Scheme 1, eq. 1).[2] Similarly, Cu-catalyzed aminations of haloenynes with hydrazines and amines followed by hydroamidation yield pyrazoles or pyrroles, respectively (Scheme 1, eq. 2).[3] 2-Naphthyridinones and 2-quinolones can be prepared using a Pd-catalyzed amidation/intramolecular aldol condensation domino synthesis (Scheme 1, eq. 3).[4] Indoles[5] and pyrroles[6] have also been synthesized *via* similar sequences.



Scheme 1. Metal-Catalyzed C-N Bond-formation/Cyclization Methods for the Synthesis of Heterocycles.

Nitrogen-containing heterocycles are present in a variety of biologically-active compounds that can be used in a wide range of therapeutic areas.[7] Specifically, 4-quinolone derivatives[8] exhibit antibacterial activity, and several quinolones, such as oxolinic acid and ciprofloxacin, have emerged as potent antibiotics (Figure 1).[7] More recently certain 2-aryl-4-quinolones and compounds containing these structures have been studied as potential treatments for a range of

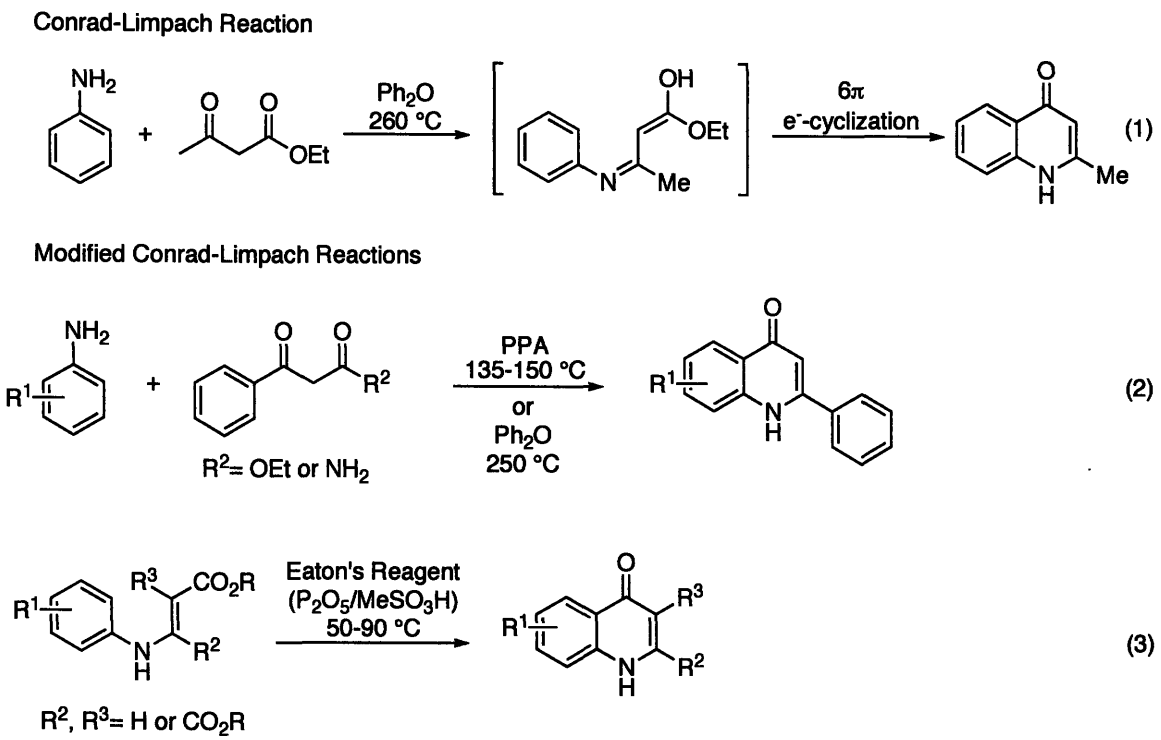
diseases[9] as they exhibit antimitotic,[10] antiplatelet,[9b] and antiviral[9f,g,i] activities and have positive cardiac effects.[9a]



Oxolinic Acid Ciprofloxacin

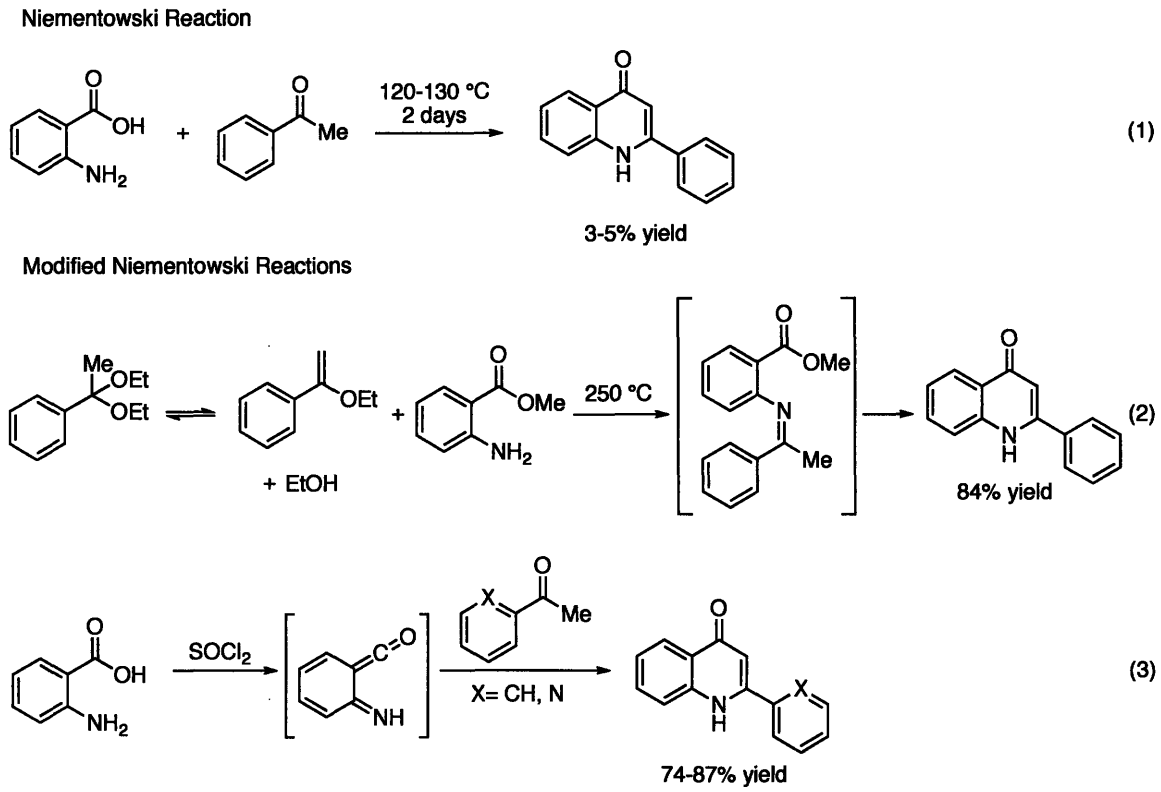
Figure 1. Structures of 4-Quinolones with Antibiotic Activity.

Multiple methods have been reported for the synthesis of 2-aryl-4-quinolones[8a] including two classical approaches, the Conrad-Limpach and Niementowski reactions.[11] The Conrad-Limpach synthesis involves the condensation of a β-ketoester with an aniline followed by a high temperature thermal cyclization (Scheme 2, eq. 1).[11a] Modifications of the method have incorporated the use of β-ketoamides and have succeeded in lowering the temperature of the cyclization by employing polyphosphoric acid (PPA) (Scheme 2, eq. 2).[9f,12] Recently several groups have reported milder conditions in which Eaton's reagent (P_2O_5/$MeSO_3H$) is used for the cyclization to 2- or 3-carboxy-4-quinolones at temperatures below 90 °C (Scheme 2, eq. 3).[13] This new protocol has not been demonstrated for the synthesis of 2-aryl-4-quinolones.



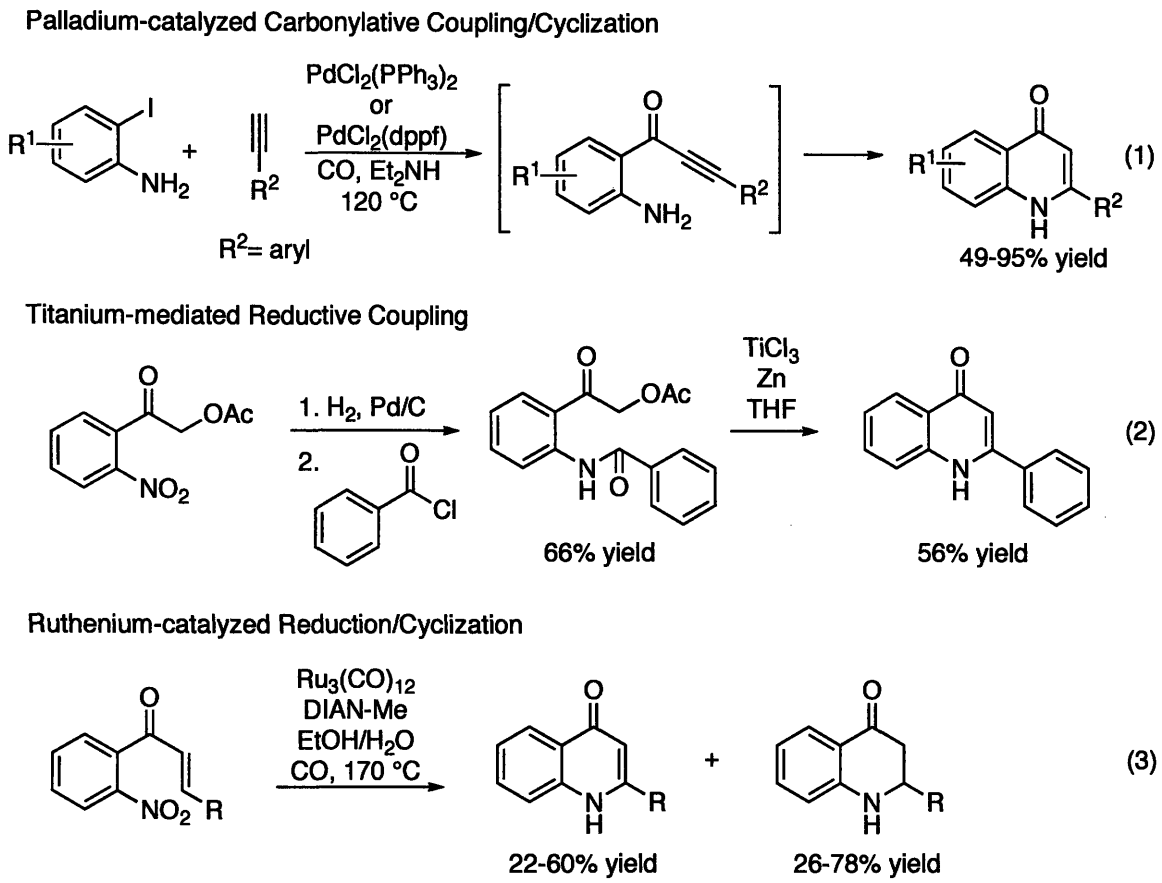
Scheme 2. Conrad-Limpach Reaction and Modifications.

The Niementowski reaction employs the condensation of anthranilic acid with a ketone or an aldehyde for the synthesis of 4-quinolones (Scheme 3, eq. 1).[11b] Initially when acetophenone was used in the reaction with anthranilic acid, only a 3-5% yield of the 2-phenyl-4-quinolone was obtained. The yield was improved to 84% by using the diethyl acetal of acetophenone as the starting material at high temperature (Scheme 3, eq. 2).[14] Even with this improvement, the temperatures employed in the reaction were still very high. Addressing these harsh reaction conditions, a new modification of the Niementowski synthesis was recently developed in which anthranilic acid was converted *in situ* to an iminoketene that cyclized *via* a [4π + 2π] cycloaddition with a ketone to yield the desired 4-quinolones (Scheme 3, eq. 3).[15] However, this synthetic route requires anthranilic acid derivatives that can withstand reaction with thionyl chloride. Less traditional syntheses of these compounds[16] make use of transition metals,



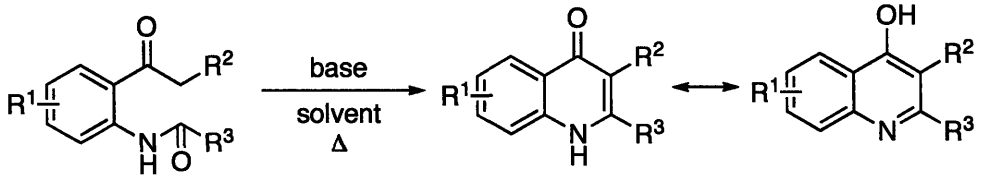
Scheme 3. Niementowski Reaction and Modifications.

including palladium-catalyzed carbonylation,[17] titanium-mediated reductive coupling,[18] and ruthenium-catalyzed reduction reactions (Scheme 4).[19]



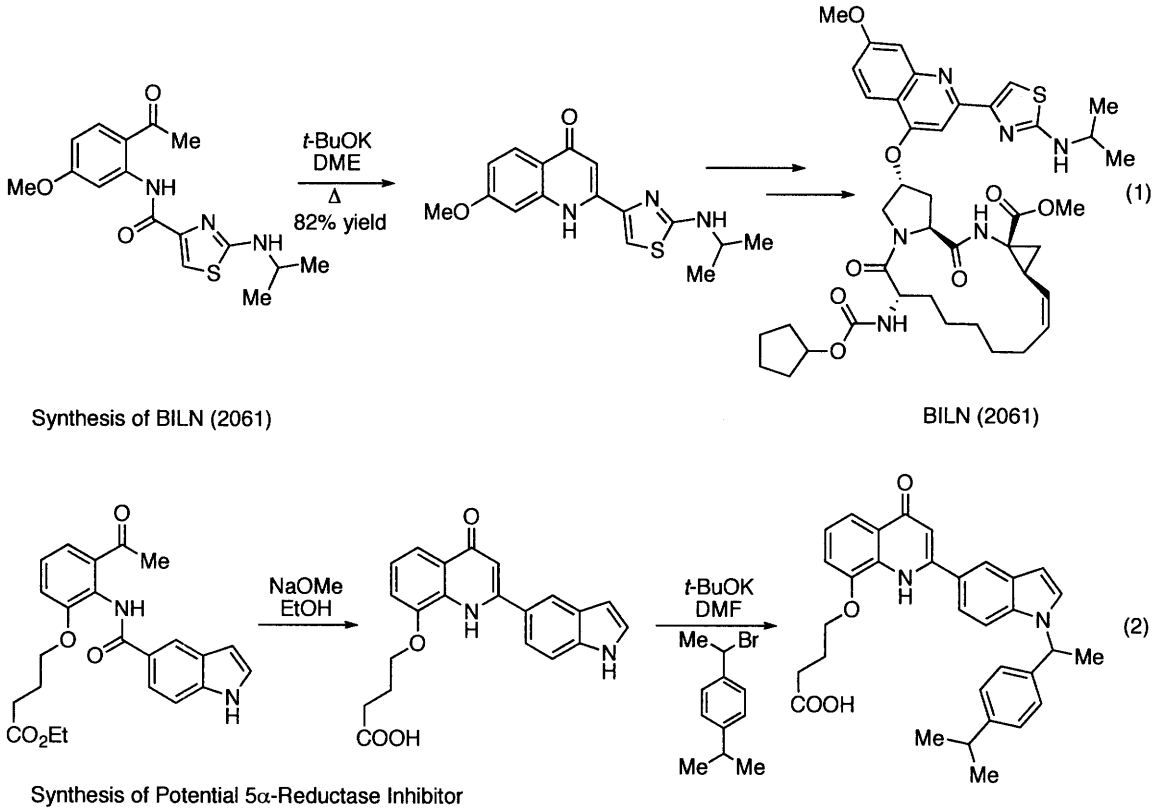
Scheme 4. Metal-promoted Syntheses of 4-Quinolones.

The base-promoted cyclization of *N*-(keto-aryl)amides (the Camps cyclization)[20] has seen widespread utilization for the synthesis of quinolones (Scheme 5).[9c,f,i,10b-f,21] Camps'



Scheme 5. Camps Quinolone Synthesis.

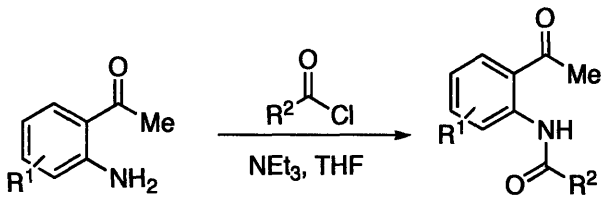
intramolecular aldol condensation was used in the scalable synthesis of BILN 2061, a drug candidate for the treatment of Hepatitis C Virus (Scheme 6, eq. 1),[9i] as well as in the preparation of the indole-substituted 4-quinolone target for SAR studies aimed at developing potent 5α-reductase inhibitors (Scheme 6, eq. 2).[9c] Several different bases and solvents have been employed in the Camps method for cyclizing *N*-(keto-aryl)amides and recently a microwave protocol was reported for the transformation.[21d]



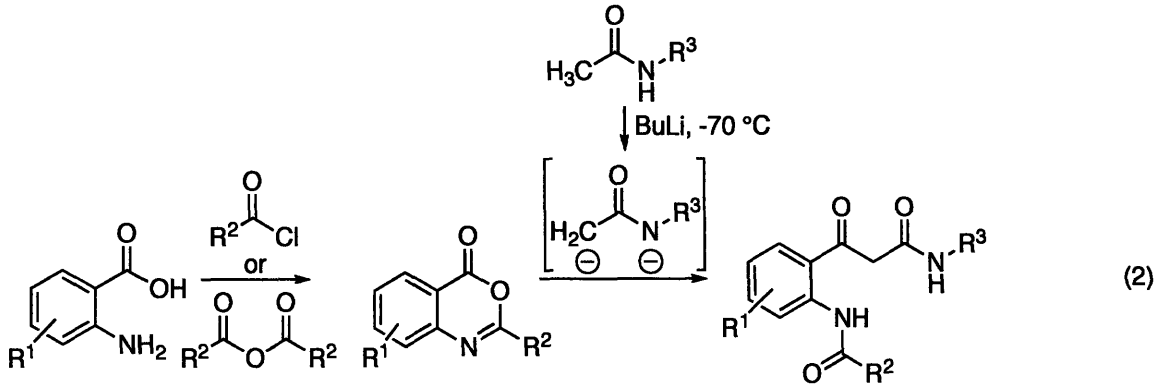
Scheme 6. Pharmaceutical Applications of the Camps Quinolone Synthesis.

Crucial to the utility of the Camps cyclization is the ability to access the *N*-(keto-aryl)amide starting materials. Known methods for the syntheses of these Camps precursors comprise condensations of *o*-aminoacetophenones and carboxylic acids[9c] or acid chlorides (Scheme 7, eq. 1),[9h,10b-e,21b,22] synthesis and subsequent opening of a benzoxazinone with the dianion of an *N*-

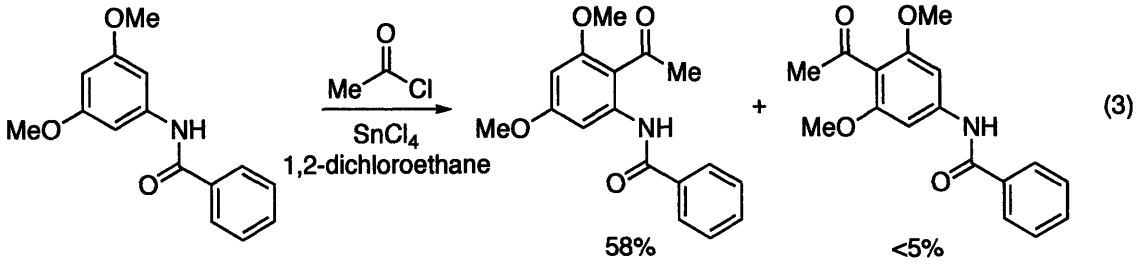
substituted acetamide (Scheme 7, eq. 2),[20b,21a] or Friedel-Crafts acylations of anilides, which often result in mixtures of products (Scheme 7, eq. 3 and 4).[9i,10f,21c]

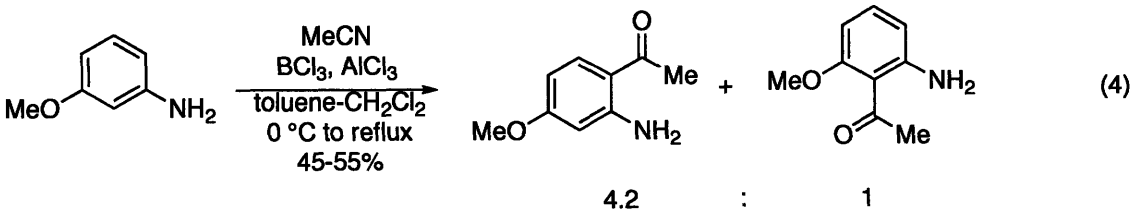


Amide Formation from Anilines and Acid Chlorides



N-(Keto-aryl)amides through a Benzoxazinone Intermediate





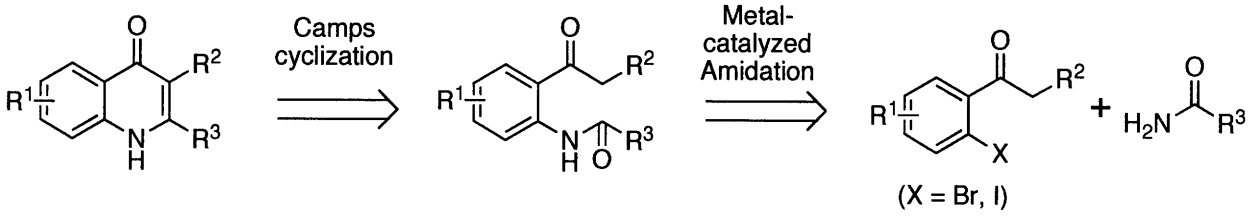
Friedel-Crafts Acylations for Installing *o*-Acetyl Groups

Scheme 7. Methods for the Formation of *N*-(Keto-aryl)amides.

In the next section we describe a simple sequence which employs a copper-catalyzed amidation reaction of 2-halophenones with aryl, heteroaryl, and vinyl amides as a means to access *N*-(keto-aryl)amides and their subsequent Camps cyclizations to 2-aryl- or 2-vinyl-4-quinolones. We also demonstrate the ability of these same amidation products to undergo McMurry titanium-mediated coupling reactions to form indoles as developed by Fürstner.[18,22,23]

II. Results and Discussion

Considering the established Camps cyclization for the synthesis of 2-aryl-4-quinolones, we envisioned that a cross-coupling reaction could be applied to prepare the *N*-(keto-aryl)amide Camps precursor. Retrosynthetic analysis of the *N*-(keto-aryl)amides suggested that a metal-catalyzed C-N bond-forming amidation approach could be utilized to install the amide portion of the compounds using *ortho*-halophenones as starting materials (Scheme 8). This approach to the *N*-(keto-aryl)amide intermediates would allow easy access to different R^3 groups by simply using diverse aryl (or vinyl) amides.



Scheme 8. Retrosynthetic Analysis of 2-Substituted-4-quinolones.

Based on the Cu(I)-catalyzed amidation of aryl halides in the presence of 1,2-diamine ligands developed in our group,[24] we focused on the application of this methodology to aryl halides with *ortho*-substituted ketones. As a test case, 2-bromoacetophenone was allowed to react with

benzamide using 10 mol% CuI, 20 mol% ligand, and 2 equivalents of K_2CO_3 in toluene at 110 °C for 24 hours. In a preliminary screen employing ligands **L1-L3,** the reaction with **L1** proceeded in the highest yield (Table 1, entry 1). We observed that 2-hydroxyacetophenone was generated from the reaction of 2-bromoacetophenone with traces of water, presumably introduced into the reaction mixture by moisture in the base. The formation of this by-product could be suppressed and the yield of the desired product improved by the use of activated molecular sieves or by a reduction in the reaction temperature to 90 °C (Table 1, entry 4).

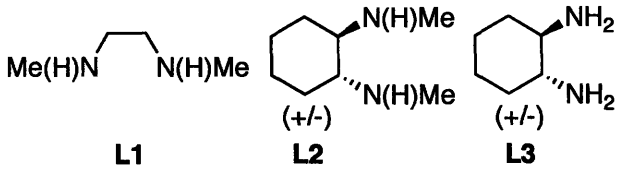
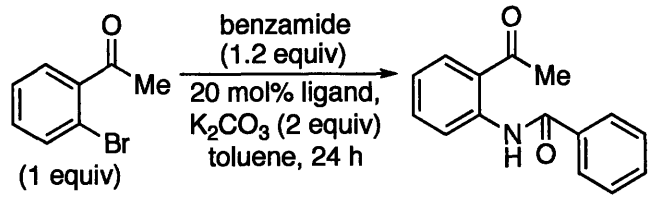


Figure 2. Diamine Ligands for Cu-catalyzed Amidation Reactions of Aryl Halides.

Table 1. Ligand Screening for Cu-Catalyzed Amidation with Benzamide.



entry	ligand	CuI (mol%)	temp (°C)	mol. sieves (5Å)	GC conversion[a] (%)	GC yield[a] (%)
1	**L1**	10	110	no	98	78
2	**L2**	10	110	no	100	54
3	**L3**	10	110	no	100	75
4	**L1**	10	90	yes	100	94
5	**L1**	0	90	yes	3	0
6	none	0	90	yes	2	0
7	none	10	90	yes	76	66

[a]GC yields and conversions are the average of two or more runs.

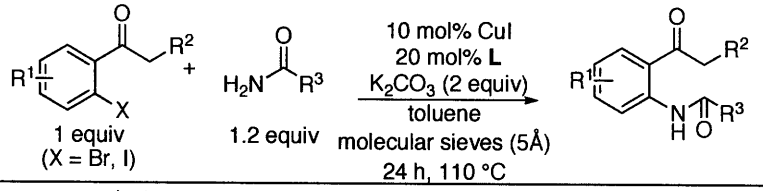
In a series of control experiments, we found that the reaction did not proceed in the absence of CuI indicating that the amidation reaction does not follow a simple nucleophilic aromatic

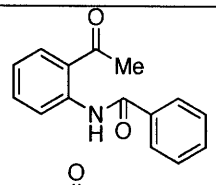
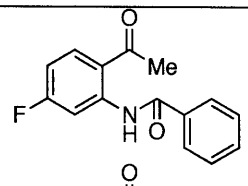
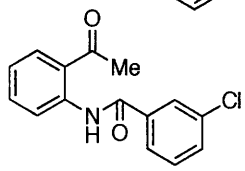
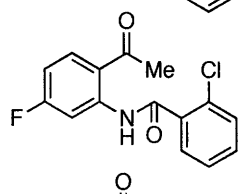
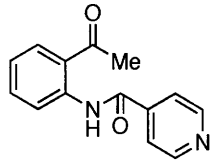
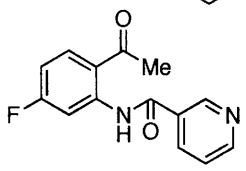
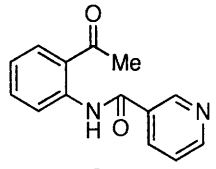
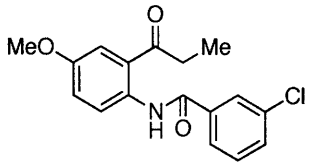
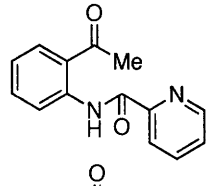
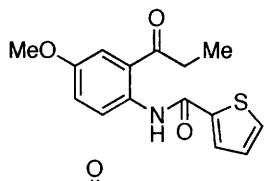
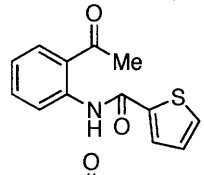
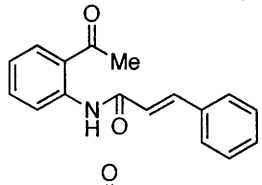
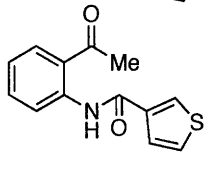
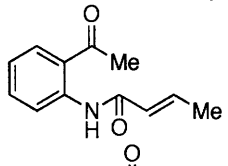
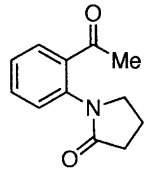
substitution mechanism (Table 1, entries 5 and 6).[25] The reaction did however yield product in the absence of ligand (Table 1, entry 7). As reported previously in the Cu-catalyzed synthesis of biaryl ethers, certain electron-withdrawing groups in the *ortho* position of the aryl halide have the ability to coordinate to copper and hasten the Ullmann-type reaction.[26] Presumably, in this amidation reaction the *o*-accelerating acetyl group had the ability to promote the coupling without the diamine ligand present. Nevertheless, the diamine ligand did enhance the rate of the amidation reaction as the ligand-free reaction did not reach completion after 24 hours.

With these reaction conditions in hand, the versatility of the Cu-catalyzed amidation reaction of 2-bromophenones and 2-iodophenones was explored (Table 2). The substrate scope of the coupling reaction encompassed 2-halophenones bearing both electron-withdrawing (**8**-**10**) and electron-donating groups (**11** and **12**). As demonstrated by the use of 2-halopropiophenones, the amidation reaction also tolerated larger ketone substituents than the methyl group (**11** and **12**). The couplings proceeded with heterocyclic amides, including 2-, 3-, and 4-pyridyl amides as well as 2- and 3-thiophenecarboxamides (**3**-**7**, **10**, and **12**). Both aryl and alkyl vinyl amides could be cross-coupled (**13** and **14**), and though the cyclic secondary amide pyrrolidinone reacted in good yield (**15**), acyclic secondary amides were not effective coupling partners.

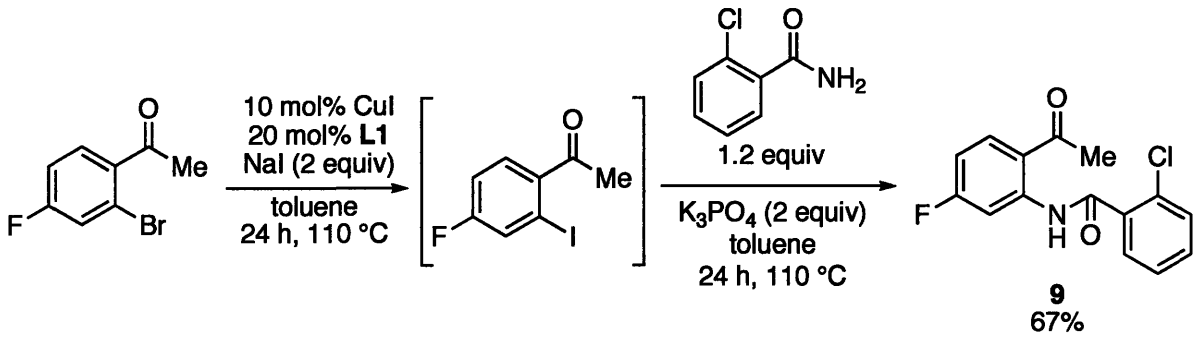
Though most reactions were conducted using the 2-bromophenones, the low reactivity of picolinamide (**5**), 2-chlorobenzamide (**9**), and crotonamide (**14**) as nucleophiles prompted us to employ the more active 2-iodophenones as substrates for these couplings.[27,28] However, even with the use of the 2-iodophenone, the yields for the syntheses of **9** and **14** were still only moderate. The synthesis of **9** from the 2-iodophenone could be accomplished in a one-pot procedure from the corresponding aryl bromide using a Cu-catalyzed halide exchange reaction[29] followed by the Cu-catalyzed amidation reaction (Scheme 9).

Table 2. Cu-catalyzed Amidation of 2-Halophenones.



X	product		yield (%)[a]	X	product		yield (%)[a]
Br		(1)	86[b]	Br		(8)	78
Br		(2)	83	I		(9)	67[e,f]
Br		(3)	80[c]	Br		(10)	77
Br		(4)	86	Br		(11)	72
I		(5)	71[d]	Br		(12)	72
Br		(6)	81[c]	Br		(13)	77[g]
Br		(7)	82	I		(14)	68[f]
				Br		(15)	89[h]

[a]Isolated yields are the average of two or more runs. [b]Heated to 90 °C. [c]Without molecular sieves. [d]Heated for 42 h with K_3PO_4. [e]Aryl iodide generated *in situ* from aryl bromide. [f]With 2 equiv K_3PO_4. [g]With 20 mol% **L2**. [h]With 5 mol% CuI, 10 mol% **L1**.

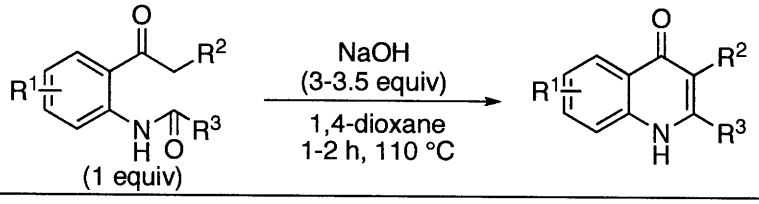


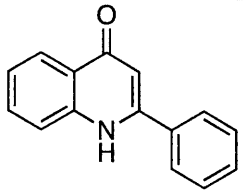
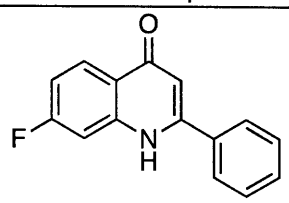
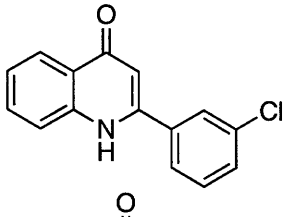
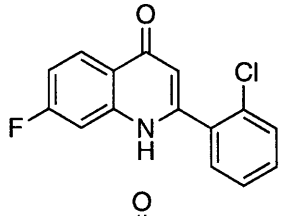
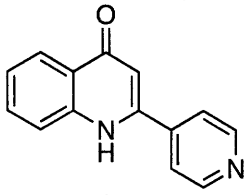
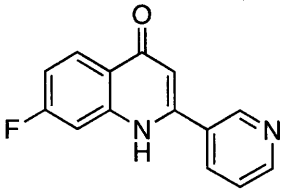
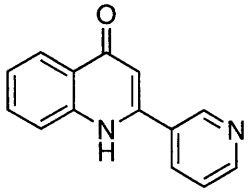
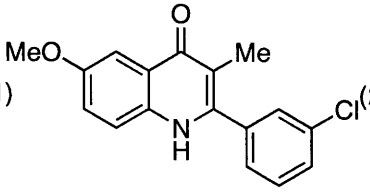
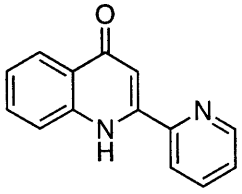
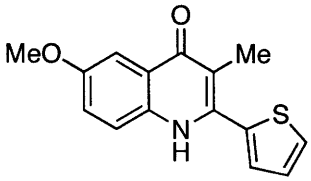
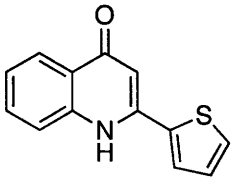
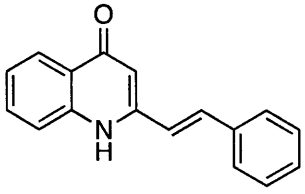
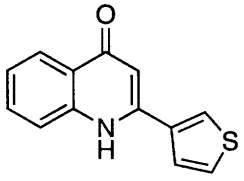
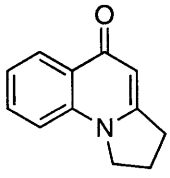
Scheme 9. Synthesis of **9** *via in situ* Formation of 2-Iodo-4-fluoroacetophenone Followed by Cu-catalyzed Amidation Reaction.

Having developed a successful method for the synthesis of *N*-(2-keto-aryl)amides, we focused on the base-catalyzed Camps cyclization to yield 2-substituted-4-quinolones. The optimal reaction conditions for the cyclization of *N*-(2-keto-aryl)amide **6** to 4-quinolone **21** were found to involve the use of 3-3.5 equivalents of NaOH in dioxane at 110 °C. The conditions proved to be generally applicable to a wide range of *N*-(2-keto-aryl)amides providing the appropriate 2-substituted-4-quinolones in good to excellent yields (Table 3). The cyclization method was also effective for the syntheses of more highly substituted quinolones **26** and **27**. Notably, when submitted to the reaction conditions, the pyrrolidinone-coupled substrate **15** provided a more complex tricyclic pyrrolo-quinolone ring system (**29**).

The workup of the 4-quinolone compounds was particularly facile as, with the exception of **29**, all the compounds shown in Table 3 could be isolated in pure form without the need to employ column chromatography; after initial concentration of the organic reaction mixture, the resulting residue was dissolved in water, and the desired products precipitated upon neutralization.

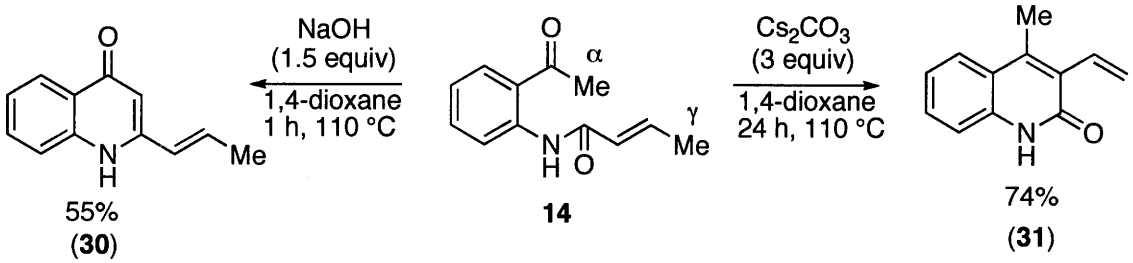
Table 3. Base-catalyzed Camps Cyclization to 2-Substituted-4-quinolones.



starting material	product	yield (%)[a]	starting material	product	yield (%)[a]
(1)		(16) 94	(8)		(23) 90
(2)		(17) 97	(9)		(24) 72
(3)		(18) 90	(10)		(25) 92
(4)		(19) 89	(11)		(26) 88
(5)		(20) 88	(12)		(27) 86
(6)		(21) 97	(13)		(28) 82[b]
(7)		(22) 92	(15)		(29) 94

[a]Isolated yields are the average of two or more runs. [b]Heated to 90 °C.

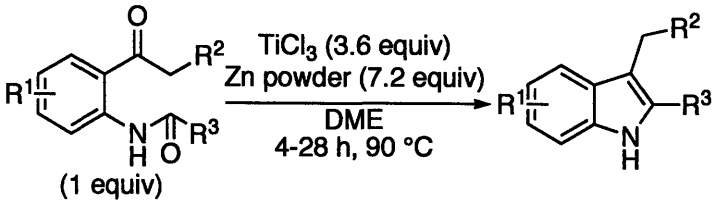
Compound **14** has the ability to cyclize to either 2-vinyl-4-quinolone (**30**) or 4-methyl-3-vinyl-2-quinolone (**31**) depending on the nature of the base utilized (Scheme 10). With NaOH, deprotonation occurred at the α position of the ketone followed by the intramolecular aldol condensation. However, the use of a weaker base (Cs_2CO_3) afforded **31** as the major product *via* γ-deprotonation of the amide. In both cases, traces of the other isomer were produced, which could be readily separated by column chromatography on silica gel. Similarly, as Camps observed,[20a] substrates with accessible protons at the α position of the amide yield a mixture of 4- and 2-quinolones rendering this method unsuitable for use with alkyl amides for the selective preparation of 2-alkyl-4-quinolones.[30] Unfortunately, the base-dependent selectivity observed for the synthesis of **30** and **31** was not seen for alkyl amides.

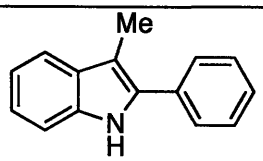
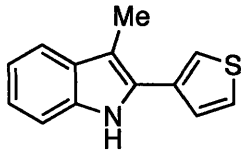
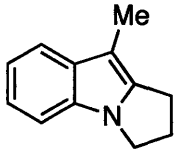


Scheme 10. Base-promoted Cyclizations to Synthesize **30** and **31**

Finally, the Cu-catalyzed amidation products in Table 2 were submitted to Fürstner's "instant" $TiCl_3$/Zn powder conditions[18] for the McMurry Ti-promoted coupling reaction to prepare 2- and 3-substituted indoles (Table 4). The yield was low when the obtained indole contained alkyl substituents in both the 2- and 3-positions (**37**).

Table 4. Ti-mediated Coupling for the Preparation of Substituted Indoles.



starting material	product		yield (%)[a]
(1)		(35)	67
(7)		(36)	71
(15)		(37)	35

[a]Isolated yields are the average of two or more runs.

In conclusion, we have demonstrated a new two-step synthesis of 2-aryl- and 2-vinyl-4-quinolones. The Cu-catalyzed amidation reaction of 2-halophenones offers access to *N*-(2-keto-aryl)amides that readily undergo base-promoted Camps cyclization to provide the desired 4-quinolones. We have also shown the accessibility of 2- and 3-substituted indoles from the *N*-(2-keto-aryl)amides via Ti-mediated reductive coupling. These sequential methods have potential for application in the synthesis of substituted nitrogen-containing heterocycles.

III. Experimental Section

General Considerations. All reactions were carried out in oven-dried resealable test tubes or Schlenk tubes under an atmosphere of argon. Potassium carbonate (Mallinckrodt or Aldrich), potassium phosphate (Riedel-de-Haën), and cesium carbonate (Chemetall) bases were stored in bulk in a glove box. Quantities of approximately 5 grams were removed from the glove box and stored in a bench-top desiccator. Sodium hydroxide pellets were crushed using a mortar and pestle and stored in the bench-top desiccator. CuI was obtained from Strem Chemicals (99.9% purity). $TiCl_3$ (99.999% purity) and Zn nanosize activated powder were both purchased from Aldrich and stored and weighed in the glove box. All three diamine ligands (**L1**, **L2**, **L3**) were obtained from Aldrich and stored in a bench-top desiccator. Amides and aryl halides were obtained from commercial sources (Aldrich, TCI, Avocado, Acros, Alfa Aesar) and used without further purification, except for 2-bromo-5-methoxypropiophenone, which was synthesized from commercially available starting materials as described in the Supporting Information. Toluene was obtained from J. T. Baker in CYCLE-TAINER kegs which were purged with argon for two hours and subsequently passed through two columns of neutral alumina and copper(II) oxide under a pressure of argon for further purification. Anhydrous 1,4-dioxane and DME were purchased from Aldrich in SureSeal® bottles. Molecular sieves (5Å) were obtained as a powder from Acros and were activated in bulk *via* flame-drying under vacuum. Silica column chromatography was performed using a Biotage SP4 Flash Purification System on KP-Sil silica cartridges.

Compounds were characterized using ^{1}H-NMR, ^{13}C-NMR, melting point, IR (KBr plate) and, in certain cases, elemental analysis. (Copies of ^{1}H-NMR and ^{13}C-NMR spectra are provided in the Supporting Information for all new compounds and any compounds that did not have

adequate elemental analysis results.) Data of known compounds were compared with existing literature characterization data and the references are given. All isolated and GC yields reported in the Results and Discussion are the average of two or more experiments. Elemental Analyses were conducted by Atlantic Microlabs, Inc., Norcross, GA. NMR spectra were obtained using Varian 500 MHz, Bruker Advance 400 MHz, or Varian 300 MHz instruments. The chemical shifts are reported in parts per million (ppm) based on the reference of the deuterated solvent. Melting points (uncorrected) were measured using a Mel-Temp II capillary apparatus. GC analysis was performed on an Agilent 6890 instrument with an FID detector and an Agilent 10m x 0.1mm DB-1 capillary column. GC yields and conversions were reported as referenced to dodecane as an internal standard. GC-MS analyses were performed on an Agilent 6850 instrument with an Agilent 5975 inert Mass Selective Detector. IR spectra were measured using a Perkin-Elmer System 2000 FT-IR. Compounds were applied in a thin film on a KBr pellet.

General Procedure A: Amidation of *o*-halophenones. An oven-dried resealable test tube with a Teflon stir bar was charged with amide (1.2 equiv, 0.60 mmol), CuI (10 mol%, 0.05 mmol), base (2 equiv, 1 mmol), and approximately 200 mg activated 5 Å molecular sieves. The test tube was sealed with a rubber septum and evacuated and refilled with Argon through a syringe needle (this sequence was performed three times). Under argon, *o*-halophenone (1.0 equiv, 0.50 mmol), *N, N'*-dimethylethylenediamine (**L1**) (20 mol%, 0.1 mmol), and toluene (1 mL) were each added *via* syringe. The rubber septum was then removed and quickly replaced with a Teflon screw-cap. The test tube was then placed in a preheated oil bath at 110 °C. The reaction was heated with stirring for 24 h and then cooled to room temperature. The reaction mixture was partitioned between EtOAc and water and the organic layer separated. The aqueous

layer was extracted with EtOAc and the organic layer combined, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to remove solvent. The product was purified by column chromatography on silica gel with EtOAc and hexane.

***N*-(2-Acetyl-phenyl)-benzamide (1).**[31,22] Following General Procedure A, benzamide (76 mg, 0.63 mmol) was coupled with 2-bromoacetophenone (67 μL, 0.50 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), K_2CO_3 (140 mg, 1.0 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). The reaction was heated to 90 °C for 24 h. **1** was purified by column chromatography using a hexane-EtOAc 98:2 to 90:10 gradient. 106 mg (88% yield) of a cream-colored solid were obtained. Mp: 99-100 °C (lit mp: 100 °C (ether)).[32] ^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.73 (s, 1H), 9.00 (dd, J = 8.5, 1.1 Hz, 1H), 8.08 (m, 2H), 7.98 (dd, J = 8.0, 1.5 Hz, 1H), 7.64 (m, 1H), 7.55 (m, 3H), 7.18 (ddd, J = 8.5, 7.3, 1.2 Hz, 1H), 2.75 (s, 3H). ^{13}C-NMR (400 MHz, $CDCl_3$): 203.3, 166.1, 141.4, 135.4, 134.8, 132.1, 131.9, 128.9, 127.5, 122.5, 121.9, 120.7, 28.6. IR (neat, cm^{-1}): 3222, 3064, 1679, 1650, 1607, 1585, 1450, 1359, 1313, 1247, 1166, 1099, 1073, 1028, 960, 896, 799, 756, 701, 609. Anal. calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48. Found: C, 75.10; H, 5.50.

***N*-(2-Acetyl-phenyl)-3-chlorobenzamide (2).** Following General Procedure A, 3-chlorobenzamide (93 mg, 0.60 mmol) was coupled with 2-bromoacetophenone (67 μL, 0.50 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), K_2CO_3 (140 mg, 1.0 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). **2** was purified by column chromatography using a hexane-EtOAc 98:2 to 90:10 gradient. 112 mg (82% yield) of a white solid were obtained. Mp: 137-139 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.75 (s, 1H), 8.95 (d, J = 8.5 Hz, 1H), 8.07 (s, 1H), 7.98 (dd, J = 8.0, 1.4 Hz, 1H), 7.94 (ddd, J =7.7, 1.7, 1.1 Hz, 1H), 7.65 (m, 1H), 7.55 (ddd, J = 8.0, 2.0, 1.1 Hz, 1H), 7.48 (t, J = 7.8 Hz, 1H), 7.20 (m, 1H),

2.74 (s, 3H). ^{13}C-NMR (400 MHz, $CDCl_3$): 203.5, 164.7, 141.2, 136.7, 135.5, 135.1, 132.1, 132.0, 130.2, 128.2, 125.3, 122.9, 122.0, 120.8, 28.7. IR (neat, cm^{-1}): 3185, 3068, 2920, 1684, 1644, 1608, 1584, 1523, 1452, 1359, 1315, 1258, 1170, 1076, 965, 904, 851, 798, 755, 739, 721, 611. Anal. calcd. for $C_{15}H_{12}ClNO_2$: C, 65.82; H, 4.42. Found: C, 65.69; H, 4.22.

***N*-(2-Acetyl-phenyl)-isonicotinamide (3).**[9h] Following General Procedure A, isonicotinamide (73 mg, 0.60 mmol) was coupled with 2-bromoacetophenone (67 μL, 0.50 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), and K_2CO_3 (140 mg, 1.0 mmol), in anhydrous toluene (1 mL). No molecular sieves were added for the synthesis of the title compound. **3** was purified by column chromatography using a hexane-EtOAc 95:5 to 50:50 gradient. 94 mg (78% yield) of a cream-colored solid were obtained. Mp: 119-120 °C (lit mp: 116-117 °C).[33] ^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.91 (s, 1H), 8.96 (dd, J = 8.5, 0.9 Hz, 1H), 8.85 (d, J = 5.3 Hz, 2H), 8.01 (dd, J = 8.0, 1.5 Hz, 1H), 7.91 (dd, J =4.6, 1.6 Hz, 2H), 7.67 (m, 1H), 7.24 (ddd, J = 8.5, 7.3, 1.2 Hz, 1H), 2.75 (s, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 203.6, 163.9, 150.9, 141.8, 140.7, 135.6, 132.0, 123.3, 122.0, 121.1, 120.8, 28.7. IR (neat, cm^{-1}): 3205, 3120, 3029, 1678, 1645, 1611, 1586, 1535, 1449, 1410, 1362, 1317, 1251, 1161, 1062, 963, 836, 756, 692, 677. Anal. calcd. for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03. Found: C, 69.96; H, 5.09.

***N*-(2-Acetyl-phenyl)-nicotinamide (4).** Following General Procedure A, nicotinamide (73 mg, 0.60 mmol) was coupled with 2-bromoacetophenone (67 μL, 0.50 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), K_2CO_3 (140 mg, 1.0 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). **4** was purified by column chromatography using a hexane-EtOAc 90:10 to 50:50 gradient. 100 mg (83% yield) of a cream-colored solid were obtained. Mp: 114-116 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.85 (s, 1H), 9.32 (d, J = 2.0 Hz, 1H), 8.96 (dd, J = 8.5, 1.1 Hz, 1H), 8.81 (dd, J = 4.8, 1.5 Hz, 1H), 8.35 (ddd, J =8.0, 2.3, 1.7

Hz, 1H), 8.00 (dd, J = 8.0, 1.6 Hz, 1H), 7.65 (m, 1H), 7.48 (ddd, J = 8.0, 4.8, 0.8 Hz, 1H), 7.22 (ddd, J = 8.5, 7.4, 1.2 Hz, 1H), 2.75 (s, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 203.5, 164.2, 152.6, 149.2, 140.9, 135.5, 134.9, 132.0, 130.3, 123.5, 123.0, 121.9, 120.7, 28.6. IR (neat, cm^{-1}): 3153, 2919, 1678, 1649, 1610, 1588, 1527, 1454, 1420, 1361, 1316, 1252, 1172, 1112, 1022, 963, 896, 827, 758, 717. Anal. calcd. for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03. Found: C, 69.69; H, 5.04.

***N*-(2-Acetyl-phenyl)-picolinamide (5).**[34] Following General Procedure A, picolinamide (73 mg, 0.60 mmol) was coupled with 2-iodoacetophenone (71 μL, 0.50 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), K_3PO_4 (210 mg, 0.99 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). The reaction was heated for 42 h. **5** was purified by column chromatography using a hexane-EtOAc 95:5 to 70:30 gradient. 85 mg (71% yield) of a pale pink solid were obtained. Mp: 109-112 °C (lit mp: 112-112.5 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 13.53 (s, 1H), 8.99 (d, J = 8.4 Hz, 1H), 8.76 (d, J = 4.3 Hz, 1H), 8.25 (d, J = 7.8 Hz, 1H), 7.92 (d, J =7.8 Hz, 1H), 7.86 (td, J = 7.7, 1.3 Hz, 1H), 7.58 (t, J = 7.4 Hz, 1H), 7.45 (m, 1H), 7.13 (t, J = 7.4 Hz, 1H), 2.68 (s, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 202.3, 164.0, 150.5, 148.8, 140.3, 137.5, 134.9, 131.8, 126.5, 123.2, 122.8, 122.8, 121.1, 28.7. IR (neat, cm^{-1}): 3207, 1684, 1656, 1576, 1517, 1451, 1430, 1363, 1312, 1251, 1169, 1111, 1042 997, 961, 900, 818, 757, 693, 610. Anal. calcd. for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03. Found: C, 69.85; H, 5.18.

***N*-(2-Acetyl-phenyl)-2-thiophenecarboxamide (6).**[35] Following General Procedure A, 2-thiophenecarboxamide (76 mg, 0.60 mmol,) was coupled with 2-bromoacetophenone (67 μL, 0.50 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), and K_2CO_3 (140 mg, 1.0 mmol) in anhydrous toluene (1 mL). No molecular sieves were utilized in the synthesis of the title compound. **6** was purified by column chromatography using a hexane-EtOAc 98:2 to 90:10 gradient. 100 mg (82% yield) of a cream-colored solid were obtained. Mp: 131-134 °C (lit mp:

129 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.74 (s, 1H), 8.90 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.97 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.85 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.62 (m, 1H), 7.58 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.17 (m, 2H), 2.74 (s, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 203.4, 160.7, 141.3, 140.4, 135.4, 132.0, 131.4, 128.8, 128.1, 122.5, 121.5, 120.5, 28.6. IR (neat, cm^{-1}): 3208, 3094, 2919, 1661, 1641, 1608, 1587, 1541, 1450, 1354, 1315, 1247, 1166, 1094, 1029, 960, 863, 811, 754, 731, 610. Anal. calcd. for $C_{13}H_{11}NO_2S$: C, 63.65; H, 4.52. Found: C, 63.39; H, 4.40.

***N*-(2-Acetyl-phenyl)-3-thiophenecarboxamide (7).** Following General Procedure A, 3-thiophenecarboxamide (76 mg, 0.60 mmol) was coupled with 2-bromoacetophenone (67 μL, 0.50 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), K_2CO_3 (140 mg, 1.0 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). **7** was purified by column chromatography using a hexane-EtOAc 98:2 to 90:10 gradient. 97 mg (79% yield) of a white solid were obtained. Mp: 90-93 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.63 (s, 1H), 8.93 (dd, *J* = 8.5, 1.1 Hz, 1H), 8.16 (dd, *J* = 3.0, 1.4 Hz, 1H), 7.97 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.69 (dd, *J* =5.1, 1.3 Hz, 1H), 7.62 (m, 1H), 7.41 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.16 (ddd, *J* = 8.5, 7.3, 1.2 Hz, 1H), 2.73 (s, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 203.4, 161.6, 141.5, 138.4, 135.5, 132.0, 129.6, 126.8, 126.5, 122.4, 121.6, 120.6, 28.7. IR (neat, cm^{-1}): 3218, 3110, 2924, 1677, 1650, 1607, 1585, 1531, 1451, 1358, 1314, 1254, 1207, 1166, 1102, 1072, 1021, 961, 865, 838, 818, 757, 741, 610. Anal. calcd. for $C_{13}H_{11}NO_2S$: C, 63.65; H, 4.52. Found: C, 63.58; H, 4.41.

***N*-(6-Acetyl-3-fluoro-phenyl)-benzamide (8).** Following General Procedure A, benzamide (76 mg, 0.63 mmol) was coupled with 2-bromo-4-fluoroacetophenone (109 mg, 0.502 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), K_2CO_3 (140 mg, 1.0 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). **8** was purified by column chromatography using a hexane-EtOAc 95:5 to 90:10 gradient. 101 mg (79% yield) of a white

solid were obtained. Mp: 123-126 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.91 (s, 1H), 8.78 (dd, *J* = 12.1, 2.6 Hz, 1H), 8.05 (m, 2H), 7.94 (dd, *J* = 8.9, 6.3 Hz, 1H), 7.55 (m, 3H), 6.81 (m, 1H), 2.67 (s, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 202.0, 166.5 (d, J_{CF} = 255 Hz), 166.2, 144.0 (d, J_{CF}= 13 Hz), 134.4 (d, J_{CF} = 11 Hz), 132.4, 130.2, 129.0, 127.6, 118.5 (d, J_{CF} = 3 Hz), 109.8 (d, J_{CF} = 23 Hz), 107.8 (d, J_{CF} = 28 Hz), 28.6. IR (neat, cm-1): 3175, 1678, 1644, 1602, 1536, 1495, 1361, 1318, 1264, 1250, 1134, 992, 873, 806, 763, 706. Anal. calcd. for $C_{15}H_{12}FNO_2$: C, 70.03; H, 4.70. Found: C, 69.86; H, 4.49.

***N*-(6-Acetyl-3-fluoro-phenyl)-2-chlorobenzamide (9).** An oven-dried resealable test tube with a Teflon stir bar was charged with CuI (9.5 mg, 0.050 mmol) and NaI (150 mg, 1.0 mmol). The test tube was covered with a rubber septum and evacuated and refilled with argon three times through a syringe needle. Under argon, 2-bromo-4-fluoroacetophenone (109 mg, 0.502 mmol), *N, N'*-dimethylethylenediamine (**L1**) (10.5 μL, 0.985 mmol), and toluene (1 mL) were each added *via* syringe. The rubber septum was then removed and quickly replaced with a Teflon screw-cap. The test tube was then placed in a preheated oil bath, at 110 °C. The reaction was heated with stirring for 24 h at which point it was cooled to room temperature. Next, 2-chlorobenzamide (93 mg, 0.60 mmol) and K_3PO_4 (210 mg, 0.99 mmol) were added quickly to the reaction mixture. The test tube was re-capped and the reaction was heated with stirring in the oil bath at 110 °C. After 24 h, the reaction was cooled to room temperature. The reaction mixture was partitioned between ethyl acetate and water and the organic layer was extracted. A second portion of ethyl acetate was used to wash the water layer and was extracted and combined with the first layer. The organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo* to remove solvent. **9** was purified by column chromatography with a hexane-EtOAc 95:5 to 90:10 gradient. 97 mg (66% yield) of a beige solid were obtained. Mp: 105-108 °C. ^{1}H-

NMR (400 MHz, $CDCl_3$): δ 12.42 (s, 1H), 8.74 (dd, J = 11.9, 2.6 Hz, 1H), 7.95 (dd, J = 8.9, 6.3 Hz, 1H), 7.62 (dd, J = 7.5, 1.8 Hz, 1H), 7.41 (m, 3H), 6.85 (dd, J = 10.0, 7.4, 2.6 Hz, 1H), 2.63 (s, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 201.6, 166.4 (d, J_{CF} = 255 Hz), 166.2, 143.2 (d, J_{CF} = 13 Hz), 135.8, 134.3 (d, J_{CF} = 11 Hz), 131.8, 131.4, 130.8, 129.4, 127.3, 118.8 (d, J_{CF} = 3 Hz), 110.3 (d, J_{CF} = 22 Hz), 108.1 (d, J_{CF} = 28 Hz), 28.7. IR (neat, cm^{-1}): 3113, 1691, 1655, 1592, 1524, 1449, 1359, 1317, 1291, 1248, 1171, 1129, 1104, 1047, 993, 956, 871, 805, 784, 744, 715. Anal. calcd. for $C_{15}H_{11}ClFNO_2$: C, 61.76; H, 3.80. Found: C, 61.55; H, 3.77.

***N*-(6-Acetyl-3-fluoro-phenyl)-nicotinamide (10).** Following General Procedure A, nicotinamide (73 mg, 0.60 mmol) was coupled with 2-bromo-4-fluoroacetophenone (109 mg, 0.502 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), K_2CO_3 (140 mg, 1.0 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). **10** was purified by column chromatography using a hexane-EtOAc 95:5 to 50:50 gradient. 97 mg (75% yield) of a white solid were obtained. Mp: 165-167 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 13.04 (s, 1H), 9.30 (s, br, 1H), 8.81 (s, br, 1H), 8,74 (dd, J = 11.9, 2.7 Hz, 1H), 8.32 (d, J =8.0 Hz, 1H), 7.99 (dd, J = 8.9, 6.2 Hz, 1H), 7.47 (dd, J = 7.7, 4.7 Hz, 1H), 6.87 (ddd, J = 10.0, 7.4, 2.6 Hz, 1H), 2.70 (s, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 203.2, 166.5 (d, J_{CF} = 256 Hz), 164.5, 153.0, 149.2, 143.6 (d, J_{CF}= 13 Hz), 135.0, 134.5 (d, J_{CF} = 11 Hz), 130.0, 123.7, 118.6 (d, J_{CF} = 3 Hz), 110.3 (d, J_{CF} = 23 Hz), 108.0 (d, J_{CF} = 28 Hz), 28.7. IR (neat, cm^{-1}): 3116, 2921, 1687, 1651, 1606, 1589, 1532, 1460, 1419, 1368, 1320, 1299, 1278, 1261, 1251, 1169, 1143, 1110, 1025, 994, 960, 882, 863, 824, 811, 779, 765, 718. Anal. calcd. for $C_{14}H_{11}FN_2O_2$: C, 65.11; H, 4.29. Found: C, 65.01; H, 4.10.

***N*-(4-Methoxy-6-propioyl-phenyl)-3-chlorobenzamide (11).** Following General Procedure A, 3-chlorobenzamide (93 mg, 0.60 mmol) was coupled with 2-bromo-5-methoxypropiophenone

(122 mg, 0.502 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), K_2CO_3 (140 mg, 1.0 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). **11** was purified by column chromatography using a hexane-EtOAc 95:5 to 90:10 gradient. 107 mg (68% yield) of a pale yellow solid were obtained. Mp: 112-114 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.43 (s, 1H), 8.85 (d, *J* = 9.2 Hz, 1H), 8.04 (s, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.49 (m, 3H), 7.18 (dd, *J* = 9.2, 3.0 Hz, 1H), 3.86 (s, 3H), 3.08 (q, *J* = 7.2 Hz, 2H), 1.25 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 205.5, 164.2, 154.6, 136.8, 135.1, 134.4, 131.8, 130.1, 128.1, 125.1, 122.9, 122.4, 119.9, 116.1, 55.7, 33.3, 8.6. IR (neat, cm^{-1}): 3221, 3087, 2986, 2968, 2947, 2915, 2838, 1668, 1651, 1642, 1615, 1572, 1531, 1454, 1423, 1383, 1320, 1291, 1265, 1252, 1195, 1176, 1050, 973, 836, 817, 730. Anal. calcd. for $C_{17}H_{16}ClNO_3$: C, 64.26; H, 5.08. Found: C, 64.07; H, 5.02.

***N*-(4-Methoxy-6-propioyl-phenyl)-2-thiophenecarboxamide (12).** Following General Procedure A, 2-thiophenecarboxamide (76 mg, 0.60 mmol) was coupled with 2-bromo-5-methoxypropiophenone (122 mg, 0.502 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), K_2CO_3 (140 mg, 1.0 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). **12** was purified by column chromatography using a hexane-EtOAc 95:5 to 90:10 gradient. 107 mg (74% yield) of a yellow solid were obtained. Mp: 153-155 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.45 (s, 1H), 8.81 (d, *J* = 9.2 Hz, 1H), 7.82 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.56 (d, *J* = 5.0, 1.1 Hz, 1H), 7.46 (d, *J* = 2.9 Hz, 1H), 7.17 (m, 2H), 3.86 (s, 3H), 3.10 (q, *J* = 7.2 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 205.5, 160.4, 154.4, 140.7, 134.6, 131.0, 128.4, 128.0, 122.5, 122.2, 120.1, 116.0, 55.7, 33.3, 8.5. IR (neat, cm^{-1}): 3216, 2983, 2911, 2830, 1643, 1616, 1595, 1521, 1420, 1352, 1314, 1287, 1261, 1192, 1175,

1056, 1044, 971, 826, 729. Anal. calcd. for $C_{15}H_{15}NO_3S$: C, 62.26; H, 5.23. Found: C, 62.06; H, 5.20.

***N*-(2-Acetyl-phenyl)-cinnamamide (13).**[36] Following General Procedure A, cinnamamide (88 mg, 0.60 mmol) was coupled with 2-bromoacetophenone (67 μL, 0.50 mmol) using CuI (9.5 mg, 0.050 mmol), *rac* trans-1,2-dimethyl-diamino-cyclohexane (**L2**) (15.8 μL, 0.100 mmol), K_2CO_3 (140 mg, 1.0 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). The reaction was heated for 25 h. **13** was purified by column chromatography using a hexane-EtOAc 98:2 to 90:10 gradient. 106 mg (80% yield) of a cream-colored solid were obtained. Mp: 90-93 °C (lit mp: 89.5-90.5 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.06 (s, 1H), 8.92 (d, J = 8.5 Hz, 1H), 7.94 (dd, J = 8.0, 1.1 Hz, 1H), 7.76 (d, J = 15.6 Hz, 1H), 7.61 (m, 3H), 7.41 (m, 3H), 7.16 (t, J = 7.2 Hz, 1H), 6.64 (d, J = 15.6 Hz, 1H), 2.71 (s, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 203.2, 165.1, 142.4, 141.5, 135.5, 134.8, 132.0, 130.2, 129.1, 128.3, 122.6, 122.3, 121.9, 121.1, 28.9. IR (neat, cm^{-1}): 3224, 3109, 3061, 3027, 1685, 1652, 1629, 1606, 1585, 1524, 1358, 1332, 1295, 1248, 1162, 975, 855, 757, 679, 614. Anal. calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70. Found: C, 76.89; H, 5.65.

***N*-(2-Acetyl-phenyl)-crotonamide (14).** Following General Procedure A, crotonamide (51 mg, 0.60 mmol) was coupled with 2-iodoacetophenone (71 μL, 0.50 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.985 mmol), K_3PO_4 (210 mg, 0.99 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). The reaction was heated at 110 °C for 24 h. **14** was purified by column chromatography using a hexane-EtOAc 98:2 to 90:10 gradient. 73 mg (71% yield) of a beige solid were obtained. Mp: 80-83 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 11.84 (s, 1H), 8.85 (dd, J = 8.5, 1.1 Hz, 1H), 7.92 (dd, J = 8.0, 1.6 Hz, 1H), 7.57 (m, 1H), 7.12 (ddd, J =8.5, 7.4, 1.2 Hz, 1H), 6.99 (dq, J = 15.3, 6.9 Hz, 1H), 6.04 (dq, J = 15.3, 1.7 Hz, 1H), 2.69 (s,

3H), 1.94 (dd, J = 6.9, 1.7 Hz, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 203.0, 165.0, 141.4, 141.3, 135.2, 131.8, 126.9, 122.3, 121.7, 120.8, 28.7, 18.0. IR (neat, cm^{-1}): 3208, 2915, 1686, 1643, 1607, 1585, 1523, 1453, 1358, 1331, 1298, 1286, 1250, 1188, 1166, 960, 928, 825, 757, 675. Anal. calcd. for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45. Found: C, 71.03; H, 6.45.

1-(2-Acetyl-phenyl)-pyrrolidin-2-one (15).[37] Following General Procedure A, 2-pyrrolidinone (46 μL, 0.61 mmol) was coupled with 2-bromoacetophenone (67 μL, 0.50 mmol) using CuI (4.8 mg, 0.025 mmol, 5 mol%), **L1** (5.3 μL, 0.050 mmol, 10 mol%), K_2CO_3 (140 mg, 1.0 mmol), and 200 mg activated 5 Å molecular sieves in anhydrous toluene (1 mL). The reaction was heated at 90 °C for 25 h. **15** was purified by column chromatography using a hexane-EtOAc 50:50 to 0:100 gradient. 87 mg (86% yield) of a white solid were obtained. Mp: 89-91 °C (lit mp: 88-89 °C). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.57 (dd, J = 7.7, 1.6 Hz, 1H), 7.43 (m, 1H), 7.29 (m, 1H), 7.17 (d, J =7.9 Hz, 1H), 3.82 (t, J = 7 Hz, 2H), 2.52 (s, 3H), 2.44 (t, J = 8 Hz, 2H), 2.15 (m, 2H). ^{13}C-NMR (300 MHz, $CDCl_3$): 200.6, 175.0, 136.8, 135.9, 131.9, 128.2, 126.8, 125.9, 50.9, 31.8, 28.6, 18.8. IR (neat, cm^{-1}): 3361, 2999, 2958, 2902, 1693, 1598, 1575, 1488, 1453, 1402, 1358, 1324, 1257, 1238, 1167, 1146, 1101, 1020, 968, 776, 656. Anal. calcd. for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45. Found: C, 70.86; H, 6.52.

General Procedure B: Base-promoted Cyclization to 2-Aryl-4-Quinolones. A resealable oven-dried test tube with Teflon stir bar was charged with *N*-(keto-aryl)amide (1 equiv) obtained in step one and crushed NaOH (3-3.5 equiv). Anhydrous 1,4-dioxane was added *via* syringe such that the reaction mixture was 0.1M in concentration. The test tube was then sealed with a Teflon screw-cap and the reaction was placed in a preheated oil bath at 110 °C. The reaction mixture was stirred for 1-2 h and then removed from the oil bath and allowed to cool to room temperature. The reaction mixture was then dissolved in ethanol and transferred to a round

bottom flask in which it was concentrated *in vacuo* to remove solvent. Next, a small amount of water and a large amount of hexane were added to the flask and the flask was sonicated for approximately two minutes. The biphasic mixture was neutralized to pH ~7 with 1M HCl and saturated $NaHCO_3$ solutions. Solid precipitated out of the water layer and the heterogeneous mixture was filtered through a Buchner funnel. The solid powder was rinsed with copious amounts of hexane and minimal water. The solid was collected and transferred to a vial with ethanol and concentrated *in vacuo* to remove residual solvent. In some cases, the hexane rinses during filtration did not completely wash away the alkyl residue and the ^{1}H-NMR showed contamination. Further purification involved a more extensive hexane wash in which hexane was added to the vial containing the compound and the mixture was sonicated. The solid was allowed to settle, and then the hexane was carefully removed *via* pipette. Hexane was added and removed twice more before the product was dried *in vacuo.*

2-Phenyl-4-quinolone (16).[17b] Following General Procedure B, **1** (98 mg, 0.41 mmol) was cyclized using NaOH (49 mg, 1.2 mmol) in 1,4-dioxane (4.1 mL). The reaction was heated for 1 h at 110 °C. After work-up and filtration, 87 mg (96% yield) of a beige solid were obtained. Mp: 247-250 °C (ethanol) (lit mp: 254 °C).[12a] ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.26 (d, J = 8.1 Hz, 1H), 7.69 (m, 4H), 7.52 (m, 3H), 7.38 (m, 1H), 6.56 (s, 1H). ^{13}C-NMR (400 MHz, $CD_3OD/CDCl_3$): 180.3, 153.0, 141.5, 135.0, 133.3, 131.6, 129.9, 128.2, 125.7, 125.4, 125.1, 119.4, 108.4. IR (neat, cm^{-1}): 3067, 2962, 1635, 1594, 1581, 1546, 1502, 1472, 1450, 1431, 1355, 1320, 1255, 1139, 839, 798, 771, 753, 689, 670.

2-(3'-Chlorophenyl)-4-quinolone (17). Following General Procedure B, **2** (107 mg, 0.39 mmol) was cyclized using NaOH (47 mg, 1.2 mmol) in 1,4-dioxane (3.9 mL). The reaction was heated for 1 h at 110 °C. After work-up and filtration, 96 mg (96% yield) of a cream-colored

solid were obtained. Mp: >260 °C. ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.26 (m, 1H), 7.76 (m, 1H), 7.67 (m, 3H), 7.50 (m, 2H), 7.40 (m, 1H), 6.55 (s, 1H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3$): 180.4, 151.4, 141.6, 137.0, 135.9, 133.5, 131.5, 131.4, 128.3, 126.7, 125.8, 125.6, 125.3, 119.5, 108.7. IR (neat, cm^{-1}): 2193, 1604, 1572, 1558, 1503, 1445, 1350, 841, 769, 757, 705.

2-(4'-Pyridyl)-4-quinolone (18).[9h] Following General Procedure B, **3** (63 mg, 0.26 mmol) was cyclized using NaOH (31 mg, 0.78 mmol) in 1,4-dioxane (2.6 mL). The reaction was heated for 2 h at 110 °C. After work-up and filtration, 52 mg (90% yield) of a beige solid were obtained. Mp: >260 °C. ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.71 (d, J = 5.0 Hz, 2H), 8.27 (dt, J = 8.2, 1.1 Hz, 1H), 7.70 (m, 4H), 7.39 (m, 1H), 6.60 (s, 1H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3$): 180.1, 150.6, 149.2, 143.2, 141.5, 133.5, 125.7, 125.6, 125.3, 122.8, 119.4, 109.0. IR (neat, cm^{-1}): 3066, 2968, 1635, 1591, 1567, 1536, 1506, 1444, 1358, 1259, 1143, 821, 796, 769, 675.

2-(3'-Pyridyl)-4-quinolone (19). Following General Procedure B, **4** (81 mg, 0.34 mmol) was cyclized using NaOH (41 mg, 1.0 mmol) in 1,4-dioxane (3.4 mL). The reaction was heated for 1 h at 110 °C. After work-up and filtration, 66 mg (88% yield) of a beige solid were obtained. Mp: >260 °C. ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.90 (dd, J = 2.4, 0.8 Hz, 1H), 8.68 (dd, J = 4.9, 1.6 Hz, 1H), 8.28 (m, 1H), 8.13 (ddd, J = 8.0, 2.4, 1.6 Hz, 1H), 7.66 (m, 2H), 7.55 (ddd, J = 8.0, 4.9, 0.8 Hz, 1H), 7.40 (m, 1H), 6.54 (s, 1H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3$): 180.1, 151.5, 149.2, 148.3, 141.4, 136.6, 133.4, 131.5, 125.8, 125.5, 125.2, 125.0, 119.2, 109.0. IR (neat, cm^{-1}): 3090, 2966, 1637, 1602, 1578, 1548, 1509, 1442, 1384, 1356, 1024, 801, 749, 704.

2-(2'-Pyridyl)-4-quinolone (20).[15] Following General Procedure B, **5** (89 mg, 0.37 mmol) was cyclized using NaOH (44 mg, 1.1 mmol) in 1,4-dioxane (3.7 mL). The reaction was heated for 1 h at 110 °C. After work-up and filtration, 71 mg (86% yield) of a beige solid were obtained.

Decomposition: 232-234 °C (ethanol). ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.77 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H), 8.27 (ddd, *J* = 8.3, 1.5, 0.6 Hz, 1H), 8.09 (d, *J* = 8.1 Hz, 1H), 7.97 (td, *J* = 7.6, 1.8 Hz, 1H), 7.78 (ddd, *J* = 8.5, 1.1, 0.6 Hz, 1H), 7.71 (m, 1H), 7.50 (ddd, *J* = 7.6, 6.9, 1.2 Hz, 1H), 7.41 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 6.98 (s, 1H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3$): 181.0, 150.2, 149.8, 147.7, 140.7, 138.7, 133.6, 126.4, 125.9, 125.8, 125.2, 122.3, 119.7, 106.6. IR (neat, cm^{-1}): 3063, 1627, 1603, 1573, 1516, 1477, 1384, 1355, 1321, 1254, 1138, 1022, 995, 781, 760, 692. Anal. calcd. for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54. Found: C, 75.45; H, 4.53.

2-(2'-Thiophenyl)-4-quinolone (21).[9a] Following General Procedure B, **6** (97 mg, 0.40 mmol) was cyclized using NaOH (48 mg, 1.2 mmol) in 1,4-dioxane (4.0 mL). The reaction was heated for 1 h at 110 °C. After work-up, filtration, and a hexane wash, 88 mg (97% yield) of a beige solid were obtained. Mp: >260 °C (lit mp: >300 °C).[21d] ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.22 (ddd, *J* = 8.2, 1.4, 0.6 Hz, 1H), 7.76 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.66 (m, 2H), 7.57 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.36 (ddd, *J* = 8.1, 6.7, 1.4 Hz, 1H), 7.19 (dd, *J* = 5.1, 3.8 Hz, 1H), 6.60 (s, 1H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3$): 179.9, 146.0, 141.1, 136.8, 133.2, 130.0, 129.1, 128.5, 125.6, 125.3, 124.8, 118.9, 107.3. IR (neat, cm^{-1}): 3058, 2184, 1598, 1557, 1503, 1443, 1347, 1256, 1136, 857, 824, 768, 756, 697.

2-(3'-Thiophenyl)-4-quinolone (22). Following General Procedure B, **7** (67 mg, 0.27 mmol) was cyclized using NaOH (33 mg, 0.83 mmol) in 1,4-dioxane (2.7 mL). The reaction was heated for 2 h at 110 °C. After work-up and filtration, 57 mg (92% yield) of a beige solid were obtained. Mp: >260 °C ($CDCl_3/CD_3OD$). ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.23 (d, *J* = 8.0 Hz, 1H), 8.01 (s, 1H), 7.63 (m, 2H), 7.55-7.33 (m, 3H), 6.61 (s, 1H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3$): 180.7, 147.8, 141.6, 136.2, 133.5, 128.6, 127.2, 126.9, 125.9, 125.7, 125.2,

119.4, 107.6. IR (neat, cm^{-1}): 3069, 2926, 1633, 1593, 1552, 1508, 1470, 1440, 1428, 1369, 1350, 1313, 1142, 1022, 830, 757, 694.

7-Fluoro-2-phenyl-4-quinolone (23).[9f] Following General Procedure B, **8** (76 mg, 0.29 mmol) was cyclized using NaOH (35 mg, 0.88 mmol) in 1,4-dioxane (2.9 mL). The reaction was heated for 2 h at 110 °C. After work-up and filtration, 63 mg (89% yield) of a cream-colored solid were obtained. Mp: >260 °C. ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.27 (dd, J = 9.1, 6.1 Hz, 1H), 7.72 (m, 2H), 7.52 (m, 3H), 7.36 (dd, J = 9.8, 2.4 Hz, 1H), 7.10 (ddd, J = 10.7, 8.3, 2.4 Hz, 1H), 6.53 (s, 1H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3/CD_2Cl_2$): 179.8, 166.1 (d, J_{CF} = 252 Hz), 153.6, 143.1 (d, J_{CF} = 13 Hz), 134.9, 131.7, 130.0, 129.0 (d, J_{CF} = 10 Hz), 128.2, 122.4 (d, J_{CF} = 1.7 Hz), 114.1 (d, J_{CF} = 24 Hz), 108.6, 104.6 (d, J_{CF} = 25 Hz). IR (neat, cm^{-1}): 3255, 3159, 3117, 3082, 3005, 1641, 1602, 1583, 1542, 1509, 1469, 1425, 1367, 1295, 1253, 1162, 1132, 1092, 869, 840, 816, 771, 744, 696.

2-(2'-Chlorophenyl)-7-fluoro-4-quinolone (24). Following General Procedure B, **9** (73 mg, 0.25 mmol) was cyclized using NaOH (30 mg, 0.75 mmol) in 1,4-dioxane (2.5 mL). The reaction was heated for 2 h at 110 °C. After work-up and filtration, 50 mg (73% yield) of a beige solid were obtained. Decomposition: 252-256 °C (ethanol). ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.30 (dd, J = 9.0, 6.0 Hz, 1H), 7.53 (m, 1H), 7.44 (m, 3H), 7.22 (dd, J = 9.6, 2.4 Hz, 1H), 7.11 (ddd, J = 10.8, 8.2, 2.1 Hz, 1H), 6.31 (s, 1H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3$): 179.4, 165.8 (d, J_{CF} = 252 Hz), 150.9, 142.4 (d, J_{CF} = 13 Hz), 134.2, 133.2, 132.1, 131.3, 130.8, 128.9 (d, J_{CF} = 11 Hz), 127.8, 122.2, 114.1 (d, J_{CF} = 24 Hz), 111.1, 104.2 (d, J_{CF} = 25 Hz). IR (neat, cm^{-1}): 3070, 1642, 1606, 1589, 1551, 1513, 1462, 1259, 1162, 1129, 966, 873, 822, 753, 732.

7-Fluoro-2-(3'-pyridyl)-4-quinolone (25). Following General Procedure B, **10** (85 mg, 0.33 mmol) was cyclized using NaOH (40 mg, 1.0 mmol) in 1,4-dioxane (3.3 mL). The reaction was

heated for 1 h at 110 °C. After work-up and filtration, further purification was needed so a hexane wash was performed. Upon drying, 87 mg (96% yield) of a beige solid were obtained. Mp: >260 °C ($CDCl_3/CD_3OD$). ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.93 (s, br, 1H), 8.72 (s, br, 1H), 8.29 (dd, J = 9.0, 6.0 Hz, 1H), 8.14 (d, J = 8.1 Hz, 1H), 7.58 (s, br, 1H), 7.34 (dd, J = 9.6, 2.4 Hz, 1H), 7.13 (ddd, J = 10.7, 8.3, 2.4 Hz, 1H), 6.52 (s, 1H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3$): 179.4, 166.1 (d, J_{CF} = 252 Hz), 151.7, 150.2, 148.4, 143.5, 136.7, 131.8, 129.0 (d, J_{CF} = 10 Hz), 125.2, 122.5 (d, J_{CF} = 1.2 Hz), 114.4 (d, J_{CF} = 24 Hz), 109.2, 104.8 (d, J_{CF} = 25 Hz). IR (neat, cm^{-1}): 3079, 2921, 2306, 2266, 1636, 1605, 1579, 1568, 1543, 1515, 1467, 1427, 1259, 1213, 1090, 852, 805, 703.

2-(3'-Chlorophenyl)-6-methoxy-3-methyl-4-quinolone (26). Following General Procedure B, **11** (66 mg, 0.21 mmol) was cyclized using NaOH (29 mg, 0.73 mmol) in 1,4-dioxane (2.1 mL). The reaction was heated for 2 h at 110 °C. After work-up and filtration, 57 mg (91% yield) of a beige crystalline solid were obtained. Mp: >260 °C. ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 7.67 (d, J = 2.9 Hz, 1H), 7.46 (m, 4H), 7.37 (m, 1H), 7.24 (dd, J = 9.1, 2.9 Hz, 1H), 3.90 (s, 3H), 2.03 (s, 3H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3$): 178.9, 157.5, 148.1, 137.8, 135.4, 135.4, 131.0, 130.5, 129.7, 128.2, 125.3, 124.4, 120.6, 115.9, 104.3, 56.1, 12.8. IR (neat, cm^{-1}): 3078, 2957, 1582, 1544, 1501, 1380, 1294, 1229, 1190, 1158, 1097, 1032, 848, 812, 768, 736, 714. Anal. calcd. for $C_{17}H_{14}ClNO_2$: C, 68.12; H, 4.71. Found: C, 68.08; H, 4.73.

6-Methoxy-3-methyl-2-(2'-thiophenyl)-4-quinolone (27). Following General Procedure B, **12** (84 mg, 0.29 mmol) was cyclized using NaOH (41 mg, 1.0 mmol) in 1,4-dioxane (2.9 mL). The reaction was heated for 1 h at 110 °C. After work-up and filtration, 73 mg (92% yield) of a pale yellow solid were obtained. Mp: >260 °C ($CDCl_3/CD_3OD$). ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 7.65 (d, J = 2.9 Hz, 1H), 7.58 (dd, J = 5.1, 1.2 Hz, 1H), 7.49 (d, J = 9.1 Hz,

1H), 7.33 (dd, J = 3.6, 1.2 Hz, 1H), 7.23 (dd, J = 9.1, 2.9 Hz, 1H), 7.18 (dd, J = 5.1, 3.6 Hz, 1H), 3.90 (s, 3H), 2.18 (s, 3H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3$): 178.9, 157.8, 143.2, 136.1, 135.7, 130.7, 129.4, 128.4, 125.5, 124.6, 120.8, 117.2, 104.4, 56.1, 13.1. IR (neat, cm^{-1}): 2951, 1589, 1541, 1488, 1439, 1375, 1256, 1228, 1161, 1026, 850, 822.7, 768, 708, 692. Anal. calcd. for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83. Found (Recrystallized from $CDCl_3/CD_3OD$): C, 66.18; H, 4.74.

2-Styryl-4-quinolone (28).[38] Following General Procedure B, **13** (101 mg, 0.38 mmol) was cyclized using NaOH (46 mg, 1.2 mmol) in 1,4-dioxane, (3.8 mL). The reaction was heated for 3 h at 90 °C. After work-up and filtration, 77 mg (82% yield) of an orange-yellow solid were obtained. Mp: >260 °C (lit mp: 279 °C). ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.22 (ddd, J = 8.2, 1.4, 0.6 Hz, 1H), 7.58 (m, 5H), 7.38 (m, 4H), 6.96 (d, J = 16.5 Hz, 1H), 6.55 (s, 1H). ^{13}C-NMR (400 MHz, $CD_3OD/CDCl_3$): 180.0, 149.5, 141.0 137.5, 136.0, 133.1, 130.3, 129.6, 128.1, 125.6, 125.6, 124.8, 121.5, 118.8, 107.0. IR (neat, cm^{-1}): 3059, 2040, 1621, 1590, 1547, 1494, 1436, 1246, 1138, 959, 752, 686.

2,3-Dihydro-pyrrolo[1,2-a]quinolin-5(1H)-one (29).[37] Following General Procedure B, **15** (71 mg, 0.35 mmol) was cyclized using NaOH (49 mg, 1.2 mmol) in 1,4-dioxane (3.5 mL). The reaction was heated for 1 h at 110 °C. After the reaction was cooled to room temperature, it was transferred into a round bottom flask with ethanol. The solvent was removed *in vacuo* and water was added. The solution was neutralized to pH ~7 with 1M HCl and saturated $NaHCO_3$ solutions and then the water was removed *in vacuo*. The title compound was purified by silica column chromatography using a EtOAc-MeOH 100:0 to 95:5 gradient. After the product was collected and concentrated, a hexane wash was performed. 60 mg (93% yield) of a beige solid were obtained. Mp: 167-173 °C (lit mp: 173-174°C). ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.24 (d,

J = 8.5, 1.5 Hz, 1H), 7.64 (ddd, J = 8.5, 7.1, 1.5 Hz, 1H), 7.36 (m, 2H), 6.19 (s, 1H), 4.26 (t, J = 7.3 Hz, 2H), 3.15 (t, J = 7.6 Hz, 2H), 2.10 (m, 2H). ^{13}C-NMR (400 MHz, $CD_3OD/CDCl_3$): 179.3, 157.8, 139.1, 133.0, 126.5, 125.8, 124.6, 116.7, 105.0, 51.3, 32.4, 21.4. IR (neat, cm^{-1}): 3480 (br), 3388 (br), 2964, 2895, 1625, 1599, 1558, 1503, 1473, 1430, 1310, 1267, 1167, 1151, 1073, 1030, 962, 840, 787, 759, 671, 621.

2-(1'-Propenyl)-4-quinolone (30).[39] Following General Procedure B, **14** (84 mg, 0.41 mmol) was cyclized using NaOH (25 mg, 0.63 mmol, 1.5 equiv) in 1,4-dioxane (4.1 mL). The reaction was heated for 1 h at 110 °C. After the reaction was cooled to room temperature, it was transferred into a round bottom flask with ethanol. The solvent was removed *in vacuo* and water was added. The solution was neutralized to pH ~7 with 1M HCl and saturated $NaHCO_3$ solutions and then the water was removed *in vacuo*. The title compound was purified by silica column chromatography using a hexane-EtOAc 50:50 to 0:100 gradient. After the product was collected and concentrated, a hexane wash was performed. 42 mg (54% yield) of a pale yellow solid were obtained. Decomposition: 240-244 °C (lit decomposition: 210 °C). ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.17 (d, J = 7.9 Hz, 1H), 7.54 (m, 2H), 7.28 (m, 1H), 6.68 (m, 1H), 6.32 (s, 1H), 6.24 (dd, J = 15.9, 1.5 Hz, 1H), 1.91 (dd, J = 6.7, 1.4 Hz, 3H). ^{13}C-NMR (500 MHz, $CD_3OD/CDCl_3$): 180.0, 149.6, 140.7, 136.4, 132.8, 125.5, 125.4, 125.2, 124.6, 118.7, 106.1, 19.2. IR (neat, cm^{-1}): 3061, 2916, 2773, 2189, 2115, 1596, 1549, 1499, 1442, 1354, 1326, 1249, 1138, 961, 835, 756.

4-Methyl-3-vinyl-2-quinolone (31).[40] Following a slight modification of General Procedure B, **14** (94 mg, 0.46 mmol) was cyclized using Cs_2CO_3 (450 mg, 1.4 mmol) in 1,4-dioxane (4.6 mL). The reaction was heated for 24 h at 110 °C. After the reaction was cooled to room temperature, it was transferred into a round bottom flask with ethanol. The solvent was removed *in vacuo* and

water was added. The solution was neutralized to pH ~ 7 with 1M HCl and saturated $NaHCO_3$ solutions and then the water was removed *in vacuo*. The title compound was purified by silica column chromatography using a hexane-EtOAc 75:25 to 100:0 gradient. After the product was collected and concentrated, a hexane wash was performed. 65 mg (76% yield) of a pale yellow solid were obtained. Decomposition: >150 °C (lit mp: 203-205°C). ^{1}H-NMR (400 MHz, $CD_3OD/CDCl_3$): δ 7.73 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.44 (m, 1H), 7.28 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.21 (m, 1H), 6.76 (dd, *J* = 17.8, 11.7 Hz, 1H), 5.77 (dd, *J* = 17.8, 2.1 Hz, 1H), 5.64 (dd, *J* = 11.7, 2.1 Hz, 1H), 2.55 (s, 3H). ^{13}C-NMR (400 MHz, $CD_3OD/CDCl_3$): 163.3, 145.3, 137.4, 131.2, 130.7, 128.3, 125.7, 123.3, 122.5, 121.7, 116.3, 16.3. IR (neat, cm^{-1}): 2944, 2845, 1648, 1603, 1551, 1503, 1431, 1380, 1270, 919, 747, 664. Anal. calcd. for $C_{12}H_{11}NO$: C, 77.81; H, 5.99. Found: C: 77.70, H: 5.96.

***N*-(2-Acetyl-phenyl)-*n*-hexanamide (32).** Following General Procedure A, hexanamide (138 mg, 1.20 mmol) was coupled with 2-iodoacetophenone (141 mL, 1.00 mmol) using CuI (9.5 mg, 0.050 mmol), **L1** (10.5 μL, 0.100 mmol), K_3PO_4 (425 mg, 2.0 mmol), and 400 mg activated 5 Å molecular sieves in anhydrous toluene (2 mL). The title compound was purified by column chromatography using a 5-10% ethyl acetate/hexane gradient. 187 mg (80% yield) of a clear, yellow oil were obtained. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 11.68 (s, 1H), 8.73 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.82 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.47 (m, 1H), 7.03 (m, 1H), 2.60 (s, 3H), 2.37 (t, *J* = 7.4 Hz, 2H), 1.70 (m, 2H), 1.32 (m, 4H), 0.86 (m, 3H). ^{13}C-NMR (300 MHz, $CDCl_3$): 202.8, 172.7, 141.2, 135.1, 131.7, 122.1, 121.6, 120.6, 38.7, 31.4, 31.4, 28.6, 25.2, 22.4, 22.4, 14.0. IR (neat, cm^{-1}): 3253, 2957, 2931, 2861, 1699, 1653, 1607, 1585, 1521, 1451, 1360, 1311, 1298, 1248, 1163, 1092, 1022, 962, 756, 606. Anal. calcd. for $C_{14}H_{19}NO_2$: C, 72.07; H: 8.21. Found: C, 72.23; H, 8.26.

3-*n*-Butyl-4-methyl-2-quinolone (33)[41] and **2-*n*-Pentyl-4-quinolone (34).**[42] Following General Procedure B, **32** (82 mg, 0.35 mmol) was cyclized using NaOH (42 mg, 3 equiv.) in 1,4-dioxane (3.5 mL). The reaction was heated for 1 h at 110 °C. After the reaction was cooled to room temperature, ethanol was added to dissolve all solid and the reaction mixture was loaded directly onto a Biotage samplet. The samplet was dried with gentle heating. The title compounds were purified by silica column chromatography using a hexane-EtOAc 75:25 to 0:100 gradient followed by a EtOAc-MeOH 100:0 to 95:5 gradient. **33** eluted faster than **34** under these conditions. After the products were collected and concentrated, hexane washes were performed on both compounds. 17 mg (23% yield) of **33** were obtained as a white solid. Mp: 171-173 °C (lit mp: 170-171 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 11.99 (s, br, 1H), 7.70 (dd. J = 8.2, 0.9 Hz, 1H), 7.46 (m, 1H), 7.38 (m, 1H), 7.21 (m, 1H), 2.83 (t, J = 7.3 Hz, 2H), 2.51 (s, 3H), 1.52 (m, 4H), 0.99 (t, J = 7.2 Hz, 3H). ^{13}C-NMR (400 MHz, $CDCl_3$): 164.1, 143.2, 137.0, 131.9, 129.3, 124.4, 122.3, 121.3, 116.2, 31.5, 26.9, 23.2, 15.3, 14.3. IR (neat, cm^{-1}): 2946, 2860, 1654, 1611, 1562, 1503, 1428, 1394, 1274, 1182, 1158, 1097, 1032, 905, 747, 706, 667, 613. 37 mg (49% yield) of **34** were obtained as a white solid. Mp: 142-145 °C (lit mp: 141-142 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 13.02 (s, 1H), 8.38 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.60 (t, J = 7.1 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 6.28 (s, 1H), 2.72 (t, J = 7.5 Hz, 2H), 1.71 (m, 2H), 1.22 (m, 4H), 0.78 (t, J = 6.8 Hz, 3H). ^{13}C-NMR (400 MHz, $CDCl_3$): 179.0, 156.0, 141.0, 131.9, 125.2, 123.8, 119.0, 108.2, 34.5, 31.5, 29.1, 22.5, 14.0. IR (neat, cm^{-1}): 3250, 3065, 2956, 2930, 2871, 1639, 1595, 1552, 1505, 1472, 1444, 1355, 1322, 1249, 1176, 1138, 1111, 844, 761, 675.

General Procedure C: McMurry-Type Coupling to Form Indoles.[18] In a glove box, $TiCl_3$ (1.8 mmol, 3.6 equiv.) and Zn powder (3.6 mmol, 7.2 equiv.) were weighed into an oven-dried Schlenk tube with a Teflon-coated stir bar. The Schlenk tube was capped with a rubber septum

and removed from the glove box. Outside of the glove box, the Schlenk tube was evacuated and refilled with Argon twice. While still under a stream of Argon, the rubber septum was removed and the *N*-(keto-aryl)amide (0.5 mmol, 1 equiv.) was added quickly to the Schlenk tube. The Schlenk tube was recapped with the septum and evacuated and refilled with Argon three more times. Anhydrous DME was added *via* syringe and the rubber septum was replaced with a Teflon Schlenk cap. The reaction was placed in a preheated oil bath at 90 °C, and the reaction was heated with stirring for 4-28 h, monitored by TLC. The reaction mixture was allowed to cool to room temperature and filtered through a pad of silica gel with copious amounts of EtOAc. The filtrate was concentrated *in vacuo*, and the crude material was purified *via* silica gel column chromatography using a hexane-EtOAc 100:0 to 92:8 gradient.

3-Methyl-2-phenylindole (35).[22] Following General Procedure C, **1** (119.6 mg, 0.50 mmol) underwent an intramolecular coupling using $TiCl_3$ (280 mg, 1.8 mmol) and Zn powder (235 mg, 3.6 mmol) in DME (6.0 mL). The reaction was heated for 28 h at 90 °C. After filtration and column chromatography, 71 mg (69% yield) of a pale yellow solid were obtained. Mp: 88-92 °C (lit mp. 90-92 °C). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.03 (s, br, 1H), 7.61 (m, 3H), 7.50 (m, 2H), 7.38 (m, 2H), 7.23 (m, 1H), 7.17 (m, 1H), 2.49 (s, 3H). ^{13}C-NMR (400 MHz, $CDCl_3$): 136.1, 134.3, 133.6, 130.3, 129,1, 128.0, 127.6, 122.6, 119.8, 119.3, 111.0, 108.9, 9.9. IR (neat, cm^{-1}): 3448, 3421, 3056, 2914, 2862, 1603, 1458, 1445, 1332, 1306, 1235, 1074, 918, 770, 739, 700.

3-Methyl-2-(3'-thiophenyl)-indole (36). Following General Procedure C, **7** (122.7 mg, 0.50 mmol) underwent an intramolecular coupling using $TiCl_3$ (280 mg, 1.8 mmol) and Zn powder (235 mg, 3.6 mmol) in DME (6.0 mL). The reaction was heated for 16 h at 90 °C. After filtration and column chromatography, 75 mg (70% yield) of a beige solid were obtained. Mp: 92-95 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.77 (s, br, 1H), 7.55 (d, J = 7.7 Hz, 1H), 7.34 (dd, J = 4.6, 3.4

Hz, 1H), 7.24 (m, 3H), 7.13 (m, 3H), 2.39 (s, 3H). ^{13}C-NMR (400 MHz, $CDCl_3$): 135.7, 134.2, 130.0, 130.0, 126.7, 126.3, 122.4, 121.3, 119.7, 119.0, 110.8, 108.6, 9.87. IR (neat, cm^{-1}): 3417, 3100, 3056, 2916, 2862, 1461, 1350, 1332, 1291, 1240, 1206, 1153, 1118, 1090, 1025, 1007, 865, 781, 741, 683, 619. Anal. calcd. for $C_{13}H_{11}NS$: C, 73.20; H, 5.20. Found: C, 73.33; H, 5.30.

2,3-Dihydro-9-methyl-1H-pyrrolo[1,2-a]indole (37).[43] Following General Procedure C, **15** (101.6 mg, 0.50 mmol) underwent an intramolecular coupling using $TiCl_3$ (280 mg, 1.8 mmol) and Zn powder (235 mg, 3.6 mmol) in DME (6.0 mL). The reaction was heated for 4.5 h at 90 °C. After filtration and column chromatography, 29 mg (34% yield) of a colorless oil were obtained. Note: Title compound readily decomposes even at low temperature. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 7.4 Hz, 1H), 7.25 (m, 1H), 7.14 (m, 2H), 4.06 (t, J = 6.9 Hz, 2H), 2.98 (t, J = 7.5 Hz, 2H), 2.63 (m, 2H), 2.32 (s, 3H). ^{13}C-NMR (400 MHz, $CDCl_3$): 141.5, 133.3, 132.7, 120.1, 118.5, 118.5, 109.3, 100.8, 43.7, 28.0, 23.1, 9.2.

2-Bromo-5-methoxypropiophenone.[44,45] 2-Bromo-5-methoxybenzoyl chloride (1.91 g, 7.67 mmol) was added to a flame-dried round bottom flask. The flask was covered with a rubber septum and then evacuated and refilled with Argon three times. Anhydrous THF (20 mL) was added *via* syringe and the reaction mixture was cooled to -78 °C. Ethyl magnesium bromide (3M in ether) was added drop-wise over approximately 30 minutes. Then the reaction mixture was allowed to warm to room temperature and was stirred for 20 h at which point saturated ammonium chloride was added. The organic layer was extracted and concentrated. Then it was partitioned between ether and water. The ether layer was extracted and then washed once more with water. The organic layer was dried over $MgSO_4$, filtered, and concentrated to dry. The title compound was purified by silica column chromatography using a hexane-EtOAc 100:0 to 90:10 gradient. 1.37 g (74% yield) of a clear, yellow oil were obtained. ^{1}H-NMR (300 MHz, $CDCl_3$): δ

7.47 (dd, J = 8.6, 0.5 Hz, 1H), 6.85 (m, 2H), 3.81 (s, 3H), 2.93 (q, J = 7.2 Hz, 2H), 1.21 (t, J = 7.2 Hz, 3H). ^{13}C-NMR (400 MHz, $CDCl_3$): 204.7, 158.8, 142.6, 134.2, 117.1, 113.6, 108.5, 55.5, 35.9, 8.0. IR (neat, cm^{-1}): 3073, 2977, 2939, 2905, 2840, 1705, 1592, 1569, 1467, 1405, 1345, 1290, 1241, 1198, 1175, 1090, 1051, 1027, 967, 874, 846, 816.

IV. References

1. (a) Jiang, L.; Buchwald, S. L. in *Metal-Catalyzed Cross-Coupling Reactions, 2nd ed.;* de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, 2004; pp 699-760. (b) Hartwig, J. F. *Synlett* **2006**, *9*, 1283-1294.

2. Zou, B.; Yuan, Q.; Ma, D. *Angew. Chem. Int. Ed.* **2007**, *46*, 2598-2601.

3. Martín, R.; Rodríguez Rivero, M.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2006**, *45*, 7079-7082.

4. Manley, P. J.; Bilodeau, M. T. *Org. Lett.* **2004**, *6*, 2433-2435.

5. (a) Ackermann, L. *Org. Lett.* **2005**, *7*, 439-442. (b) Tang, Z.-Y.; Hu, Q.-S. *Adv. Synth. Catal.* **2006**, *348*, 846-850. (c) Liu, F.; Ma, D. *J. Org. Chem.* **2007**, ASAP.

6. Rodríguez Rivero, M.; Buchwald, S. L. *Org. Lett.* **2007**, *9*, 973-976.

7. Pozharskii, A. F.; Soldatenkov, A. T.; Katritzky, A. R. Heterocycles and Health. in *Heterocycles in Life and Society*; John Wiley: Chichester, U.K., 1997; pp 135-164.

8. It is known that 4-quinolines have two tautomeric forms and can be drawn as either the 4-hydroxyquinolines in the enol-form or as 4-quinolones in the keto-form (Scheme 5). Both forms are important in understanding the characterization data and the chemical reactivity of such compounds. However, it is believed that in the solid state, as well as in many solvents, these compounds exist primarily in the keto-form. Therefore, for the purposes of this publication, we will refer to and draw the products as 4-quinolones. For discussions on the tautomerization of hydroxyquinolines: (a) Reitsema, R. H. *Chem. Rev.* **1948**, *43*, 43-68. (b) Katritzky, A. R.; Lagowski, J. M. Prototropic Tautomerism of Heteroaromatic Compounds: II. Six-Membered Rings. in *Advances in Heterocyclic Chemistry, vol. 1*; Katritzky, A. R.; Ed.; Academic Press, Inc.: New York, 1963, pp. 339-437. (c) Mphahlele, M. J.; El-Nahas, A. M. *J. Mol. Struct.* **2004**, *688*, 129-136.

9. (a) Osawa, T.; Ohta, H.; Akimoto, K.; Harada, K.; Soga, H.; Jinno, Y. 4(1H)quinolone Derivatives. Eur. Patent 0 343 574, 1994. (b) Huang, L.-J.; Hsieh, M.-C.; Teng, C.-M.; Lee, K.-H.; Kuo, S.-C. *Bio. Med. Chem.* **1998**, *6*, 1657-1662. (c) Takami, H.; Kishibayashi, N.; Ishii, A.; Kumazawa, T. *Bio. Med. Chem.* **1998**, *6*, 2441-2448. (d) Lee, H.-Z.; Lin, W.-C.; Yeh, F.-T.; Wu,

C.-H. *Eur. J. Pharmacol.* **1998**, *354*, 205-213. (e) Jackson, S. P.; Robertson, A. D.; Kenche, V.; Thompson, P.; Prabaharan, H.; Anderson, K.; Abbott, B.; Goncalves, I.; Nesbitt, W.; Schoenwaelder, S.; Saylik, D. Inhibition of Phosphoinostide 3-Kinase Beta. PCT Int. Patent WO 2004/016607, 2004. (f) Llinàs-Brunet, M.; Bailey, M. D.; Ghiro, E.; Gorys, V.; Halmos, T.; Poirier, M.; Rancourt, J.; Goudreau, N. *J. Med. Chem.* **2004**, *47*, 6584-6594. (g) Wu, F. X. H.; Nakajima, S.; Or, Y. S.; Lu, Z.-H.; Sun, Y.; Miao, Z.; Wang, Z. Aza-Peptide Macrocyclic Hepatitis C Serine Protease Inhibitors. PCT Int. Patent WO 2005/010029, 2005. (h) Pal, M.; Khanna, I.; Subramanian, V.; Padakanti, S.; Pillarisetti, S. Heterocyclic and Bicyclic Compounds, Compositions and Methods. PCT Int. Patent WO 2006/058201, 2006. (i) Frutos, R. P.; Haddad, N.; Houpis, I. N.; Johnson, M.; Smith-Keenan, L. L.; Fuchs, V.; Yee, N. K.; Farina, V.; Faucher, A.-M.; Brochu, C.; Haché, B.; Duceppe, J.-S.; Beaulieu, P. *Synthesis* **2006**, *15*, 2563-2567.

10. Selected references on 2-aryl-4-quinolones as antitumor agents: (a) Kuo, S.-C.; Lee, H.-Z.; Juang, J.-P.; Lin, Y.-T.; Wu, T.-S.; Chang, J.- J.; Lednicer, D.; Paull, K. D.; Lin, C. M.; Hamel, E.; Lee, K.-H. *J. Med. Chem.* **1993**, *36*, 1146-1156. (b) Li, L.; Wang, H.-K.; Kuo, S.-C.; Wu, T.-S.; Lednicer, D.; Lin, C. M.; Hamel, E.; Lee, K.-H. *J. Med. Chem.* **1994**, *37*, 1126-1135. (c) Li, L.; Wang, H.-K.; Kuo, S.-C.; Wu, T.-S.; Mauger, A.; Lin, C. M.; Hamel, E.; Lee, K.-H. *J. Med. Chem.* **1994**, *37*, 3400-3407. (d) Sui, Z.; Nguyen, V. N.; Altom, J.; Fernandez, J.; Hilliard, J. J.; Bernstein, J. I.; Barrett, J. F.; Ohemeng, K. A.; *Eur. J. Med. Chem.* **1999**, *34*, 381-387. (e) Xia, Y.; Yang, Z.-Y.; Xia, P.; Hackl, T.; Hamel, E.; Mauger, A.; Wu, J.-H.; Lee, K.-H. *J. Med. Chem.* **2001**, *44*, 3932-3936. (f) Hadjeri, M.; Peiller, E.-L.; Beney, C.; Deka, N.; Lawson, M. A.; Dumontet, C.; Boumendjel, A. *J. Med. Chem.* **2004**, *47*, 4964-4970. (g) Hradil, P.; Krejcí, P.; Hlavác, J.; Wiedermannová, I.; Lycka, A.; Bertolasi, V. *J. Heterocyclic Chem.* **2004**, *41*, 375-379. (h) Lai, Y.-Y.; Hung, L.-J.; Lee, K.-H.; Xiao, Z.; Bastow, K. F.; Yamori, T.; Kuo, S.-C. *Bioorg. Med. Chem.* **2005**, *13*, 265-275. (i) Ferlin, M. G.; Chiarelotto, G.; Gasparotto, V.; Via, L. D.; Pezzi, V.; Barzon, L.; Palu, G.; Castagliuolo, I. *J. Med. Chem.* **2005**, *48*, 3417-3427. (j) Gasparotto, V.; Castagliuolo, I.; Chiarelotto, G.; Pezzi, V.; Montanaro, D.; Brun, P.; Palu, G.; Viola, G.; Ferlin, M. G. *J. Med. Chem.* **2006**, *49*, 1910-1915.

11. (a) Li, J. J. Conrad-Limpach Reaction in *Name Reactions: A Collection of Detailed Reaction Mechanisms, 2nd ed.*; Springer-Verlag: Berlin, 2003; p 81. (b) Niementowski, S. *Ber. Dtsch. Chem. Ges.* **1894**, *27*, 1394-1403.

12. (a) Staskun, B.; Israelstam, S. S. *J. Org. Chem.* **1961**, *26*, 3191-3193. (b) Giardina, G. A. M.; Sarau, H. M.; Farina, C.; Medhurst, A. D.; Grugni, M.; Rveglia, L. F.; Schmidt, D. B.; Rigolio, R.; Luttmann, M.; Vecchietti, V.; Hay, D. W. P. *J. Med. Chem.* **1997**, *40*, 1794-1807.

13. (a) Dorow, R. L.; Herrinton, P. M.; Hohler, R. A.; Maloney, M. T.; Mauragis, M. A.; McGhee, W. E.; Moeslein, J. A.; Strohbach, J. W.; Veley, M. F. *Org. Process Res. Dev.* **2006**, *10*, 493-499. (b) Zewge, D.; Chem, C.-Y.; Deer, C.; Dormer, P. G.; Hughes, D. L. *J. Org. Chem.* **2007**, ASAP.

14. (a) Fuson, R. C.; Burness, D. M. *J. Am. Chem. Soc.* **1946**, *68*, 1270-1272. (b) Ogata, Y.; Kawasaki, A.; Tsujimura, K. *Tetrahedron* **1971**, *27*, 2765-2770.

15. Son, J. K.; Kim, S. I.; Jahng, Y. *Heterocycles* **2001**, *55*, 1981-1986.

16. (a) Tang, J.; Huang, X. *Synth. Commun.* **2003**, *33*, 3953-3960. (b) Beifuss, U.; Ledderhose, S. *Synlett* **1997**, 313-315. (c) Strekowski, L.; Wydra, R. L.; Cegla, M. T.; Czarny, A.; Harden, D. B.; Patterson, S. E.; Battiste, M. A.; Coxon, J. M. *J. Org. Chem.* **1990**, *55*, 4777-4779.

17. (a) Kalinin, V. N.; Shostakovsky, M. V.; Ponomaryov, A. B. *Tetrahedron Lett.* **1992**, *33*, 373-376. (b) Torii, S.; Okumoto, H.; Xu, L. H.; Sadakane, M.; Shostakovsky, M. V.; Ponomaryov, A. B.; Kalinin, V. N. *Tetrahedron* **1993**, *49*, 6773-6784.

18. Fürstner, A.; Hupperts, A.; Ptock, A.; Janssen, E. *J. Org. Chem.* **1994**, *59*, 5215-5229.

19. Tollari, S.; Cenini, S.; Ragaini, F.; Cassar, L. *J. Chem. Soc., Chem. Commun.* **1994**, 1741-1742.

20. (a) Camps, R. *Chem. Ber.* **1899**, *32*, 3228-3234. (b) Pflum, D. A. Camps Quinolinol Synthesis. in *Name Reactions in Heterocyclic Chemistry*; Li, J. J., Corey, E. J., Eds.; Wiley-Interscience: Hoboken, NJ, 2005; pp 386-389.

21. (a) Clémence, F.; Le Martret, O.; Collard, J. *J. Heterocyclic Chem.* **1984**, *21*, 1345-1353. (b) Dubroeucq, M.-C.; Bains, E. L.; Paris, J.-M.; Marne, V. S.; Renault, C. Quinolyloxyacetamides. U.S. Patent 5017576, 1991. (c) Hadjeri, M.; Mariotte, A.-M.; Boumendjel, A. *Chem. Pharm. Bull.* **2001**, *49*, 1352-1355. (d) Ding, D.; Li, X.; Wang, X.; Du, Y.; Shen, J. *Tetrahedron Lett.* **2006**, *47*, 6997-6999.

22. Fürstner, A.; Jumbam, D. N. *Tetrahedron* **1992**, *48*, 5991-6010.

23. For a review: Fürstner, A.; Bogdanovic, B. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2442-2469.

24. (a) Klapars, A.; Antilla, J. C.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7727-7729. (b) Klapars, A.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 7421-7428. (c) Streiter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4120-4121.

25. References indicating catalyst-free amination reactions: (a) Beller, M.; Breindl, C.; Riermeier, T. H.; Tillack, A. *J. Org. Chem.* **2001**, *66*, 1403-1412. (b) Shi, L.; Wang, M.; Fan, C.-A.; Zhang, F.-M.; Tu, Y.-Q. *Org. Lett.* **2003**, *5*, 3515-3517. (c) De Lange, B.; Lambers-Verstappen, M. H.; Schmieder-van de Vondervoort, L.; Sereinig, N.; de Rijk, R.; de Vries, A. H. M.; de Vries, J. G. *Synlett* **2006**, *18*, 3105-3109.

26. (a) Lindley, J. *Tetrahedron* **1984**, *40*, 1433-1456. (b) Nicolaou, K. C.; Boddy, C. N. C.; Natarajan, S.; Yue, T.-Y.; Li, H.; Bräse, Ramanjulu, J. M. *J. Am. Chem. Soc.* **1997**, *119*, 3421-3422. (c) Cai, Q.; Zou, B.; Ma, D. *Angew. Chem. Int. Ed.* **2006**, *45*, 1276-1279.

27. Aryl iodides were found to be better starting materials for the more difficult Cu-catalyzed amidation reactions of 2-halophenones with alkyl amides, which are not discussed in this publication due to their problematic reactivity in the Camps cyclization.

28. K_3PO_4 was employed for reactions with 2-iodophenones due to the superiority of K_3PO_4 for the facilitation of Cu-catalyzed amidation with aryl iodides reported in our earlier work (Reference 24b).

29. (a) Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124,* 14844-14845. (b) Antilla, J. C.; Baskin, J. M.; Barder, T. E.; Buchwald, S. L. *J. Org. Chem.* **2004**, *69*, 5578-5587.

30. For example, *N*-(2-acetyl-phenyl)-*n*-hexanamide (**32**) cyclized to afford 25% of 4-methyl-3-*n*-butyl-2-quinolone (**33**) and 49% of 2-*n*-pentyl-4-quinolone (**34**).

31. (a) Gribble, G. W.; Bousquet, F. P. *Tetrahedron* **1971**, *27*, 3785-3794. (b) Mudry, C. A.; Frasca, A. R. *Tetrahedron* **1973**, *29*, 603-613.

32. Grammaticakis, P. *Bull. Soc. Chim. Fr.* **1953**, 93-99.

33. Shirakawa, N.; Tomioka, H.; Koizumi, M.; Takeuchi, M.; Sugiyama, H.; Okada, M.; Yoshimoto, M.; Iwane, Y.; Murakami, Y. Isonicotinanilide Derivatives, Process for Preparing the Same and Plant Growth Regulator Containing the Same. Eur. Pat. Appl. 48998, 1982.

34. Soloshonok, V. A.; Cai, C.; Hruby, V. J.; Meervelt, L. V.; Yamazaki, T. *J. Org. Chem.* **2000**, *65*, 6688-6696.

35. Amino phénones, leur preparation et leur utilization en thérapeutique. Fr. Patent 2121391, 1972.

36. Kövendi, A.; Kircz, M. *Chem. Ber.* **1965**, *98*, 1049-1059.

37. Möhrle, H.; Gerloff, J. *Arch. Pharm.* **1979**, *312*, 219-230.

38. (a) Troger, J.; Dunker, E. *J. Prakt. Chem.* **1925**, *109*, 88-123. (b) Jayabalan, L.; Shanmugam, P. *Synthesis* **1991**, 217-220.

39. (a) Gottstein, W. J.; Roberts, H.; Wells, I. C.; Cheney, L. C. J. Org. Chem. 1964, 29, 3065-3067. (b) Cheney, L. C.; Gottstein, W. J. Cinchoninic Acids and Use in Process for Quinolinols. US Patent 3301859, 1967.

40. Shanmugam, P.; Lakshminarayana, P. *Tet. Lett.* **1971**, *25*, 2323-2324.

41. Searles, A. L.; Lindwall, H. G. *J. Am. Chem. Soc.* **1946**, *68*, 988-990.

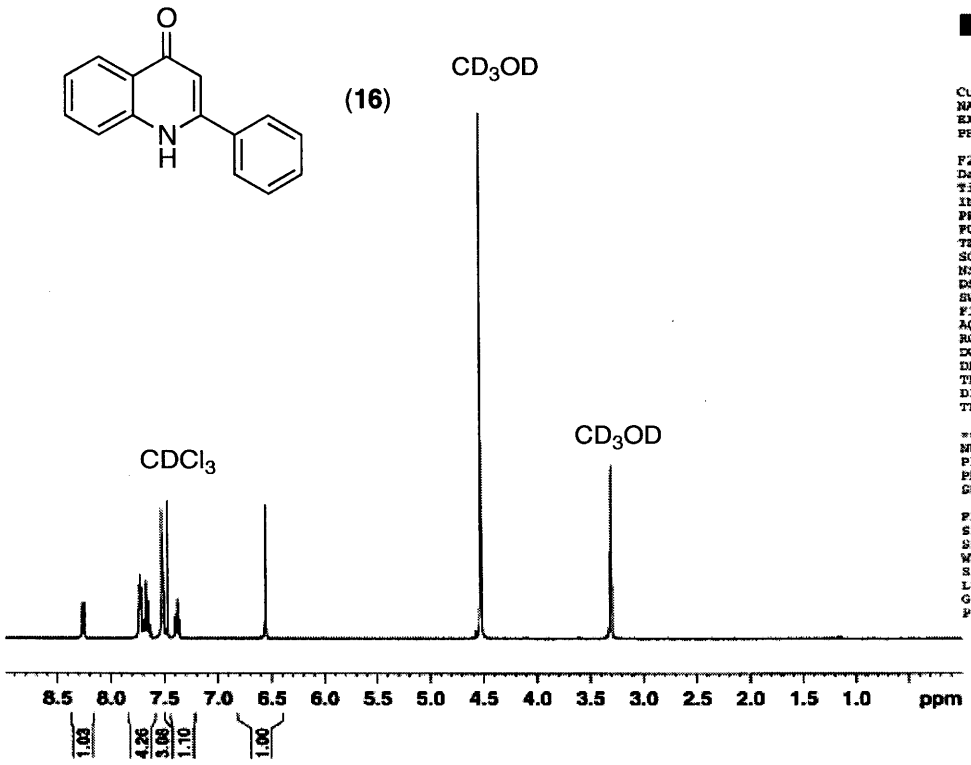
42. Back, T. G.; Parvez, M.; Wulff, J. E. *J. Org. Chem.* **2003**, *68*, 2223-2233.

43. (a) Lee, J.; Ha, J. D.; Cha, J. K. *J. Am. Chem. Soc.* **1997**, *119*, 8127-8128. (b) Ishikura, M.; Ida, W.; Yanada, K. *Tetrahedron* **2006**, *62*, 1015-1024.

44. Fleming, I.; Woolias, M. *J. Chem. Soc., Perkin Trans. 1* **1979**, *3*, 829-837.

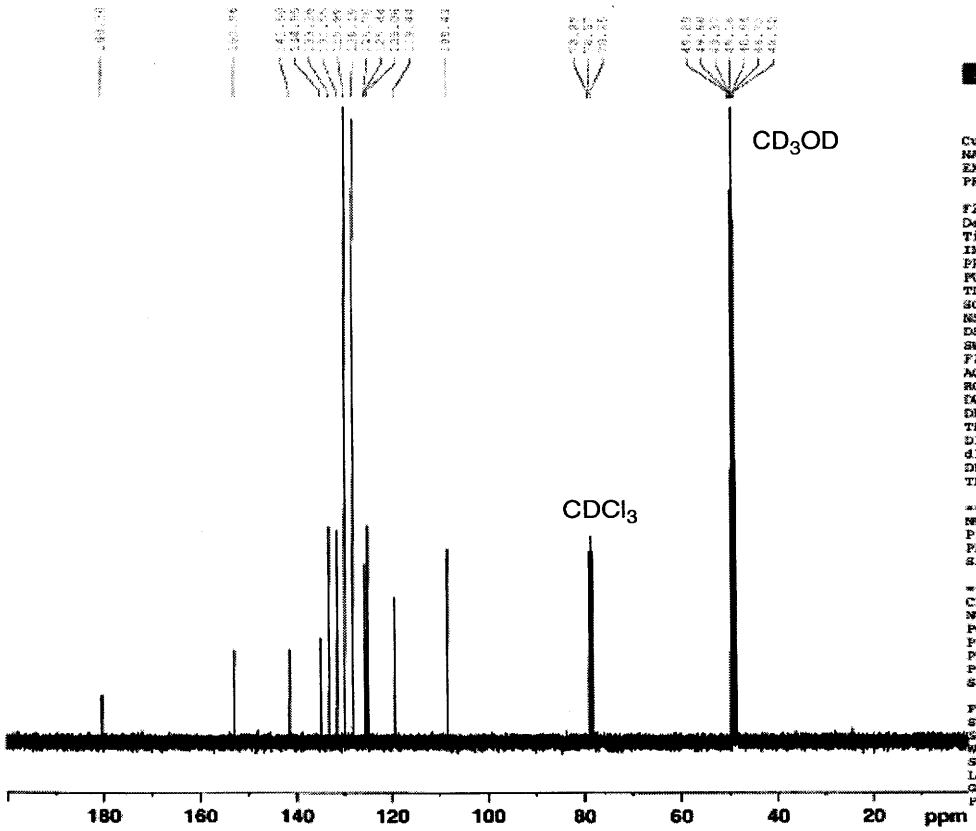
45. Procedure for the synthesis of 2-bromo-5-methoxypropiophenone was modified from the procedure for the synthesis of *o*-bromopropiophenone in Wang, S.; Morrow, G. W.; Swenton, J. S. *J. Org. Chem.* **1989**, *54*, 5364-5371.

V. Appendix A: Selected NMR Spectra



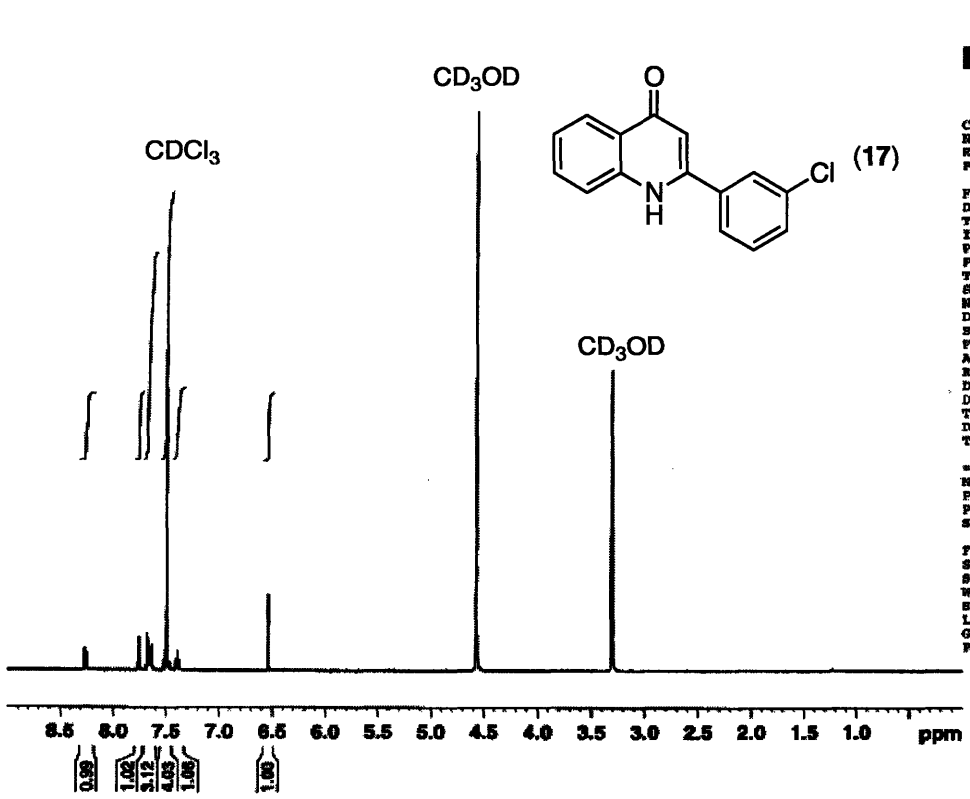
BRUKER

```
Current Data Parameters
NAME                  CJ-2-20
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20061201
Time                   11.05
INSTRUM                spect
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    228.1
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     15.07 usec
PL1                     0.00 dB
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF             400.1311021 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```



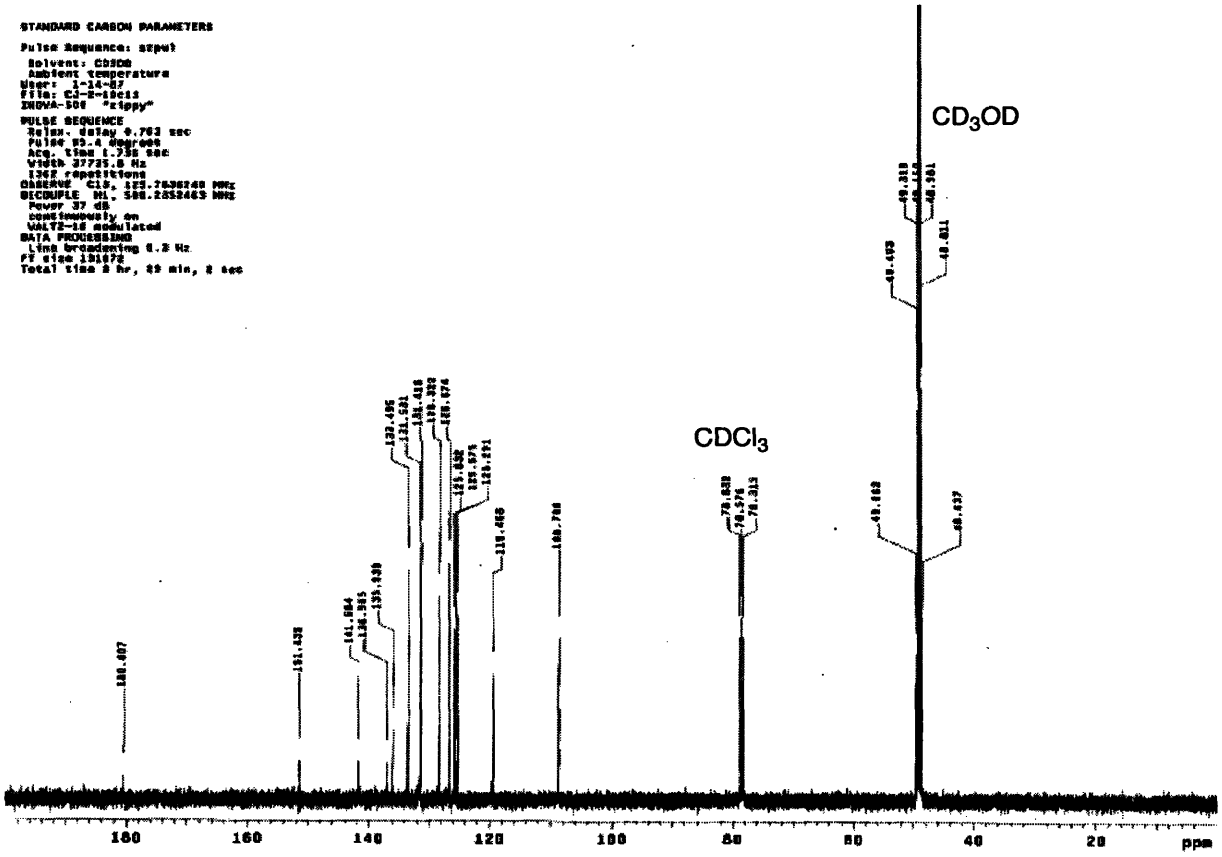
BRUKER

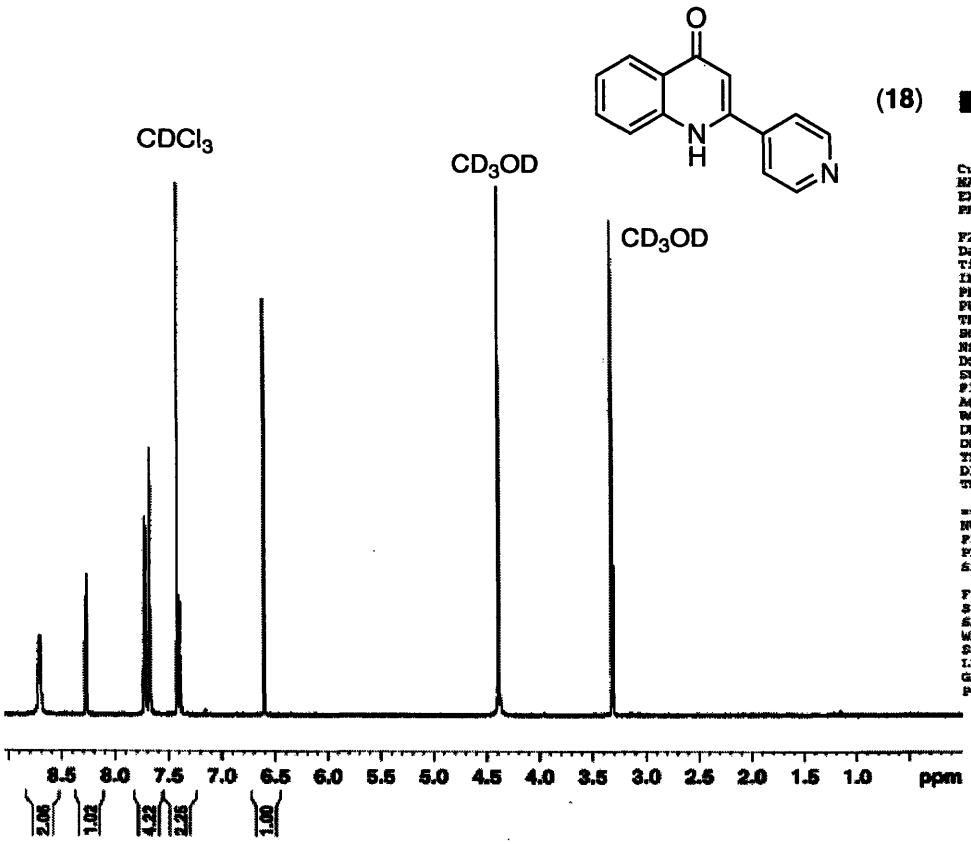
```
Current Data Parameters
NAME          CJ-2-20c13mecd
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070316
Time                   12.28
INSTRUM                spect
PROBHD    5 mm BBO BB-1H
PULPROG             zgpg30
TD                    65536
SOLVENT               MeOD
NS                     1597
DS                        2
SWH               23980.814 Hz
FIDRES            0.365918 Hz
AQ                1.3664756 sec
RG                     8152
DW                   20.850 usec
DE                    6.00 usec
TE                   294.2 K
D1                2.00000000 sec
d11               0.03000000 sec
DELTA             1.89999998 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                  90.00 usec
PL2                    -1.00 dB
PL12                   14.52 dB
PL13                   18.00 dB
SFO2           400.1316005 MHz

F2 - Processing parameters
SI                    65536
SF             100.6126744 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.40
```



BRUKER

```
Current Data Parameters
NAME                  CJ-2-19
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20061130
Time                   10.30
INSTRUM                spect
PROBHD   5 mm QNP 1H/13
PULPROG                zg30
TD                    65536
SOLVENT                MeOD
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    645.1
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      1H
P1                     14.00 usec
PL1                     0.00 dB
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                        65536
SF             400.1300083 MHz
WDW                         no
SSB                          0
LB                        0.00 Hz
GB                           0
PC                        1.00
```





(18)

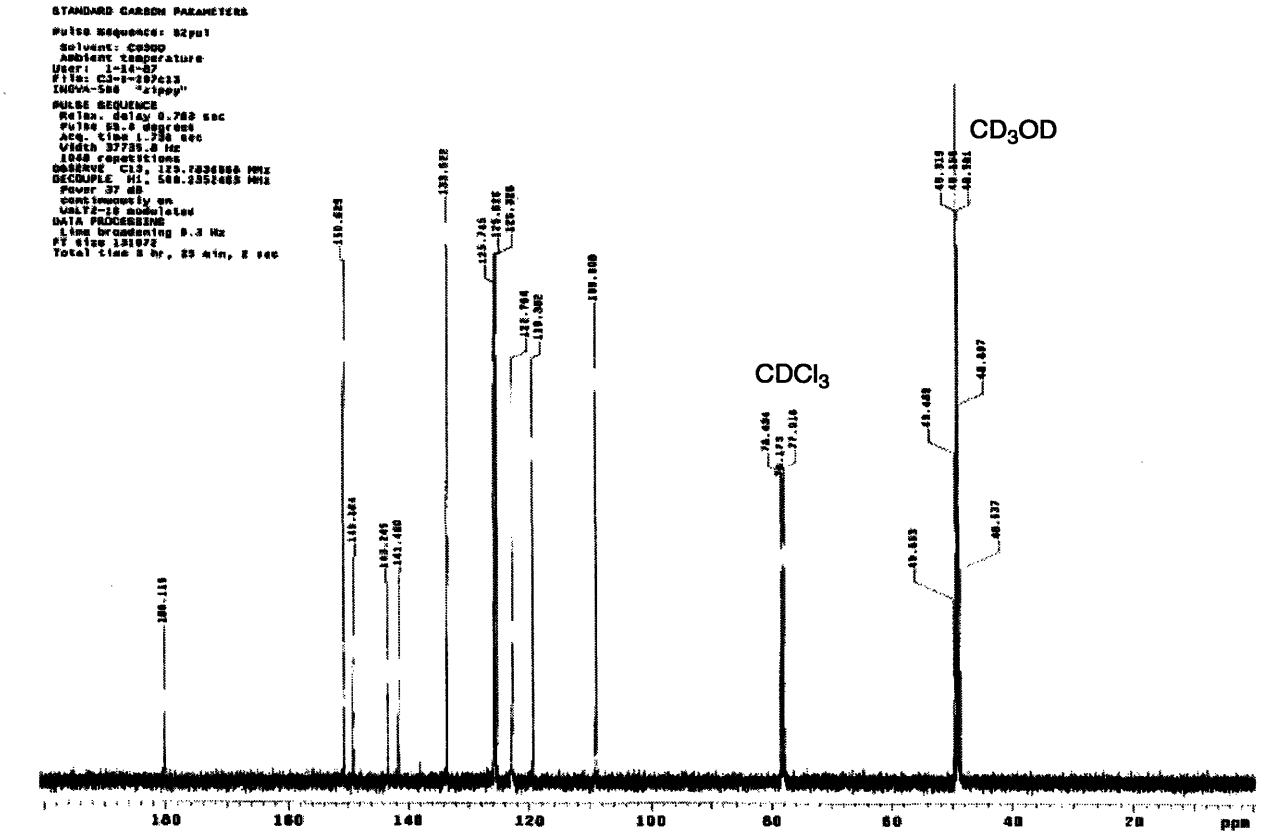
BRUKER

Current Data Parameters
NAME CJ-1-297
EXPNO 1
PROCNO 1

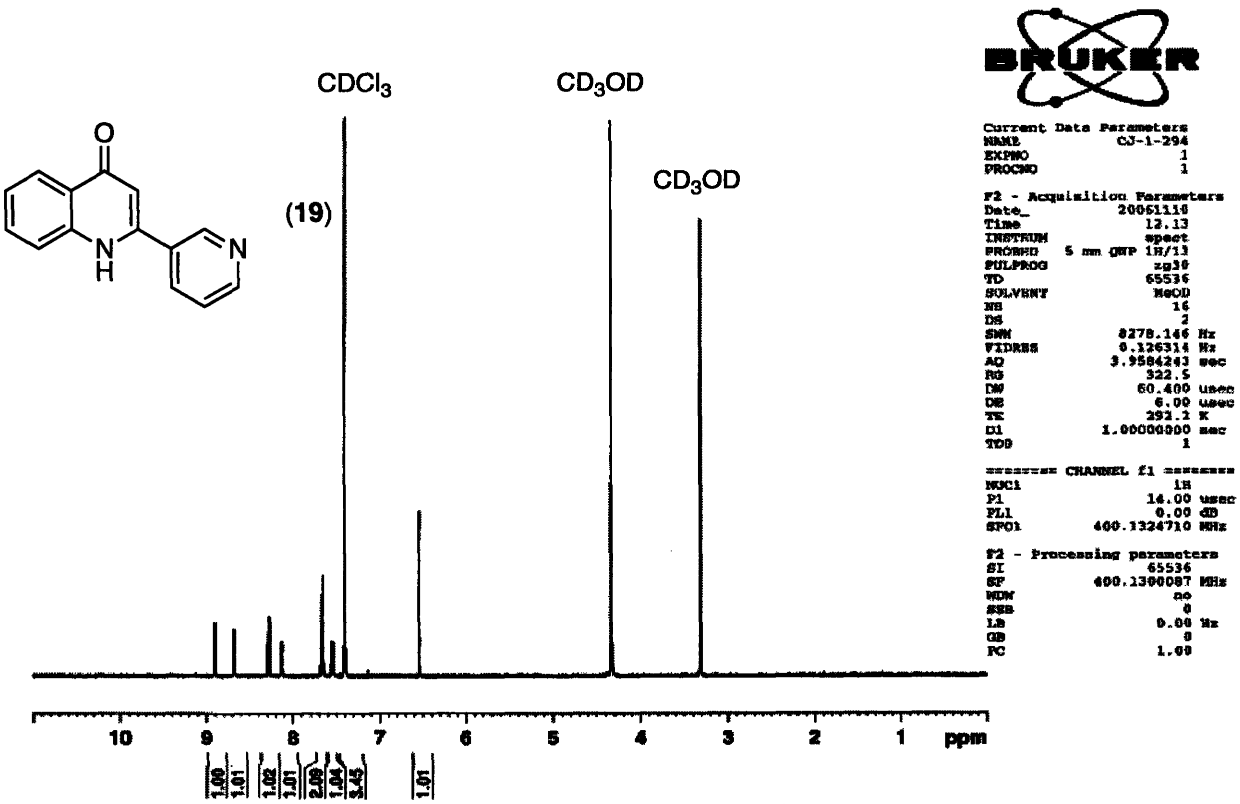
F2 - Acquisition Parameters
Date_ 20061115
Time 11.17
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT MeOD
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 162
DW 60.400 usec
DE 6.00 usec
TE 292.2 K
D1 1.00000000 sec
TD0 1

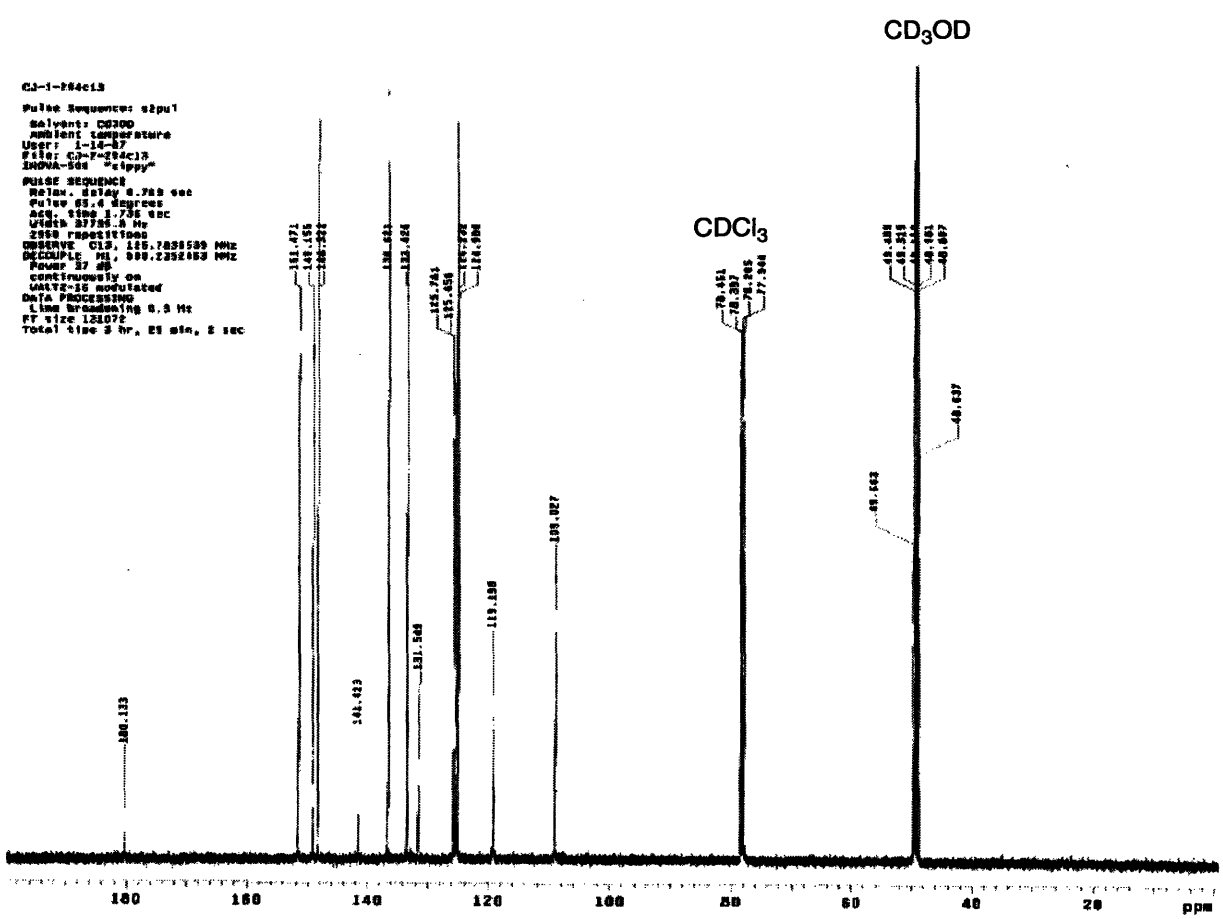
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
SFO1 400.1324710 MHz

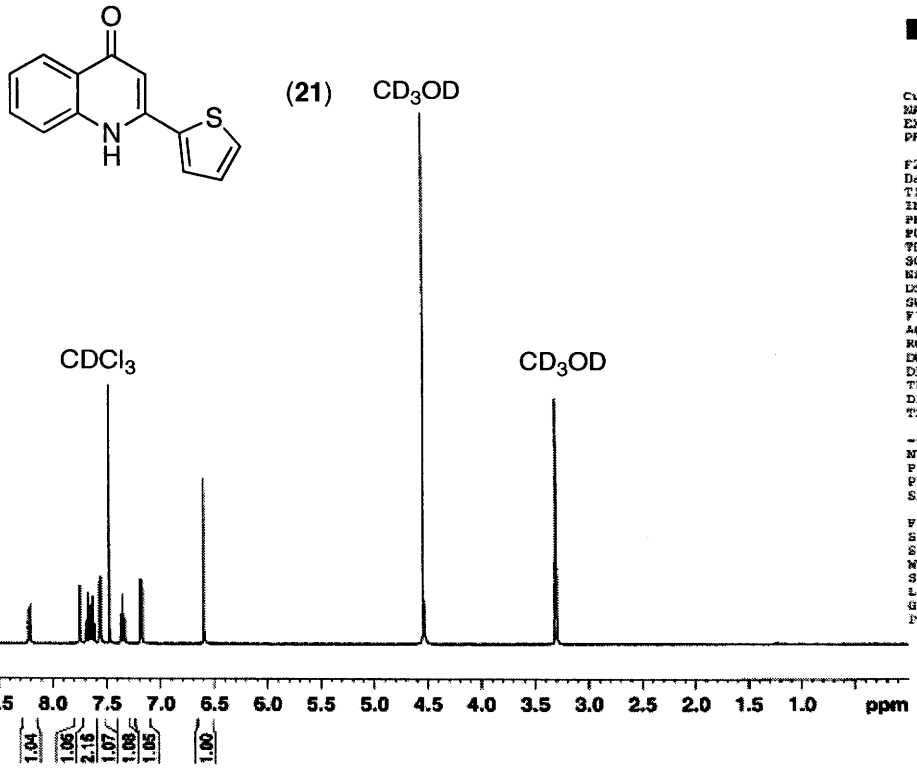
F2 - Processing parameters
SI 65536
SF 400.1300088 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00



(19)

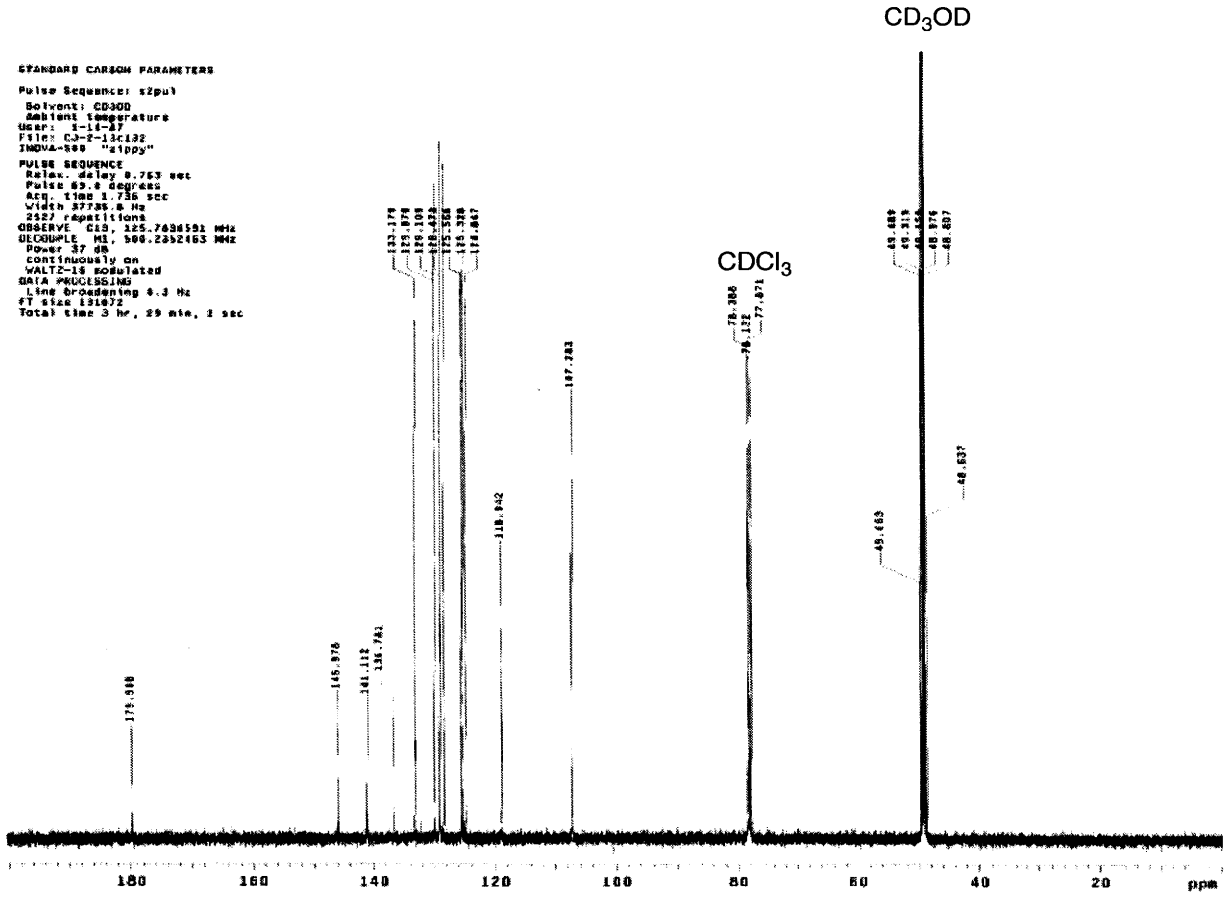

CDCl3
CD3OD
CD3OD
Current Data Parameters
NAME CJ-1-294
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20061116
TD 65536
SOLVENT MeOD
NS 16
DS 2
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 65536
SF 400.1300087 MHz
ppm


CD3OD
CDCl3
ppm

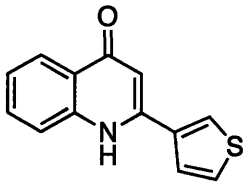


BRUKER

```
Current Data Parameters
NAME                  CJ-2-13-2
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_              20061203
Time                      14.31
INSTRUM                   spect
PROBHD     5 mm CNP 1H/13
PULPROG                   zg30
TD                       65536
SOLVENT                   MeOD
NS                           16
DS                            2
SWH                6278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                       456.1
DW                    60.400 usec
DE                     6.00 usec
TE                      293.2 K
D1                 1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                         1H
P1                        14.00 usec
PL1                        3.00 dB
SFO1             400.1329710 MHz

F2 - Processing parameters
SI                       65536
SF               400.1300093 MHz
WDW                         no
SSB                          0
LB                        0.30 Hz
GB                           0
PC                        1.00
```

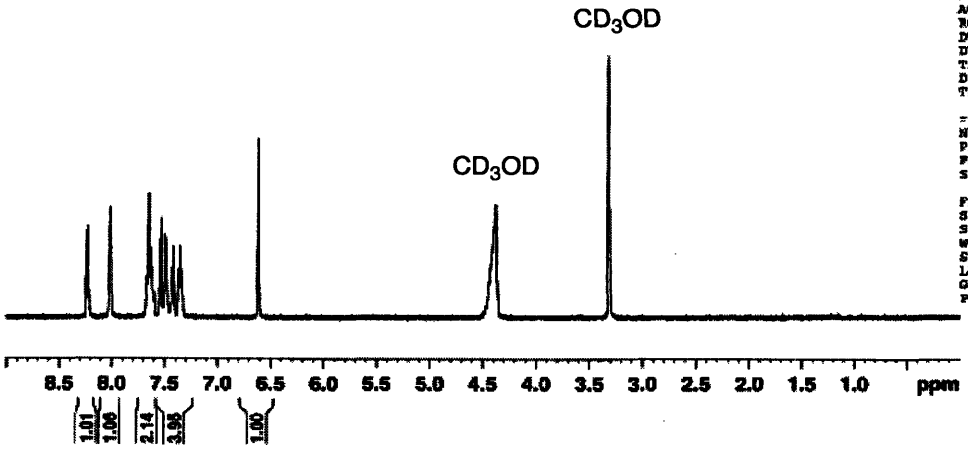


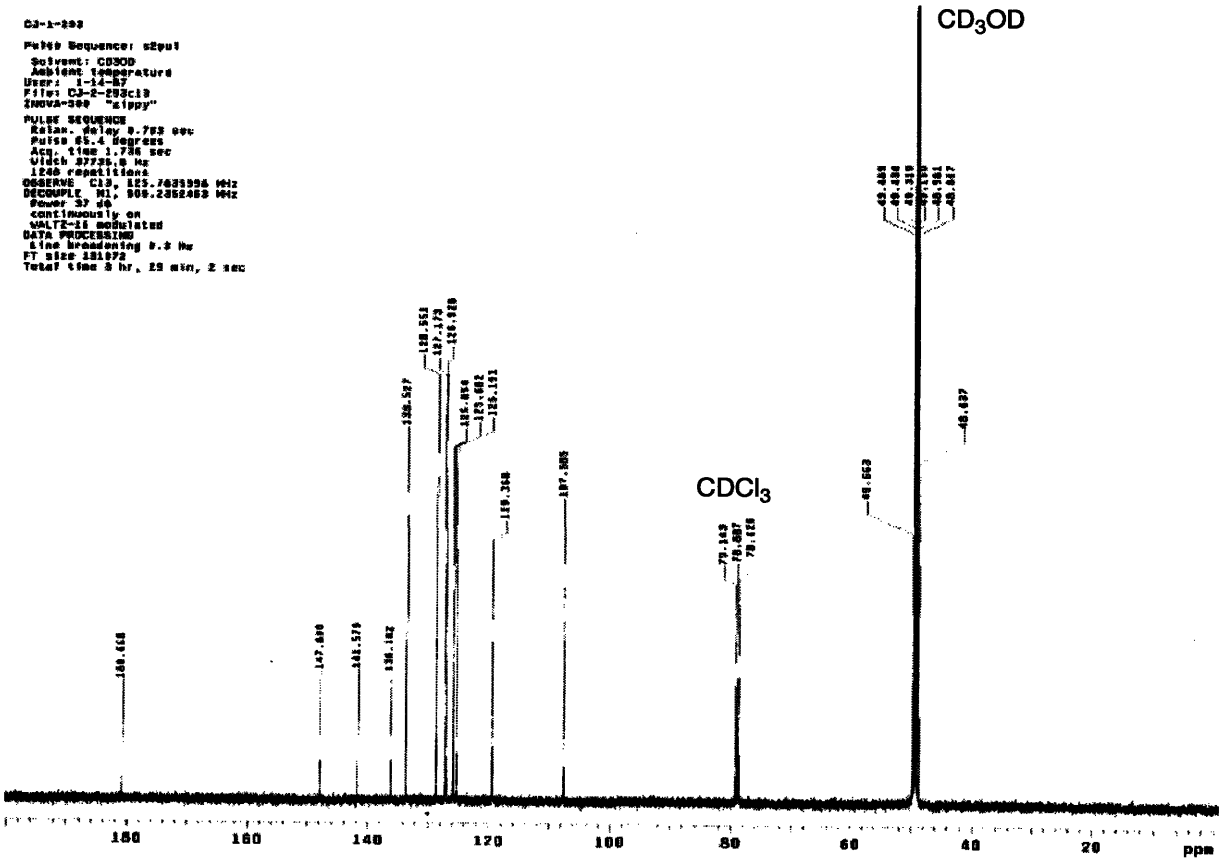

```
STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul
 Solvent: CD3OD
 Ambient temperature
User:   S-16-87
File: CJ-2-13c132
INOVA-500  "z1ppy"

PULSE SEQUENCE
 Relax. delay 0.753 sec
 Pulse 63.8 degrees
 Acq. time 1.736 sec
 Width 37735.8 Hz
 2327 repetitions
OBSERVE   C13, 125.7836591 MHz
DECOUPLE  H1, 500.2352483 MHz
 Power 37 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 0.3 Hz
FT size 131072
Total time 3 hr, 29 min, 2 sec
```

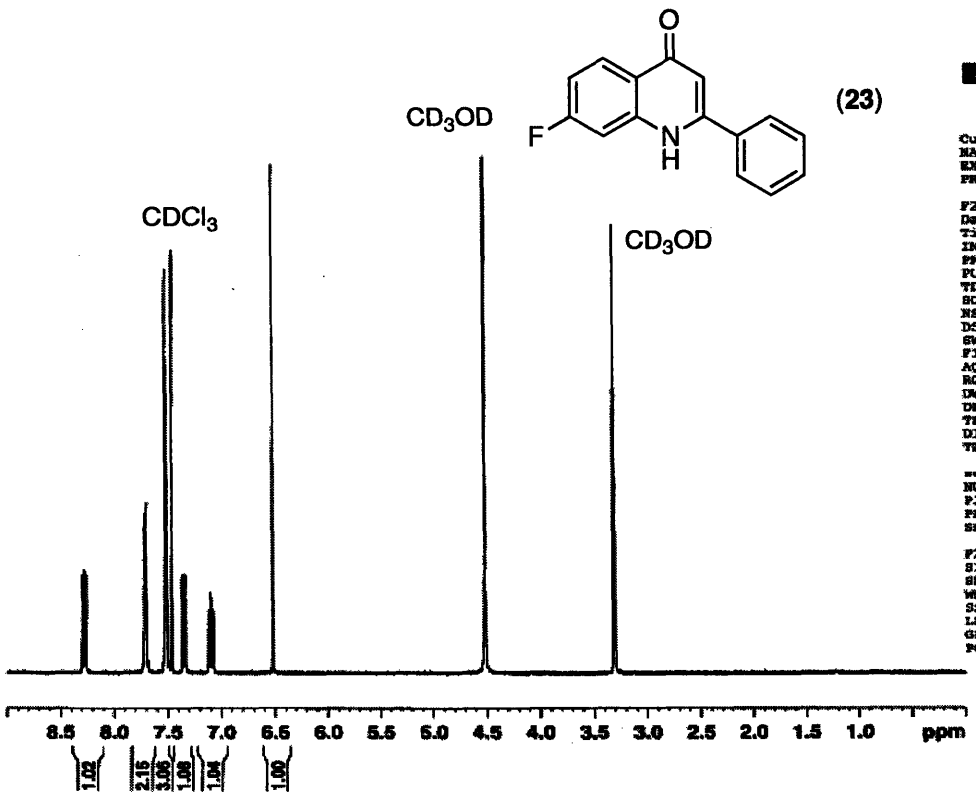


(22)

```
Current Data Parameters
NAME                  CJ-1-293
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20061115
Time                   11.04
INSTRUM                spect
PROBHD     5 mm QNP 1H/13
PULPROG                zg30
TD                     65536
SOLVENT                MeOD
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                       57
DW                   60.400 usec
DE                    6.00 usec
TE                   292.2 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                     1H
P1                    14.00 usec
PL1                    0.00 dB
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                       65536
SF             400.1300093 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```







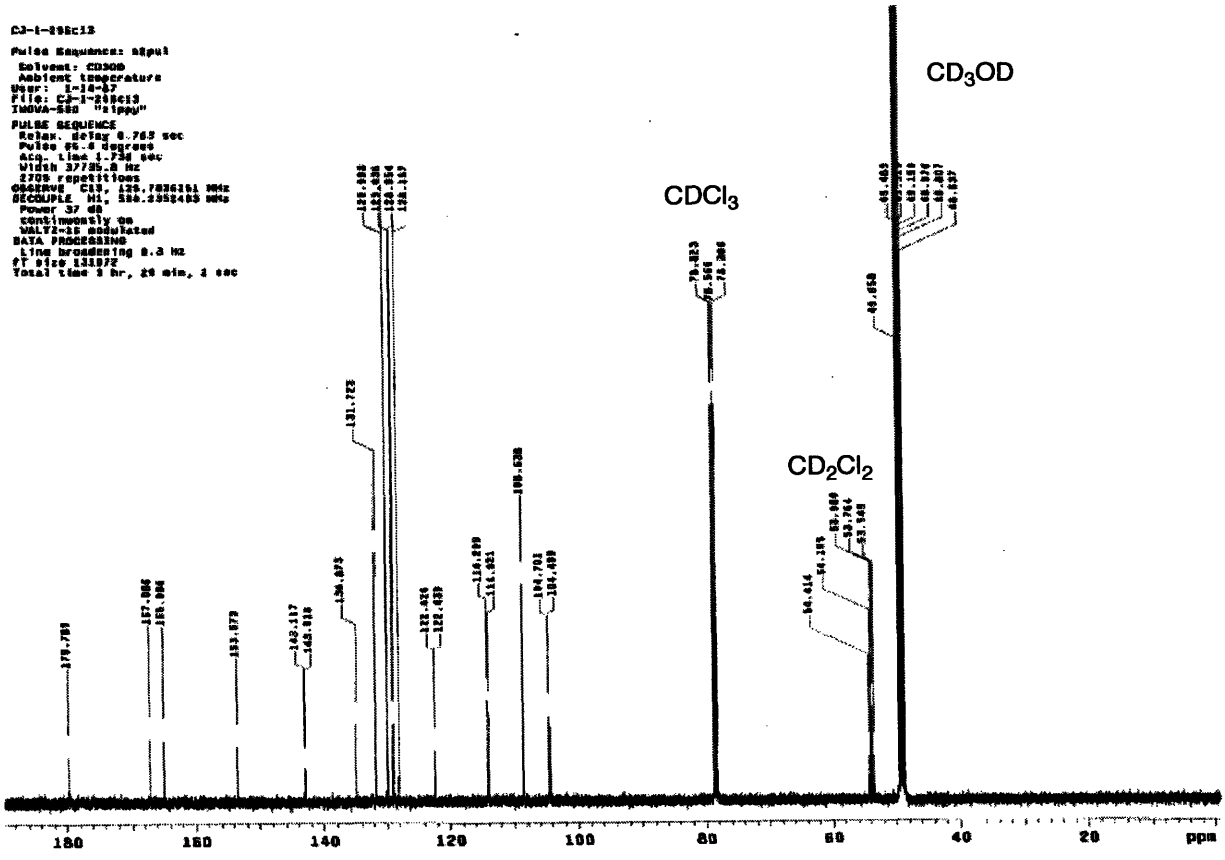
BRUKER

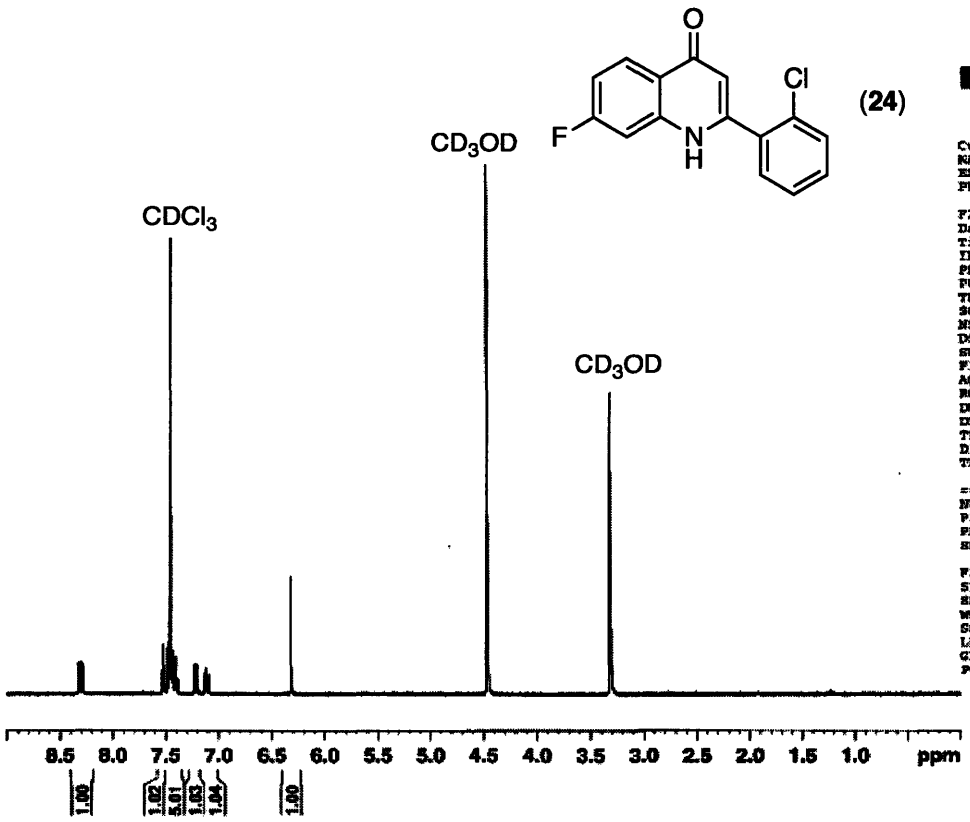
Current Data Parameters
NAME CJ-1-296
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20061115
Time 11.11
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT MeOD
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 322.5
DW 60.400 usec
DE 6.00 usec
TE 292.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
SFO1 400.1324710 MHz

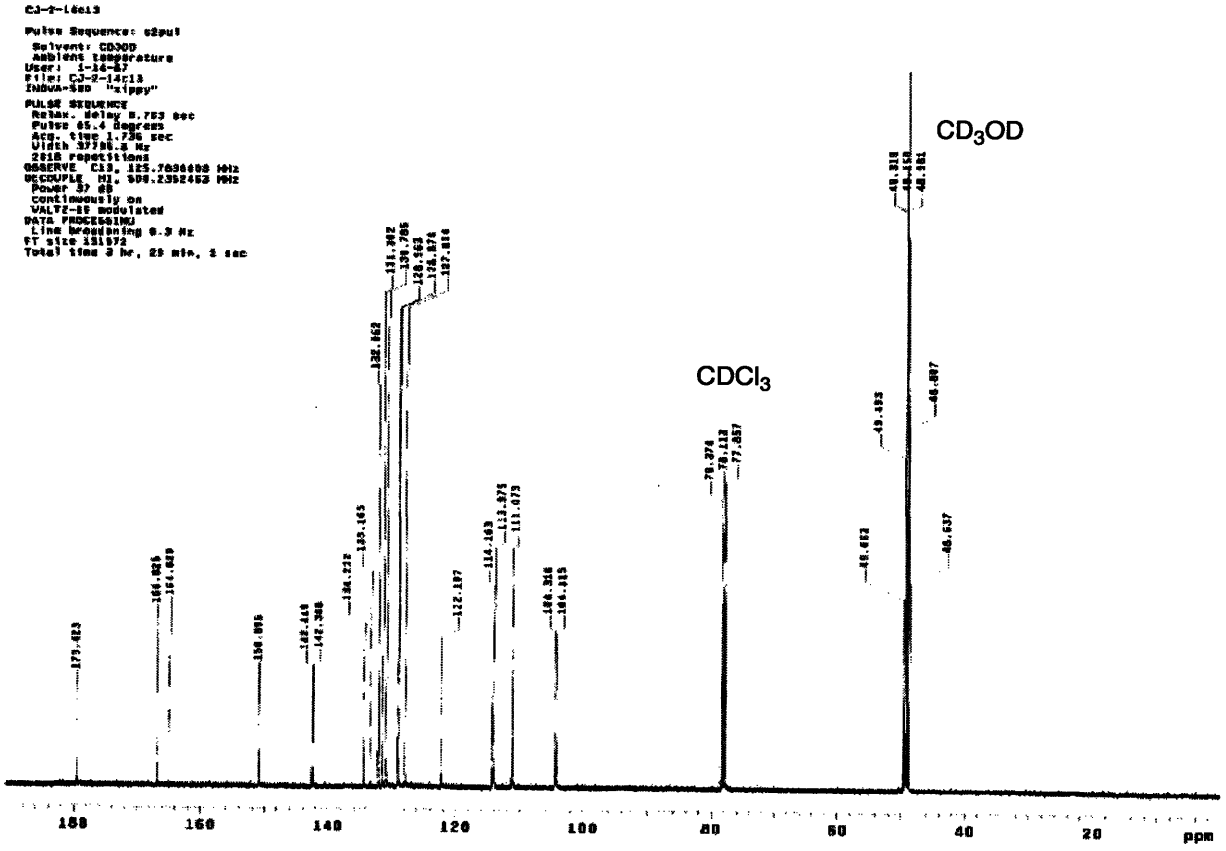
F2 - Processing parameters
SI 65536
SF 400.1300088 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

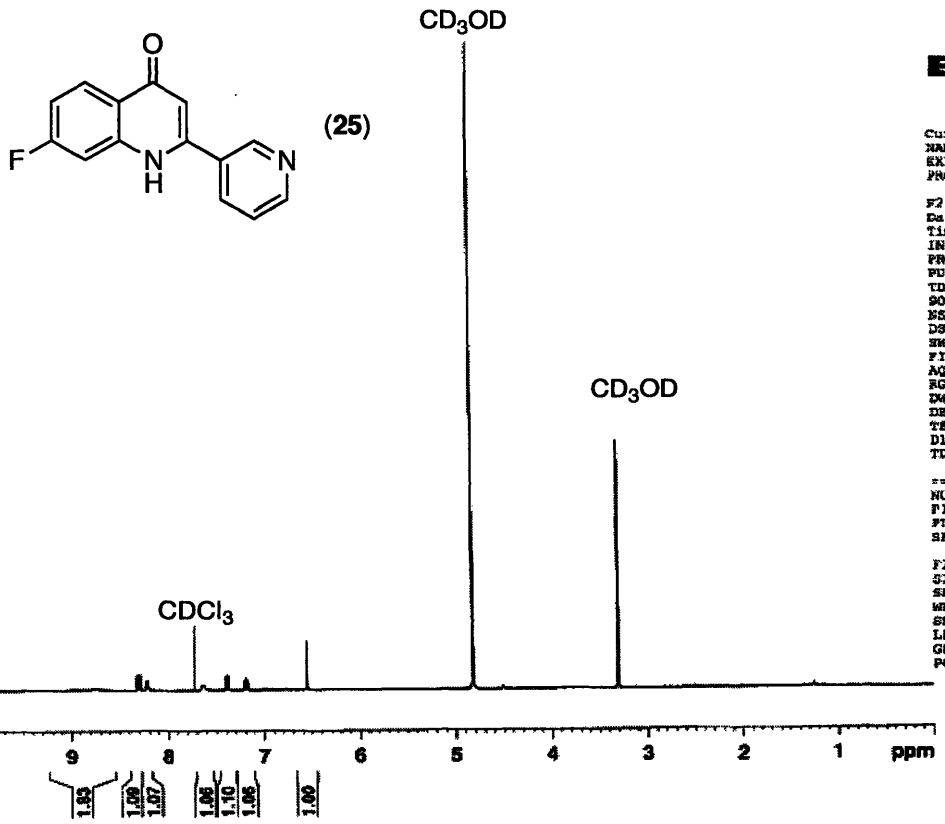




BRUKER

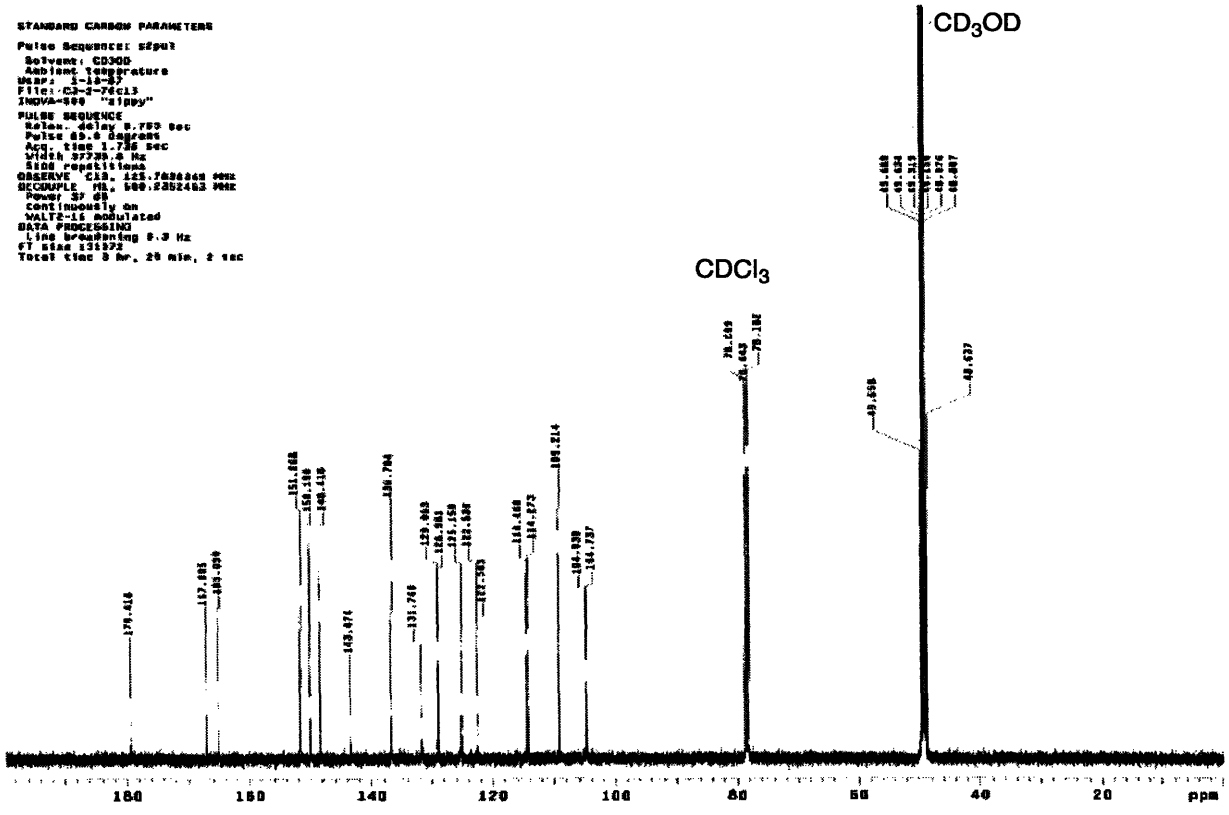
```
Current Data Parameters
NAME                  CJ-2-14
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20061122
Time                  15.10
INSTRUM               spect
PROBHD   5 mm QNP 1H/13
PULPROG               zg30
TD                   65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    574.7
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    1H
P1                   14.00 usec
PL1                   0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF            400.1315033 MHz
WDW                      EM
SSB                       0
LB                     0.60 Hz
GB                        0
PC                     1.00
```

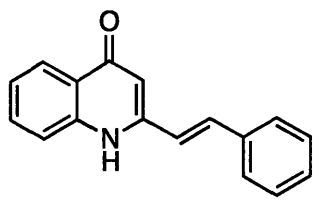




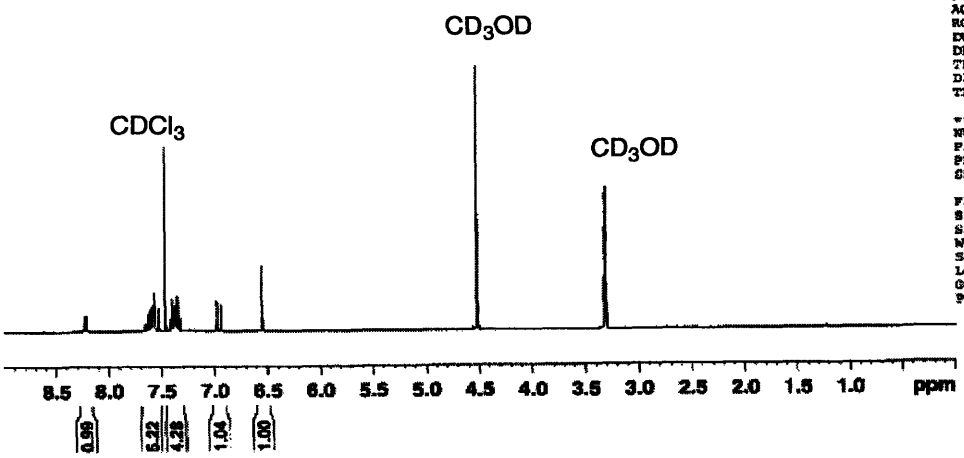
BRUKER

```
Current Data Parameters
NAME                  CJ-1-295-3
EXPNO                          1
PROCNO                         1

F2 - Acquisition Parameters
Date_               20070321
Time                      13.58
INSTRUM                   spect
PROBHD     5 mm QNP 1H/13
PULPROG                   zg30
TD                       65536
SOLVENT                   MeOD
NS                           16
DS                            2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                          362
DW                     60.400 usec
DE                      6.00 usec
TE                       293.2 K
D1                1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                         1H
P1                        14.00 usec
PL1                        0.00 dB
SFO1               400.1324710 MHz

F2 - Processing parameters
SI                       65536
SF                 400.1300099 MHz
WDW                         no
SSB                          0
LB                        0.00 Hz
GB                           0
PC                        1.00
```



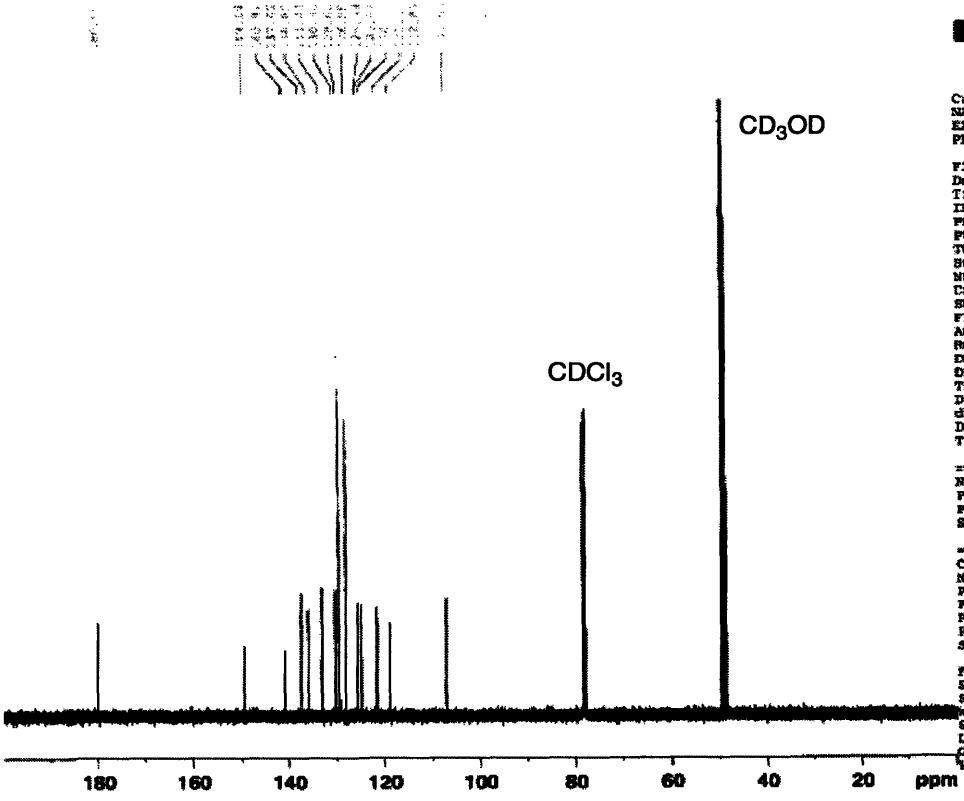


(28)



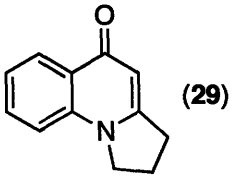
BRUKER

```
Current Data Parameters
NAME                  CJ-2-132
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20070417
Time                    16.34
INSTRUM                 spect
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                 MeOD
NS                        16
DS                         2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                     228.1
DW                    60.400 usec
DE                     6.00 usec
TE                    283.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     15.07 usec
PL1                     0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                     65536
SF            400.1300075 MHz
WDW                       no
SSB                        0
LB                      0.00 Hz
GB                         0
PC                      1.00
```

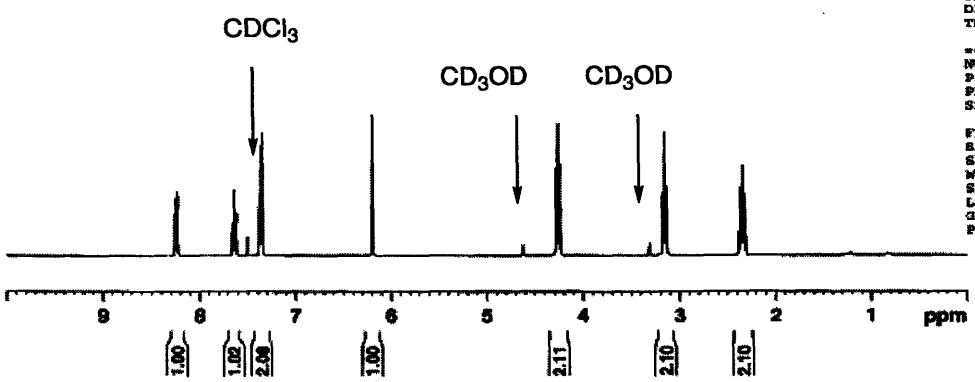


BRUKER

```
Current Data Parameters
NAME                CJ-2-133c13
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20070428
Time                    16.56
INSTRUM                 spect
PROBHD    5 mm BBO BB-1H
PULPROG                 zgpg30
TD                     65536
SOLVENT                 MeOD
NS                        946
DS                         2
SWH               23980.814 Hz
FIDRES             0.365918 Hz
AQ                 1.3664756 sec
RG                      8192
DW                    20.850 usec
DE                     6.00 usec
TE                    294.2 K
D1                 2.00000000 sec
d11                0.03000000 sec
DELTA              1.89999998 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                      8.75 usec
PL1                    -3.00 dB
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                      1H
PCPD2                  90.00 usec
PL2                    -1.00 dB
PL12                   14.52 dB
PL13                   18.00 dB
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                     65536
SF            100.6126918 MHz
WDW                       no
SSB                        0
LB                      0.00 Hz
GB                         0
PC                      1.40
```

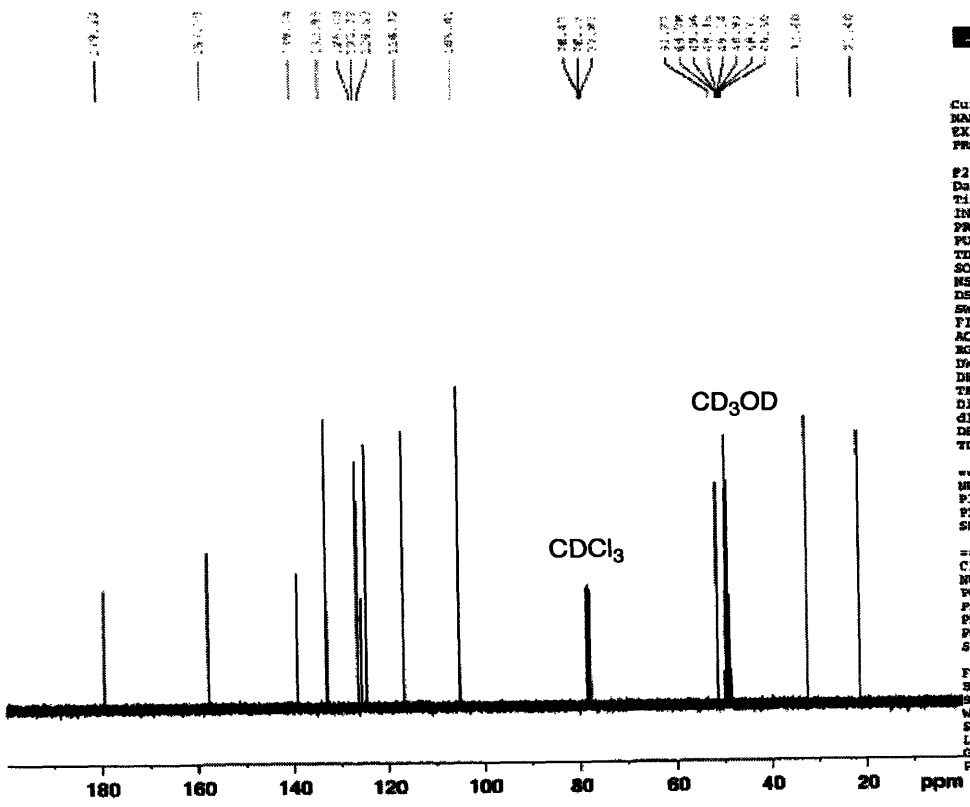


(29)



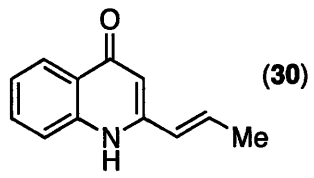
BRUKER

```
Current Data Parameters
NAME          CJ-2-104-2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20070307
Time               9.33
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG           zg30
TD                65536
SOLVENT            MeOD
NS                   16
DS                    2
SWH            8278.146 Hz
FIDRES         0.126314 Hz
AQ             3.9584243 sec
RG                  128
DW               60.400 usec
DE                6.00 usec
TE               294.2 K
D1            1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                  1H
P1                15.07 usec
PL1               0.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                65536
SF           400.1300083 MHz
WDW                  no
SSB                   0
LB                0.00 Hz
GB                    0
PC                 1.00
```



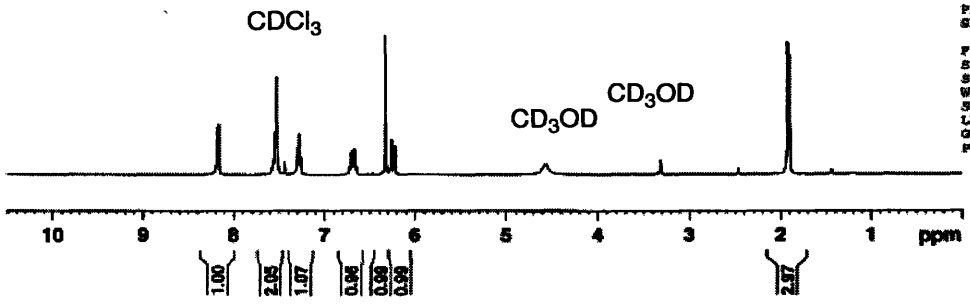
BRUKER

```
Current Data Parameters
NAME          CJ-2-104c13-2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20070309
Time               15.22
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT            MeOD
NS                  128
DS                    2
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664756 sec
RG                18390.4
DW               20.850 usec
DE                6.00 usec
TE               294.2 K
D1            2.00000000 sec
d11           0.03000000 sec
DELTA         1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                8.75 usec
PL1               -3.00 dB
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             90.00 usec
PL2               -1.00 dB
PL12              14.52 dB
PL13              18.00 dB
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                65536
SF           100.6127048 MHz
WDW                  no
SSB                   0
LB                0.00 Hz
GB                    0
PC                 1.40
```

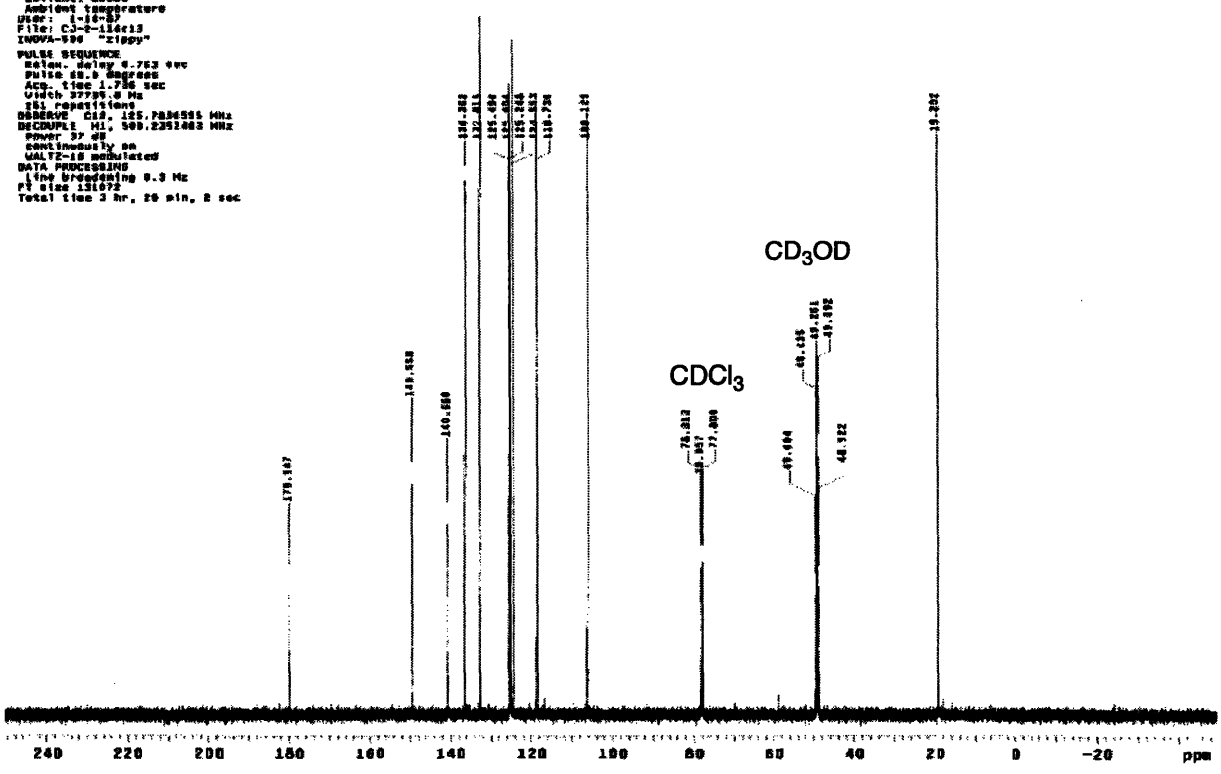


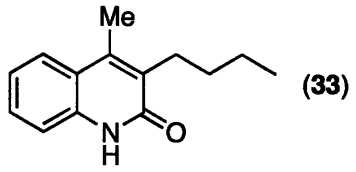
(30)


```
Current Data Parameters
NAME                  CJ-2-114-2
EXPNO                          1
PROCNO                         1

F2 - Acquisition Parameters
Date_               20070329
Time                     13.43
INSTRUM                  spect
PROBHD    5 mm BBO BB-1H
PULPROG                  zg30
TD                      65536
SOLVENT                  MeOD
NS                         16
DS                          2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                        128
DW                   60.400 usec
DE                    6.00 usec
TE                     293.2 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     15.07 usec
PL1                     0.00 dB
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                       65536
SF               400.1300082 MHz
WDW                         no
SSB                          0
LB                        0.00 Hz
GB                           0
PC                        1.00
```

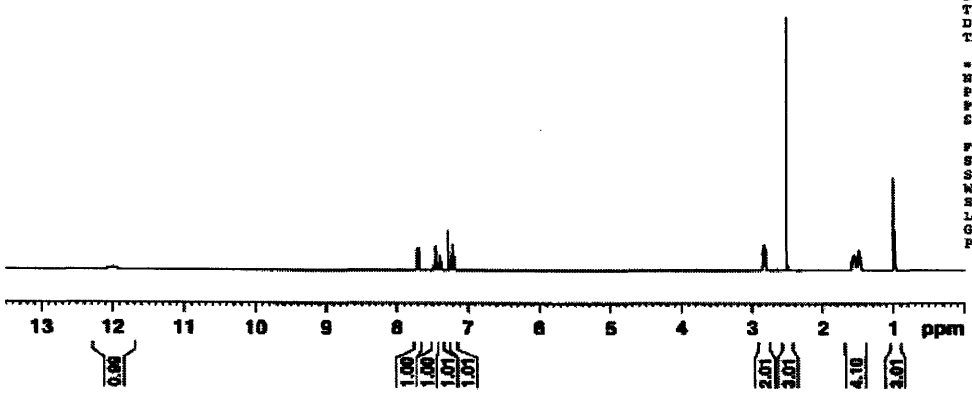



```
STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul
 Solvent: CD3OD
 Ambient temperature
User:  L-16-07
File: CJ-2-114r13
INOVA-500  "zippy"

PULSE SEQUENCE
 Relax. delay 0.763 sec
 Pulse 48.9 degrees
 Acq. time 1.736 sec
 Width 27795.0 Hz
 251 repetitions
OBSERVE C13, 125.7836515 MHz
DECOUPLE  H1, 500.2351483 MHz
 Power 37 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 0.3 Hz
FT size 131072
Total time 3 hr, 26 min, 2 sec
```





(33)



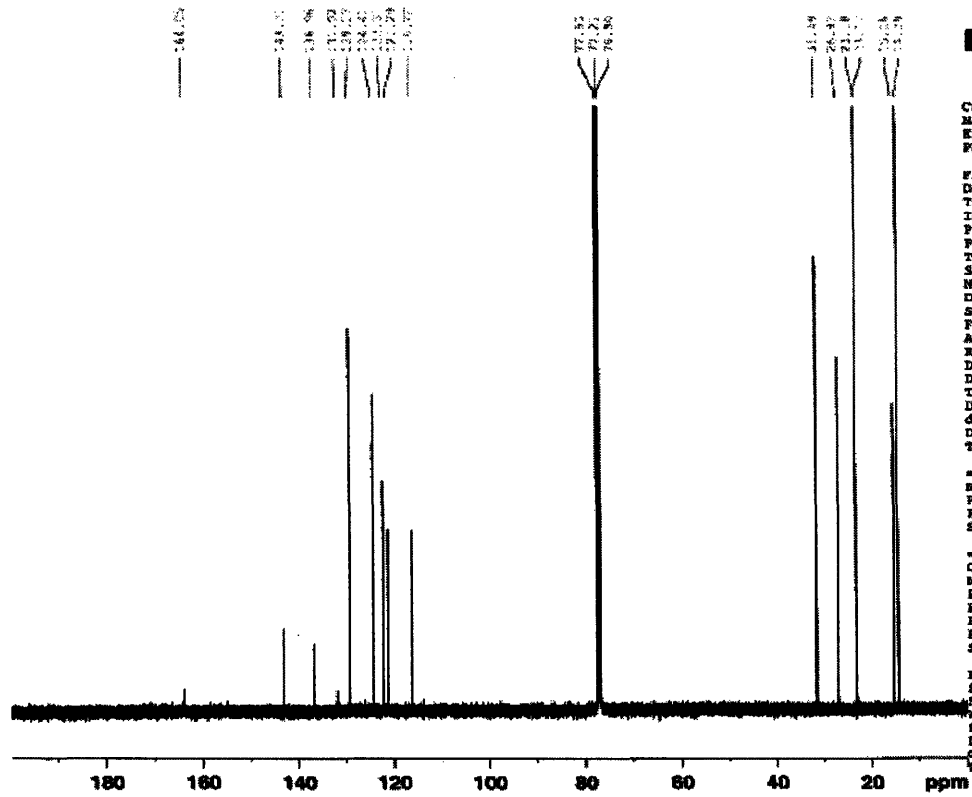
BRUKER

Current Data Parameters
NAME CJ-2-23hex
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20070511
Time 10.53
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 256
DW 60.400 usec
DE 6.00 usec
TE 293.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 14.06 usec
PL1 0.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 65536
SF 400.1300068 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00



BRUKER

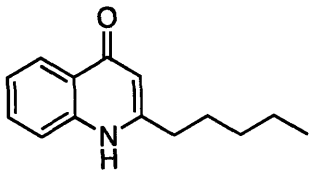
Current Data Parameters
NAME CJ-2-23hexc13
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20070512
Time 12.15
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 3108
DS 2
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 8192
DW 20.850 usec
DE 6.00 usec
TE 293.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

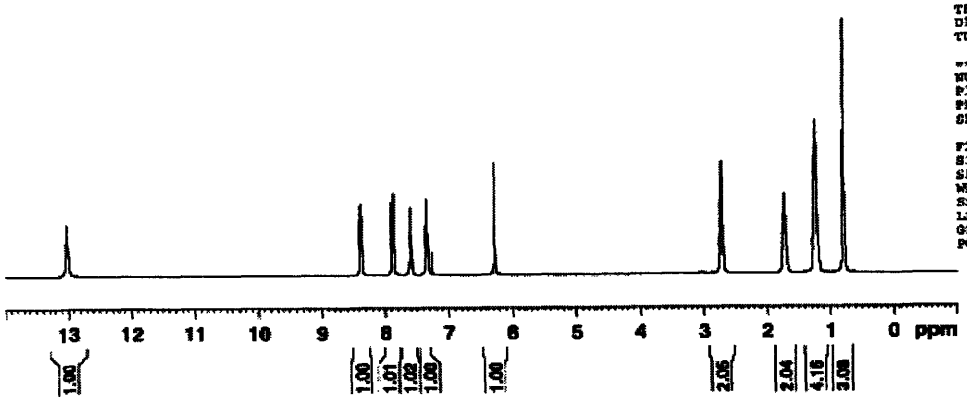
======== CHANNEL f1 ========
NUC1 13C
P1 8.75 usec
PL1 -1.00 dB
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -1.00 dB
PL12 14.52 dB
PL13 18.00 dB
SFO2 400.1316005 MHz

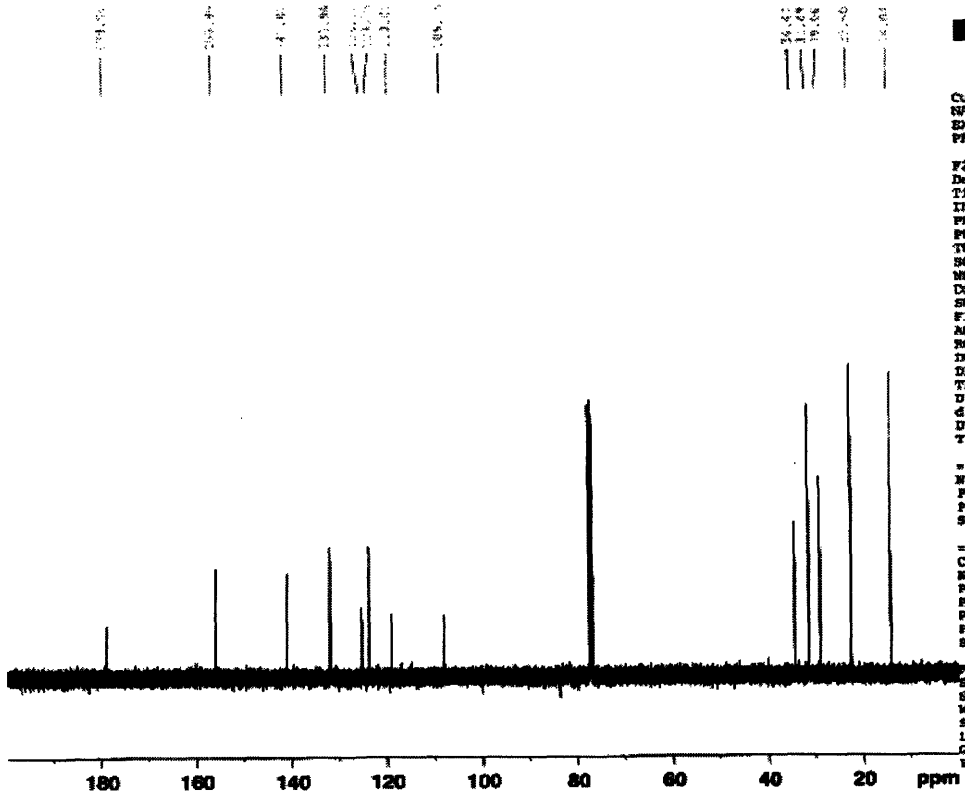
F2 - Processing parameters
SI 65536
SF 100.6127521 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40



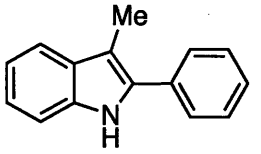
(34)



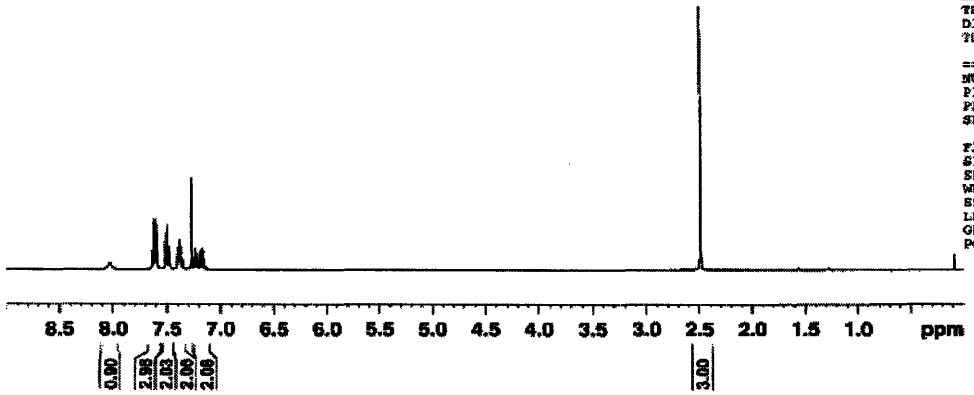

```
Current Data Parameters
NAME          CJ-2-23shex
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20070511
Time                8.54
INSTRUM            spect
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           8278.146 Hz
FIDRES        0.126314 Hz
AQ            3.9584243 sec
RG                  71.8
DW                60.400 usec
DE                 6.00 usec
TE                293.2 K
D1          1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 15.07 usec
PL1                 0.00 dB
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 65536
SF          400.1300059 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.00
```



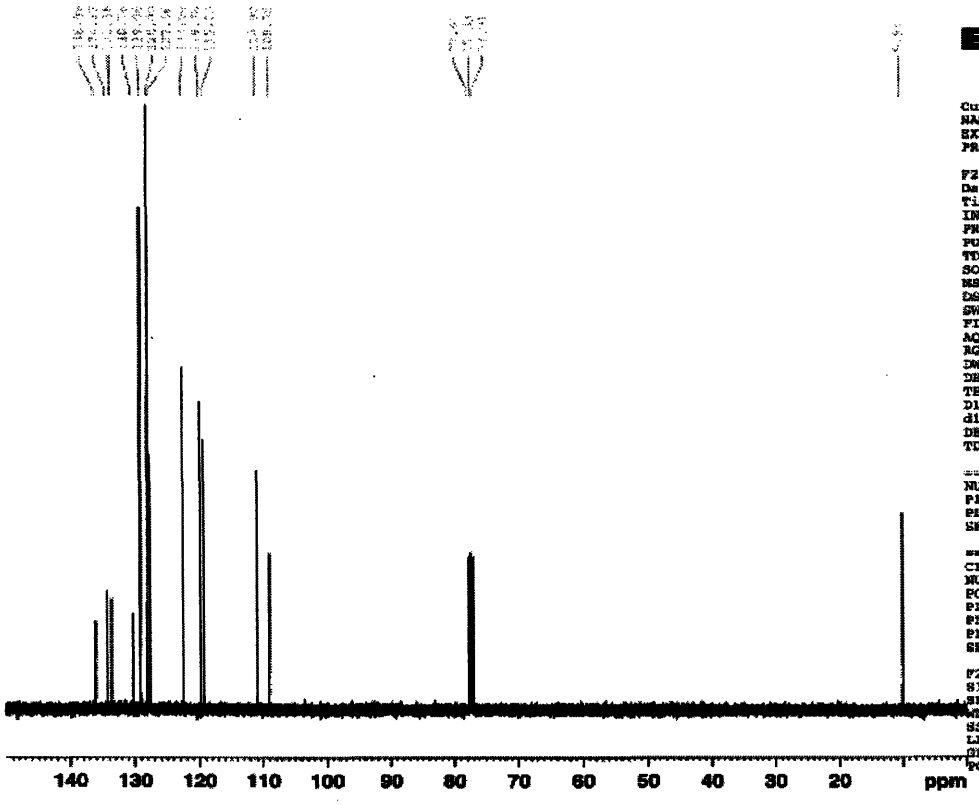

```
Current Data Parameters
NAME       CJ-2-23shexc13
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20070511
Time                9.06
INSTRUM            spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   128
DS                     2
SWH          23980.814 Hz
FIDRES        0.365918 Hz
AQ            1.3664756 sec
RG                14596.5
DW                20.850 usec
DE                 6.00 usec
TE                294.2 K
D1          2.00000000 sec
d11         0.03000000 sec
DELTA       1.89999998 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                 8.75 usec
PL1               -3.00 dB
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              90.00 usec
PL2               -1.00 dB
PL12               14.52 dB
PL13               16.00 dB
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                 65536
SF          100.6127545 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.40
```



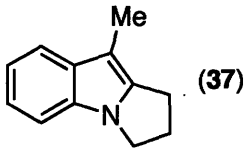
(35)



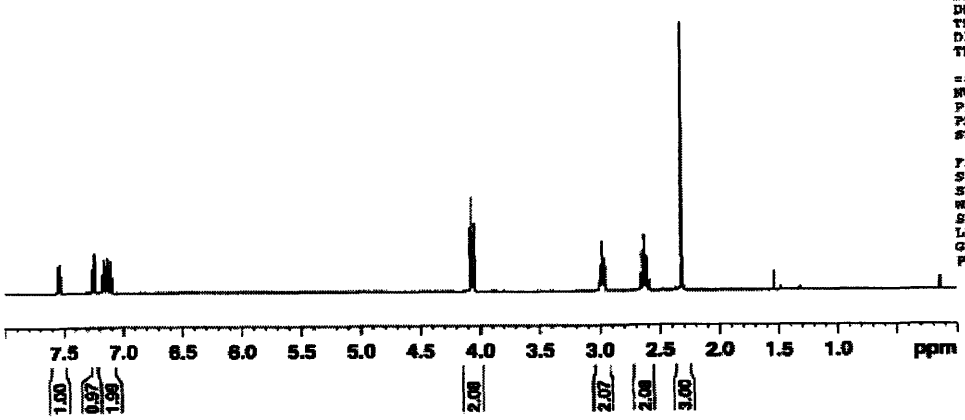

```
Current Data Parameters
NAME          CJ-1-289-2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20070406
Time               9.55
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG           zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            8278.146 Hz
FIDRES         0.126314 Hz
AQ             3.9584243 sec
RG                  256
DW                60.400 usec
DE                 6.00 usec
TE                293.2 K
D1            1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                1H
P1                15.07 usec
PL1                0.00 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                65536
SF           400.1300064 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.00
```




```
Current Data Parameters
NAME      CJ-1-289-2c132
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20070406
Time              10.36
INSTRUM           spect
PROBHD   5 mm CNP 1H/13
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  128
DS                    2
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664756 sec
RG                 4096
DW                20.850 usec
DE                 6.00 usec
TE                293.2 K
D1            2.00000000 sec
d11           0.03000000 sec
DELTA         1.89999998 sec
TD0                   1

========== CHANNEL f1 ==========
NUC1                13C
P1                9.38 usec
PL1                0.00 dB
SFO1         100.6228298 MHz

========== CHANNEL f2 ==========
CPDPRG2          waltz16
NUC2                1H
PCPD2             90.00 usec
PL2                0.00 dB
PL12              16.10 dB
PL13              19.80 dB
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                65536
SF           100.6127528 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.40
```

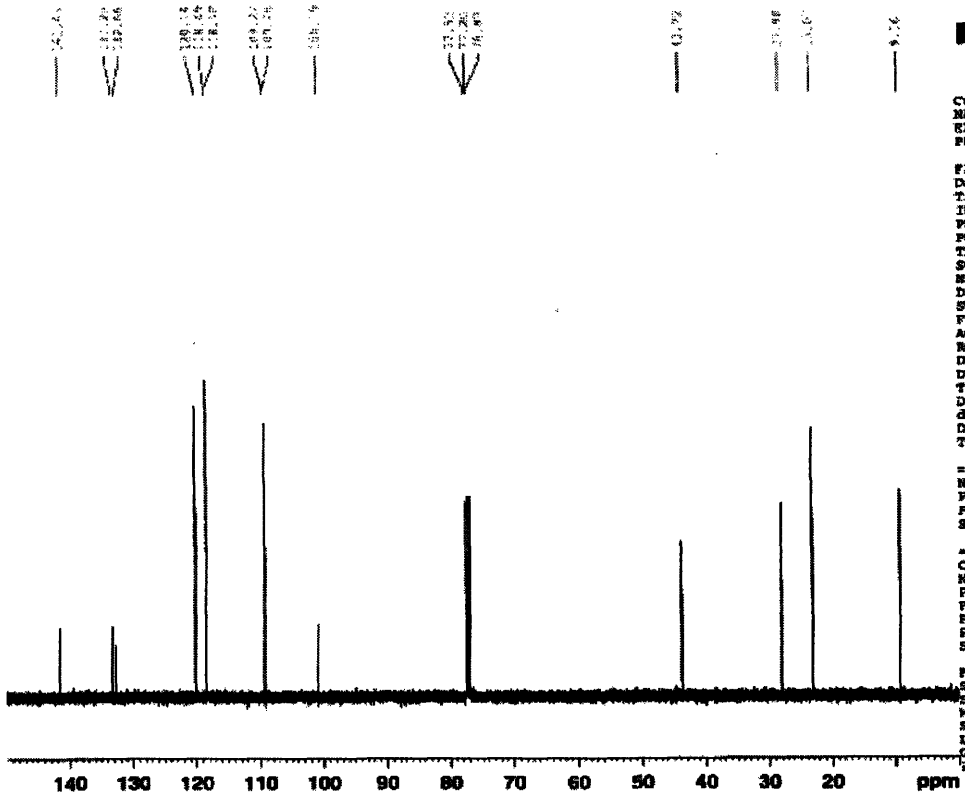


(37)



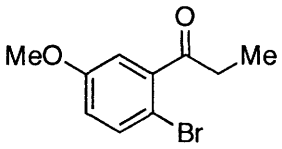
BRUKER

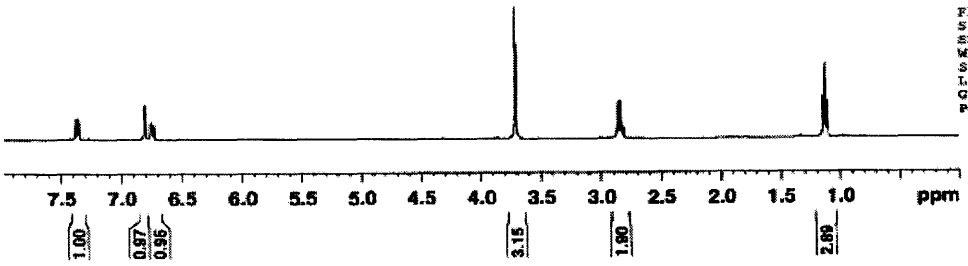
```
Current Data Parameters
NAME                  CJ-2-119
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20070322
Time                   12.32
INSTRUM                spect
PROBHD     5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      128
DW                   60.400 usec
DE                    6.00 usec
TE                   293.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     15.07 usec
PL1                     0.00 dB
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    65536
SF          400.1300063 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```



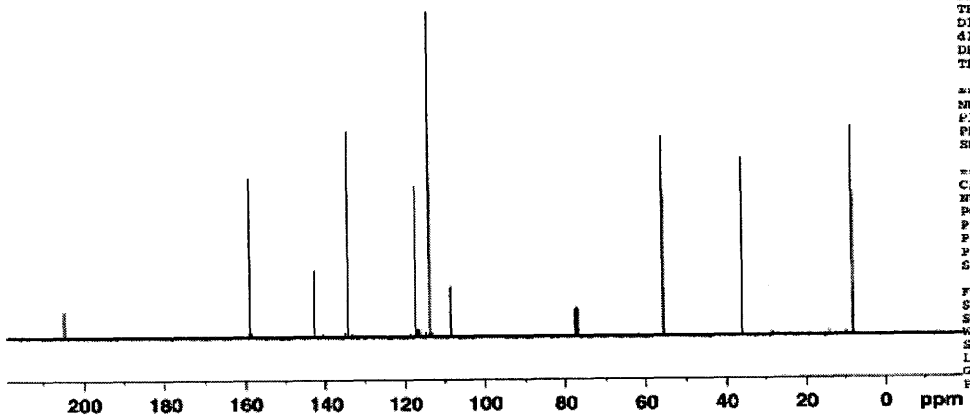
BRUKER

```
Current Data Parameters
NAME              CJ-2-119c13
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20070322
Time                   12.34
INSTRUM                spect
PROBHD     5 mm BBO BB-1H
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      128
DS                        2
SWH               23980.814 Hz
FIDRES             0.365918 Hz
AQ                 1.3664756 sec
RG                   18390.4
DW                   20.850 usec
DE                    6.00 usec
TE                   293.2 K
D1                2.00000000 sec
d11               0.03000000 sec
DELTA             1.89999998 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                     8.75 usec
PL1                   -1.00 dB
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                 90.00 usec
PL2                   -1.00 dB
PL12                  14.52 dB
PL13                  18.00 dB
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                    65536
SF          100.6127587 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.40
```






```
Current Data Parameters
NAME                  CJ-2-39-2
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_               20070511
Time                      9.13
INSTRUM                  spect
PROBHD     5 mm BBO BB-1H
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                       28.5
DW                     60.400 usec
DE                      6.00 usec
TE                     293.2 K
D1                  1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      15.07 usec
PL1                      0.00 dB
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                      65536
SF                 400.1300056 MHz
WDW                        no
SSB                         0
LB                       0.00 Hz
GB                          0
PC                       1.00
```




```
Current Data Parameters
NAME                  CJ-2-39c13
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_               20070511
Time                      9.25
INSTRUM                  spect
PROBHD     5 mm BBO BB-1H
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                        128
DS                          2
SWH                23980.814 Hz
FIDRES              0.365918 Hz
AQ                  1.3664756 sec
RG                      13004
DW                     20.850 usec
DE                      6.00 usec
TE                     294.2 K
D1                  2.00000000 sec
d11                 0.03000000 sec
DELTA               1.89999998 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                       8.75 usec
PL1                     -3.00 dB
SFO1            100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                       1H
PCPD2                   90.00 usec
PL2                     -1.00 dB
PL12                    14.52 dB
PL13                    18.00 dB
SFO2            400.1316005 MHz

F2 - Processing parameters
SI                      65536
SF                 100.6127718 MHz
WDW                        no
SSB                         0
LB                       0.60 Hz
GB                          0
PC                       1.40
```

VI. Appendix B: Curriculum Vitae

472 Cambridge St. Apt. 3
Cambridge, MA 02141

Phone: 908-304-4781
E-mail: carriepjones@gmail.com

Carrie Preston Jones

Objective

An intellectually challenging position which utilizes my creativity, enthusiasm, and analytical and problem-solving skills

Education

September 2005-present — Massachusetts Institute of Technology, Cambridge, MA
Master of Science/Organic Chemistry — (Expected Sept. 2007)
- Teaching Award 2006
- MIT Presidential Fellow 2005-2006
- Completed Master's thesis: *Development of a Copper-catalyzed Amidation-Base-promoted Cyclization Sequence for the Synthesis of 2-Aryl- and 2-Vinyl-4-quinolones*

September 1998-June 2002 — Williams College, Williamstown, MA
Bachelor of Arts/Chemistry — June 2002
- Highest Honors, Magna Cum Laude, Phi Beta Kappa, Sigma Xi
- Chemistry GPA: 3.89; Career GPA: 3.78
- Received ACS Connecticut Valley Section 2002 Achievement Award
- Received 1999 CRC Press First-Year Chemist Achievement Award
- Dean's List for all eight semesters
- Completed year-long chemistry research thesis: *Metallomesogenic Platinum Complexes with 2,2'-Bipyridyl-Based Ligands: Progress Towards 1-D Conductive Materials*

Work Experience

January 2006-present — Buchwald Lab, MIT
Lab Research Assistant
- Developed a copper-catalyzed method for the synthesis of nitrogen heterocycles: 2-aryl-4-quinolones.
- Research culminated in written thesis (above) and publication (below) and involved regular presentations at group meetings

September 2005-December 2005 — MIT, Cambridge, MA
Teaching Assistant
- Held biweekly recitations and office hours for Course 5.13: Organic Chemistry (2nd semester), graded problem sets and exams

April 2003-July 2005 — Merck & Co., Inc., Rahway, NJ
Chemist
- Worked in Medicinal Chemistry department performing organic synthesis of small molecules for drug discovery
- Received promotion in Spring 2005
- Presented work at Merck's annual Associate Research Symposium (June 2005)

September 2002-January 2003 — Waynflete School, Portland, ME
Substitute Teacher

June 2001-May 2002 — Inorganic Chemistry Lab, Williams College
Lab Research Assistant
- Performed organic syntheses and scale-ups of bipyridyl-based ligands and inorganic syntheses of Pt-coordinated complexes
- Research culminated in written thesis (above) and included two oral presentations

Publications

"Sequential Cu-Catalyzed Amidation-Base-mediated Camps Cyclization: A Two-step Synthesis of 2-Aryl-4-quinolones from *ortho*-Halophenones." Jones, C. P., Anderson, K. W., Buchwald, S. L. Manuscript submitted.

"A Highly Activated Catalyst System for the Heteroarylation of Acetone." Liu, P., Lanza, T. J., Jewell, J. P., Jones, C. P., Hagmann, W. K., Lin, L. S. *Tetrahedron Lett.* 2003, **44**, 8869-8871.

"Mesomorphic Properties of Novel 2,2'-Bipyridines and Their Metal Complexes." Park, L. Y., Fulmer, S. L., Hensley, L. A., Jones, C. P., McGehee, E. A., Scroggins, S. T., Walrod, M. D. Manuscript submitted.

Skills

Computer Proficiency: Microsoft Office, ChemDraw, Mac and PC systems; Chemistry Instrumentation: NMR, GC, GC-MS, LC-MS, HPLC, IR, silica chromatography, DSC, polarized optical microscopy, microwave