Library

A STUDY OF THE FAVORSKII REARRANGEMENT

by

George Andrew Frank

B.S., Colorado State University
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of the Requirements for the
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Certified by Signature redacted
Thesis Supervisor

Accepted by Signature redacted
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Signature redacted

Professor Frederick D. Greene____________________
(Chairman)

Signature redacted

Professor Herbert O. House____________________
(Thesis Supervisor)

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Professor Arthur C. Cope____________________

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Submitted to the Department of Chemistry at the Massachusetts Institute of Technology on January 26, 1965, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

ABSTRACT

Part I: THE WITTIG REACTION OF STABLE YLIDS

The reaction of carbomethoxymethylenetriphenylphosphorane (**1**) with chloroacetaldehyde afforded both the methyl *cis*- and *trans*-γ-chlorocrotonates (**10** and **9**). The new ylid **8** was prepared and its reaction with chloroacetaldehyde afforded only *trans*-1-phenyl-5-chloro-3-penten-2-one (**7a**).

Part II: FAVORSKII REARRANGEMENT OF KETONES **8** AND **9**

trans- and *cis*-9-Chloro-1-decalones (**8** and **9**) underwent stereospecific Favorskii rearrangement with sodium methoxide in 1,2-dimethoxyethane to afford *trans*-3a-carbomethoxyperhydroindane (**18**) and *trans*-1-carbomethoxyperhydroindane (**20**) and *cis*-3a-carbomethoxyperhydroindane (**19**), *cis,trans*- and *cis,cis*-1-carbomethoxyperhydroindane (**21** and **22**). In methanolic sodium methoxide the products were the 9- and 2-methoxy-1-decalones **12** - **15**.

APPENDIX

Part I: *trans*-1-Phenyl-5-chloro-3-penten-2-one or a mixture of its enol acetates was transformed to 2-benzylfuran when heated or treated with acid.

Part II: Chlorination of the $\Delta^{1,9}$-enol acetate of 1-decalone afforded a mixture of the *cis*- and *trans*-9-chloro-1-decalones. These, when heated, were converted to the $\Delta^{8,9}$- and $\Delta^{9,10}$-1-octalones, respectively. The nitrosyl chloride adduct of $\Delta^{1,9}$-octalin is the nitroso dimer. Heating this in acid yielded $\Delta^{9,10}$-1-octalone. The Diels-Alder reaction between 2-chloro-2-cyclohexen-1-one and butadiene followed by reduction of the double bond failed to give *cis*-9-chloro-1-decalone.

Thesis Supervisor: Herbert O. House
Title: Professor of Chemistry

FOR MY PARENTS

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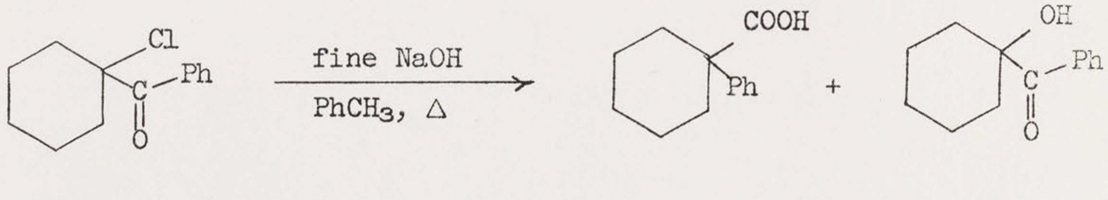
INTRODUCTION

The Favorskii rearrangement is the base-catalyzed skeletal rearrangement of α-halo ketones.[1] Derivatives of carboxylic acids containing the same number of carbon atoms are products of these reactions. The first example of a Favorskii rearrangement was described by Demarcay[2] in 1880 and involves an α,α-dibromo ketone.

It is generally accepted that the presence of an α'-hydrogen atom is necessary for a successful Favorskii rearrangement to occur. There are, however, several examples of the so-called *quasi*-Favorskii rearrangement where such a proton is not present,[3] as is shown in the following example:



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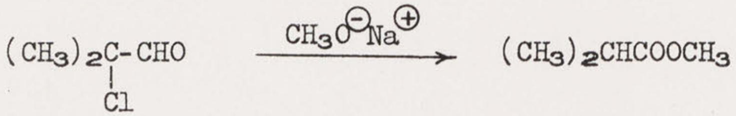
[1] A. Favorskii, J. Russ. Phys. Chem. Soc., 26, 559 (1894).

[2] M. Demarcay, Ann. chim. et phys., (5)20, 433 (1880).

[3] C. L. Stevens and E. Farkas, J. Am. Chem. Soc., 74, 5352 (1952).

Base catalyzed Favorskii rearrangements of α-halo aldehydes belong in the same category. The product of such reaction[4] may arise from the adduct of the aldehyde with base through a hydride shift either directly or from an intermediate epoxide.



$$(CH_3)_2\underset{\displaystyle Cl}{\underset{|}{C}}-CHO \xrightarrow{CH_3O^{\ominus}Na^{\oplus}} (CH_3)_2CHCOOCH_3$$

The history of the Favorskii rearrangement is a long series of widely assorted reactions under alkaline conditions of haloketones punctuated by mechanisms proffered to explain the experimentally obtained facts. These early mechanisms, in chronological order, by Favorskii,[5] Richard,[6] Tchoubar,[7] and McPhee and Klingsberg[8] are described in the exhaustive review by Kende.[9] We shall mainly concern

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(4) A. Kirrmann and H. I. Joschek, Bull. soc. chim. France, 2483 (1963)

(5) A. Favorskii, J. prakt. Chem., (2)88, 641 (1913).

(6) G. Richard, Compt. rend., 197, 1432 (1933).

(7) B. Tchoubar and O. Sackur, Compt. rend., 208, 1020 (1939).

(8) W. D. McPhee and E. Klingsberg, J. Am. Chem. Soc., 66, 1132 (1944).

(9) A. S. Kende, Org. Reactions, 11, 261 (1960).

ourselves with those mechanisms extant, the stereochemical implications derived from these, and recent developments in the Favorskii rearrangement.

It was noted[8] that α-halo ketones yield the same products during Favorskii rearrangement as their α'-halo isomers, and to prove that a symmetrical intermediate, one in which the α- and α'-carbon atoms become formally equivalent, e.g. cyclopropanone, is involved Loftfield has carried out an ingenious experiment with C^{14}-labelled 2-chlorocyclohexanone.[10] The intermediacy of cyclopropanone has been invoked as far back as 1892 by Hantzsch[11] in the cyanide ion-catalyzed rearrangement of ethyl α-chloroacetoacetate to both α- and γ-cyano compounds. 1,2-C^{14}-2-Chlorocyclohexanone (**1**) was treated with ethanolic sodium ethoxide and the resulting carboethoxycyclopentane (**2**) showed a distribution of C^{14}-labeling to be suggestive of a cyclopropanone intermediate or any other that makes the C_1 and C_2 carbon atoms equivalent. Results of recovery and degradation of unchanged starting material from a reaction with deficient base disproved the possibility of reversible halogen migration.

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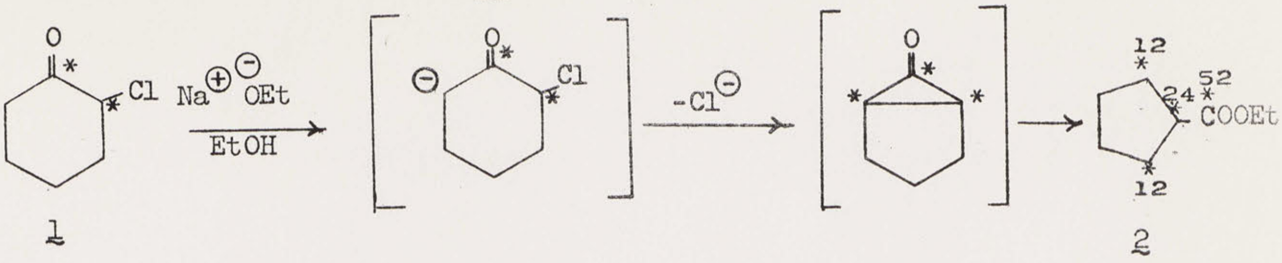
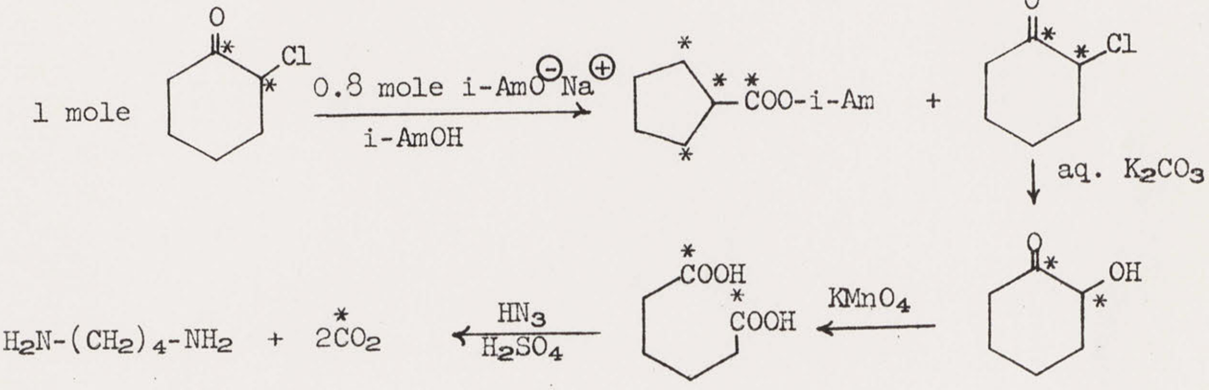
(10) (a) R. B. Loftfield, J. Am. Chem. Soc., *72*, 632 (1950); (b) R. B. Loftfield, *ibid*., *73*, 4707 (1951).

(11) A. Hantzsch and H. Schiffer, Ber., *25*, 728 (1892).



Scheme A



Had any halogen migration occured during the incomplete rearrangement the recovered tetramethylene diamine would have showed radioactivity.

Shortly thereafter appeared a suggestion by Aston and Newkirk[12] that loss of halide ion from the intermediate anion precedes closure to the cyclopropanone. From kinetic results of the previous work[10] showing the Favorskii rearrangement to be first order with respect to both base and ketone the only conclusion to be drawn was the rate-determining formation of the enolate anion or loss of the hydrogen halide. Thus, Aston's mechanism may be depicted as follows:

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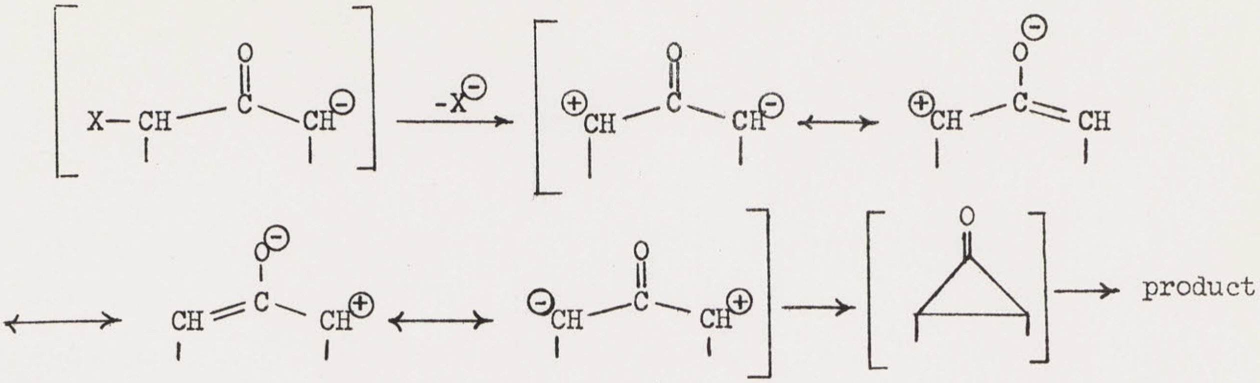
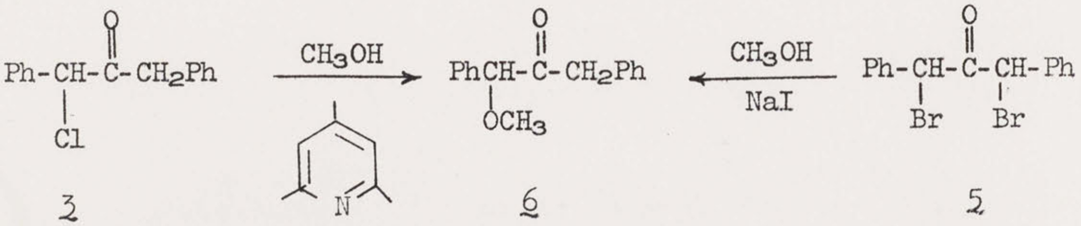
(12) J. G. Aston and J. D. Newkirk, J. Am. Chem. Soc., 73, 3900 (1951).



Scheme B

This "mesomeric zwitterion" mechanism found further support in conclusions derived from solvolytic studies on 1-chloro-1,3-diphenylacetone (3) and the Favorskii-type rearrangement of 6-(3,5,5-trimethyl-2-cyclohexen-1-one)-yl p-toluenesulfonate (4) by Fort.[13] The lutidine-catalyzed methanolysis of the ketone 3, as well as the sodium iodide treatment in presence of methanol of 1,3-dibromo-1,3-diphenylacetone (5), yielded 1-methoxy-1,3-diphenylacetone (6). The tosylate 4, when brought in contact with methanolic sodium methoxide, afforded two solvolytic and two rearrangement products:



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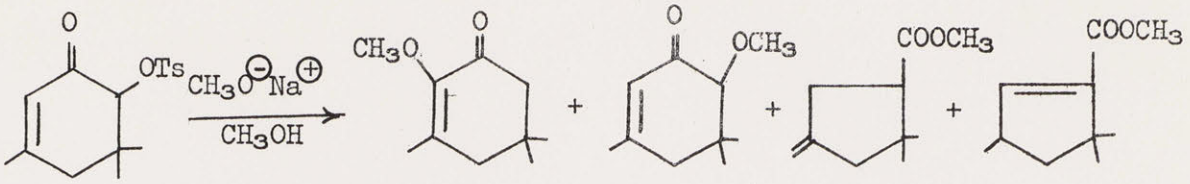
(13) (a) A. W. Fort, J. Am. Chem. Soc., 84, 2620 (1962); (b) A. W. Fort, *ibid*., 84, 2625 (1962).



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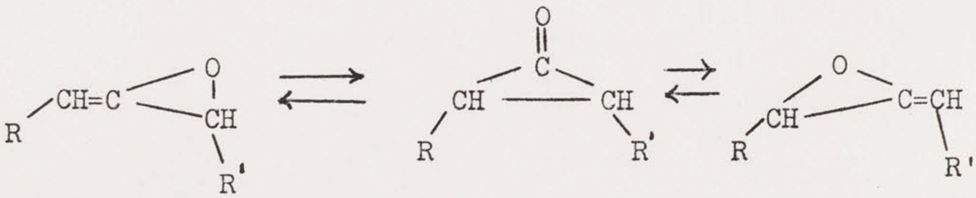
The former reaction showed second-order kinetics and the rate was found to be independent of lutidinium ion concentration thus excluding enolization and loss of chloride ion as rate-determining step and suggesting an elimination-addition mechanism involving a delocalized intermediate. Since the first step of a Favorskii rearrangement is also presumably the loss of hydrogen halide it is conceivable that this same delocalized intermediate, formally analogous to earlier proposals,[12] is operative in the rearrangement. The results of the second reaction[14] may similarly be explained on the

basis of this intermediate depicted below:



Beyond interpretive chemical evidence quantum mechanical calculations have been carried out to arrive at a mechanism for the

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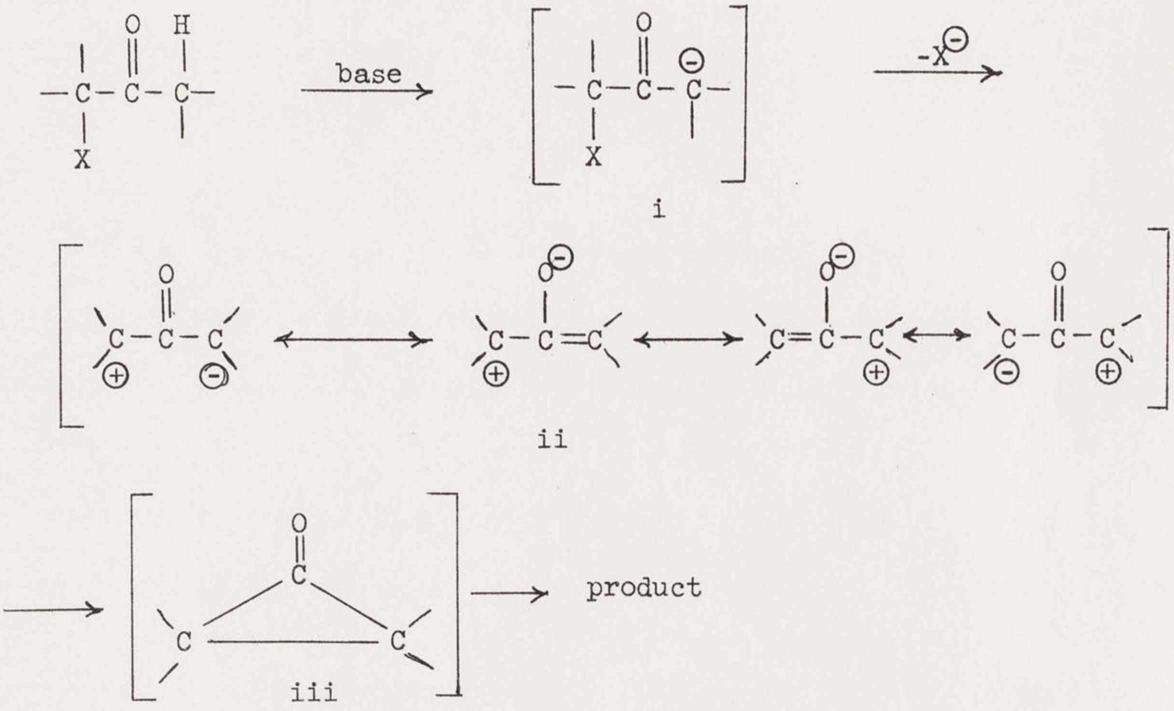
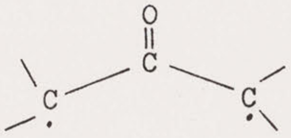
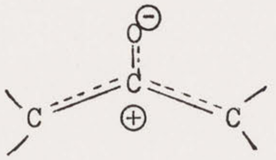
(14) Treatment of the tosylate 4 with sodium iodide in methanol allowed recovery of the starting material showing that the second product did not arise through an S_N2 displacement of the tosylate group by methanol.

Favorskii rearrangement consistent with the body of facts available. The following sequence of steps was suggested by Burr and Dewar[15] based on computation by the LCAO-MO method of conjugation energies of the proposed intermediates:




iv


v

Calculations show that the intermediate ii - variously represented by the authors as the "no-bond" canonical form iv or the electronically more meaningful form v - has total π-electron energy 7.420 β

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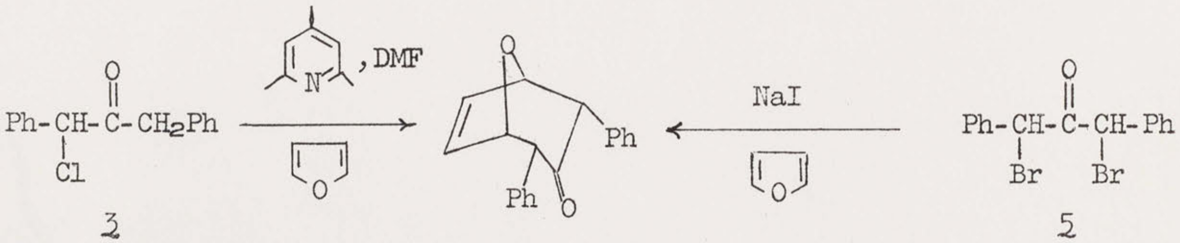
(15) J. G. Burr and M. J. S. Dewar, J. Chem. Soc., 1201 (1954).

as compared to 6.687β for the enolate anion i, thus showing the former to have ~14 kcal. higher resonance energy. The conjugation energy of ii is ~40 kcal. and the strain energy of a three-membered ring ~30 kcal., the formation energy of a carbon-carbon bond, however, is 81 kcal. and therefore, the process ii → iii is still an exothermic one, thus making the sequence i → ii → iii plausible. The possibility of going directly from i to iii is excluded on stereochemical grounds since there is very little overlap between the p-orbital and the σ-bond of the carbon-halogen bond required for the S_N2 process.

In recent years there have been several successful attempts at trapping various intermediates in the Favorskii rearrangement or like reactions. Both Fort[16] and Cookson[17] have isolated a bicyclic product of an intermediate like ii with furan from the reaction of the chloro ketone 3 with lutidine and the dibromo ketone 5 with sodium iodide, respectively, in presence of furan. In the latter work



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(16) A. W. Fort, J. Am. Chem. Soc., 84, 4979 (1962).

(17) R. C. Cookson and M. J. Nye, Proc. Chem. Soc., 129 (1963).

the course of the reaction was followed by infrared spectral analysis. The results -- there is an initial drop of the carbonyl stretching frequency to 1714 cm.$^{-1}$ accompanied by formation of sodium bromide followed by the appearance of a band at 1754 cm.$^{-1}$ due to an intermediate, e.g. ii, and liberation -- show that this intermediate does not arise *via* a direct reduction by iodide ion of the starting ketone. The final product shows absorption at 1703 cm.$^{-1}$.

A bicyclic adduct of this nature, along with a derivative of cyclopropanone, has been isolated in the course of irradiation of 2,2,4,4-tetramethyl-1,3-cyclobutanedione[18] adding further evidence

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(18) (a) N. J. Turro, G. W. Byers, and P. A. Leermakers, J. Am. Chem. Soc., *86,* 955 (1964); (b) H. G. Richey, J. M. Richey, and D. C. Clagett, *ibid.*, *86,* 3906 (1964); (c) R. C. Cookson, M. J. Nye, and G. Subrahmanyam, Proc. Chem. Soc., 144 (1964); (d) P. A. Leermakers, G. F. Vesley, N. J. Turro, and D. C. ckers, J. Am. Chem. Soc., *86,* 4213 (1964).

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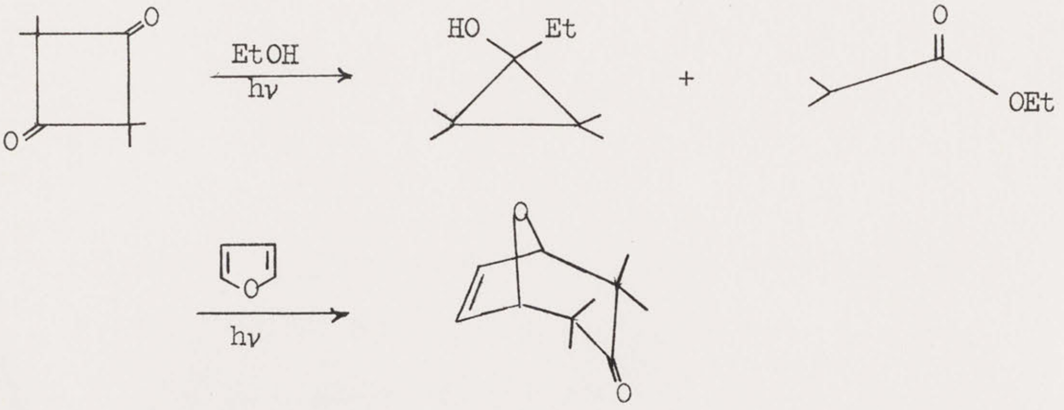
to the possible existence of species like ii (or iv).



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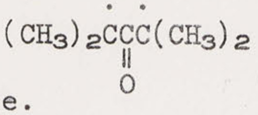
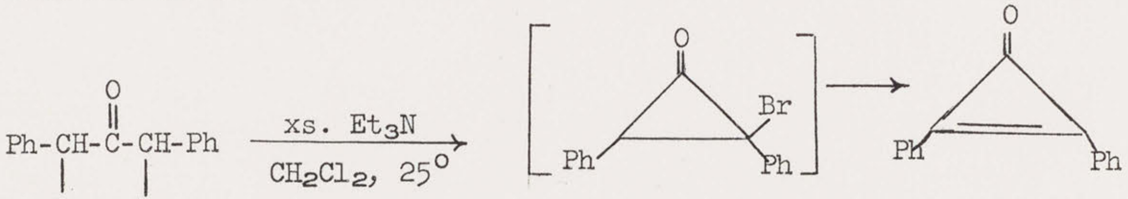
* The three minor products may have arisen from the hemi-ketal on work-up. When so tried the minor products actually appeared.

These products are explicable on the basis of the fragmentation to dimethylketene and a diradical  $(CH_3)_2\dot{C}\underset{\underset{O}{\|}}{C}\dot{C}(CH_3)_2$ postulated to exist[15] in the more stable singlet state.

Breslow[19] has treated several α,α'-dibromo ketones with a tertiary amine and was able to isolate the corresponding cyclopropenones. These must, by necessity, discounting the unlikely formation of bis-carbenes, arise by the dehydrohalogenation of the intermediate halocyclopropanones. There is a report in the chemical literature,[20] aside from the several dealing with its derivatives, of the detection by infrared spectral means of cyclopropanone itself formed through the addition of diazomethane to an excess of ketene in a cold ethereal solution.



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At least one discordant note has been struck by Conia[21]

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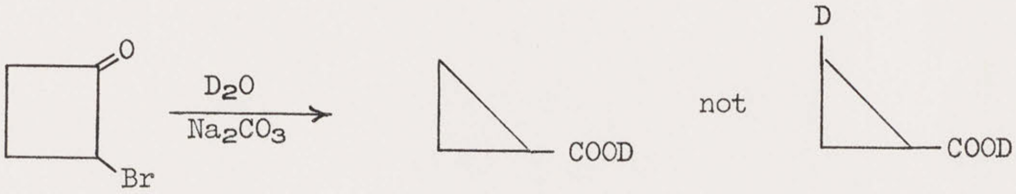
[19] R. Breslow, J. Posner, and A. Krebs, J. Am. Chem. Soc., 85, 234 (1963).

[20] (a) A. S. Kende, Ph. D. Thesis, Harvard University, 1956; (b) W. B. Demore, H. O. Pritchard, and N. Davidson, J. Am. Chem. Soc., 81, 5874 (1959).

against the intermediacy of cyclopropanone in the Favorskii rearrangement. In the treatment of 2-bromocyclobutanone with deuterium oxide and sodium carbonate the expected Favorskii rearrangement product, if a cyclopropanone were an intermediate, would have been cyclopropanecarboxylic acid deuterated at the 2-position. Nuclear magnetic resonance data clearly showed no deuterium on the ring. The results are explicable in terms of a semibenzilic rearrangement and may be rationalized by the inherent strain involved in forming a cyclopropanone ring as part of a bicyclo(1.1.0)system or by the high susceptibility of a cyclobutanone to nucleophilic attack.



A more accurate insight into the nature of the intermediate may be gained by the examination of stereochemical results of the Favorskii rearrangement. The intermediates discussed thus far are kinetically indistinguishable. If, however, closure to cyclopropanone is synchronous with loss of halide ion, i.e. an S_N2 process, or at least if the leaving ion does not recede past shielding range before closure, then the net result of this would be a Walden

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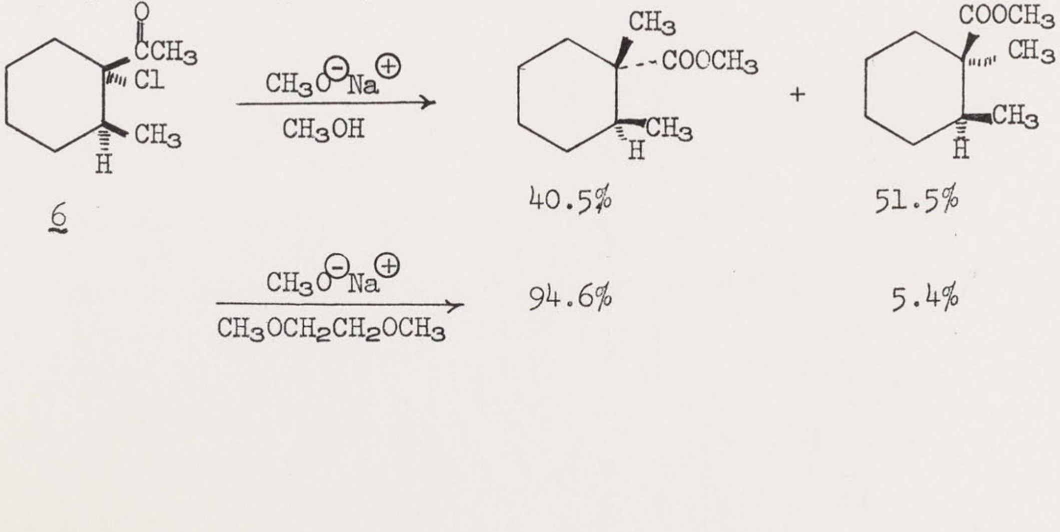
(21) J. H. Conia and J. Salaün, Tet. Letters, No. 18, 1175 (1963).

inversion at the halogen-bearing carbon atom. A fast, prior loss of halide ion, on the other hand, from the enolate anion i resulting in a discrete species ii would mean racemization at the α-carbon atom. It was found[22] that the methanolic sodium methoxide catalyzed Favorskii rearrangement of 17α-bromo-3α-acetoxypregnane-11,20-dione yielded an approximately equal mixture of the epimeric 17-methyl-17-carboxylic esters. Subsequent work[23] on the Favorskii rearrangement of 1-chloro-cis-1-acetyl-2-methyl-cyclohexane (6) in methanol and in 1,2-dimethoxyethane revealed that while in polar media the rearrangement proceeds with loss of steric integrity at the α-carbon atom in less polar solvents the reaction is stereospecific yielding essentially complete inversion.



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(22) N. L. Wendler, R. P. Graber, and G. G. Hazen, Tetrahedron, 3, 144 (1958).

(23) (a) G. Stork and I. J. Borowitz, J. Am. Chem. Soc., 82, 4307 (1960); (b) H. O. House and W. F. Gilmore, ibid., 83, 3980 (1961).

That the stereochemical course of these reactions is solvent dependent and not due to prior isomerization of the ketone 6 to either its 1-chloro-trans-1-acetyl- or chloromethylketone- isomers was also shown by these authors.[23] Whether the polar medium facilitates ionization to the intermediate ii or causes loss of stereospecificity through the conjugate acid of intermediate iii is open to argument. These results[23] then, coupled with similar observations made[24] using the same ketone 6 and several base and solvent systems alleviate the need for invoking reversible bromine migration earlier used to explain the stereochemical outcome of the Favorskii rearrangement.[22] Further work investigating the significance of stereochemistry of products in Favorskii rearrangements of α,β-epoxy ketones,[25,26] e.g. piperitone oxide, bears out earlier conclusions reached about increasing stereospecificity achieved through using less polar media. In these cases, as in many others,[9] use of increasingly more polar solvents results in the appearance of side products, mainly

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(24) A. Gandemar, J. Parello, A. Skrobek, and B. Tchoubar, Bull. soc. chim. France, 2405 (1963).

(25) H. O. House and W. F. Gilmore, J. Am. Chem. Soc., 83, 3972 (1961).

(26) S. A. Achwad and G. W. K. Cavill, Australian J. Chem., 16, 858 (1963).

solvolysis products and those arising from nucleophilic attack on the carbonyl group helped by better solvation of the resulting negative charge, i.e. higher rates of nucleophilic attack than enolate anion formation.[27]

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(27) R. B. Loftfield and L. J Schaad, J. Am. Chem. Soc., 76, 35 (1964).

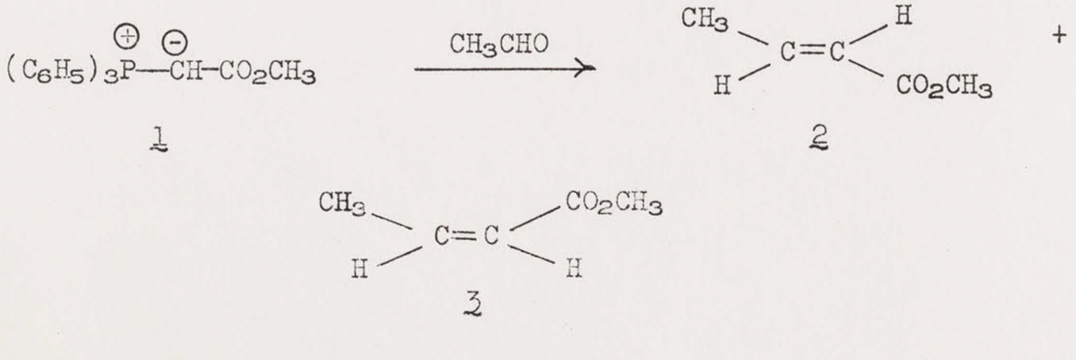
The final answer to the mechanism of the Favorskii rearrangement is far from settled and no uniform answer will ever be found, for the slightest change in reaction conditions or in the nature of the halo ketone may radically alter the outcome of the reaction.

PART I

THE WITTIG REACTION OF STABLE YLIDS

The Wittig reaction has achieved quick prominence and has been amply reviewed in the chemical literature.[1]

Earlier investigations[2] of a specific aspect of the Wittig reactions of aldehydes with ylids stabilized by the presence of carbonyl substituents at the *alpha* position (*e.g.* 1) have indicated that the predominant stereoisomer in the olefinic product is that isomer in which the carbonyl substituent is *trans* to the larger group at the β-carbon atom (*e.g.* 2).



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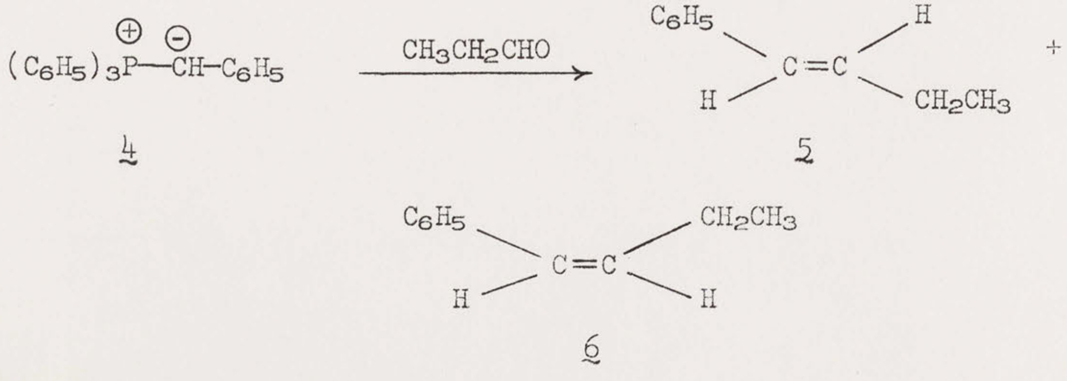
(1) (a) G. Wittig and G. Geissler, Ann., *580*, 44 (1953); (b) G. Wittig and U. Schöllkopf, Chem. Ber., *87*, 1318 (1954); (c) J. Levisalles, Bull. soc. chim. France, 1021 (1958); (d) U. Schöllkopf, Angew. Chem., *71*, 260 (1959); (e) S. Trippett in R. Raphael, E. Taylor, and M. Wynberg, editors, "Advances in Organic Chemistry: Methods and Results", Vol. I, Intersicence Publishers, New York, 1960, pp. 83-102.

(2) (a) S. Trippett, Quart. Revs., *17*, 406 (1963); (b) H. O. House and G. H. Rassmusson, J. Org. Chem., *26*, 4278 (1961); (c) H. O. House and H. Babad, *ibid.*, *28*, 90 (1963); (d) H. J. Bestmann and O. Kratzer, Chem. Ber., *95*, 1894 (1962); (e) R. Ketcham, D. Jambotkar, and L. Martinelli, J. Org. Chem., *27*, 4666 (1962); (f) A. J. Speziale and D. E. Bissing, J. Am. Chem. Soc., *85*, 3878 (1963); (g) S. Fliszar, R. F. Hudson, and G. Salvadori, Helv. Chim. Acta, *46*, 1580 (1963).

Other studies of the stereochemistry of the Wittig reaction[3,4] have indicated that the degree of stereoselectivity observed is somewhat dependent on the substituents present and is markedly influenced by changes in the reaction medium. For example, the reaction of the benzylidene phosphoranes **4** with propionaldehyde in benzene solution was found to yield a mixture of olefins **5** and **6** containing 26% of the *cis*-isomer **6**. However, if the solution of the ylid **4** was treated successively with a *suspension* of lithium bromide or lithium iodide (obtained from *n*-butyllithium and hydrogen bromide or hydrogen iodide) and then with propionaldehyde, the proportion of the *cis*-stereoisomer **6** in the product was reported to be increased to over 90%.



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6

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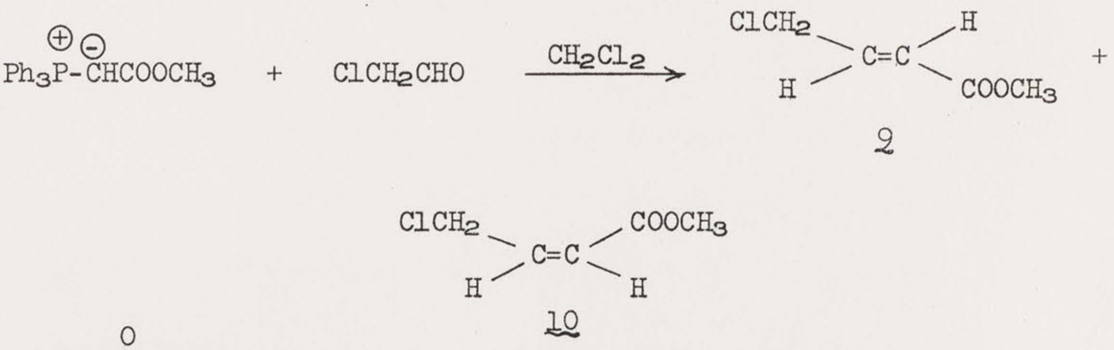
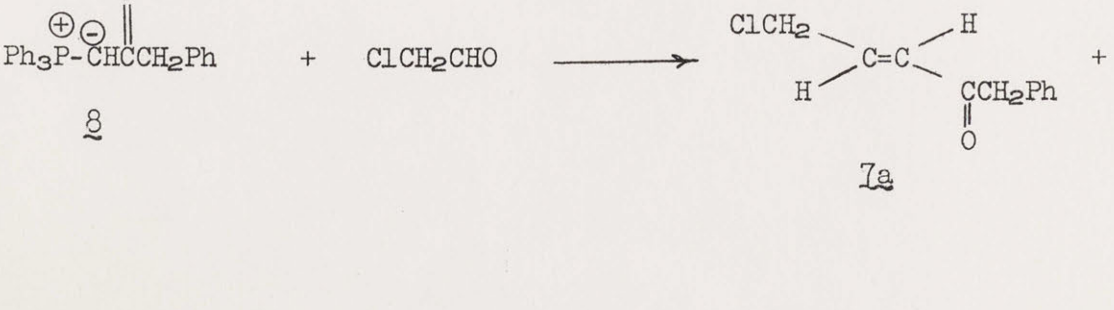
(3) (a) A. J. Speziale and K. W. Ratts, J. Am. Chem. Soc., 85, 2790 (1963); (b) C. F. Hanser, T. W. Brooks, M. L. Miles, M. A. Raymond, and G. B. Butler, J. Org. Chem., 28, 372 (1963).

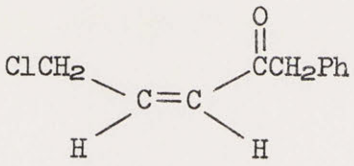
(4) (a) L. D. Bergelson and M. M. Shemyakin, Tetrahedron, 19, 149 (1963); (b) L. D. Bergelson, V. A. Vaver, L. I. Barsukov, and M. M. Shemyakin, Izv. Akad. Nauk SSSR Otd. Khim. Nauk, 1053 (1963); (c) L. D. Bergelson and M. M. Shemyakin, Angew. Chem., 76, 113 (1964).

These results came under closer scrutiny as possible means for obtaining the vinylogous α-halo ketone 7 unsuccessfully sought through other pathways. The class of reactions of the type ylid 8 with chloroacetaldehyde seemed to provide a general method toward γ-halo-α,β-unsaturated compounds needed in our planned study under conditions of the Favorskii rearrangement. Since neither reports of reactions of α-halo aldehydes with stabilized ylids existed nor was the ylid 8 known a model system employing the simple stable ylid 1 in a reaction with chloroacetaldehyde was studied.

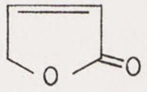
When carbomethoxymethylenetriphenylphosphorane (1) and chloroacetaldehyde were made to react in methylene chloride a mixture of methyl *cis*- and *trans*-γ-chlorocrotonate (9 and 10) resulted. Based on these results 3-phenyl-1-acetonyltriphenylphosphorane (8) was treated with chloroacetaldehyde. There was, however, only the *trans*-ketone 7a isolated and no evidence for the formation of the *cis*-ketone 7b could be found.







7b



18

From these and subsequently gathered data[5] the following conclusions may be drawn: The proportion of the *cis*-isomer is enhanced by the presence in the reaction *solution* of a Lewis acid such as a proton-donating solvent or a lithium cation; the results are not consistent with the idea of a prior coordination of the ylid with a Lewis base.[2,4] Most studies with reactive ylids have utilized the reaction of phosphonium salts with organolithium reagents to form an ylid accompanied by a lithium salt whereas the stable ylids are usually isolated free from extraneous materials.

Both the catalysis of Wittig reactions of stabilized ylids by proton-donating solvents[2f] or additives[6] and the enhanced

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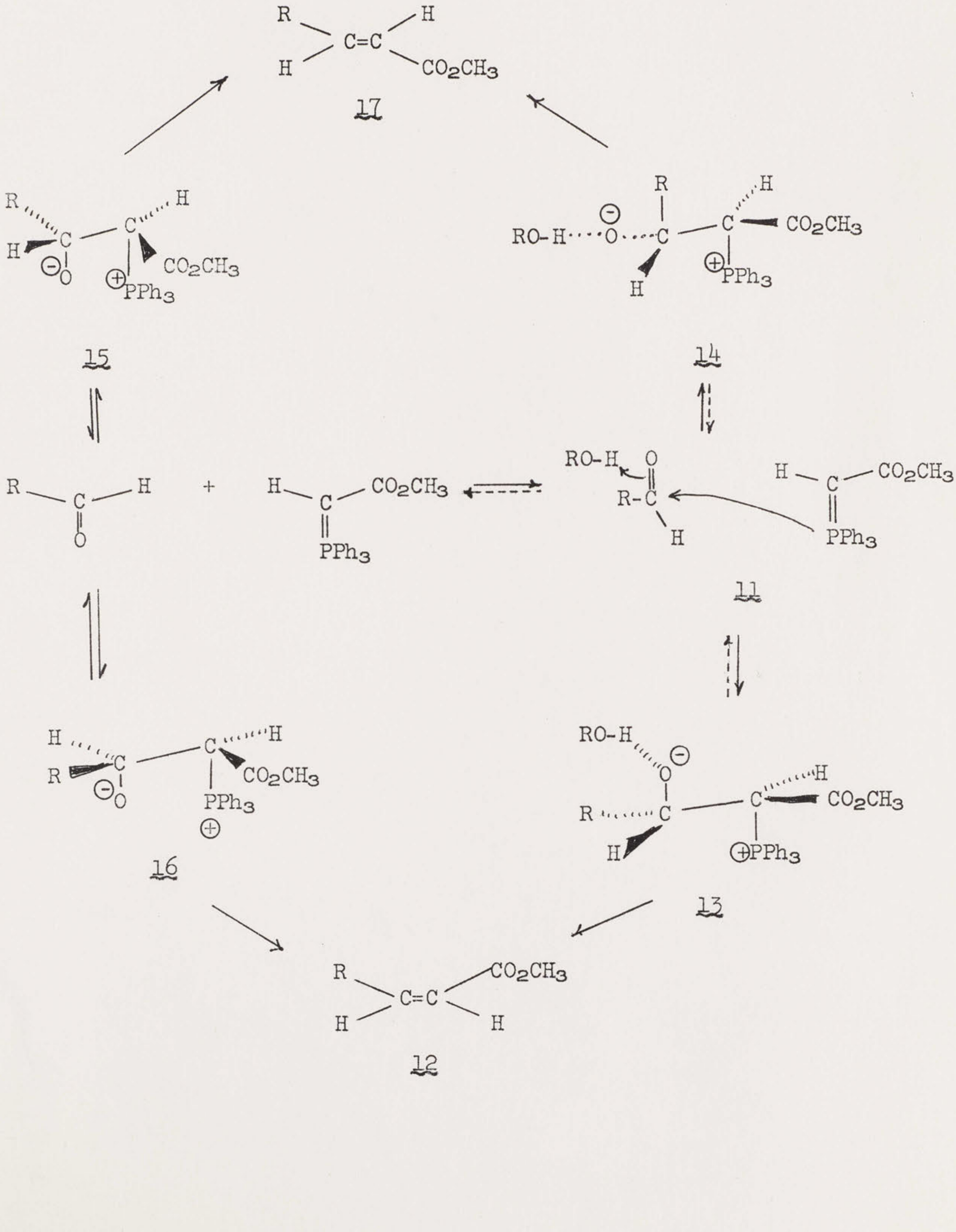
(5) H. O. House, V. K. Jones, and G. A. Frank, J. Org. Chem., **29**, 3327 (1964).

(6) C. Rüchardt, S. Eichler, and P. Panse, Angew. Chem., (Int. Ed.), **2**, 619 (1963).

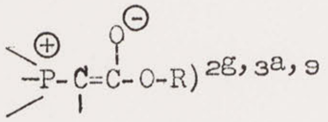
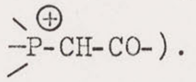
proportions of *cis* isomer formed in the presence of dissolved Lewis acids (methanol, water, lithium salts) would appear to be explicable in terms of coordination of the Lewis acid with the carbonyl oxygen atom in the addition step as illustrated in structure **11**. Such a process has ample analogy in the addition of other nucleophiles to carbonyl functions. The increased proportion of the *cis*-isomer **12** formed under such circumstances would appear to be the result of one or both of the following factors. Interconversion of the two stereosiomeric solvated betaines **13** and **14** (either by reversal of the addition reaction[2f] or by way of an intermediate ylid resulting from loss of a proton from **13** or **14**[2a]) may be slower than the corresponding interconversion of the unsolvated betaines **15** and **16**. If the relative rates of decomposition of betaines **15** or **14** to **17** and **16** or **13** to **12** remain unaltered, the result will be to make the reaction less stereoselective. Even if the rate of interconversion of the betaines is not retarded by solvation, the ratio of the steady-state concentrations of betaines **15** and **16** would be expected to differ from the corresponding ratio of concentrations for solvated betaines **13** and **14**. For electrostatic reasons, both betaines **15** and **16** would be expected to exist primarily in the indicated conformations. However, the solvated betaines **13** and **14** should have much less preference for corresponding conformations where the phosphorous and oxygen atoms are near one another because the negative charge remaining at the oxygen atom has been lessened substantially. Hence, for a combination of electrostatic and steric reasons, the betaine **15** (leading to *trans* olefin **17**) is expected to be more stable than its isomer **16**. However, the relative stabilities of solvated betaines **13** and **14** would be expected to be more nearly equal and may possibly favor the isomer **13** leading to *cis* olefin **12**.



The fact that there is a relatively high ratio of the *cis*-ester **10** formed from the ylid **1** in a non-polar medium may be explained by structure **16**, R = CH_2Cl, where the electrostatic interaction between the chlorine and phosphorus atoms is making this isomer a larger contributor.

16

Experimental

Preparation of carbomethoxymethylenetriphenylphosphorane (1).- Carbomethoxymethylenetriphenylphosphorane (1), prepared as previously described,[7] was obtained as fine white prisms, m.p. 160-163° (lit.[7] 162-163°), from an ethyl acetate-petroleum ether mixture. The material has strong infrared absorption[8] at 1620 cm.$^{-1}$ (this peak is apparently characteristic of the system  $>\overset{\oplus}{P}-\underset{|}{C}=\overset{O^{\ominus}}{\overset{|}{C}}-O-R)$[2g, 3a, 9] and an n.m.r.[10] multiplet in the region 7.2-8.0 δ (15 H, aryl C-H) as well as a singlet at 3.50 δ (3 H, O-CH_3) and a broad peak centered at 3.20 δ (1 H,  $>\overset{\oplus}{P}-CH-CO-$).

Preparation of 3-phenyl-1-acetonyltriphenylphosphorane (8) *and its precursors*.- To an ethereal solution of 10.82 g. (0.07 mole) of

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(7) O. Isler, H. Gutmann, M. Montavon, R. Rüegg, G. Ryser, and P. Zeller, Helv. Chim. Acta, 40, 1242 (1957).

(8) Determined as a solution in chloroform.

(9) (a) F. Ramirez and S. Dershowitz, J. Org. Chem., 22, 41 (1957); (b) A. J. Speziale and K. W. Ratts, *ibid*., 28, 465 (1963).

(10) Determined as a solution in deuteriochloroform.

phenylacetyl chloride was added, dropwise and with stirring, cold (0°) ethereal solution containing 0.14 mole of diazomethane. The resulting solution was allowed to stand overnight and then treated with dry hydrogen chloride until the yellow color of the diazo ketone was discharged. After the ethereal solution had been washed with aqueous sodium bicarbonate, dried and concentrated, distillation afforded 8.17 g. of a fraction, b.p. 110-118° (6 mm.), n^{25}_{D} 1.5308,[11] containing[12] approximately 80% of 3-chloro-1-phenyl-2-propanone, the remainder of the fraction being a mixture of methyl phenylacetate and ethyl phenylacetate. A solution of 8.43 g. (0.05 mole) of this crude chloro ketone and 13.1 g. (0.05 mole) of triphenylphosphine in 75 ml. of methylene chloride was stirred at room temperature for 30 min. and then concentrated and mixed with ether. The crude salt which separated was collected and recrystallized from a methanol-ethyl acetate mixture to separate 12 g. (85%) of the salt as white needles, melting with decomposition over the range 153-200°. This 3-phenylacetonyltriphenylphosphonium chloride apparently forms a

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(11) W. D. McPhee and E. Klingsberg [J. Am. Chem. Soc., <u>66</u>, 1132 (1944)] report b.p. 130-133° (17 mm.) and n^{25}_{D} 1.5357-1.5361 for 3-chloro-1-phenyl-2-propanone.

(12) A column packed with Dow Corning Silicone Fluid, No. 710, suspended on Chromosorb P was employed.

series of solvates since repeated efforts to obtain an analytically pure sample were unsuccessful. A sample of the salt which had been cyrstallized several times from ether-methylene chloride mixtures and then dried at 85° for several days melted with decomposition at 204-207° and had a composition [Found: C, 73.65; H, 6.11; Cl, 7.83. Calcd. for $C_{27}H_{24}ClOP\cdot\frac{1}{2}H_2O$: C, 73.61; H, 5.73; Cl, 8.06] suggesting that the material is a hemihydrate. The material had infrared absorption[8] at 1715 cm.$^{-1}$ (ester C=O) with n.m.r. absorption[10] in the region 7.1-8.0 δ (20 H, aryl C-H) as well as a doublet (J ~ 12 c.p.s.) centered at 6.26 δ (2H, $-\overset{|\oplus}{\underset{|}{P}}-CH_2$) and broad peak at 4.32 δ (2. H, $-CO-CH_2-Ph$). A suspension of 4.3 g. (0.01 mole) of this phosphonium salt in a mixture of 15 ml. of water and 12 ml. of methylene chloride was treated with sufficient 10% aqueous sodium hydroxide to make the aqueous layer alkaline. The organic layer was separated, washed with water, dried and concentrated. Recrystallization of the residue (2.6 g.) from an ethyl acetate-methylene chloride layer separated 2.38 g. (58%) of the ylid **11** as white needles, m.p. 102-102.5°. The product exhibits a strong infrared band[8] at 1535 cm.$^{-1}$ ($-\overset{|\oplus}{\underset{|}{P}}-CH=\overset{O\ominus}{\overset{|}{C}}-$),[2g,3a,9] ultraviolet maxima[13] at 267 mμ (ε 7560), 273 mμ (ε 7230) and 287 mμ (ε 6520) and an n.m.r.[10] multiplet in the region 7.1-7.9 δ (20 H, aryl C-H) with a partially resolved multiplet (apparently an AB pattern superimposed on other absorption) in the region 3.4-3.9 δ

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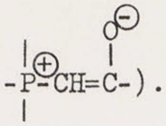
(13) Determined as a solution in 95% ethanol.

-CH$_2$ and 
$-\overset{|}{\underset{|}{P}}{}^{\oplus}-CH=\overset{O^{\ominus}}{\overset{|}{C}}-)$.

Anal. Calcd. for $C_{27}H_{23}PO$: C, 82.21; H, 5.88. Found: C, 82.24; H, 6.00.

Preparation of chloroacetaldehyde.- Reaction of either the dimethyl acetal or the diethyl acetal of chloroacetaldehyde with oxalic acid as previously described[14] produced crude chloroacetaldehyde, b.p. 88-93° which was converted[14] to its trimer as white needles from ethanol, m.p. 85-87° (lit.[14] 87.5°). The trimer has no absorption[15] in the 6 μ region of the infrared attributable to a carbonyl function and exhibits n.m.r. peaks[15] at 5.30 δ (3 H, triplet with J = 5 c.p.s., $-O-\overset{|}{C}H-O-$) and at 3.72 δ (6 H, doublet with J = 5 c.p.s., Cl-CH$_2$-). Distillation of this trimer immediately before use yielded chloroacetaldehyde, b.p. 85-86° (lit.[14] 86°), with infrared absorption[15] at 1730 cm.$^{-1}$ (C=O).

Reaction of Ylid 1 with chloroacetaldehyde.- To a solution of 2.58 g. (33 mmoles) of chloroacetaldehyde in 25 ml. of methylene

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[14] P. J. De Bievre, G. P. Van der Kelen, G. Cornille, and Z. Eckhaut, Bull. soc. chim. Belges, *68*, 550 (1959).

[15] Determined as a solution in carbon tetrachloride.

chloride was added, dropwise and with stirring over a period of 1 hr., a solution of 11.1 g. (33 mmoles) of the phosphorane **1** in 40 ml. of methylene chloride. After the resulting mixture had been refluxed for 2 hr. and allowed to stand overnight, it was concentrated and diluted with petroleum ether (b.p. 30-60°) to precipitate the bulk of the triphenylphosphine oxide (8.26 g. or 90%). The remaining solution was concentrated and distilled through a 30 cm. Holtzmann column to separate 2.4872 g. (57%) of fractions, b.p. 72-78° (18-19 mm.), n^{25}_{D} 1.4600-1.4630, containing[16] 33% of the *cis*-ester **10** (first eluted) and 67% of the *trans*-ester **9** (second eluted). Each of the pure isomers was collected from the chromatograph[16] and redistilled for characterization.[17] The *cis*-isomer **10**, b.p. 55° (12 mm.), n^{24}_{D} 1.4590, has infrared absorption[15] at 1730 cm.$^{-1}$ (C=O) and at 1650 cm.$^{-1}$ (C=C) and at 1650 cm.$^{-1}$ (C=C) with an ultraviolet maximum[13] at 207 mμ (ε 12,600) and n.m.r. absorption[10] attributable to the vinyl protons at 6.12 δ (1 H, pair of overlapping triplets with J = 6 and 11 c.p.s.) and at 5.67 δ (1 H, pair of triplets with J = 1 and 11

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[16] A column packed with 20 M Carbowax suspended on ground firebrick was employed.

[17] R. Rambaud and M. Brini-Fritz [Bull. soc. chim. France, 1426 (1958)] have reported methyl γ-chlorocrotonate (stereochemistry not specified) to be a liquid, b.p. 80-81° (19 mm.), n^{14}_{D} 1.469.

c.p.s.) as well as a pair of doublets (J = 1 and 6 c.p.s.) centered at 4.51 δ (2 H, $-CH_2-Cl$) and a singlet at 3.61 δ (3 H, $-O-CH_3$). The *trans*-isomer **9**, b.p. 68.5° (11 mm.), $n^{24}D$ 1.4650, has infrared absorption[15] at 1730 cm.$^{-1}$ (C=O), at 1665 cm.$^{-1}$ (C=C) and at 975 cm.$^{-1}$ (*trans* CH=CH) with an ultraviolet maxima[13] at 206 mμ (ε 14,400). The sample has n.m.r. peaks[10] attributable to vinyl protons at 6.86 δ (1 H, pair of triplets with J = 6 and 15 c.p.s.) and at 5.89 δ (1H, pair of triplets with J = 1 and 15 c.p.s.) as well as a pair of doublets (J = 1 and 6 c.p.s.) centered at 4.03 δ (2 H, $-CH_2-Cl$) and a singlet at 3.63 δ (3 H, $-O-CH_3$).

Anal. Calcd. for $C_5H_7ClO_2$: C, 44.64; H, 5.25; Cl, 26.23; mol. wt., 134, 136. Found for *cis*-isomer: C, 44.74; H, 5.47; Cl, 26.25; mol. wt., 134 and 136 (mass spectrum). Found for *trans*-isomer: C, 44.55; H, 5.22; Cl, 26.06; mol. wt., 134 and 136 (mass spectrum).

During separation of the chlorocrotonic esters **9** and **10** the *cis*-isomer **10** was observed to be converted to crotonolactone (**18**) on gas chromatograhy columns at high temperatures. Consequently an authentic sample of this lactone **18** was prepared to establish its absence among the reaction products. The absence of crotonolactone (**18**) in the products eluted from the gas chromatograph[12] was demonstrated both by collection of samples (which lacked infrared absorption characteristic of the lactone **18**) and by comparison of retention times [on the column used the lactone **18** was eluted after both the *cis*-ester **10** (first eluted) and the *trans*-ester **9** (second eluted)].

Preparation of crotonolactone (18) and its precursors.- To a solution of 165 g. of an acetic acid solution containing 0.85 mole of peracetic acid in 350 ml. of ethyl acetate was added 15 g. of sodium acetate. To this mixture, kept at 23°, was added, dropwise and with stirring, 92.6 g. (0.81 mole) of ethyl 3-butenoate.[18] The reaction mixture was stirred for 60 hr. at 23-25° and then neutralized to pH 7.5 by the addition of aqueous sodium carbonate. After separation of the organic layer, the aqueous phase was extracted with ether. The combined organic solutions were dried, concentrated, and distilled to separate 28 g. of the starting ester, b.p. 72-75° (18 mm.), $n^{25}D$ 1.4208 and 60.22 g. (57.4% of ethyl 3,4-epoxybutyrate as a colorless liquid, b.p. 79° (18 mm.), $n^{25}D$ 1.4208.[19] This epoxy ester has infrared absorption[15] at 1735 cm.$^{-1}$ (ester C=O) with no significant ultraviolet absorption (ϵ 75 at 210 mμ)[13] and exhibits a single peak on gas chromatography.[20]

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(18) This ester was kindly supplied by Dr. D. L. Heywood, Union Carbide Chemicals Co.

(19) R. Ramboud, S. Ducher, A. Broche, M. Brini-Fritz, and M. Vessiere [Bull. soc. chim. France, 877 (1955)] report b.p. 75.5-76° (16 mm.), $n^{15}D$ 1.427.

(20) A column packed with 1540 Carbowax suspended on ground firebrick was employed.

A mixture of 10 g. (77 mmoles) of ethyl 3,4-epoxybutyrate and 30 g. of 10% aqueous sulfuric acid was stirred for 2 hr. at 40-46° and then continuously extracted with ether for 36 hr. The organic extract was concentrated and distilled[21] to separate 1.75 g. (27.3%) of crotonolactone (**18**) as a colorless liquid, b.p. 71-73° (2.9 mm.), n^{25}_{D} 1.4659 [lit.[22] b.p. 100-102° (18 mm.), n^{25}_{D} 1.4660], which contained[20] less than 1% of impurities. The lactone **18** has infrared absorption at 1740 and 1775 cm.$^{-1}$ (C=O)[23] with an ultraviolet maximum[24] at 208 mμ (ε 5140) and n.m.r. absorption corresponding to the published[25] spectrum.

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(21) If the acid in the extract was neutralized prior to distillation the distillate was primarily 3-hydroxybutyrolactone. Cf. ref. 19.

(22) N. C. Kaas, F. Limborg, and K. Glens, Acta Chem. Scand., *6*, 531 (1952).

(23) The carbonyl doublet in these lactones is thought to arise from Fermi resonance. See R. N. Jones, C. L. Angell, T. Ito, and R. J. D. Smith, Can. J. Chem., *37*, 2007 (1959).

(24) Determined in isoöctane solution.

(25) "N.M.R. Spectra Catalog," Varian Associates, Palo Alto, California, 1962, Spectrum No. 51.

Reaction of the Ylid 8 with Chloroacetaldehyde.- A solution of 10.2 g. (25 mmoles) of the phosphorane 8 and 1.997 g. (25 mmoles) of freshly distilled chloroacetaldehyde in 120 ml. of methylene chloride was refluxed for 2 hr., allowed to stand overnight and then concentrated. After the residual solid had been continuously extracted with pentane for 120 hr., concentration of the pentane extract separated 3.14 g. (64.4%) of the crude, crystalline unsaturated ketone 7a, m.p. 35-40°. Sublimation (25° at 0.02 mm.) of this material afforded the pure ketone 7a as white prisms, m.p. 39.5-40.5°, with infrared absorption[15] at 1685 and 1670 $cm.^{-1}$ (conj. C=O), at 1630 $cm.^{-1}$ (conj. C=C) and at 977 $cm.^{-1}$ (trans CH=CH) as well as ultraviolet maxima[26] at 212 mμ (ε 1800) and 188 mμ (ε 4500). The sample has broad n.m.r. absorption[10] at 7.39 δ (5 H, aryl C-H) with a singlet at 3.90 δ (2 H, $Ar-CH_2-CO$), a doublet (J = 5.5 c.p.s.) at 4.19 δ (2 H, $Cl-CH_2-$) and absorption attributable to the vinyl protons at 6.48 δ (1 H, doublet with J = 16 c.p.s., long range coupling perceptible but not resolved) and at 6.97 δ (1 H, pair of triplets with J = 5.5 and 16 c.p.s.).

Anal. Calcd. for $C_{11}H_{11}ClO$; C, 67.87; H, 5.70; Cl, 18.22; mol. wt., 194, 196. Found: C, 68.00; H, 5.94; Cl, 18.14; mol. wt., 194, 196 (mass spectrum).

Various efforts to isolate or confirm the presence of the cis-chloro ketone 7b in the reaction mixtures were unsuccessful. We are therefore uncertain of the degree of stereoselectivity in this reaction.

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(26) Determined as a solution in n-heptane.

PART II

THE FAVORSKII REARRANGEMENT OF CIS- AND TRANS 9-CHLORO-1-DECALONES

It was the aim of this work to study the mechanism of the Favorskii rearrangement. Earlier studies[1] have amply demonstrated a strong dependence of both product composition and stereochemistry on reaction conditions in the Favorskii rearrangement. To achieve high yields of esters as products of a stereospecific rearrangement (inversion at the *α*-carbon atom) the use of strong bases in aprotic, non-nucleophilic, and non-polar solvents has been recommended[1d,e,f] along with *α*-halo ketones capable of assuming coplanarity of the halogen atom with the carbonyl group.[2] Some of these generalizations were tested during the course of this thesis using the bromo ketone **1** and the *trans*- and *cis*-9-chloro-1-decalones **8** and **9** with sodium methoxide in methanol and in 1,2-dimethoxyethane (DME).

As may be seen from the following summary of results in case of the ketone **1** radical changes in product composition occured caused by the change of solvents. In both solvents, however, the Favorskii rearrangement product ester **2** was a minor product only.[3]

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(1) (a) A. S. Kende, Org. Reactions, **11**, 261 (1960); (b) A. A. Sachs and J. G. Aston, J. Am. Chem. Soc., **73**, 3902 (1951); (c) G. Stork and I. J. Borowitz, J. Am. Chem. Soc., **82**, 4307 (1960); (d) H. O. House and W. F. Gilmore, J. Am. Chem. Soc., **83**, 3980 (1961); (e) H. O. House and W. F. Gilmore, J. Am. Chem. Soc., **83**, 3972 (1961); (f) A. Gandemer, J. Parello, A. Shrabek, and B. Tchoubar, Bull. soc. chim. France, 2405 (1963).

(2) H. O. House and H. W. Thompson, J. Org. Chem., **28**, 164 (1963).

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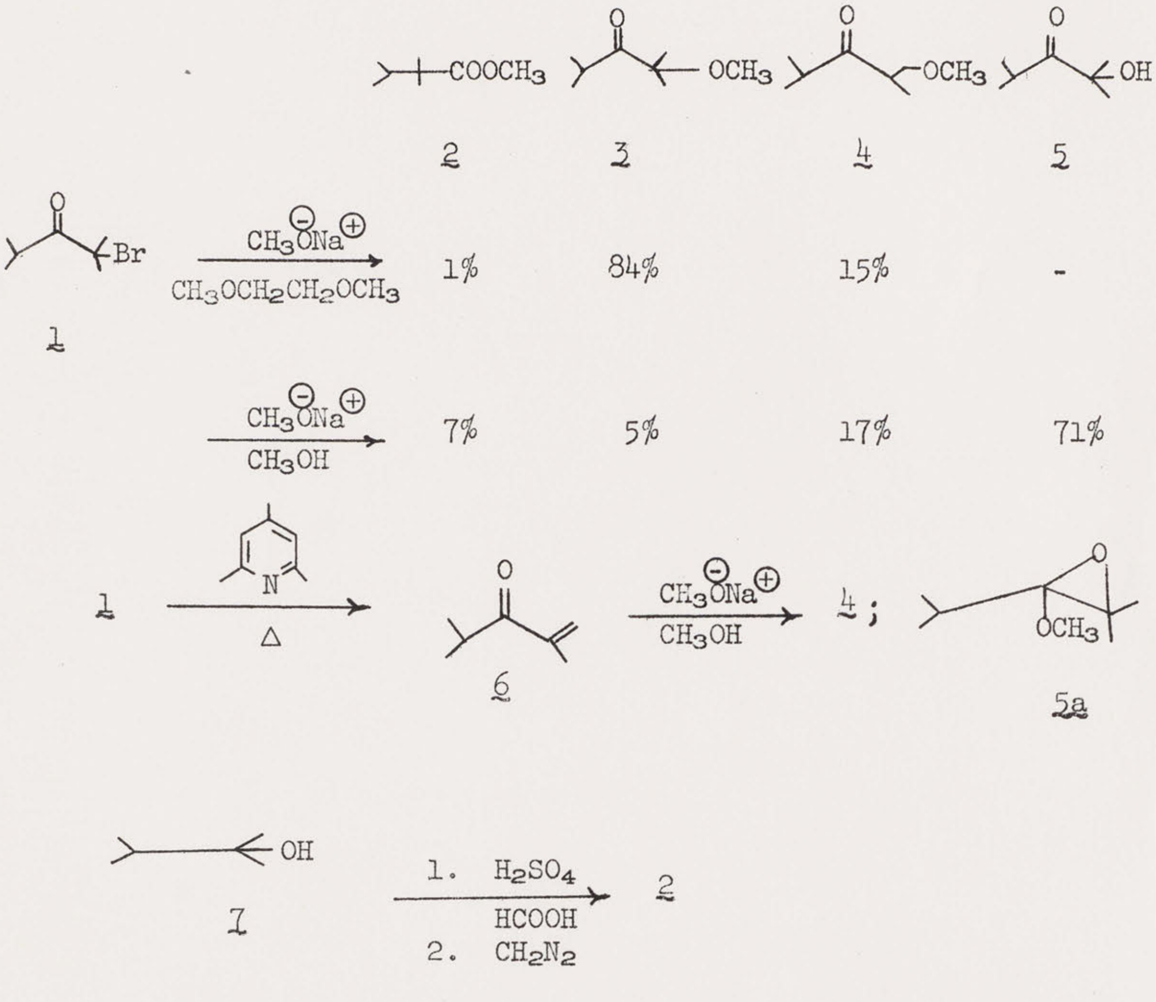
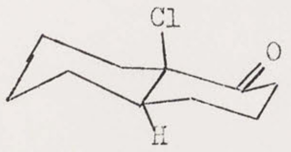
(3) Sachs and Aston (ref. 1b) found only the ketone 3 in low yield from the bromo ketone 1 and sodium methoxide in ether. These authors obtained small quantities of Favorskii rearrangement products when sodium isopropoxide or sodium benzyloxide was employed.

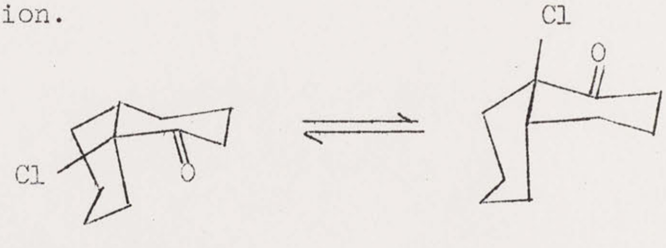


The β-methoxy ketone 4 is believed to be a secondary product arising from the Michael addition of methanol to the dehydrohalogenated ketone 6 initially formed in the reaction mixture; the α-hydroxy ketone 5 is probably the hydrolysis product of the epoxy ether 5a.[1a,4] The formation of this epoxy ether 5a through the nucleophilic attack of methoxide ion on the carbonyl group, followed by displacement of the bromide ion, is facilitated in the more polar methanolic medium. We shall defer discussion on formation of the α-methoxy ketone 3 to correlate with similar products from the chloro decalones.

The *trans*-9-chloro-1-decalone (8) is unfavorable, at least in the chair conformation, to internal nucleophilic displacement of the halogen atom. The *cis*-isomer 9, however, is expected to exist in a mobile equilibrium of the forms 9a and 9b providing the conformation 9a favorable to internal nucleophilic displacement by an initially formed enolate anion.



8a



9a

9b

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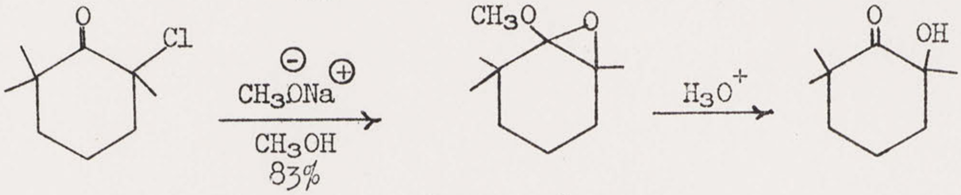
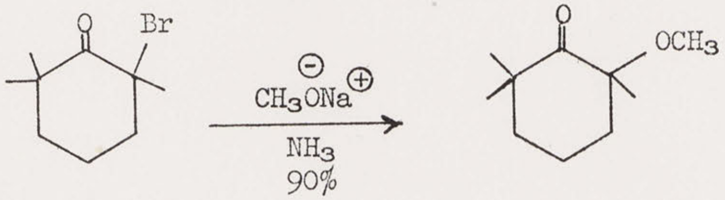
(4) A sequence of papers by C. L. Stevens and co-workers, the last one of which is No. XX, C. L. Stevens et al., J. Org. Chem., 29, 3146 (1964), deals with the preparation and reactions of epoxy ethers; e.g. C. L. Stevens and A. J. Weinheimer, J. Am. Chem. Soc., 80, 4072 (1958) report the following:





Sodium methoxide catalyzed rearrangements of the *trans*- and *cis*-chloro ketones **8** and **9** in methanol and in dimethoxyethane afforded product mixtures containing either the methoxy ketones **12** - **15** (from methanol) or the mixture of esters **18** - **22** (from DME) with different product *ratios* resulting from the *trans*- and *cis*-ketones **8** and **9**.[5] When a dimethoxyethane solution which was 4.4 *M* in methanol and 0.9 *M* in sodium methoxide was used, a mixture of the ketones **12** - **15** and esters **18** - **22** was obtained. Chart I represents the results of these experiments; the product composition shown for the *cis*-chloro ketone **9** was calculated from product composition obtained from the ketone mixture **8** and **9**, assuming approximately 45% of **9** and 55% of **8** (see Experimental). Based on the reasonable assumption that esters **19** and **21** arise from the approximately 5% *cis*-ketone present in the *trans*-ketone **8** (see n.m.r. spectrum) the Favorskii rearrangement of these two ketones **8** and **9** in 1,2-dimethoxyethane appears to be completely stereospecific.

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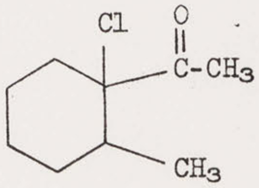
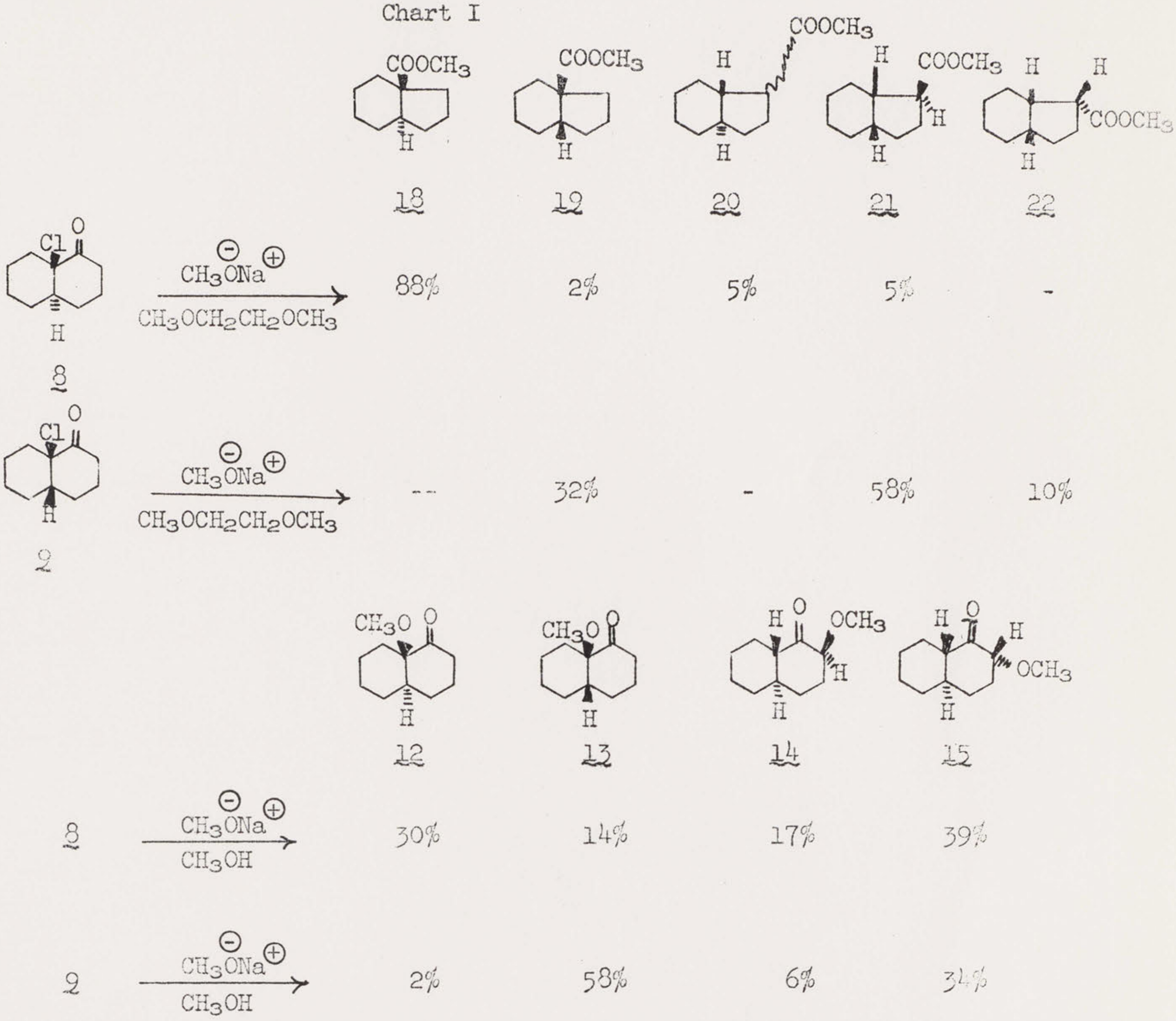
(5) When, *e.g.* the chloro ketone **i** was treated under the same conditions Favorskii rearrangement products were obtained.[1e,f]



i

Chart I

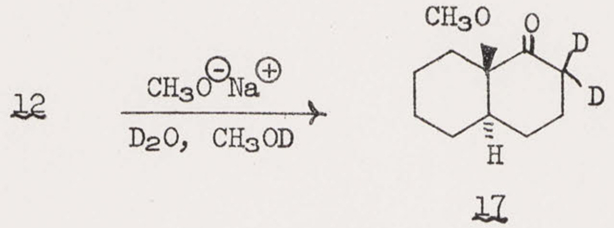


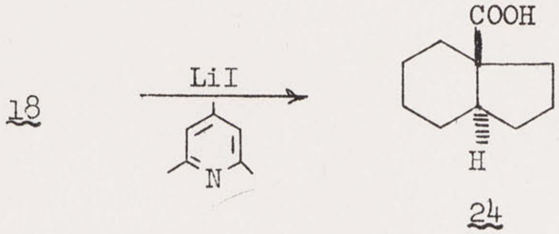
		18	19	20	21	22
8	CH$_3$O$^{\ominus}$Na$^{\oplus}$, CH$_3$OCH$_2$CH$_2$OCH$_3$	88%	2%	5%	5%	-
9	CH$_3$O$^{\ominus}$Na$^{\oplus}$, CH$_3$OCH$_2$CH$_2$OCH$_3$	--	32%	-	58%	10%

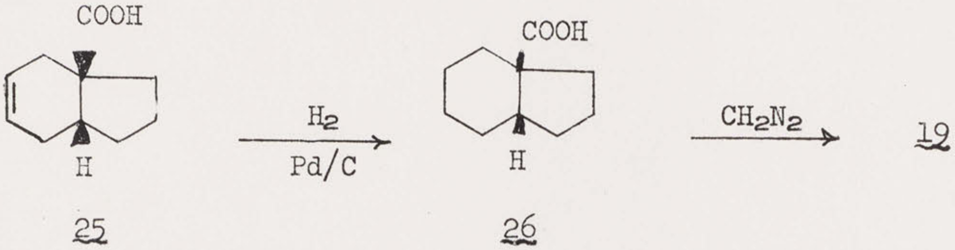
		12	13	14	15
8	CH$_3$O$^{\ominus}$Na$^{\oplus}$, CH$_3$OH	30%	14%	17%	39%
9	CH$_3$O$^{\ominus}$Na$^{\oplus}$, CH$_3$OH	2%	58%	6%	34%

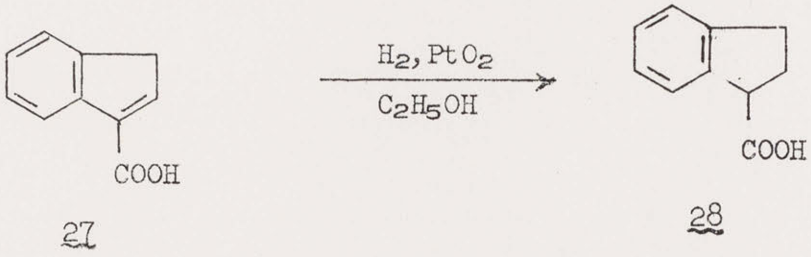
Separate experiments showed that the methoxy ketones 14 and 15 and the esters 21 and 22 were present amont the reaction products in equilibrium concentrations.

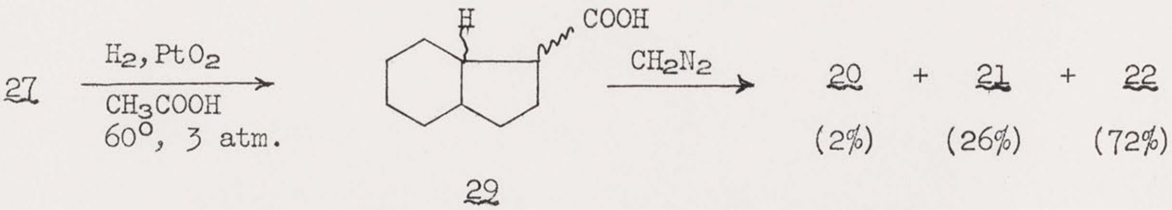
The following chart depicts the sequences of reactions used for the necessary structure proofs. For additional information concerning the methoxy ketones **12** - **15** see ref. 2.











If one discards the rearrangement of initially formed epoxy ethers from the α-halo ketones to the α-methoxy ketone products in these reactions[1a,4] then a choice has to be made from the many possible pathways following the enolate anion formation.[6] Clearly, since all of the above reactions of the chloro decalones **8** and **9** show a large degree of stereospecificity, the mesomeric zwitterion form **31**,[7] with its total lack of steric integrity, cannot be the sole intermediate. Our choice for the explanation lies with the cyclopropanone intermediate although to form such an intermediate, taking into consideration the objections raised by Burr and Dewar,[8]

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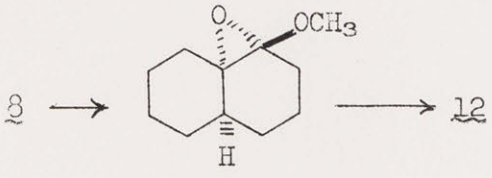
(6) Epoxy ethers have been isolated previously[1a,4] and hydrolyzed to α-hydroxy ketones, though we know of no instance where these rearranged to α-methoxy ketones in the manner acetoxy ethers are known to rearrange to α-acetoxy ketones. [See H. O. House and H. W. Thompson, J. Org. Chem., 26, 3729 (1961)]. While such an intermediate as **i** could explain the stereospecific formation of the 9-methoxy ketones **12** and **13** one would be in a dilemma over the formation of the 2-methoxy compounds **14** and **15** from **i** unless a second mechanism were involved.

e.g.



i

(7) J. G. Aston and J. D. Newkirk, J. Am. Chem. Soc., 73, 3900 (1951).

(8) J. G. Burr and M. J. S. Dewar, J. Chem. Soc., 1201 (1954).

some solvated, stereochemically protected form of **31** has to intervene. Backside shielding of the incipient carbonium ion by the π-orbital of the enolate anion accomplishes the same task. Consider the cyclopropanones **32** and **33** which are attacked immediately after formation by excess methoxide ion, less solvated in dimethoxyethane, at the carbonyl group to open, stereospecifically, both possible ways to produce, on the one hand, the esters **18** and **20** from **32**, and the esters **19**, **21**, and **22** from **33**, on the other. If attack on the cyclopropanone is not instantaneous an equilibrium, through **31**, may be established[9] very slowly with the sterically less strained

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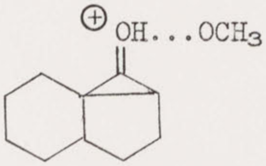
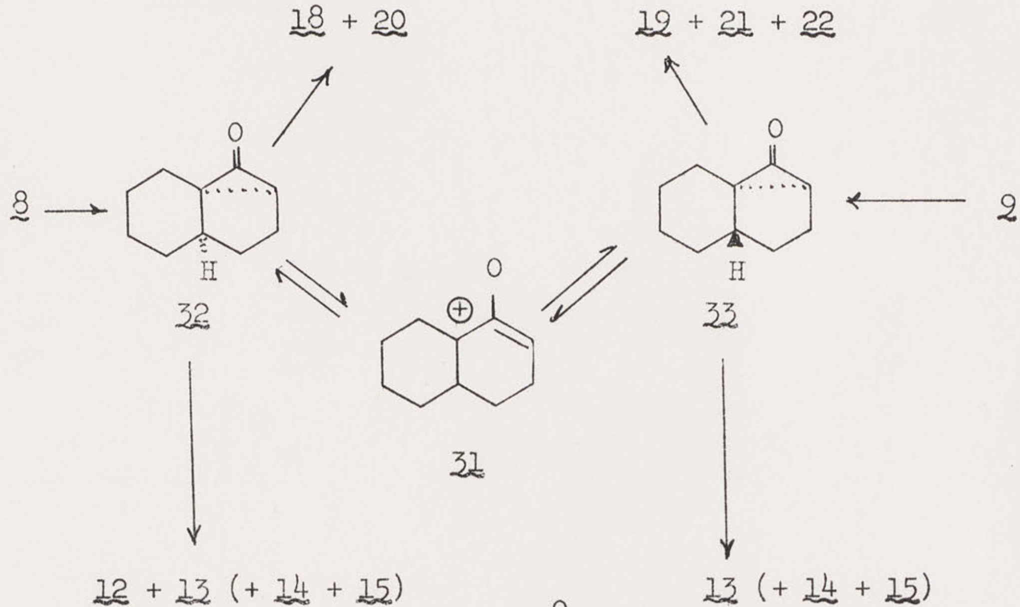
(9) One explanation for this is the stabilization of the cyclopropanone intermediate through solvation in the more polar methanolic medium to give rise to **i**. The experiment designed to

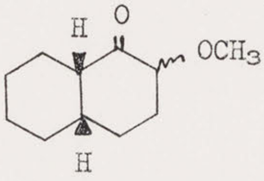


i

shed some light on this point, increasing the concentration from the usual *ca.* 0.15 M methanol in DMF to *ca.* 5 M, proved inconclusive. *If* this were the mechanism the reaction would be second order in methanol and the *ca.* 30-fold increase in methanol concentration should lead *to* an approximately 1000-fold increase in the formation of methoxy ketones **12** - **15**. Actually, of the reaction products the esters **18** - **22** accounted for 80% and the methoxy ketones **12** - **15** for 20%. Methanol, however, may help the establishment of the equilibrium through solvation of **31**.

33, the one arising from the *cis*-ketone 9, predominating. This would explain the presence of some of the *cis*-9-methoxy ketone 13 from the *trans*-ketone 8.





16

The 2-methoxy-*cis*-1-decalone (16), obtained in impure form from experiments designed to detect the kinetically controlled product, appears to be the product of kinetic protonation after ring opening of 32 and/or 33.

The α-methoxy ketones 3, 14, and 15 may also arise from the first formed enolate anions through direct attack at the α'-position by methanol or methoxide ion and expulsion of the halide ion. The traditional objection of attacking an electron-rich center by a nucleophile may be tempered if one assumes the presence of a small amount of enol, in equilibrium with the enolate anion, which can undergo the attack.

Results of reactions of alcohols with hemi ketals of a cyclopropanone[10] pose the interesting question concerning the almost total lack of formation of the Favorskii rearrangement product 2 from the ketone 1 when sodium methoxide is the base used. When, however,

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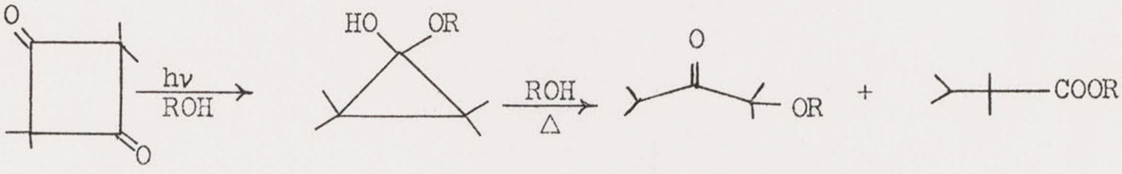
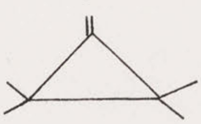
(10) N. J. Turro, G. W. Byers, and P. A. Leermakers, J. Am. Chem. Soc., 86, 955 (1964); H. G. Richey, J. M. Richey, and D. C. Clagett, *ibid.*, 86, 3906 (1964); P. A. Leermakers, G. F. Vesley, N. J. Turro, and D. C. Neckers, *ibid.*, 86, 4213 (1964) have found the hemiketal i as the major product from irradiation of ketone ii. The hemiketal i, when refluxed with an alcohol afforded both the alkoxy ketone iii and the ester iv.



ii i iii iv

This ester iv must, of necessity, arise through the cyclopropanone v, while the ketone iii may be a product from v or directly from i through an S_N2' process.



v

different bases are used as high as 30% of Favorskii rearrangement products can be realized.[1b]

The body of data available to date, however extensive, needs further additions to clarify the exact nature of intermediates in the Favorskii rearrangement.

Experimental[11]

2-Bromo-2,4-dimethyl-3-pentanone (1).- This bromo ketone, obtained by the bromination of diisopropyl ketone in chloroform solution, was obtained as a colorless liquid, b.p. 85° (16 mm.), n^{25}_{D} 1.4526 [lit.[12,18] b.p. 50-51° (10 mm.), 166-168° (760 mm.), 59-61° (18-20 mm.)]. The bromo ketone has infrared absorption[13] at 1715 cm.$^{-1}$ (C=O) with n.m.r. peaks[13] at 3.51 δ (1 H, 7 lines with J = 6.5 c.p.s., $>$CH-CO), at 1.89 δ (6 H singlet, $CH_3-\overset{|}{\underset{|}{C}}-Br$), and at 1.18 δ (6 H doublet with J = 6.5 c.p.s., CH_3). The mass spectrum of the compound has weak molecular ion peaks at m/e 192 and 194 with abundant fragment peaks at m/e 121 and 123 ($CH_3-\overset{\oplus}{C}{<}^{Br}_{CH_3}$), at 71 [$(CH_3)_2C\equiv\overset{\oplus}{O}$], and at

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[11] All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin Elmer, Model 237, infrared recording spectrophotometer fitted with a grating. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14. The NMR spectra were determined at 60 mc. with a Varian, Model A-60, NMR spectrometer. The mass spectra were obtained with a CEC, Model 21-130, Mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates and by the Scandinavian Microanalytical Laboratory.

[12] (a) A. J. Oumoff, Bull. soc. chim. France, [2]43, 568 (1928).
(b) A. Unnowa, J. prakt. Chem., [2]88, 641 (1913).

[13] Determined as a solution in carbon tetracloride.

43 $[(CH_3)_2CH^{\oplus}]$.

*Reaction of the Bromo Ketone **1** with Methanolic Sodium Methoxide*.- A solution of 2.895 g. (15 mmoles) of the bromoketone in 20 ml. of methanol was added to a solution of sodium methoxide prepared from 2.327 g. (100 mg.-atom) of sodium and 30 ml. of methanol. After the resulting mixture had been stirred for 10 hr. at room temperature, it was diluted with saturated aqueous sodium chloride and extracted with ether. The ethereal extract was dried and concentrated; distillation of the residue (1.647 g. of light yellow liquid) in a short-path still (100-120° at 0.1 mm.) afforded 1.1216 g. of colorless liquid. This liquid contained,[14] in order of increasing retention time, the ester **2** (*ca*. 8%), the α-methoxy ketone **3** (*ca*. 8%), the β-methoxy ketone **4** (*ca*. 14%) and the hydroxy ketone **5** (*ca*. 70%). In a comparable reaction (employing 2.890 g. or 15 mmoles of the bromo ketone **1**), 73.3 mg. of 1-methylcyclohexene was added as an internal standard and the crude, undistilled product (1.2644 g.) was analyzed.[14] The product contained the ester **2** (7%), the α-methoxy ketone **3** (5%), the β-methoxy ketone **4** (17%), and the hydroxy ketone **5** (71%), the calculated yield being 4% of **2**, 3% of **3**, 10% of **4**, and 43% of **5**. No higher boiling or acidic products were found. To determine the composition and yield values, a calibration curve

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(14) A gas chromatography column packed with Carbowax 20M, suspended on ground firebrick was employed.

was prepared with mixtures containing known weights of the products and the internal standard.

Samples of each of the products from the reaction were calibrated[14,15] and the ester **2** and α-methoxy ketone **3** were identified with subsequently described samples by comparison of retention times and infrared spectra. A collected sample of the hydroxy ketone **5**, n^{25}_{D} 1.4182 (lit.[16] n^{25}_{D} 1.4190), has infrared absorption[13] at 3600 and 3480 (unassoc. and assoc. O-H) and at 1710 cm.$^{-1}$ (C=O) with n.m.r. absorption[13] at 3.43 δ (1 H, broad, OH), at 3.03 δ (1 H, 5 lines of expected 7 line pattern discernible, J = 6.5 c.p.s., $>$CH-CO), at 1.32 δ [6 H singlet, $(CH_3)_2\overset{|}{C}-OH$] and at 1.08 δ [6 H doublet with J = 6.5 c.p.s., methyl groups of $(CH_3)_2CH-CO-$]. The mass spectrum has a molecular ion peak at m/e 130 with abundant fragment peaks at m/e 87 $[(CH_3)_2\overset{OH}{\overset{|}{C}}-\overset{\oplus}{C}\equiv O]$, 71 $[(CH_3)_2CH-\overset{\oplus}{C}\equiv O]$, 59 $[(CH_3)_2\overset{\oplus}{C}=OH]$ and 43 $[(CH_3)_2CH^{\oplus}]$. To obtain an authentic sample of the hydroxy ketone **5**, a mixture of 9.65 g. (50 mmoles) of the bromo ketone **1** and 100 ml. of 2 M aqueous potassium carbonate was refluxed for 14 hr.[17] The ether extract of

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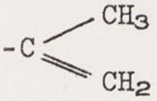
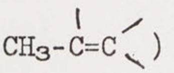
(15) A gas chromatography column packed with Silicone Rubber, No. SE 30, suspended on ground firebrick was employed.

(16) R. Paul, Compt. rend., 200, 1481 (1935).

(17) The procedure of J. Colonge and J. C. Dubrin, Bull. soc. chim. France, 1180 (1960).

the reaction mixture was dried and concentrated; distillation of the residual yellow liquid (8.174 g.) separated 7.633 g. of a colorless liquid, b.p. 53-55° (7 mm.), which contained[15] approximately equal amounts of the starting bromo ketone 1 and the hydroxy ketone 5. A collected sample of the hydroxy ketone, n^{25} D 1.4196 [lit.[16,17] b.p. 59° (17 mm.) n^{25} D 1.4190] was identified with the previous sample by comparison of retention times and infrared spectra.

A collected sample of the β-methoxy ketone 4 has infrared absorption[13] at 1715 cm.$^{-1}$ (C=O) with n.m.r. absorption[13] at 3.34 δ (2 H, doublet with J = 7.5 c.p.s., $-CH_2-O$) and at 3.22 δ (3 H singlet, $O-CH_3$) with complex absorption in the region 2.4-3.2 δ (2 H, $>CH-CO-$) and three overlapping doublets (J = 7 c.p.s. in each case) at 1.03, 1.01, and 0.97 δ (9 H, CH_3-). The mass spectrum of the product has a molecular ion peak at m/e 144 with abundant fragment peaks at m/e 101 $[CH_3OCH_2(CH_3)CH\text{-}\overset{\oplus}{C}{\equiv}O]$, 73 $[CH_3OCH_2(CH_3)CH^{\oplus}]$, 71 $[(CH_3)_2CH\text{-}\overset{\oplus}{C}{\equiv}O]$, 45 $(CH_3\text{-}\overset{\oplus}{O}{=}CH_2)$ and 43 $[(CH_3)_2CH^{\oplus}]$.

To obtain an authentic sample of the β-methoxy ketone 4, a solution of 4.83 g. (25 mmoles) of the bromo ketone 1 in 25 ml. of *γ*-collidine was refluxed overnight under a nitrogen atmosphere. The reaction mixture was poured into aqueous acid and extracted with ether. After the ether solution had been washed with aqueous sodium chloride, dried and concentrated, distillation of the residue in a short-path still (70° at 10 mm.) separated 1.1637 g. (42%) of 2,4-dimethyl-1-penten-3-one (6) as a colorless liquid, n^{25} D 1.4251 [lit.[17] b.p. 50° (60 mm.), n^{25} D 1.4260], which exhibits a single peak in gas chromatography.[15] The product has infrared absorption[13] at 1680 (conj. C=O) at 1625 (conj. C=C), and at 860 and 927 cm.$^{-1}$ ($C=CH_2$) with n.m.r. peaks[13] at 5.88 δ (1 H, broad but coupling not resolved) and 5.73 δ (1 H, partially resolved quartet with J = 1.5 c.p.s.) attributable to the vinyl protons of the grouping  $-C(CH_3){=}CH_2$ as well as absorption at 3.26 δ (1 H, 7 lines with J = 6.5 c.p.s.), a partially resolved multiplet at 1.86 δ (3 H,  $CH_3-C{=}C<$) and a doublet (J = 6.5 c.p.s.) at 1.07 δ (6 H, $-CH_3$).

A solution of 1.1637 g. (10 mmoles) of the unsaturated ketone **6** in 3 ml. of methanol was added to a cold (0°) solution of 1.0 mmole of sodium methoxide in 1 ml. of methanol. The resulting mixture was stirred for 3 hr. and then acidified with dilute, aqueous hydrochloric acid and extracted with ether. After the extract had been dried and concentrated, the residual light yellow liquid (1.09 g.) was found to contain[15] 13% of the starting unsaturated ketone **6** and 87% of the β-methoxy ketone **4**. A collected[15] sample of the methoxy ketone **4** was identified with the previously described sample by comparison of retention times and infrared, n.m.r., and mass spectra.

Anal. Calcd. for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.45; H, 10.94.

Reaction of the Bromo Ketone 1 with Sodium Methoxide in 1,2-Dimethoxyethane.- A suspension of sodium methoxide was prepared by refluxing a mixture of 3.2 g. (0.1 mole) of methanol and 30 ml. of

1,2-dimethoxyethane with 2.3 g. (0.1 g.-atom) of sodium under a nitrogen atmosphere until all the sodium was consumed. To this suspension was added 2.855 g. (0.015 mole) of the bromo ketone 1 and the resulting mixture was stirred at room temperature for 10 hr. and then poured into aqueous sodium chloride. After the resulting mixture had been extracted with ether, the extract was dried and concentrated to leave 1.282 g. of light yellow liquid which contained[14] the ester 2 (1%), the α-methoxy ketone 3 (86%) and the hydroxy ketone 5 (13%). In a comparable experiment where 274 mg. of 1-methylcyclohexene was added as an internal standard, the composition of the crude product was 2 (1%), 3 (84%) and 5 (15%), the calculated yields being 1% of 2, 53% of 3 and 9% of 5. No higher boiling or acidic products were found. The ester 2 was identified with an authentic sample by comparison of retention times. A collected[15] sample of the hydroxy ketone 5 was identified with the previously described sample by comparison of retention times and infrared and mass spectra. A collected[15] sample of the previously described[1b,18] α-methoxy ketone 3, n^{25}_{D} 1.4101, has infrared absorption[13] at 1715 $cm.^{-1}$ (C=O) with n.m.r. absorption[13] at 1.00 δ (6 H doublet with J = 6.5 c.p.s., (3 H, O-CH_3) superimposed on a multiplet in the region 2.9-3.5 δ (1 H, $>$CH-CO). The mass spectrum of the product has a very weak

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[18] The authors in ref. 1b report b.p. 149-151°, n^{20}_{D} 1.4113-1.4120, for the methoxy ketone 3.

molecular ion peak at m/e 144 with abundant fragment peaks at m/e 73 $[(CH_3)_2C{=}\overset{\oplus}{O}\text{-}CH_3]$ and 43 $[(CH_3)_2CH^{\oplus}]$.

Methyl-2,2,3-trimethylbutyrate (**2**).- 2,3-Dimethyl-2-butanol (**7**), b.p. 115-118°, n^{25} D 1.4136 [lit.[19] 118-118.6° (757 mm.], was prepared in 61% yield by the reaction of 3-methyl-2-butanone with excess methylmagnesium bromide. The product has infrared absorption[13] at 3600 and 3400 cm.$^{-1}$ (unassoc. and assoc. O-H) with n.m.r. peaks[13] at 2.26 δ (1 H, O-H), at 1.08 δ (6 H singlet, CH_3) and at 0.87 δ (6 H, doublet with J = 6.5 c.p.s., CH_3) as well as a multiplet in the region 1.1-1.8 δ (1 H, $>CH-$). The mass spectrum exhibits no molecular ion peak but has abundant fragment peaks at m/e 87 $[(CH_3)_2CH\text{-}\overset{\oplus OH}{\overset{\|}{C}}\text{-}CH_3]$, 59 $[(CH_3)_2C{=}\overset{\oplus}{O}H]$ and 43 $[(CH_3)_2CH^{\oplus}]$.

To a solution of 10.2 g. (0.1 mole) of the alcohol **7** in 110 g. of cold (0°), concentrated sulfuric acid was added, dropwise and with stirring over a 20-min. period, 13.8 (0.3 mole) of formic acid.[20] The resulting cold mixture was stirred for 1 hr. and then poured onto 200 g. of ice and extracted with ether. The ethereal solution was extracted with aqueous sodium hydroxide. After the resulting

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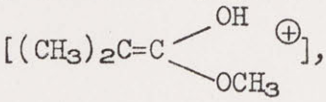
(19) M. Delacre, Bull. soc. chim. France, *[4]1*, 456 (1907).

(20) (a) The procedure of W. Haaf and H. Koch, Ann., *618*, 251 (1958); (b) *ibid*., *638*, 122 (1960).

aqueous extract had been acidified with hydrochloric acid and extracted with ether, the ether solution was dried and concentrated to leave 1.0606 g. of crude acidic product. Distillation in a short path still (110° at 10 mm.) afforded 732.2 mg. of 2,2,3-trimethylbutyric acid [lit.[10b] b.p. 111° (20 mm.)] with infrared absorption[13] at 3000 (broad, assoc. O-H) and 1710 cm.$^{-1}$ (carboxyl C=O). Esterification of this acid sample with excess ethereal diazomethane followed by filtration and evaporation of the ether afforded 0.81 g. of the crude ester 2 as a colorless liquid. A collected[15] sample of the pure ester 2 has infrared absorption[13] at 1735 cm.$^{-1}$ (ester C=O); the mass spectrum of the sample has a molecular ion peak at m/e 144 with abundant fragment peaks at m/e 102  $[(CH_3)_2C{=}C(OH)(OCH_3)^{\oplus}]$, 85 $[(CH_3)_2CH\text{-}\overset{\oplus}{C}(CH_3)_2]$ and 43 $[(CH_3)_2CH^{\oplus}]$.

Preparation of the 9-chloro-1-decalones 8 and 9.- 1-Decalone (60.8 g. or 0.40 mole) was chlorinated with sulfuryl chloride in carbon tetrachloride as previously described.[21] Repeated crystallization of the crude product from petroleum ether at Dry Ice temperature separated 7.494 g. (10%) of the trans-chloro ketone 8, m.p. 39-40° (lit.[11c] 40-41°). Distillation of the crude product recovered from the mother liquor separated 67 g. of pale yellow liquid,

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[21] (a) E. W. Warnhoff, Ph. D. Dissertation, University of Wisconsin, 1953; (b) E. W. Warnhoff and W. S. Johnson, J. Am. Chem. Soc., 75, 494 (1953); (c) H. O. House and H. W. Thompson, J. Org. Chem., 26, 3729 (1961).

b.p. 80-87° (0.4-0.8 mm.) which was estimated from its spectra and gas chromatogram[14,22] to contain more than 90% of the two chloro ketones **8** and **9**. Repeated fractional distillation of this material separated 9.0509 g. of a mixture containing[14,22] 97% of the chloro ketones **8** and **9**, b.p. 68° (0.35 mm.), n^{25}_{D} 1.5043, as well as other fractions containing predominantly the chloro ketones **8** and **9** as well as varying amounts of 1-tetralone and 1-decalone. The gas chromatogram[14,22] of the above mentioned mixture of chloro ketones **8** and **9** exhibits peaks for the dehydrochlorinated products **10** and **11** in the proportions 38% of **11** and 62% of **10** indicating that 40% or more of the mixture is the *cis*-chloro ketone **9**. The subsequently described ester mixtures from Favorskii rearrangement suggest that the mixture contains 47% of the *cis*-isomer **9** and 53% of the *trans*-isomer **8**. We therefore conclude that this mixture is approximately 45% *cis*-chloro ketone **9** and 55% *trans*-chloro ketone **8**. Since our efforts to obtain pure samples of the *cis*-chloro ketone **9** have thus far been unsuccessful, this mixture (containing *ca.* 45% of **9**) was used along with the pure *trans*-chloro ketone in subsequent experiments.

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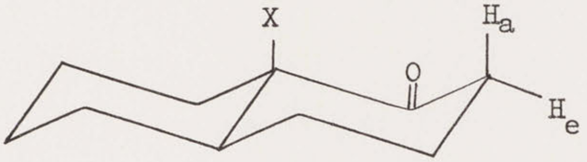
(22) On the column (ref. 14) employed for analysis, both chloro ketones **8** and **9** were dehydrohalogenated to form unsaturated ketones **10** and **11**. The major dehydrohalogenated product from the pure *trans* ketone **8** under these conditions was the unsaturated ketone **10** (> 95%), whereas mixtures containing the *cis*-chloro ketone **9** also formed the octalone **11**.

The pure trans-chloro ketone 8 has the previously noted[21c] infrared[13] and ultraviolet[22a] peaks at 1718 cm.$^{-1}$ (C=O) and 300.5 mμ (ε 45) as well as complex n.m.r. absorption[13] in the region 1.1-2.5 δ (14 H) and a complex, partially resolved multiplet in the region 2.7-3.5 δ (1 H). The same pattern attributable to one proton in the lower field region of the spectrum is found in the n.m.r. spectrum of the subsequently described 9-methoxy-trans-1-decalone (12). The low-field absorption is believed to arise from the axial 2-proton (Ha in structure 30) which is deshielded by the nearby axial, electronegative substituent (X in structure 30).[23]



30 X = Cl or OCH_3

The previously described mixture of chloro ketones (ca. 45% 9 and 55% 8) has infrared absorption[13] at 1725 cm.$^{-1}$ with ultraviolet

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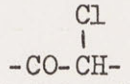
(22) (a) Determined in ethanol solution.

(23) (a) The deshielding of an axial methyl group by a nearby axial halogen atom has been noted by E. R. Malinowski, M. S. Manhas, G. H. Müller, and A. K. Bose, Tetrahedron Letters, No. 18, 1161 (1963); (b) for an example of long range deshielding by a nitro group, see A. C. Huitric and W. F. Trager, J. Org. Chem., 27 1926 (1962).

maxima[22a] at 247 mμ (ε 365, tetralone and/or octalone impurities) and 297 mμ (ε 69). The n.m.r. spectrum[13] of this mixture resembles the spectrum of the *trans*-isomer **9** but has an additional broad peak centered at *ca.* 2.55 δ; however, the spectrum exhibits no absorption at lower field than 3.5 δ (indicating the absence of protons in the environment  $-CO-\overset{Cl}{\overset{|}{C}}H-$ and allowing us to conclude that the mixture is free of the 2-chloro-1-decalones.

Reaction of the 9-chloro-1-decalones **8** *and* **9** *with Sodium Methoxide in Methanol*. *A. General Procedure and Product Analysis*.- Samples of either the pure *trans*-chloro ketone **8** or the mixture of chloro ketones (*ca.* 45% of **9** and 55% of **8**) were added to a cold (0°) solution of sodium methoxide in methanol; the quantities used are listed in Table I. After the resulting mixtures (from which sodium chloride began to precipitate within 1-2 min. after mixing) had been stirred at room temperature for the specified times, 10 ml. of water and 10 ml. of petroleum ether were added and the layers were separated. The aqueous phase was washed with petroleum ether and the combined organic layers were washed with saturated, aqueous sodium chloride and dried. After a weighed quantity of benzotrichloride had been added as an internal standard, the solutions were concentrated and the residual liquid was analyzed by gas chromatography to determine the yields and product compositions (Table I). A known mixture of authentic samples was prepared in order to calibrate the gas chromatography columns used for analysis.

TABLE I

Reaction of the 9-Chloro-1-decalones with Sodium Methoxide in Methanol

Chloro ketone,[a] mg. (mmoles)	Sodium methoxide, mmoles	methanol, ml.	Reaction time, min.	Product composition, %[b]					yield,[c] %
				12	**13**	**14**	**15**	**16**	
8, 914.2 (4.9)	30.3	20	600	29	14	15	42	--	74
8, 932.6 (5.0)	30.4	20	600	30	14	20	36	--	80[e]
8, 745.2 (4.0)	26.2	25	10	39	21	22	10	8	74
			1	36	20	7	1	36	77[d]
8 + **9**, 1016.4 (5.4)	29.6	15	600	16	36	11	37	--	79
8 + **9**, 978.1 (5.3)	30.0	15	600	18	32	10	40	--	83[f]
8 + **9**, 986.8 (5.3)	28.4	15	10	16	38	11	34	1	78
8 + **9**, 1007.6 (5.4)	28.2	15	1	24	39	11	4	22	39[d]

[a] As noted in the experimental section, the mixture of chloro ketones employed contained ca. 45% of the cis-isomer **9** and 55% of the trans-isomer **8**.

[b] The values listed refer to the proportion of each methoxy ketone identified in the mixture of the five methoxy ketones **12** - **16**. Other unidentified minor by-products were also present.

[c] The yield calculated from gas chromatographic data for the five methoxy ketones **12** - **16**.

[d] Some starting material was present in this product mixture.

[e] After a solution of 2.4 mmoles of this product mixture in 10 ml. of methanol containing 16.1 mmoles of sodium methoxide had been refluxed for 10 hr., the recovered product (76% recovery) contained 34% of **12**, 16% of **13**, 11% of **14** and 39% of **15**.

[f] After a solution of 2.8 mmoles of this product mixture in 10 ml. of methanol containing 15.0 mmoles of sodium methoxide, had been refluxed for 10 hrs., the recovered product (79% recovery) contained 18% of **12**, 40% of **13**, 6% of **14** and 36% of **15**.

Two gas chromatography columns were employed for analysis. With the Carbowax 20M column employed,[14] the retention times of the methoxy ketones were: *trans*-9-methoxy ketone **12**, 12.4 min.; *cis*-9-methoxy ketone **13**, 15.4 min.; an unresolved mixture of the thermally equilibrated 2-methoxy ketones **14** and **15** as a broad peak, 24.8 min. With a combination column,[24] the retention times were: *trans*-9-methoxy ketone **12**, 33.0 min.; axial 2-methoxy ketone **14**, 36.4 min.; *cis*-9-methoxy ketone **13**, 39.2 min., equatorial 2-methoxy ketone **15**, 86.0 min. Although resolution of the peaks for ketones **12**, **13** and **14** on the latter column was not complete, utilizing the combined data from both columns,[14, 24] we believe our analysis to be in error by less than ± 5% in all cases. From reactions run for short periods of time, the unstable 2-methoxy ketone **16** appeared on our neutral column[24] as a new peak eluted slightly before the equatorial 2-methoxy ketone **15** (relative retention times were **16**, 55.6 min., and **15**, 60.6 min.). As expected, this unstable ketone **16** was epimerized by the ordinary Carbowax column[14] and appeared under the same

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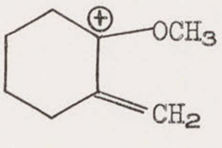
(24) The first half of the gas chromatography column was packed with Silicone Fluid, No. 710 suspended on Chromosorb W and the second half of the column was packed with Carbowax 20M suspended on Chromosorb W. The column fluids were washed with aqueous sodium bicarbonate prior to use. The inert support (Chromosorb W) and interior glass surfaces of the column were treated with a solution of dichlorodimethylsilane in toluene and then washed successively with toluene and methanol following a procedure provided by Dr. R. J. Highet of the National Heart Institute. The resulting column did not epimerize the 2-methoxy ketones **14** and **15**.

broad peak as 2-methoxy ketones 14 and 15.

B. *Identification of Products*.- Samples of each of the four methoxy ketones 12 - 15 were collected from appropriate gas chromatography columns^{14,24} and identified with previously described^{2} samples by comparison of infrared and mass spectra. The equatorial 2-methoxy ketone 15 has an ultraviolet maximum^{22a} at 279 mμ (ϵ 79). The mass spectra of the 9-methoxy ketones 12 and 13 differ from the spectra of the 2-methoxy ketones 14 and 15 in that both 9-methoxy compounds give abundant fragment peaks at m/e 125 and 111 which are only minor peaks in the spectra of the 2-methoxy compounds. In the mass spectrum of the subsequently described 9-methoxy-2,2-dideuterio *trans*-1-decalone (17) these peaks are found at m/e 125 and at 111, 112 and 113 suggesting that the 125 peak is attributable to the ion



and that the 111 peak arises from several ions. The mass spectra of the 2-methoxy ketones 14 and 15 differ from the 9-methoxy isomers in having very abundant fragment peaks at m/e 71 and 58; these peaks are much less intense in the spectra of the 9-methoxy isomers. The corresponding peaks in the previously described^{2} 2,9-dideuterio derivative of the 2-methoxy ketone 15 are found at m/e 72 and 59 suggesting that these peaks are attributable to ions $CH_2=CH\text{-}CH=\overset{\oplus}{O}\text{-}CH_3$

and $[(\mathrm{CH_2{=}CH\text{-}O\text{-}CH_3}]^{\oplus}$, respectively.

After a sample of the *trans*-9-methoxy ketone **12** had been subjected to a series of three exchanges with a refluxing solution of sodium methoxide in a deuterium oxide-methanol-d_1 (1:3 by volume) mixture, the neutral material was recovered and the deuterated ketone **17** was collected.[24] The material which contained 6% d_0 species, 34% d_1 species and 60% d_2 species, has infrared absorption[13] at 2110 (shoulder), 2155, 2215 (shoulder) and 2245 cm.$^{-1}$ (C-D stretching). The n.m.r. spectrum[13] of this deuterated sample **17** differs from the previously described[2] spectrum of the ketone **12** in lacking the complex absorption in the region 2.2-2.8 δ attributable to one proton. As noted earlier both the absorption and the analogous absorption in the 9-chloro-*trans*-1-decalone (**8**) are believed attributable to the axial hydrogen atom at position 2 which is deshielded by the nearby axial electronegative 9-substituent (cf. structure **30**).

A 50-μl. sample of the 2-methoxy ketones **14** and **15** was dissolved in 2 ml. of methanol containing 2.0 mmoles of sodium methoxide and the resulting solution was refluxed for 10 hr. After use of the previously described isolation procedure, the recovered methoxy ketone mixture contained[24] 15.5% of **14** and 84.5% of **15** corresponding to an equilibrium constant of 5.5 for the process, axial 2-methoxy ketone $\rightleftharpoons$ equatorial 2-methoxy ketone. The value, corresponding to a free energy change of *ca.* 1 kcal/mole, is in reasonable agreement with previous estimates[25] of 0.5-0.7 kcal./mole as the energy difference

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(25) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book, Co., New York, N.Y., 1962, p. 236.

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between axial and equatorial methoxyl groups.

A collected sample of the 2-methoxy ketone 16 had infrared absorption[13] at 1730 $cm.^{-1}$ (C=O) with abundant fragment peaks at m/e 71, 58 and 55 in its mass spectrum as well as a molecular ion peak at m/e 182. It has n.m.r. absorption[13] at 3.32 δ (3 H singlet, $-O-CH_3$) and complex absorption at 0.9 - 2.5 δ (15 H, aliphatic C-H).

To ensure that none of the aforementioned methoxy ketones was derived from one of the octalones 10 or 11, each of these octalones was stirred with methanolic sodium methoxide for 10 hr. at room temperature under a nitrogen atmosphere and the reaction mixture was subjected to the usual isolation procedure. From the $\Delta^{9,10}$-octalone 10 (1.0658 g. or 7.12 mmoles) after reaction with 15 ml. of methanol containing 28.5 mmoles of sodium methoxide, only the starting ketone was recovered (83% recovery). From reaction of 960 mg. (6.41 mmoles) of the $\Delta^{8,9}$-octalone 11 with 15 ml. of methanol containing 34.6 mmoles of sodium methoxide, the crude pale yellow oil (685.3 mg.) recovered contained[24] the starting ketone 11 (56% of mixture, retention time 57.2 min.) and two other components 1-decalone (20%, 30.0 min.) and the octalone 10 (24%, 66.4 min.), neither of which corresponded in retention time to any of the five methoxy ketones 12 - 16. A relatively insoluble and non-volatile yellow solid, m.p. 91-100° dec., also separated during the isolation procedure. A collected[24] sample of the octalone 10 was identified with an authentic sample by comparison of retention times and infrared spectra. A collected sample of 1-decalone has infrared spectra and mass spectrum identical with the spectra of an authentic sample.

Reaction of the 9-Chloro-1-decalones 8 and 9 with Sodium Methoxide in 1,2-Dimethoxyethane. A. General Procedure and Product Analysis.-- Finely divided suspensions of sodium methoxide in 1,2-dimethoxyethane were obtained by refluxing a suspension of sodium in 1,2-dimethoxyethane containing 1 equiv. of methanol for 24 hr. at which time all the sodium was consumed. Solutions of either the trans-chloro ketone 8 or the mixture of chloro ketones (ca. 45% of 9 and 55% of 8) in 1,2-dimethoxyethane were added to these suspensions and the resulting mixtures were stirred, at room temperature and under a nitrogen atmosphere, for 10 hr. The crude product mixtures were isolated by the addition of water and petroleum ether followed by separation of the organic layer as in the previous cases. The combined organic extracts from each run were mixed with a weighed quantity of m-methoxytoluene as an internal standard and then dried, concentrated and analyzed[24] to obtain the data presented in Table II. A known mixture of authentic samples was prepared in order to calibrate the gas chromatography equipment. With the gas

TABLE II

Reaction of the 9-Chloro-1-decalones with Sodium Methoxide in 1,2-Dimethoxyethane

Chloro ketone,[a] mg. (mmoles)	Sodium methoxide, mmoles	1,2-Dimethoxyethane, ml.	Product Composition, %[b]					Yield,[c] %
			18	**19**	**20**	**21**	**22**	
8, 666 (3.57)	23.2	35	88	2	5	5	-	88
8, 670.2 (3.59)	22.4	35	88	2	5	5	-	88
8 + **9**, 1050.1 (5.63)	31.7	30	46	16	3	30	5	84
8 + **9**, 916.8 (4.92)	28.5	30	46	16	3	30	5	88

[a] As noted in the Experimental section, the mixture of chloro ketones employed contained ca. 45% of the cis-isomer **9** and 55% of the trans-isomer **8**.

[b] The values listed refer to the proportion of each ester in the mixture of esters **18** - **22**. Other unidentified minor products were also present in some cases.

[c] The yield calculated from gas chromatography data for the five methyl esters **18** - **22**.

chromatography column used,[24] the products are eluted in the following order: *trans*-ester 18, 16.6 min.; *cis*-ester 19, 21.8 min.; ester 20, 24.0 min.; ester 21, 29.0 min., ester 22, 35.6 min. All of these materials except ester 22 are eluted more rapidly than the methoxy ketones 12 - 16.

In an additional experiment, a solution of 34.2 mmoles of sodium methoxide in a mixture of 6.16 g. of methanol and 30 ml. of 1,2-dimethoxyethane (4.4 *M* in methanol) was mixed with 1.0858 g. (5.81 mmoles) of a mixture of approximately equal quantities of the chloro ketone 8 and 9 and the resulting mixture was stirred at room temperature for 10 hr. Application of the previously described isolation and analysis procedures afforded 864.5 mg. of a crude product containing[24] the ester 18 (22%), the ester 19 (19%), the ester 20 (*ca*. 2%), the ester 21 (32%), a mixture of the ester 22 and 9-methoxy ketones 12 and 13 (14%) and the methoxy ketone 15 (11%). The calculated yield of these products was 79.5%.

B. *Identification of Products*.- Samples of each of the esters 18 - 22 were collected[24] from appropriate reaction mixtures. The reaction of 1.9844 g. (10.64 mmoles) of the *trans*-chloro ketone 8 with 60.8 mmoles of sodium methoxide in 70 ml. of 1,2-dimethoxyethane was repeated to yield 1.5828 g. of a crude neutral product as a yellow liquid. Distillation in a short-path still (120° at 10 mm.) afforded 1.2979 g. (67%) of a mixture of esters containing[26]

88% of the *trans*-ester 18. A collected[26] sample of the *trans*-ester 18, b.p. 218-219°, n^{25}_{D} 1.4723, has infrared absorption[13] at 1735 cm.^{-1} (ester C=O) with a molecular ion peak at m/e 182 in the mass spectrum as well as abundant fragment peaks at m/e 123 (M- CO_2CH_3), 81, 67, and 41. The ester has n.m.r. absorption[13] at 3.65 δ (3 H singlet, $-CO_2CH_3$) with broad, complex absorption in the region 1.0-2.1 δ (14 H, aliphatic C-H) and two broad peaks at 2.32 and 2.46 δ together probably attributable to 1 H (bridgehead C-H).

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.44; H, 9.91

A solution of 910.4 mg. (5.0 mmoles) of the *trans*-ester 18 and 4.4 g. (33 mmoles) of lithium iodide in 100 ml. of freshly distilled *γ*-collidine was refluxed for 9 hr.[27] and then poured into a mixture of ether, methylene chloride and cold, dilute, aqueous hydrochloric acid. After the organic layer had been separated, the aqueous layer was saturated with sodium chloride and extracted with an ether-methylene chloride mixture. The combined organic layers

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(26) A gas chromatography column packed with Silicone fluid, No. 710, suspended on ground firebrick was employed.

(27) The procedure of F. Elsinger, J. Schreiber, and A. Eschenmoser, [Helv. Chim. Acta, *43*, 113 (1960)] for the cleavage of hindered esters.

were washed with saturated, aqueous sodium chloride, dried and concentrated to leave 905 mg. of the crude acid as a white solid. Recrystallization from aqueous acetic acid afforded 510 mg. (60.7%) of the pure acid as fine, white crystals, m.p. 94-94.5° (lit.[28] 91-93.5°). The product, which was identified with an authentic sample[28] by a mixed melting-point determination and by comparison of infrared and mass spectra, has infrared absorption[29] at 2950 (broad, assoc. O-H) and at 1695 cm.$^{-1}$ (carboxyl C=O) with a molecular ion peak at m/e 168 in the mass spectrum as well as abundant fragment peaks at m/e 123 (M- CO_2H), 113, 81, 67, 55, 41, and 39.

Hydrogenation of a solution of 996 mg. (6.00 mmoles) of the unsaturated acid 25[30] in 10 ml. of ethanol over 100 mg. of a 20% palladium-on-carbon catalyst at room temperature and atmospheric

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(28) In unpublished work, Professor W. G. Dauben, University of California at Berkeley, and his associates have prepared and characterized this acid. We are grateful to Prof. Dauben for providing us with a sample of this material. The corresponding carboxamide has also been prepared both by Professor Dauben and his associates and by W. L. Meyer and J. F. Wolfe [J. Org. Chem., 29, 170 (1964)].

(29) Determined as a solution in chloroform.

(30) R. K. Kronenthal and E. I. Becker, J. Am. Chem. Soc., 79, 1095 (1957).

pressure resulted in the uptake of 144.0 ml. (0.98 equiv.) of hydrogen. After the resulting solution had been filtered and concentrated crystallization of the residue from aqueous acetic acid afforded 788 mg. (77%) of the cis-acid 26 as a waxy white solid, m.p. 39-40° [lit. 43.5-44.5°,[31] 43.5-45.5° or 49°[30]].

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(31) (a) W. G. Dauben, J. W. McFarland, and J. B. Rogan, J. Org. Chem., 26, 297 (1961); (b) the acid has also been prepared by H. Koch and W. Haaf, Chem. Ber., 94, 1252 (1961).

A solution of this acid 26 (788 mg. or 4.6 mmoles) was esterified with excess ethereal diazomethane. Distillation of the crude product (640 mg. of colorless liquid) in a short-path still (117° at 11 mm.) separated 468.4 mg. (56%) of the pure[26] ester 19, n^{25}_D 1.4733 [lit.[30] n^{25}_D 1.4701, b.p. 116° (20 mm.)]. The material has infrared absorption[13] at 1735 cm.$^{-1}$ (ester C=O) with n.m.r. absorption[32] at 3.77 δ (3 H singlet, $-CO_2CH_3$) as well as complex absorption in the region 1.0-2.1 δ (14 H, aliphatic C-H) and a broad peak centered at 2.48 δ (1 H, bridgehead C-H). The mass spectrum of the material has a molecular ion peak at m/e 182 with abundant fragment peaks at m/e 123 (M- CO_2CH_3), 81, 67, and 41. This sample was identified with a collected[24] sample of ester 19 from the chloro ketone rearrangement by comparison of the infrared and mass spectra of the two samples.

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(32) Determined as a solution in deuteriochloroform.

A collected[24] sample of the ester 21 has infrared absorption[13] at 1735 cm.$^{-1}$ (ester C=O) with n.m.r. absorption[13] at 3.60 δ (3 H singlet, $-CO_2CH_3$) as well as complex absorption in the region 1.0-2.8 δ (15 H, aliphatic C-H). The mass spectrum has a molecular ion peak at m/e 182 with abundant fragment peaks at m/e 150, 96, 87, 81, 67, 55, and 41.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.32; H, 9.96.

A collected[24] sample of ester 20 has infrared absorption[13] at 1740 cm.$^{-1}$ (ester C=O) with n.m.r. absorption[13] at 3.63 δ (3 H singlet $-CO_2CH_3$) as well as complex absorption in the region 1.0-2.6 δ (15 H, aliphatic C-H). The mass spectrum has a molecular ion peak at m/e 182 with abundant fragment peaks at m/e 150, 108, 87, 81, 67, 55, and 41.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.16; H, 9.88.

A collected[24] sample of the ester 22 was shown to be identical with a subsequently described sample by comparison of retention times as well as infrared and mass spectra.

In a larger scale reaction, 30.982 g. (0.166 mole) of the mixture of chloro ketones 8 and 9 and 0.7676 mole of sodium methoxide in 500 ml. of 1,2-dimethoxyethane were stirred at room temperature under a nitrogen atmosphere for 10 hr. and then diluted with 200 ml. of water. An aliquot of the neutral organic product separated at this time contained:[24] **18**, 45%; **19**, 16%; **20**, 3%; **21**, 32%; and **22**, 4%. The mixture was refluxed for 7.5 hr. with aliquots of the neutral organic product being separated periodically for analysis. After this reaction period when the selective saponification of the unhindered esters **20**, **21** and **22** was essentially complete, the organic layer was separated and the aqueous phase was extracted with petroleum ether. The combined organic layers were dried and concentrated to leave 21.88 g. of pale yellow oil containing[24] the *trans*-ester **18** (*ca*. 70%), the *cis*-ester **19** (*ca*. 25%) and the ester **21** (*ca*. 5%). Distillation of this material afforded 13.817 g. of fractions, b.p. 87-98° (7 mm.). Fractional distillation of this material through a 30-cm. spinning band column separated 7.6307 g. of fractions, b.p. 75-83° (6 mm.), containing 92-97% of the *trans*-ester **18** [n^{25}_{D} 1.4721 for fraction, b.p. 81-82° (6 mm.) containing 97% of ester **18**] and 3.7012 g. of fractions, b.p. 83-88° (6 mm.), containing esters **18** (55-25%), **19**, (38-59%) and **21** (7-16%).

A 7.1-g. (40-mmole) sample of the above *trans*-ester **18** was cleaved with 36 g. (0.3 mole) of lithium iodide in 400 ml. of refluxing *γ*-collidine as previously described to give 5.627 g. (89%) of the acid **24**, m.p. 90-93°. An additional recrystallization from aqueous acetic acid narrowed the melting range of the acid **24** to 92-93°.

The aqueous layer from the above selective saponification was acidified, saturated with sodium chloride, and extracted with ether. This ethereal solution of acidic products was dried, concentrated and esterified with excess diazomethane and then concentrated. Distillation of the residue (7.3 g. of light yellow liquid) afforded 7.1 g. of a mixture of esters, b.p. 137-142° (7 mm.), containing[24] the *cis* ester **19** (2%), the ester **20** (8%), the ester **21** (79%) and the ester **22** (11%). Collected[24] samples of each of the esters **20**, **21** and **22** were identified with previously desdribed samples by comparison of retention times and infrared spectra.

Hydrogenation of Indene-3-carboxylic Acid (**27**). A. **Partial Hydrogenation to 28**.- A solution of 1.60 g. (10 mmoles) of indene-3-carboxylic acid (**27**)[33] in 25 ml. of ethanol was hydrogenated at room temperature and atmospheric pressure over the catalyst from 157 mg. of platinum oxide. After the hydrogen uptake (240 ml. or 1.0 equiv.) ceased, the reaction mixture was filtered and concentrated to leave 1.551 g. of crude acidic product. Crystallization from petroleum ether afforded 860.4 mg. (53%) of the pure acid **28** as white needles, m.p. 58-59° (lit.[34] 57-58°), with infrared

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(33) This sample, obtained from the Aldrich Chemical Company, melted at 158-159° after recrystallization. The reported melting point for this acid is 159-161°; A. Melera, M. Claesen, and H. Vanderhaeghe, J. Org. Chem., **29**, 3705 (1964).

(34) R. A. Heacock, R. L. Wain, and F. Wightman, Ann. Appl. Biol. **46**, 352 (1958).

absorption[13] at 3000 (broad O-H) and at 1710 cm.$^{-1}$ (carbonyl C=O), a molecular ion peak at m/e 162 in the mass spectrum and n.m.r. absorption[13] at 12.20 δ (1 H, -CO_2H) as well as complex absorption in the regions 7.0-7.5 δ (4 H, aryl C-H) and 2.0-4.3 δ (5 H, aliphatic C-H).

B. **Complete Hydrogenation to Acid 29**.- A solution of 9.6 g. (0.060 mole) of the unsaturated acid **27** in 120 ml. of acetic acid was hydrogenated at 60° and 2-3 atm. pressure over the catalyst from 1.0 g. of platinum oxide. The hydrogen uptake (0.256 mole or 1.07 equiv.) ceased after 12 hr. and the reaction mixture was filtered and concentrated to leave 9.083 g. of the crude acid **29**[35] as a broan oil. An ethereal solution of this product was esterified with excess diazomethane to give, after washing, drying and concentration, 6.928 g. (64% based on the starting unsaturated acid **27**) of a mixture of esters as a pale yellow liquid. This material contained[24] the ester **20** (2%, 15.4 min.), the ester **21** (18.6 min.) partially resolved from a small amount of an unknown component A (*ca.* 20 min.) (total 25%), the ester **22** (67%, 23.4 min.) and two

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(35) Preparations of the acid **29** have been reported by (a) D. W. Mathieson, [J. Chem. Soc., 3251 (1953)] who reports m.p. 94-95° for one isomer believed to have a *cis*-fused ring juncture and (b) M. J. LeGoffic and F. LeGoffic [Compt. rend., 255, 539 (1962)] who prepared a *p*-bromophenacyl ester derivative, m.p. 88-89°, of uncertain stereochemistry.

additional compounds **B** (1%, 29.4 min.) and **C** (5%, 38.6 min.). Collected[24] samples of esters **20**, **21**, and **22** were identified with previously described samples by comparison of retention times and infrared and mass spectra. The collected sample of ester **22** has infrared absorption[13] at 1740 cm.$^{-1}$ (ester C=O) with a molecular ion peak at m/e 182 in its mass spectrum as well as abundant fragment peaks at m/e 150, 108, 87, 81, 67, 55, and 41. The n.m.r. spectrum[13] of ester **22** has a singlet at 3.74 δ (3 H, $-CO_2CH_3$) with a broad multiplet centered at 2.85 δ (1 H, $CH-CO_2R$), and complex absorption in the region 1.0-2.5 δ (14 H, aliphatic C-H).

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.62; H, 10.05.

A collected sample of component **B**, with infrared absorption at 1710 and 1645 cm.$^{-1}$ and a molecular ion peak at m/e 180 in the mass spectrum, appears to be one or more of the tetrahydroindane carboxylic esters. No further characterization of components **A**, **B**, and **C** was attempted.

The above ester mixture (602.2 mg. or 3.4 mmoles) from hydrogenation and subsequent esterification was dissolved in 5 ml. of methanol containing 16 mmoles of sodium methoxide. After the resulting mixture had been refluxed for 24 hr., it was diluted with water and petroleum ether. The organic layer was separated, dried and concentrated at which time the residual yellow liquid contained[24] primarily the ester **21** accompanied by smaller amounts of esters **20** and **22** as well as components **B** and **C**. A collected sample of ester **21** from this reaction was identified with the previously described material by comparison of retention times and infrared spectra. A comparable equilibration employing 28.2 mg. (0.16 mmole) of the pure[24] ester **22** in 1 ml. of methanol containing 0.9 mmole of sodium methoxide afforded a mixture composed of[24] 88% of the ester **21** and 12% of the ester **22**.[36] Application of the same equilibration procedure to the ester **20** failed to reveal the formation of a second component. However, it is possible that the two epimers of the *trans*-fused ester (**20** and its C_1 epimer) were not resolved by the gas chromatography column[24] used.

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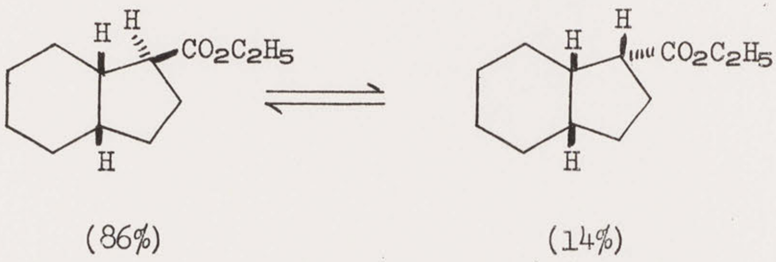
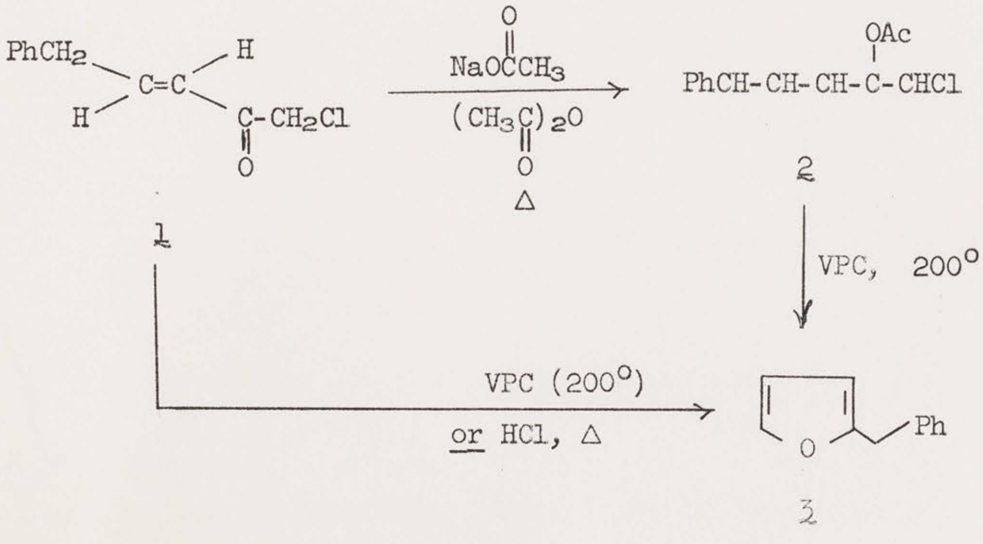
(36) G. J. Fonken and W. Moran, [Chem. Ind. (London), 1841 (1963)] reports the equilibrium values indicated in the following equation for the corresponding ethyl esters.



APPENDIX

PART I: Reactions of *trans*-1-phenyl-5-chloro-3-penten-2-one (**1**).- As part of our studies of the Favorskii rearrangement the *trans* ketone **1**,[1] a vinylogous α-halo ketone,[2] was prepared. Since its reactions with sodium methoxide in methanol and dimethoxyethane under different conditions yielded only an ill-defined dimeric (or polymeric) solid the investigation of the first-formed enolate anion was undertaken. The results are summarized in the following chart:



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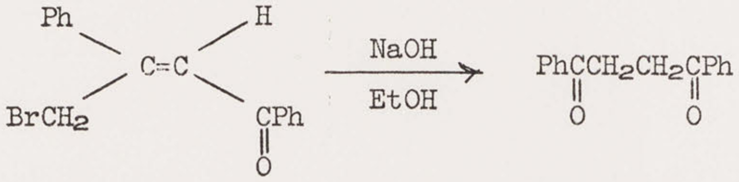
(1) (a) Part I of this Thesis; (b) H. O. House, V. K. Jones, and G. A. Frank, J. Org. Chem., 29, 3327 (1964).

(2) R. E. Lutz, L. T. Slade, and P. A. Zoretic, J. Org. Chem., 28, 1359 (1963) report the reaction of γ-bromodypnone with base:



Preparation of the enol acetate mixture 2.- A suspension of freshly fused sodium acetate (0.178 g., 2.0 mmoles) in 20 ml. of acetic anhydride was refluxed in an inert atmosphere to expel oxygen. To the refluxing mixture was added the *trans*-ketone **1** (0.1946 g., 1.0 mmole). After the reaction mixture had been stirred at reflux temperature for 45 min. and at 25° for 10 hr., it was poured into a pentane-saturated aqueous sodium bicarbonate solution. The layers were separated, the aqueous layer was washed with pentane, and the combined organic layers were dried and concentrated to afford 0.1507 g. (64%) of a yellow liquid which still contained a halogen atom, as shown by a positive Beilstein test. Distillation, oven at 120° at 0.05 mm., yielded 80 mg. of material, the infrared spectrum[3] of which exhibits peaks at 1765 $(C=C-O-\overset{\overset{O}{\|}}{C})$ and 1190 $cm.^{-1}$

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(3) Determined in 5% carbon tetrachloride solution.

(C-O). The mass spectrum shows a molecular ion peak m/e 236 and a large fragment peak at m/e 194 ($M- CH_2=C=O$). The complex n.m.r. spectrum[4] also indicates the presence of a mixture of enol acetates.

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(4) Determined in carbon tetrachloride solution with tetramethylsilane at internal standard.

Gas chromatography[5] of the mixture showed a single peak (retention

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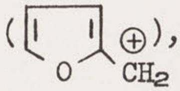
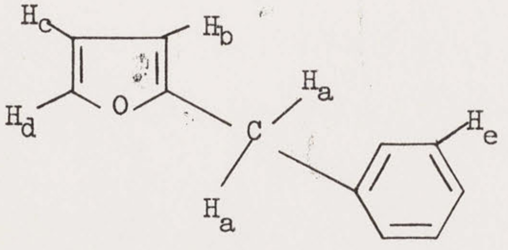
(5) A column packed with Carbowax 20M on Chromosorb P was employed.

time 17.4 min. at 200°) which was enhanced when a mixture of the starting ketone **1** and product mixture **2** was injected. When this peak, both from **1** and from **2**, was collected, the material was shown by infrared,[3] mass spectral, and retention time[5] comparison to be identical with the subsequently described 2-benzylfuran (**3**).

Preparation of 2-benzylfuran (**3**).- A mixture of the *trans* ketone **1** (0.1063 g., 0.55 mmole) and 50 µl. of conc. hydrochloric acid was heated, in an inert atmosphere, to 180° for 10 min. Short path distillation (oven at 120° at 0.1 mm.) afforded 35 mg. of a clear liquid, n^{25}_{D} 1.5440, (lit.[6] b.p. 114-116°/23 mm., n^{19}_{D} 1.5451). The infrared spectrum[3] shows peaks at 1590, 1500, and 1005 $cm.^{-1}$. The mass spectrum has a strong molecular ion peak at m/e 158 and abundant fragment peaks at m/e 129, 115, 91 ($PhCH_2^{\oplus}$), 81 (), 77, 64, and 51. It has n.m.r. absorption[4] at 7.22 δ (6 H, multiplet, H_e and H_d), at 6.22 δ (1 H, multiplet, H_c), at 5.93 δ (1 H, multiplet, H_b), and at 3.94 δ (2 H, singlet, H_a) of structure:



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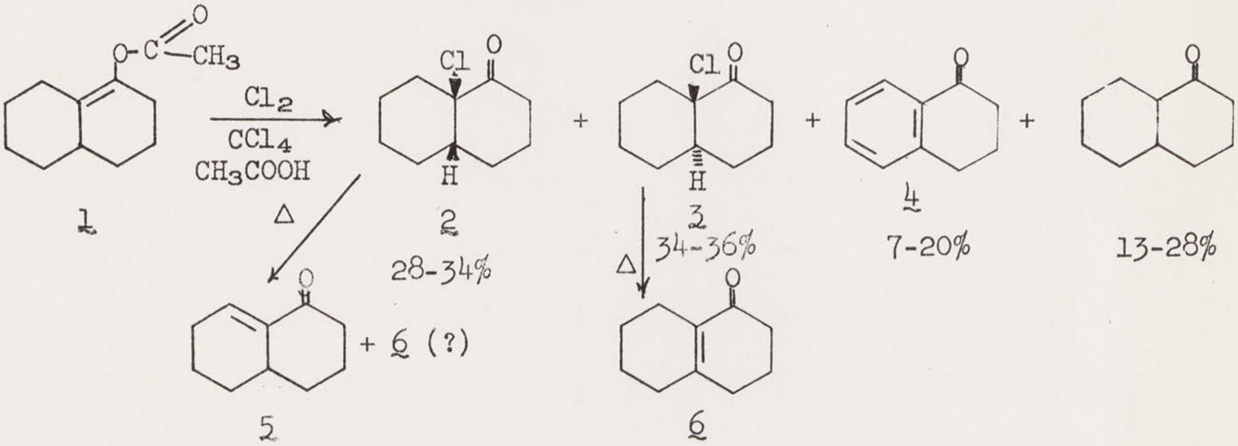
(6) (a) R. Paul, Compt. rend., 200, 1481 (1935); (b) R. Paul, Bull. soc. chim. France, 2227 (1935).

Part II: *Syntheses, precursors, and derivatives of 9-chloro-1-decalones*.

A. *Chlorination of the enol acetate* 1.- This reaction was explored as a possible means toward the isomeric 9-chloro-1-decalones 2 and 3 needed in our study of the Favorskii rearrangement. Results of our experiments are charted below. Relative product ratios varied with reaction time and amount of chlorine used.



Preparation of 1-acetoxy-$\Delta^{1,9}$*-octalin (1)*.- The method of House and Thompson[1] was followed using 1-decalone (30 g., 0.198 mole), acetic anhydride (66 g., 0.642 mole), and 1.0 g. of *p*-toluenesulfonic acid. Final distillation, b.p. 64-68° (0.17 mm.), [lit.[1] b.p. 79-80° (1.32 mm.)], afforded 32.5 g. (88% yield) of a clear liquid. It shows infrared absorption[2] at 1755 cm.$^{-1}$ (C=O) and

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(1) H. O. House and H. W. Thompson, J. Org. Chem., 26, 3729 (1961).

(2) Determined in a 10% carbon tetrachloride solution.

at 1450 cm.$^{-1}$ (C-CH_3) and was found to be[3] a single component not contaminated with the $\Delta^{1,2}$-isomer.

Chlorination of the enol acetate 1.- To the enol acetate 1 (3.9234 g., 0.02 mole) dissolved in 35 ml. of glacial acetic acid was added first 4 g. of freshly fused sodium acetate and then chlorine gas (10 g., 0.028 mole) as a solution in 150 ml. of carbon tetrachloride. During the addition the reaction mixture was kept at 0° in the dark. Stirring was continued for 84 hr. after which time the previously described[4] work-up procedure afforded 2.2453 g. (60%) of a pale yellow liquid containing[3] approximately 34% of each 2 and 3,[5] 13% of 1-decalone resulting from the hydrolysis during work-up of unreacted 1, and 20% of α-tetralone (4). 1-Decalone was identified by its infrared,[2] n.m.r.[6] and mass spectra, and by comparison

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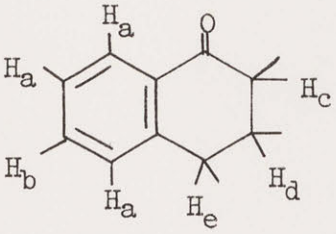
(3) A gas chromatography column packed with Carbowax 20M on Chromosorb P was used.

(4) E. R. H. Jones and D. J. Wluka, J. Chem. Soc., 911 (1959).

(5) Quantities of the <u>cis</u>- and <u>trans</u>-ketones 2 and 3 were judged on the basis of relative intensities of peaks corresponding to the ketones 5 and 6.[1] See Part II of this Thesis.

(6) Determined in carbon tetrachloride solution with tetramethylsilane as internal standard.

of retention times[3] with an authentic sample. α-Tetralone arises in larger quantities as the chlorination is allowed to proceed for a longer time. After a reaction time of 18 hr., the rate of chlorination of starting material approximates the rate of chlorination of the mono-chlorinated products eventually producing α-tetralone (**4**). The ketone **4** was shown to be identical to a commercial sample[7] of α-tetralone. It has infrared absorption[2] at 1690 cm.$^{-1}$ (unsat. C=O), the mass spectrum shows a strong molecular ion peak at m/e 146 and abundant fragment peaks at m/e 118, 90, and 77. The n.m.r. spectrum[6] shows the following peaks: 7.80 δ (1 H, multiplet, H_b), 7.13 δ (3 H, multiplet, H_a), 2.87 δ (2 H, multiplet, H_e), 2.43 δ (2 H, multiplet, H_c), and 2.08 δ (2 H, multiplet, H_d) in structure:



We were unable, by means of physical methods - elution, gas, and quantitative thin layer chromatography and distillation-to separate the *cis*- and *trans*-ketones **2** and **3**.

B. **The nitrosyl chloride adduct of $\Delta^{1,9}$-octalin (7)**.- Addition of nitrosyl chloride to olefins generally results in deriva-

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(7) Eastman Chemical Company.

tives of α-chloro ketones.[8] Depending on the amount of substitution on the double bond and reaction conditions used chloro nitroso compounds,[8a] chloro oximes,[9] and nitroso dimers[10,13] are produced.

In a few cases these latter two can be converted to the parent α-chloro ketones.[11] While the widely assumed ionic mechanism[12] would

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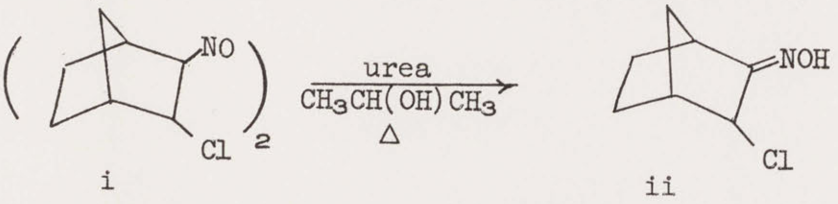
(8) (a) J. L. Simonsen, "The Terpenes", Cambridge University Press, London, 1931, 1st edition, Vol. 1, pp. 135-8; (b) W. Hückel, Ann., 474, 124 (1931); (c) W. Hückel, ibid., 474, 139 (1931); (d) W. Hückel and H. Naab, ibid., 502, 138 (1933).

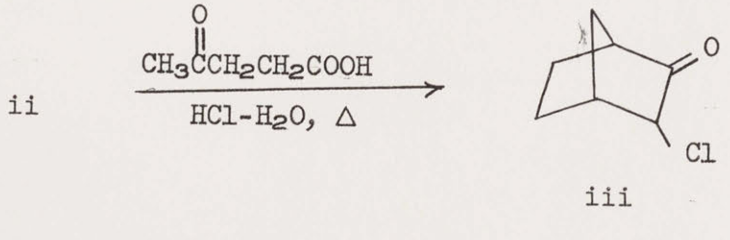
(9) H. Wieland and F. Bergel, Ann., 446, 13 (1926).

(10) J. B. Miller, J. Org. Chem., 26, 4905 (1961).

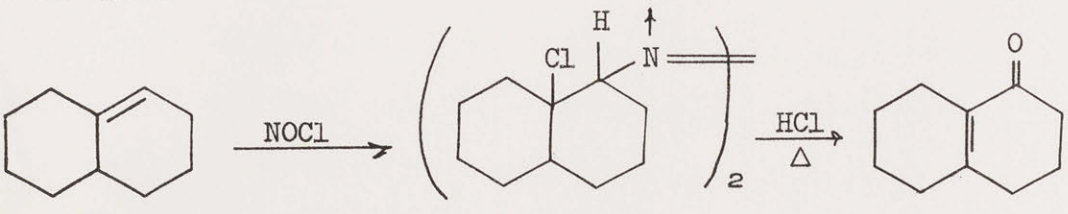
(11) (a) C. Bordenka, R. K. Allison, and P. H. Dirstine, Ind. Eng. Chem., 43, 1196 (1951) report the conversion:



and (b) C. H. DePuy and B. W. Pender, J. Am. Chem. Soc., 81, 4629 (1959) carried out the following:



give rise to stereoisomeric chloro- derivatives there has been at least one report in the literature^{13} of a stereospecific *cis* addition of nitrosyl chloride to norbornene. Formation of a chloro-oxime **8** from $\Delta^{1,9}$-octalin (**7**) has been reported^{8d,14} and it was hoped that its hydrolysis^{11} may lead to the desired *cis*-ketone **2**. Treatment of the olefin **7** with nitrosyl chloride, however, yielded not the described oxime^{8d,14} but a nitroso dimer believed to have the structure **9**. Its treatment under hydrolytic conditions afforded the octalone **6** leading us to believe the dimer **9** to have the *trans* ring-juncture and thus not useful for the preparation of the *cis*-ketone **2**.



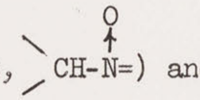
7 **9** **6**

Several nitroso dimers, however, lost hydrogen chloride during these hydrolysis procedures.^{11a}

(12) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, New York, 1953, pp. 669-670.

(13) J. Meinwald, Y. C. Meinwald, and T. N. Baker, J. Am. Chem. Soc., **86**, 4074 (1964).

(14) E. A. Benkeser, R. E. Robinson, D. M. Sauve, and O. H. Thomas, J. Am. Chem. Soc., **77**, 3230 (1955).

Preparation of the dimer 9.- The method of Pike[15] was followed using the following quantities: Octalin 7 (1.52 g., 0.011 mole), ethyl nitrite (2.6 g., 0.044 mole), 3 ml. of glacial acetic acid and 3 ml. of conc. hydrochloric acid. The resulting white solid, 0.4238 g., was recrystallized from acetone to afford white prisms, m.p. 126-127° (lit.[8d] m.p. 127°). The white solid exhibits infrared absorption[2] at 1395, 1355, and 1205 cm.$^{-1}$ (characteristic[16] of C-nitroso dimers), ultraviolet absorption[17] at λ_{max} 232 mµ (ϵ 2796), and n.m.r.[6] bands at 5.77 δ (1 H, multiplet,  $>CH-\overset{O}{\overset{\uparrow}{N}}=$) and 1.66 δ (15 H, multiplet). Osmometric molecular weight determination gave a value of 390 (calc. 403).

Treatment of the dimer 9 with 2,4-dinitrophenylhydrazine[14] afforded the hydrazone of 6, m.p. 265-267° (lit.[14] m.p. 266-267°), and infrared spectrum[2] matching the one earlier described.[1]

Refluxing of the white dimer 9 (100 mg., 0.25 mole) in an inert atmosphere in 2 ml. of conc. hydrochloric acid for 6 hr.

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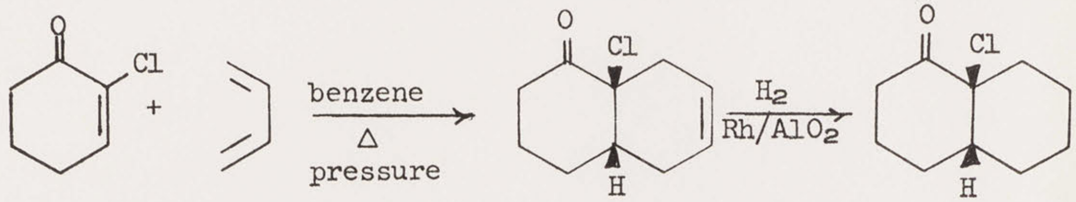
(15) R. A. Pike, Ph. D. Thesis, Massachusetts Institute of Technology, 1953.

(16) B. G. Gowenlock and W. Lüttke, Quart. Rev., 12, 320 (1958).

(17) Determined in ethanol solution.

followed by extraction with ether, drying, and concentration left a dark residue. Distillation (oven at 120°, 1 mm.) afforded 24 mg. of a clear liquid which was shown to be the octalone 6 through retention time[3] and infrared spectral comparison with an authentic sample.

C. **Diels-Alder reaction of 2-chloro-2-cyclohexen-1-one (10) with butadiene.**- The scheme as described below led to a complex reaction mixture from which no ketone 2 could be separated:



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Preparation of the ketone 10.- The methods of Ohno[18] [potassium tert.-butoxide (22.4 g., 0.2 mole), 100 ml. of tetrahydrofuran, N-morpholinyl-1-cyclopentene (13 g., 0.1 mole), and chloroform (11 g., 0.1 mole) resulted, after sublimation, in 2.02 g. (16%) of white prisms, m.p. 69.5-71° (lit.[18] m.p. 70-71°)] and Kötz and Richter[19]

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(18) M. Ohno, Tet. Letters, No. 25, 1753 (1963).

(19) A. Kötz and K. Richter, J. prakt. Chem., 111, 373 (1925).

[2-cyclohexenone (9.6 g., 0.1 mole) and aqueous hypochlorous acid (prepared from 141 g. of Chlorox solution containing 0.1 mole of sodium hypochlorite and 10 g. of conc. hydrochloric acid) were mixed and after the solution had been stirred for 3 hr. at 0-5° it was extracted with ether. The organic layer was mixed with a 30% solution of 20 g. of conc. sulfuric acid and heated on a steam bath for 1.5 hr. After the mixture had been cooled overnight, it was extracted with ether, dried and concentrated to afford 8.086 g. of a light brown solid. Recrystallization from water yielded 7.4 g. (57%) of white prisms, m.p. 67-69° (lit.[19] m.p. 70°)] were followed. The material exhibits infrared absorption[2,18] at 1698 $cm.^{-1}$ unsat.C=O) and 1610 $cm.^{-1}$ (conj. C=C), it shows n.m.r.[6,18] bands at 7.08 δ (1 H, triplet, J = 5 c.p.s.) and two multiplets centered at 2.5 δ and 2.1 δ of 4 and 2 protons, respectively.

BIOGRAPHICAL NOTE

The author was born on April 6, 1938 in Budapest, Hungary. He graduated from Eötvös Gymnasium in Budapest in 1956 and came to the United States in 1957. After graduation from Colorado State University with High Distinction in 1960 he entered M.I.T. where he has worked since then as a graduate student in Professor H. O. House's research group.

In 1962 he became an American citizen.

The author is a member of the American Chemical Society, the Honor Society of Phi Kappa Phi, and the Society of Sigma Xi.

The author has accepted a position as a research chemist with the Rohm and Haas Company.