The Chemistry of Carbanions. V. The Enolates Derived from Unsymmetrical Ketones[1a]

HERBERT O. HOUSE AND VERA KRAMAR[1b]

Department of Chemistry, Massachusetts Institute of Technology, Cambridge 39, Massachusetts

Received March 15, 1963

The equilibrium compositions for solutions of potassium enolates derived from several acyclic (**2**–**6**) and alicyclic (**7** and **8**) unsymmetrical ketones have been determined. The reactions of enolate mixtures from ketones **2**, **4**, **5**, and **7** with methyl iodide to form ketones **9** to **20** have been investigated. The related enol acetates **26** to **41** and enol ethers **44** to **53** have been prepared and the positions of their acid-catalyzed equilibria have been measured. Generalizations regarding the composition and reactions of enolate mixtures derived from unsymmetrical ketones are discussed.

Although a variety of useful synthetic reactions involve the preparation and subsequent reaction of enolate anions, there is remarkably little information available dealing with the effect of structure on the stability of such ions.[2] In particular, there are no direct measurements of the equilibrium concentration of the isomeric enolate ions derived from unsymmetrical ketones even though arguments based on presumed equilibrium enolate concentrations are often employed to rationalize product compositions.[3] The purpose of the study reported here was to develop methods which could be used to measure equilibrium concentrations of solutions of enolate anions derived from unsymmetrical ketones. In subsequent papers of the series we will examine in more detail how changes in reaction conditions alter the equilibrium concentration of enolate ions and what relationships exist between equilibrium enolate concentrations and the composition of products derived from further reactions of enolate ions.

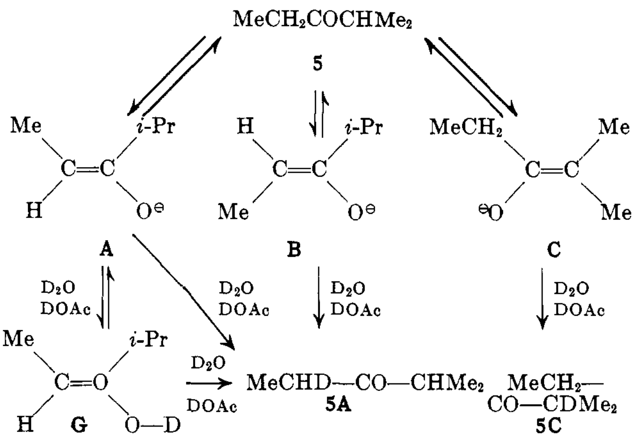
For the majority of the studies reported here solutions of the enolate ions were prepared by reaction of the ketone with triphenylmethylpotassium[4] in 1,2-dimethoxyethane.[5] The addition of ketones to this base–solvent system until the red color of the triphenylmethyl anion was just discharged permitted us to effect essentially complete conversion of the ketone to a solution of its enolate anions. To ensure that equilibration was achieved among the various enolate anions produced in this way, a mixture of the ketone **3** and its pentadeuterated derivative **3d** was converted to a solution of its potassium enolates and then quenched in aqueous acetic acid under conditions which would not remove hydrogen (or deuterium) bonded to the α-carbon atom of the ketone **3**. Analysis of the recovered ketone by mass spectrometry (eq. 1) demonstrated that equilibration of the α-hydrogen and α-deuterium atoms was complete in 15 min. or less. A comparable control experiment was performed with 2-methylcyclohexanone (**7**) and its trideuterated derivative.

$$\underset{\mathbf{3}}{i\text{-PrCH}_2\text{COCH}_3} + \underset{\mathbf{3d}}{i\text{-PrCD}_2\text{COCD}_3} \xrightarrow{\text{Ph}_3\text{C}^{\ominus}\text{K}^{\oplus}} \text{potassium enolates} \qquad (1)$$

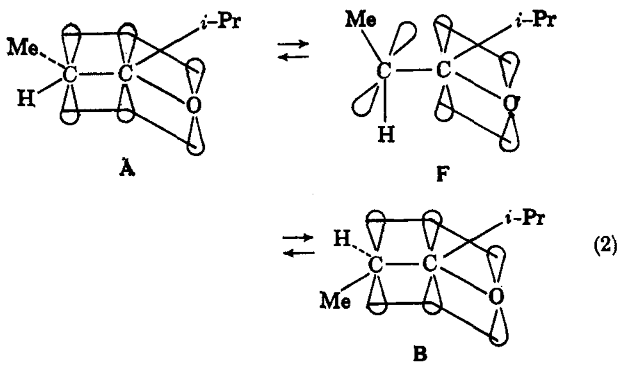
$$\downarrow \text{H}_3\text{O}^{\oplus}$$

$$i\text{-PrCH}_2\text{COCH}_3 \text{ containing } 37\%\ d_0,\ 41\%\ d_1,\ 18\%\ d_2,\ 3.5\%\ d_3, \text{ and } 0.5\%\ d_4 \text{ species}$$

CHART I



A study of the composition of the enolate anions derived from most unsymmetrical ketones involves the determination of the concentration of both structural isomers and stereoisomers. For example, the ketone **5** can yield (Chart I) the three isomeric enolates **A**, **B**, and **C**, two of which (**A** and **B**) form the same product (*e.g.* **5A**) upon further reaction at carbon. It is nonetheless appropriate to consider stereoisomeric enolates **A** and **B** as separate entities since the energy barrier separating the two stereoisomers must be appreciable. Equation 2 illustrates the fact that during this interconversion the carbonyl π-orbital and car-



(2)

---

[1] (a) This research has been supported in part by Grant No. 594-A from the Petroleum Research Fund; (b) Forris Jewett Moore Fellow, 1962–1963.

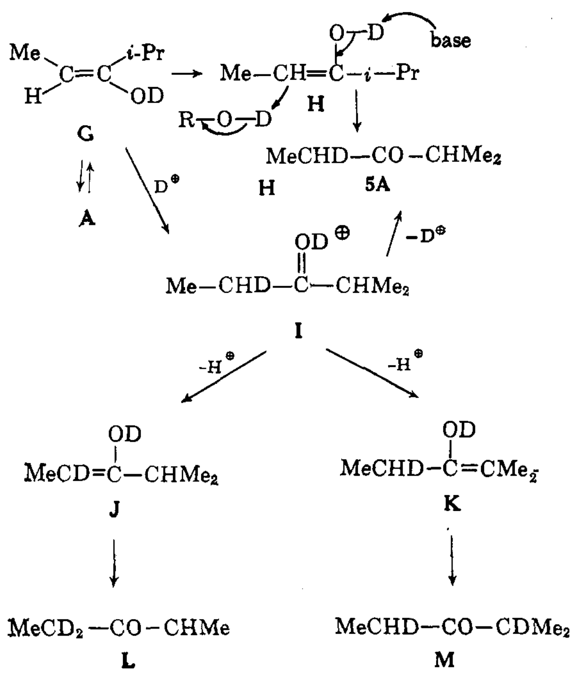
[2] (a) R. G. Pearson and R. L. Dillon, *J. Am. Chem. Soc.*, **75**, 2439 (1953); (b) W. L. Rellahan, W. L. Gumby, and H. D. Zook, *J. Org. Chem.*, **24**, 709 (1959).

[3] (a) J. M. Conia and P. Gosselin, *Bull. soc. chim. France*, 836 (1961); (b) *in addition*, for a review of earlier work, see J. M. Conia, *ibid.*, 1040 (1956); (c) H. M. E. Cardwell, *J. Chem. Soc.*, 2442 (1951); see also H. M. E. Cardwell and A. E. H. Kilner, *ibid.*, 2430 (1951); (d) J. M. Conia, *Record Chem. Progr.* (Kresge-Hooker Science Library), **24**, 43 (1963).

[4] H. O. House and V. Kramar, *J. Org. Chem.*, **27**, 4146 (1962).

[5] The advantages of this solvent for organic preparative work are discussed with leading references by A. J. Parker, *Quart. Rev.* (London), **16**, 163 (1962).

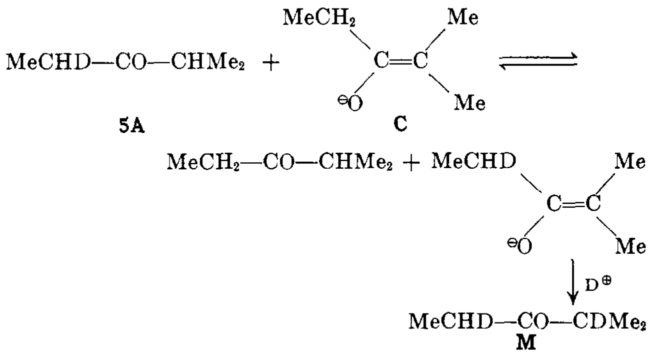
Chart II



banion *p*-orbital lie at right angles (as in **F**) and electron delocalization is no longer possible.[6]

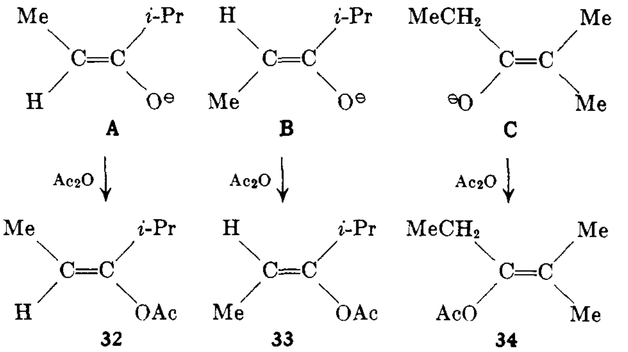
The first method utilized to measure enolate concentrations consisted of quenching an aliquot of the solution of enolates **A**, **B**, and **C** in a deuterioacetic acid–deuterium oxide mixture (Chart I) followed by isolation of the mixture of monodeuterated ketones **5A** and **5C**. The composition of the mixture of monodeuterated ketones **5A** and **5C** was determined by mass spectrometry taking advantage of the fact that two of the intense fragment peaks in the mass spectra of dialkyl ketones arise from the acylonium ions [*e.g.*, $(CH_3)_2CH-C\equiv O^{\oplus}$ and $CH_3CH_2C\equiv O^{\oplus}$ from the ketone **5**].[7] The concentration of deuterioacetic acid in the quenching bath was such that the final pH of the mixture after quenching was in the range of 5 to 6. Appropriate control experiments demonstrated that under the conditions used for quenching none of the ketones underwent exchange of hydrogen (or deuterium) bound to carbon. It is very probable that the quenching procedure employed results in rapid and reversible addition of a deuteron to the oxygen atom of the enolate to form an enol (*e.g.*, **A** → **G**) as well as the slower, nonreversible (under the experimental conditions employed) addition to the carbon atom to form a ketone (*e.g.*, **A** → **5A**).[8] The fate of this enol (*i.e.*, **G** from **A** or comparable structures from **B** and **C**, Chart II) may be to return to the enolate **A**, to undergo a termolecular conversion (as in **H**) to the ketone **5A** or react with a deuteron to form the conjugate acid **I** of the ketone **5A**.[9] This last reaction path could, in principle, result in the isomerization of the enol **G** to two new enols **J** and **K**. However, it will be noted that such an isomerization would lead to the dideuterated ketones **L** and **M**. The efficiency of our quenching conditions also had to be questioned since one could argue that enolate **A** reacts with a deuteron more rapidly than enolate **C** and a subsequent exchange occurs as illustrated in Chart III. However, it will be noted that any such exchange will lead to a dideuterated ketone. The fact that in all cases, except for the quenching of a solution of the sodium enolates of ketone **2** in dimethyl sulfoxide, the recovered ketones contained no significant amount of dideuterated species allowed us to be confident that the proportions of monodeuterated ketones obtained (*e.g.*, **5A** and **5C**) provided a measure of the equilibrium concentration of the enolates. It will be noted that this method only provides information about the sum of the concentrations of the stereoisomeric enolates **A** and **B** relative to the concentration of the structurally isomeric enolate **C**.

Chart III



The second method used to measure composition of enolate solutions consisted of adding solutions of the enolates to an excess of acetic anhydride to form a mixture of enol acetates (Chart IV). This mixture was analyzed by gas chromatography. In all cases the enol acetate mixture (*e.g.*, **32**, **33**, and **34**) was the major product (yields, 57–81%), the other major component present in the product mixtures being the starting ketone (recovery, 6–26%). Although minor amounts of C-acetylated products (*i.e.*, 1,3-dicarbonyl compounds) may have been produced, we have no evidence for their presence. Apart from its pertinence to this study, this observation has intrinsic interest in view of

Chart IV



---

(6) (a) From the estimated pK_a values for acetone (~20) and methane (~40), one may calculate the maximum delocalization energy to be about 27 kcal./mole [*cf.* H. E. Zimmerman, L. Singer, and B. S. Thyagarajan, *J. Am. Chem. Soc.*, **81**, 108 (1959)]. The actual value must be somewhat lower since this estimate ignores the inductive effect of the carbonyl function. (b) An analogous energy barrier to rotation in allylic radicals has been demonstrated by C. Walling and W. Thaler, *ibid.*, **83**, 3877 (1961).

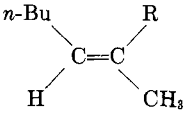
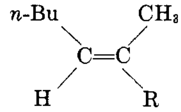
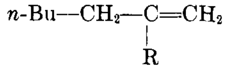
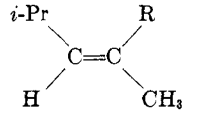
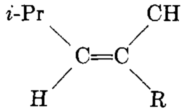
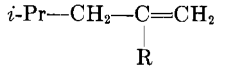
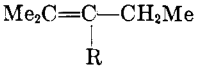
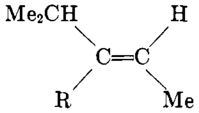
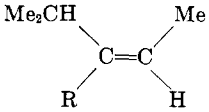
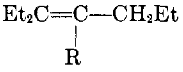
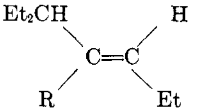
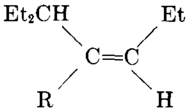
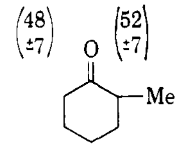
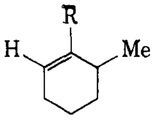
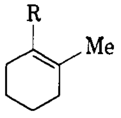
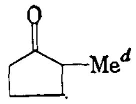
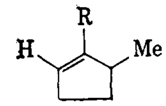
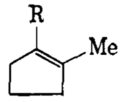
(7) See K. Bieman, "Mass Spectrometry, Organic Chemical Applications," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, for discussion and leading references.

(8) *Cf.* (a) S. K. Malhotra and H. J. Ringold, *J. Am. Chem. Soc.*, **85**, 1538 (1963); (b) H. J. Ringold and S. K. Malhotra, *ibid.*, **84**, 3402 (1962).

(9) (a) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1956, pp. 198–199; (b) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1959, pp. 374–375.

TABLE I

EQUILIBRIUM POSITIONS FOR THE POTASSIUM ENOLATES (IN 1,2-DIMETHOXYETHANE), THE ENOL ACETATES, AND THE ENOL ETHERS

Ketone (enolate equilibrium position from deuterium quenching indicated as % in parentheses)[a]	Equilibrium for enolates (enolate acetylation procedure), enol ethers, and enol acetates indicated as % in parentheses[b]		
(42) (58) $n\text{-Bu—CH}_2\text{—CO—CH}_3$ 2	 $R = O^{\ominus}$ (39) **27**, R = OAc (69)	 $R = O^{\ominus}$ (10) **26**, R = OAc (28)	 $n\text{-Bu—CH}_2\text{—C(R)=CH}_2$ $R = O^{\ominus}$ (51) **28**, R = OAc (3)
(18) (82) $i\text{-Pr—CH}_2\text{—CO—CH}_3$ 3	 $R = O^{\ominus}$ (18) **30**, R = OAc (73)	 $R = O^{\ominus}$ (7) **29**, R = OAc (22)	 $i\text{-Pr—CH}_2\text{—C(R)=CH}_2$ $R = O^{\ominus}$ (75) **31**, R = OAc (5)
(>98) (<2) $\text{Ph—CH}_2\text{—CO—CH}_3$ 4			
(10) (90) $\text{Me}_2\text{CH—CO—CH}_2\text{—Me}$ 5	 $\text{Me}_2\text{C=C(R)—CH}_2\text{Me}$ $R = O^{\ominus}$ (12) **46**, R = OEt (55) **34**, R = OAc (55)	 $R = O^{\ominus}$ (74) **45**, R = OEt (32) **33**, R = OAc (42)	 $R = O^{\ominus}$ (14) **44**, R = OEt (13) **32**, R = OAc (3)
(3) (97) $\text{Et}_2\text{CH—CO—CH}_2\text{—Et}$ 6	 $\text{Et}_2\text{C=C(R)—CH}_2\text{Et}$ $R = O^{\ominus}$ (3) **49**, R = OEt (18)[e] **37**, R = OAc (61)	 $R = O^{\ominus}$ (49) **48**, R = OEt (72)[e] **36**, R = OAc (35)	 $R = O^{\ominus}$ (48) **47**, R = OEt (10)[e] **35**, R = OAc (4)
 7	 $R = O^{\ominus}$ (~35)[c] **50**, R = OEt (51) **38**, R = OAc (~5)[c]		 $R = O^{\ominus}$ (~65)[c] **51**, R = OEt (49) **39** R = OAc (>95)[c]
 8	 $R = O^{\ominus}$ (30) **52**, R = OEt (50) **40**, R = OAc (2)		 $R = O^{\ominus}$ (70) **53**, R = OEt (50) **41**, R = OAc (98)

[a] The values listed are averages of two or more determinations. Unless otherwise noted, the average deviations did not exceed 2%. [b] The values for the enolate acetylations are averages of two or more values. Unless otherwise noted the average deviations did not exceed 2%. The values for the enol ethers and acetates were obtained by heating mixtures of the enol acetates or enol ethers of varying composition with *p*-toluenesulfonic acid to 100° until the composition of the enol acetate or enol ether mixture became constant. [c] Since these enol acetates were not resolved by gas chromatography, it was necessary to estimate the composition of the mixture from its n.m.r. spectrum. [d] No deuterium quenching experiments were run with this ketone. [e] These structural assignments are tentative. See Experimental.

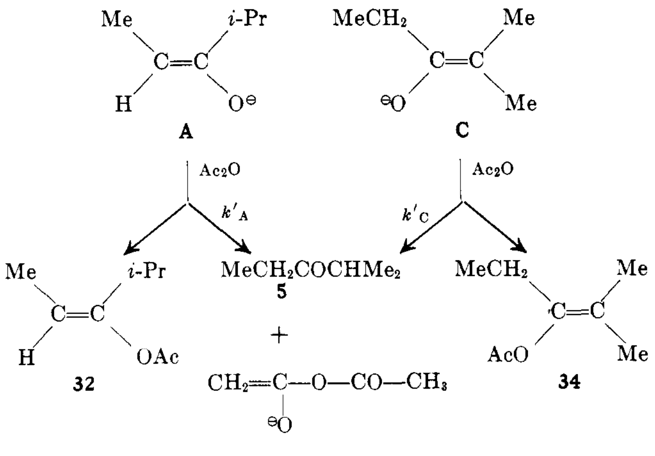
several reports[10] that 1,3-dicarbonyl compounds may be synthesized by reaction of enolates with acid chlorides or acid anhydrides. In view of our results, it is clear that even *the enolates of simple unhindered ketones react with acid anhydrides* (and presumably acid chlorides) *to give primarily O-acylated products* (*cf.* ref. 3b). The formation of C-acylated products must then result from reaction of the initially formed enol esters with excess of enolate which is employed.[10b] In our studies where the acid anhydride was present in large excess this subsequent reaction of the enol ester with excess enolate anion was not possible.

Since there is no *a priori* reason to expect the reaction rate for each enolate (*e.g.*, **A**, **B**, and **C**) with acetic anhydride to be the same and reactions other than O-acylation (*e.g.*, proton transfer from acetic anhydride to the enolate) are possible, the question arises whether

---

(10) (a) C. R. Hauser, F. W. Swamer, and J. L. Adams, *Org. Reactions*, **8**, 59 (1954); (b) B. O. Linn and C. R. Hauser, *J. Am. Chem. Soc.*, **78**, 6066 (1956).

Chart V

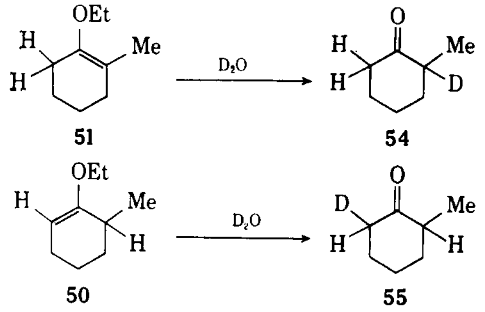


it is correct to assume that the relative quantities of enol acetates (*e.g.*, **32**, **33**, and **34**) produced are a measure of the relative concentrations of enolates. Rather compelling evidence that such an assumption is essentially correct may be derived from comparing (Table I) the position of equilibrium determined by this enolate acetylation procedure with the corresponding results from the previously described deuterium quenching experiments. The maximum difference between the two values for the acyclic ketones studied was 8%.

For the one cyclic ketone **7** where the equilibrium position was determined by both methods, the difference between the two values was 13%. We believe it is significant that the direction of this deviation was always such that the enolate acetylation procedure indicated a higher equilibrium concentration of the more highly substituted enolate. It seems probable that this deviation represents the error which is inherent in the enolate acetylation procedure because each enolate reacts with acetic anhydride either to transfer a proton or to form the enol acetate as is illustrated for enolates **A** and **C** in Chart V. As has been noted elsewhere,[3c] it is very probable that $k_A' > k_C'$. Consequently, the enolate acetylation procedure should yield an enol acetate mixture containing a percentage of the more highly substituted enol acetate which is slightly greater than the percentage of the corresponding enolate in the equilibrium mixture of enolates. We, therefore, believe that the procedure offers a reasonable estimate of the position of the various enolate equilibria and offers the advantage of measuring the relative quantities of stereoisomeric enolates such as **A** and **B**.

The results of applying these methods to solutions in 1,2-dimethoxyethane of the potassium enolates from the ketones **2** to **8** are summarized in Table I. Also included in this table are the values obtained by the acid-catalyzed equilibration of the corresponding enol acetates and of the ethyl enol ethers derived from ketones **5**, **6**, **7**, and **8**. We were unable to obtain data for the enol ethers derived from the methyl ketone **2** and the data for the enol ethers of ketone **6** are questionable because of the tendency of these materials to dimerize or polymerize in the presence of acids.

In order to analyze the mixtures of monodeuterated ketones **54** and **55** derived from the enolates of 2-methylcyclohexanone (**7**), it was necessary to prepare pure samples of each of these ketones. The preparative procedures employed, the hydrolysis of the enol ethers **50** and **51** with a mixture of methanol-d_1 and deuterium oxide in the presence of a buffer, would appear to be generally applicable to the synthesis of specifically labeled α-deuterio ketones. Interestingly, although the C–D infrared stretching frequencies (see Experimental) of the ketone **54** suggest that the deuterium atom occupies an axial position as expected, the corresponding peaks in the spectrum of ketone **55** suggest that the deuterium atom occupies both equatorial and axial positions.[11,12]



Some preliminary results of studies of the effects of changing the cation on the equilibrium position of the enolates from the ketones **2**, **3**, and **5** are summarized in Table II along with the effects of changing the solvent from 1,2-dimethoxyethane to dimethyl sulfoxide. As has been noted in Table II, the data for the ketone **2** in dimethyl sulfoxide are of only qualitative value because of the formation of significant quantities (7% d_2 and 3% d_3) of polydeuterated ketones during the quenching. An appropriate control experiment with mixture of the ketone **2** and its pentadeuterated

Table II

The Effect of the Cation on the Position of Enolate Equilibria

Ketone	Cation	Solvent	Position of equilibrium, %	
5			$\mathrm{Me_2CH{-}\underset{O^{\ominus}}{C}{=}CH{-}Me}$	$\mathrm{Me_2C{=}\underset{O^{\ominus}}{C}{-}CH_2Me}$
	K	DME[a]	90	10
	Na	DME	82	18
	Li	DME	98	2
	Na	DMSO[b]	90	10
3			$i\text{-}\mathrm{PrCH_2{-}\underset{O^{\ominus}}{C}{=}CH_2}$	$i\text{-}\mathrm{Pr{-}CH{=}\underset{O^{\ominus}}{C}{-}CH_3}$
	K	DME	82	18
	Na	DMSO	67	33
2			$n\text{-}\mathrm{Bu{-}CH_2{-}\underset{O^{\ominus}}{C}{=}CH_2}$	$n\text{-}\mathrm{Bu{-}CH{=}\underset{O^{\ominus}}{C}{-}CH_3}$
	K	DME	58	42
	Li	DME	88	12
	Na	DMSO	30[c]	70[c]

[a] 1,2-Dimethoxyethane. [b] Dimethyl sulfoxide. [c] Since the ketone recovered from this quenching experiment contained 7% d_2 and 3% d_3, the validity of these results is open to question.

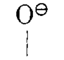
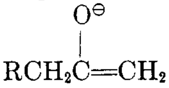
---

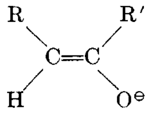
[11] For a discussion of C–D infrared stretching frequencies in rigid cyclohexane systems, see E. J. Corey, M. G. Howell, A. Boston, R. L. Young, and R. A. Sneen, *J. Am. Chem. Soc.*, **78**, 5036 (1956).

[12] (a) For a discussion of the kinetically controlled protonation of enols, see H. E. Zimmerman in P. de Mayo, "Molecular Rearrangements," Vol. I, Interscience Publishers, New York, N. Y., 1963, pp. 345–372; (b) the formation (or hydrolysis) of enol ethers under the conditions employed here involving an addition–elimination sequence, see K. B. Wiberg and K. A. Saegebarth [*J. Org. Chem.*, **25**, 832 (1960)] and S. Sarel, E. Breuer, and J. S. Menahem [*J. Chem. Soc.*, 66 (1963)].

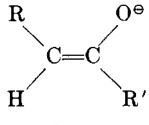
derivative demonstrated that equilibration of a solution of the lithium enolates in 1,2-dimethoxyethane, although slower than equilibration of the potassium enolates, was essentially complete in 1 hr. at room temperature.

From our data, it is clear that even an α-phenyl substituent (as in **4**) will provide sufficient additional stabilization to control the direction of enolate formation in an unsymmetrical ketone. The results of product studies with enolates derived from β,γ(or enolizable α,β)-unsaturated ketones[3,8,13] suggest that an α-vinyl substituent behaves similarly. Both pK_a measurements[2a] and a vast number of preparative experiments attest to the fact that carbonyl functions, nitro groups, cyano groups, and sulfone groups substituted at the alpha position of a ketone will control the direction of enolate formation. Thus, the generalization that a ketone possessing a phenyl group, a vinyl group, a carbonyl function, a nitrile group, etc. as an α-substituent will yield predominately an enolate whose carbon–carbon double bond is adjacent to this α-substituent is on firm ground.

For unsymmetrical ketones which have only alkyl groups as α-substituents, the following generalizations appear warranted for the sodium or potassium enolates in 1,2-dimethoxyethane solution: (1) acyclic ketones of the type $R_2CHCOCH_2R$ (*e.g.*, **5** and **6**) form the less highly substituted enolate  $R_2CHC(O^\ominus)=CHR$ as the predominate structural isomer in the equilibrium mixture; (2) ketones of the type RCH_2COCH_3 form approximately equal amounts of the structurally isomeric enolates if R is an unbranched alkyl group (*e.g.*, **2**) and form predominately the less highly substituted enolate  $RCH_2C(O^\ominus)=CH_2$ if R is a branched alkyl group (*e.g.*, **3**); (3) cyclic ketones (*e.g.*, **7** and **8**) afforded approximately equal amounts of the structural isomeric enolates; (4) where stereoisomeric enolates of types

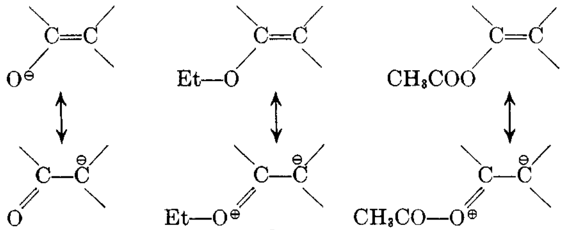


and



are possible (*e.g.*, **2**, **3**, **5**, and **6**), the latter structure will predominate. Since the energy differences between many of the enolates studied are small (1 kcal./mole or less), appreciable changes in the position of the enolate equilibria are observed by changing the cation or solvent (Table II) or by making relatively small changes in the steric bulk of alkyl substituents (*cf.* **2** and **3**). In view of these small differences the previously mentioned dominant effect of α-phenyl and α-vinyl substituents in controlling the direction of enolate formation is not surprising. Our preliminary results (Table II) on cation and solvent effects suggest that changing the cation from sodium or potassium to lithium will favor the less highly substituted enolate whereas changing the solvent from the relatively nonpolar 1,2-dimethoxyethane to the polar dimethyl sulfoxide will favor the more highly substituted enolate.[14] Thus, our results are not in agreement with the earlier general suggestion[3] that the more highly substituted enolate will be more stable. It should be noted that the anions derived from aliphatic nitro compounds do appear to be stabilized by alkyl substitution.[2a,3c,15]

Comparison of the positions of enolate and enol acetate equilibria (Table I) reveals that the relative stability of the more highly substituted enolate is always less than the relative stability of the corresponding more highly substituted enol acetate. A similar trend is seen when the cyclic enol ethers and enol acetates derived from ketones **7** and **8** are compared. We believe this tendency of enolates and enol ethers to favor the less highly substituted carbon–carbon double bond isomer when compared with the corresponding enol acetates is the result of at least two factors. Both the equilibrium positions of the various geometrical isomers listed in Table I and conformational free energy differences[16] suggest that an acetoxyl group has less steric bulk than an ethoxyl group and an alkoxide ion (with whatever atoms or molecules are associated with it in solution). Consequently, steric repulsion between the *cis*-alkyl group and the alkoxy group (or alkoxide ion) in the trisubstituted enol derivative should be greater than the corresponding repulsion between the alkyl group and the acetoxyl group. The enhanced preference for the less highly substituted enolate in equilibrium mixtures involving lithium enolates (see **2** and **5** in Table II) presumably reflects the fact that lithium salts have more covalent character than potassium salts[17] and, consequently, the alkoxide ion and the closely associated and solvated lithium cation is sterically more bulky than the analogous structure with a potassium cation. A second factor which may be important in the effect of alkyl substituents on enolate equilibria is based on delocalization of the type illustrated in structures **N**, **O**, and **P** which should be more extensive for enolates **N** and enol ethers **O**[18] than



N **O** **P**

---

(13) For examples, see (a) C. Djerassi, J. Osiecki, and E. J. Eisenbraun, *J. Am. Chem. Soc.*, **83**, 4433 (1961); (b) H. J. Ringold and S. K. Malhotra, *Tetrahedron Letters*, No. **15**, 669 (1962); (c) J. M. Conia and A. Sandre-Le Craz, *ibid.*, No. **12**, 505 (1962).

(14) *Cf.* G. Stork, P. Rosen, and N. L. Goldman, *J. Am. Chem. Soc.*, **85**, 207 (1963).

(15) H. Schechter, P. W. K. Flanagan, H. Stone, J. G. Troynkam, and F. T. Williams, Jr., Abstracts of Papers, 136th National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1959, p. 33P.

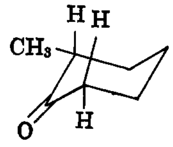
(16) The A values for an acetoxyl group and an ethoxyl group are 0.4–0.7 and 1.0 kcal./mole respectively. E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962 p. 236.

(17) In other studies ethereal solutions of lithium enolates have been found to be substantially less reactive than the corresponding potassium enolates. See H. D. Zook and W. L. Gumby, *J. Am. Chem. Soc.*, **82**, 1386 (1960). Also, organopotassium compounds are reported to be stronger bases than organosodium and organolithium compounds. See W. I. O'Sullivan, F. W. Swamer, W. J. Humphlett, and C. R. Hauser, *J. Org. Chem.*, **26**, 2306 (1961).

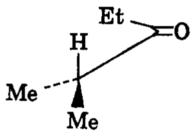
(18) The n.m.r. spectra of simpler enol ethers [J. Feeny, A. Ledwith, and L. H. Sutcliffe, *J. Chem. Soc.*, 2021 (1962)] have suggested that this type of delocalization makes a significant contribution. Comparison of the enol ethers and enol acetates prepared in this study reveals that the β-vinyl proton resonance of the enol ethers occurs at 0.40 to 1.12 p.p.m. (average 0.67 p.p.m.) higher field than the β-vinyl proton resonance of the corresponding enol acetate which is consistent with the idea that there is a higher electron density at the β-carbon atom of the enol ethers.

for enol acetates **P**. Since the electron-donating inductive effect of alkyl groups at the β-carbon atom should oppose this delocalization, the expected result is for trisubstituted enolates and enol ethers to be less stable than the corresponding enol acetates.

To obtain crude estimates of relative rates of proton extraction, the ketones **2**, **5**, and **7** were each allowed to exchange their α-hydrogen atoms for deuterium in a solution containing sodium carbonate in a methanol-d_1–deuterium oxide mixture. Aliquots of these solutions were quenched after various periods of time and the recovered ketones were analyzed by mass spectrometry. From the data obtained in this way we are able to estimate that in an aqueous methanol medium the rate of proton removal from C-4 of 2-methyl-3-pentanone (**5**) is approximately twenty times as fast as the rate of proton removal from C-2. Similarly, for 2-heptanone (**2**) the rate of proton removal at C-1 is approximately four times as rapid as at C-3 and for 2-methylcyclohexanone (**7**) the rate of proton removal at C-6 is approximately equal to the rate of proton removal at C-2. These results are consistent with expectations based on conformational grounds if one recalls that the formation of the enolate anion by an energetically favorable pathway requires the orientation of the C–H bond being broken perpendicular to the plane of the carbonyl group.[12a] For 2-methylcyclohexanone (**7**), which presumably exists mainly in the conformation **56**, there should be little preference for the removal of the axial proton at C-2 rather than the axial proton at C-6. For acyclic ketones such as 2-methyl-3-pentanone (**5**), the conformation **57** necessary for the removal of a proton at C-2 is definitely not favorable with respect to other conformations which are possible. Our results are in general agreement with more detailed studies concerning the rates of abstraction of an α-proton from symmetrical ketones or ketones which enolize in only one direction and analogous studies of hydrocarbons.[19]

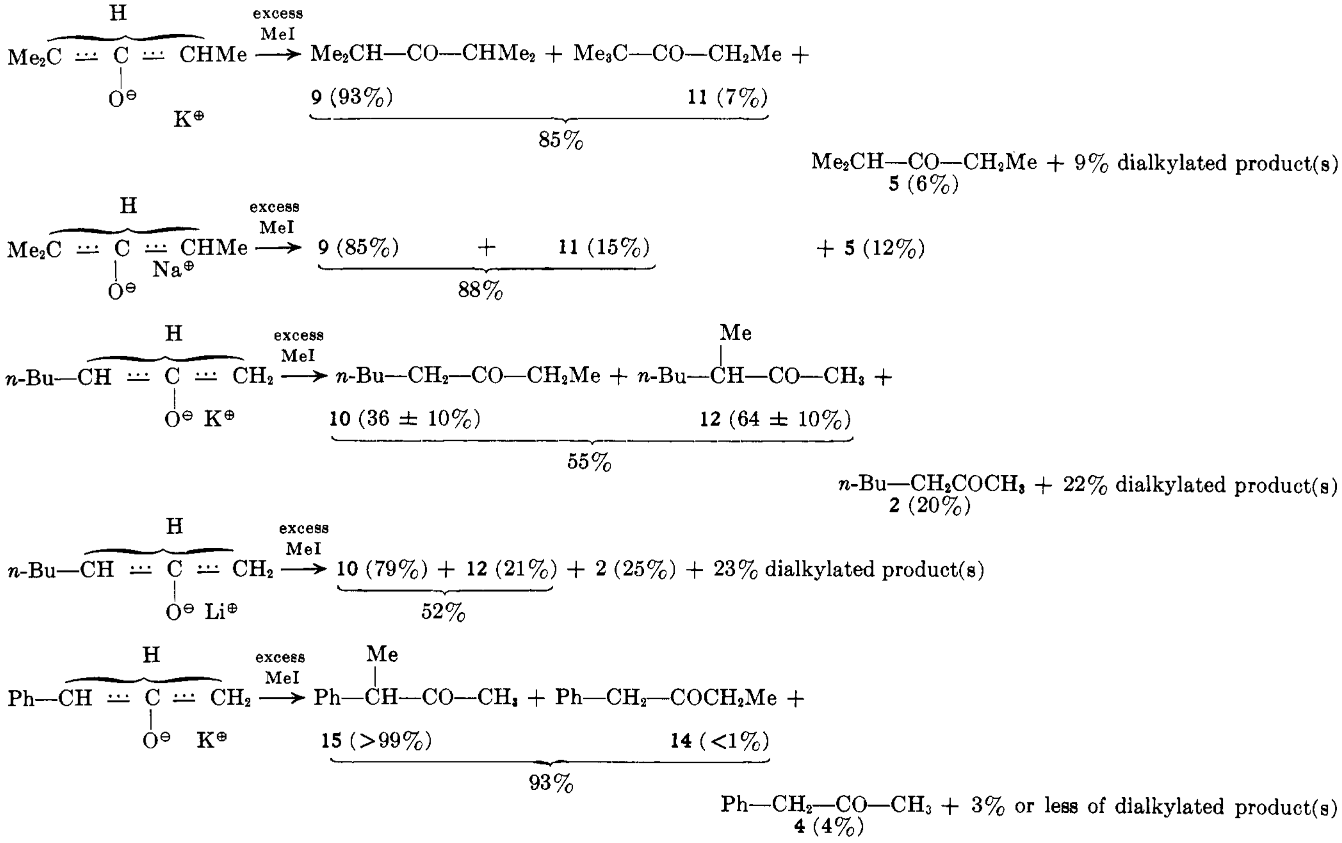


56



57

Finally the reactions of methyl iodide with the enolate mixtures derived from ketones **2**, **4**, **5**, and **7** were examined. The reaction with the enolates of ketones **2**, **4**, and **5** was carried out by adding solutions of the enolates in 1,2-dimethoxyethane to a large excess of methyl iodide in order to minimize di- and trialkylation. The results are indicated in the set of accompanying equations where both the composition of a typical product mixture and the average composition of the monoalkylated product from two or more runs are indicated. It will be noted that dialkylation was a serious side reaction with the ketone **2** in spite of the precautions taken and, as a result, the composition of the monoalkylated product varied substantially from one run to another presumably because the rates of further proton abstraction from **10** and **12** are not the



$$\overbrace{\mathrm{Me_2C} \mathrel{\overset{..}{-}} \underset{\substack{|\\ \mathrm{O^{\ominus}}}}{\mathrm{C}} \mathrel{\overset{..}{-}} \mathrm{CHMe}}^{\mathrm{H}}\ \mathrm{K^{\oplus}} \xrightarrow{\substack{\text{excess}\\ \mathrm{MeI}}} \underbrace{\underset{\mathbf{9}\ (93\%)}{\mathrm{Me_2CH{-}CO{-}CHMe_2}} + \underset{\mathbf{11}\ (7\%)}{\mathrm{Me_3C{-}CO{-}CH_2Me}}}_{85\%} + \underset{\mathbf{5}\ (6\%)}{\mathrm{Me_2CH{-}CO{-}CH_2Me}} + 9\%\ \text{dialkylated product(s)}$$

$$\overbrace{\mathrm{Me_2C} \mathrel{\overset{..}{-}} \underset{\substack{|\\ \mathrm{O^{\ominus}}}}{\mathrm{C}} \mathrel{\overset{..}{-}} \mathrm{CHMe}}^{\mathrm{H}}\ \mathrm{Na^{\oplus}} \xrightarrow{\substack{\text{excess}\\ \mathrm{MeI}}} \underbrace{\mathbf{9}\ (85\%) + \mathbf{11}\ (15\%)}_{88\%} + \mathbf{5}\ (12\%)$$

$$\overbrace{n\text{-}\mathrm{Bu{-}CH} \mathrel{\overset{..}{-}} \underset{\substack{|\\ \mathrm{O^{\ominus}}}}{\mathrm{C}} \mathrel{\overset{..}{-}} \mathrm{CH_2}}^{\mathrm{H}}\ \mathrm{K^{\oplus}} \xrightarrow{\substack{\text{excess}\\ \mathrm{MeI}}} \underbrace{\underset{\mathbf{10}\ (36 \pm 10\%)}{n\text{-}\mathrm{Bu{-}CH_2{-}CO{-}CH_2Me}} + \underset{\mathbf{12}\ (64 \pm 10\%)}{n\text{-}\mathrm{Bu{-}}\overset{\substack{\mathrm{Me}\\ |}}{\mathrm{C}}\mathrm{H{-}CO{-}CH_3}}}_{55\%} + \underset{\mathbf{2}\ (20\%)}{n\text{-}\mathrm{Bu{-}CH_2COCH_3}} + 22\%\ \text{dialkylated product(s)}$$

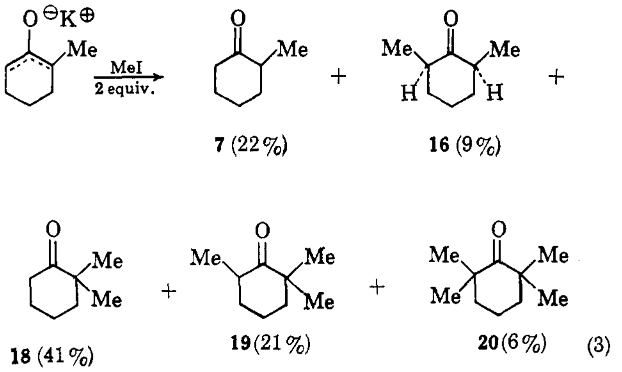
$$\overbrace{n\text{-}\mathrm{Bu{-}CH} \mathrel{\overset{..}{-}} \underset{\substack{|\\ \mathrm{O^{\ominus}}}}{\mathrm{C}} \mathrel{\overset{..}{-}} \mathrm{CH_2}}^{\mathrm{H}}\ \mathrm{Li^{\oplus}} \xrightarrow{\substack{\text{excess}\\ \mathrm{MeI}}} \underbrace{\mathbf{10}\ (79\%) + \mathbf{12}\ (21\%)}_{52\%} + \mathbf{2}\ (25\%) + 23\%\ \text{dialkylated product(s)}$$

$$\overbrace{\mathrm{Ph{-}CH} \mathrel{\overset{..}{-}} \underset{\substack{|\\ \mathrm{O^{\ominus}}}}{\mathrm{C}} \mathrel{\overset{..}{-}} \mathrm{CH_2}}^{\mathrm{H}}\ \mathrm{K^{\oplus}} \xrightarrow{\substack{\text{excess}\\ \mathrm{MeI}}} \underbrace{\underset{\mathbf{15}\ (>99\%)}{\mathrm{Ph{-}}\overset{\substack{\mathrm{Me}\\ |}}{\mathrm{C}}\mathrm{H{-}CO{-}CH_3}} + \underset{\mathbf{14}\ (<1\%)}{\mathrm{Ph{-}CH_2{-}COCH_2Me}}}_{93\%} + \underset{\mathbf{4}\ (4\%)}{\mathrm{Ph{-}CH_2{-}CO{-}CH_3}} + 3\%\ \text{or less of dialkylated product(s)}$$

---

[19] (a) A. K. Mills and A. E. W. Smith, *Helv. Chim. Acta*, **43**, 1915 (1960); (b) D. J. Cram, B. Rickborn, C. A. Kingsbury, and P. Haberfield, *J. Am. Chem. Soc.*, **83**, 3678 (1961); (c) R. E. Dessy, Y. Okuzumi, and A. Chen, *ibid.*, **84**, 2899 (1962); (d) H. Shechter, M. J. Collis, R. Dessy, Y. Okuzumi, and A. Chen, *ibid.*, **84**, 2905 (1962); (e) A. Schriesheim, R. J. Muller, and C. A. Rowe, Jr., *ibid.*, **84**, 3164 (1962); (f) H. Hart and R. E. Crocker, *ibid.*, **82**, 418 (1960); (g) A. Streitwieser and co-workers, *ibid.*, **84**, 244, 249, 251, 254, 258 (1962); (h) A. Schriesheim and C. A. Rowe, Jr., *ibid.*, **84**. 3160 (1962); (i) A. Schriesheim, J. E. Hofmann, and C. A. Rowe, Jr., *ibid.*, **83**, 3731 (1961).

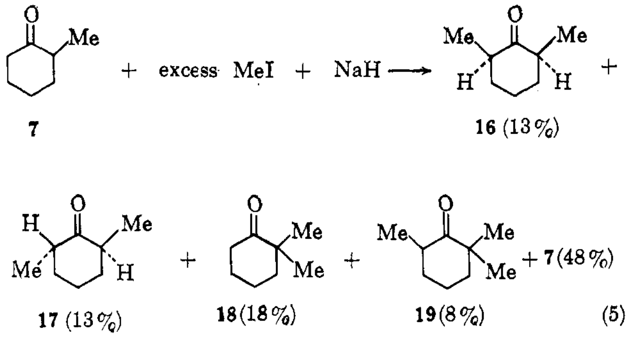
same. The alkylation of 2-methylcyclohexanone (**7**) was carried out as a typical preparative reaction where two equivalents of methyl iodide was added to the enolate partially as a solution and partially as a suspension in 1,2-dimethoxyethane. As is seen from the composition of the reaction mixture (indicated in eq. 3) di- and trialkylation are serious side reactions under these conditions. Under such circumstances, the assumption[3b] that the distribution of monoalkylated products (*e.g.*, **16** and **18** from **7**) provides a measure of the composition of the enolate mixture is definitely fallacious since for such an assumption to be valid the rates of enolate formation and subsequent alkylation of both monoalkylated products would have to be the same. As noted earlier, it is most probable that proton abstraction from **16** (with two axial protons) is approximately twice as rapid as proton abstraction from **18** (with one axial proton).



7 (22%) **16** (9%) **18** (41%) **19** (21%) **20** (6%) (3)

Since our studies indicated that the enolates **A** and/or **B** (Chart I) were formed from 2-methyl-3-pentanone (**5**) approximately twenty times as fast as enolate **C**, it was clear that a more selective alkylation of ketone **5** could be achieved if one could make use of this kinetic preference. We were able to achieve this objective by generating the enolates from the ketone **5** *in the presence of the alkylating agent*, methyl iodide, employing sodium hydride in 1,2-dimethoxyethane. The results, summarized in eq. 4, indicate the increased selectivity, the proportion of ketone **9** in the monoalkylated product being increased from 85% to 96%. Similarly, the distribution of monoalkylated products from a comparable alkylation of 2-methylcyclohexanone (**7**) produced approximately equal amounts of the 2,6 isomers **16** and **17** and the 2,2 isomer **18** as would be anticipated from the relative rates of proton removal (see eq. 5). Since our experiments were not designed to determine whether the distribution of the *cis*- (**16**) and *trans*- (**17**) isomers obtained are the result of a kinetically controlled process or incomplete equilibration (**16** is more stable than **17**), further discussion of this point and of the aforementioned enol ether **50** hydrolysis will be deferred to a subsequent paper in this series.

$$\underset{\mathbf{5}}{\mathrm{Me_2CH{-}CO{-}CH_2Me}} + \text{excess MeI} + \text{NaH} \longrightarrow \underbrace{\underset{\mathbf{9}\ (96\%)}{\mathrm{Me_2CH{-}CO{-}CHMe_2}} + \underset{\mathbf{11}\ (4\%)}{\mathrm{Me_3C{-}CO{-}CH_2Me}}}_{77\%} + \mathbf{5}\,(19\%) + 4\%\ \text{dialkylated products} \qquad (4)$$



7 **16** (13%) **17** (13%) **18** (18%) **19** (8%) + **7** (48%) (5)

For each of the alkylations studied where dialkylation was not a serious competing reaction, it will be noted that the composition of the monoalkylated product is similar to the composition of the equilibrium mixture of enolates. This observation indicates that the reaction of the enolates with the excess methyl iodide is more rapid than interconversion of the enolates and suggests that the structurally isomeric enolates (*e.g.*, **C** *vs.* **A** + **B** in Chart I) react with methyl iodide at similar rates.[3d,20] The generality of this observation for alkylation reactions is being explored further.

Experimental[21]

Preparation of Starting Materials.—2-Methyl-3-pentanone (**5**) was obtained as previously described,[22,23] b.p. 112–115°, $n^{25}\mathrm{D}$ 1.3963; lit.[22] b.p. 113.7–114.5°, $n^{25}\mathrm{D}$ 1.3961; $\bar{\nu}_{\mathrm{C=O}}$[24] 1717 cm.$^{-1}$; $\lambda_{\max}$[25] 281 mμ (ϵ 30). A sample of 2-methylcyclohexanone (**7**), b.p. 76–77° (25 mm.), $n^{25}\mathrm{D}$ 1.4460; lit.[26] b.p. 104–107° (116 mm.), $n^{23}\mathrm{D}$ 1.4473, was prepared as previously described,[26] $\bar{\nu}_{\mathrm{C=O}}$[24] 1710 cm.$^{-1}$, with broad n.m.r. absorption[28] in the region 7.5–8.8 τ and a doublet (J = 6 c.p.s.) centered at 9.03 τ ($\mathrm{CH_3{-}CH}<$).

A cold (0°) solution of 62 g. (0.46 mole) of α-ethylbutyryl chloride and 0.3 g. of cuprous chloride in 100 ml. of ether was treated with an ethereal solution of *n*-propylmagnesium bromide prepared from 43 g. (0.35 mole) of *n*-propyl bromide, 9.0 g. (0.37 g.-atom) of magnesium, and 400 ml. of ether. The resulting crude product was stirred with excess aqueous potassium hydroxide at steam bath temperature to remove the remaining unchanged acid chloride. Recovery and distillation of the water-insoluble residue afforded 33.7 g. (68%) of material, b.p. 67–78° (25 mm.), $n^{25}\mathrm{D}$ 1.4174, which contained[27] 90% of 3-ethyl-4-heptanone (**6**). Fractional distillation through a 40-cm. spinning-band column separated the pure ketone **6**, $n^{25}\mathrm{D}$ 1.4178, lit.[28] b.p. 174.5–175.5° (741 mm.), $\bar{\nu}_{\mathrm{C=O}}$[24] 1708 cm.$^{-1}$, $\lambda_{\max}$[25] 286 mμ (ϵ 39), complex n.m.r. multiplets[24] in the region 7.5–8.0 (3H), 8.1–8.9 (6H), and 9.0–9.4 τ (9H).

Anal. Calcd. for $\mathrm{C_9H_{18}O}$: C, 75.99; H, 12.76; mol. wt., 142. Found: C, 75.92; H, 13.02; mol. wt., 142 (mass spectrum).

---

[20] *Cf.* H. D. Zook and W. L. Rellahan, *J. Am. Chem. Soc.*, **79**, 881 (1957).

[21] 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 either a Baird, Model B, or a Perkin-Elmer, Model 21, infrared recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14. The n.m.r. spectra were determined at 60 Mc. with a Varian, Model A-60, n.m.r. 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.

[22] C. G. Overberger, W. F. Hale, M. B. Berenbaum, and A. G. Finestone, *J. Am. Chem. Soc.*, **76**, 6185 (1954).

[23] A gas chromatography column packed with Dow Corning No. 550 silicone oil suspended on ground firebrick was employed for analysis.

[24] Determined in carbon tetrachloride solution.

[25] Determined in 95% ethanol solution.

[26] A. S. Hussey and R. H. Baker, *J. Org. Chem.*, **25**, 1434 (1960).

[27] A gas chromatography column packed with Dow Corning No. 710 silicone oil suspended on ground firebrick was employed for this analysis.

[28] E. Zener, *Monatsh.*, **32**, 677 (1911). This ketone, previously prepared by the trialkylation of acetone, was reported not to form a semicarbazone.

2-Methyl-2-carboethoxycyclopentanone, b.p. 116–118° (38–40 mm.), $n^{24}\mathrm{D}$ 1.4482, $\bar{\nu}_{C=O}{}^{24}$ 1750 cm.$^{-1}$; lit.[29] b.p. 94.5° (8 mm.), $n^{20}\mathrm{D}$ 1.4460, was prepared as previously described[30] and then hydrolyzed and decarboxylated[31] to yield 2-methylcyclopentanone (**8**), b.p. 135–138°, $n^{24.5}\mathrm{D}$ 1.4330, $\bar{\nu}_{C=O}{}^{24}$ 1735 cm.$^{-1}$, lit.[31] b.p. 139–140°.

Authentic Samples of the Alkylation Products.—An authentic sample of 2,2-dimethyl-3-pentanone (**11**) had been prepared previously.[32] A supposedly pure commercial sample[33] of 3-methyl-2-heptanone (**12**) was found to contain (in order of elution)[23] 3-methyl-2-heptanone (**12**, 15% of the mixture), 3-octanone (**10**, 40% of the mixture), and an unknown conjugated ketone (45% of the mixture). A pure sample of the desired 3-methyl-2-heptanone (**12**), collected[23] from this mixture, $\bar{\nu}_{C=O}{}^{24}$ 1710 cm.$^{-1}$, formed a semicarbazone, m.p. 81–82°, lit.[34] m.p. 82°.

Reaction of isopropylmagnesium bromide with trimethylacetamide as previously described[35] yielded trimethylacetonitrile, 18%, $\bar{\nu}_{C\equiv N}{}^{24}$ 2260 cm.$^{-1}$, b.p. 104–107°, $n^{25}\mathrm{D}$ 1.3740; lit.[35] b.p. 104° (738 mm.), $n^{20}\mathrm{D}$ 1.3792, and 2,2,4-trimethyl-3-pentanone (**13**), 6.7%, $\bar{\nu}_{C=O}{}^{24}$ 1705 cm.$^{-1}$, b.p. 136–137°, $n^{25}\mathrm{D}$ 1.4033; lit.[35] b.p. 134–135° (744 mm.), $n^{20}\mathrm{D}$ 1.4060–1.4070.

1-Phenyl-2-nitro-1-butene, b.p. 127–136° (11 mm.), $n^{25}\mathrm{D}$ 1.5825; lit.[36] b.p. 125–129° (10 mm.), $n^{25}\mathrm{D}$ 1.5832, was reduced and hydrolyzed as previously described[36] to form 1-phenyl-2-butanone (**14**), $\bar{\nu}_{C=O}{}^{24}$ 1715 cm.$^{-1}$, b.p. 95–106° (9–11 mm.), $n^{25}\mathrm{D}$ 1.5102–1.5120, lit.[36] b.p. 101–102° (10 mm.). 2-Phenylpropionaldehyde, b.p. 56° (2 mm.), $n^{26}\mathrm{D}$ 1.5147, prepared as previously described,[37] was oxidized at 0° with potassium permanganate in aqueous acetone to yield 2-phenylpropionic acid, b.p. 114–121° (2.2–2.8 mm.), $n^{25}\mathrm{D}$ 1.5230, lit.[38] b.p. 189° (48 mm.). Reaction of the corresponding acid chloride with dimethylcadmium in benzene produced, after fractional distillation, pure[23] 3-phenyl-2-butanone (**15**), b.p. 96–99° (25 mm.), $n^{25}\mathrm{D}$ 1.5069; lit.[39] b.p. 107–108° (22 mm.), $n^{25}\mathrm{D}$ 1.5074; $\bar{\nu}_{C=O}{}^{24}$ 1718 cm.$^{-1}$, $\lambda_{max}{}^{25}$ 249 (113), 253 (138), 259 (157), 265 (148) and 286 mμ (ϵ 143).

A mixture[23] of stereoisomeric 2,6-dimethylcyclohexanols, b.p. 173–175°, $n^{25}\mathrm{D}$ 1.4615; lit.[40] b.p. 171–173°, $n^{20}\mathrm{D}$ 1.4625, was oxidized[40] to a mixture[23] of 79% of the *cis*-2,6-dimethylcyclohexanone (**16**, first eluted) and 21% of the *trans*-2,6-dimethylcyclohexanone (**17**, second eluted).[41] A sample of each ketone was identified by comparison of its infrared spectrum with the published spectra[42] for ketones **16** and **17**. Additionally, the mass spectrum of each ketone indicated that each sample had a molecular weight of 126. A 13.7-g. (0.083 mole) sample of the pyrrolidine enamine of 2-methylcyclohexanone[43] was added, portionwise and with stirring, to 30.9 g. (0.166 mole) of methyl *p*-toluenesulfonate. After a slightly exothermic reaction, the resulting viscous yellow liquid was divided into three fractions which were sealed under nitrogen. One fraction, containing 24 g. of material, was allowed to stand for 3 weeks at room temperature and then heated to 140° for 24 hr. The resulting viscous liquid was heated on a steam bath with 10 ml. of water for 1 hr. and then extracted with ether. The ethereal solution was washed successively with aqueous hydrochloric acid, aqueous sodium bicarbonate, and saturated aqueous sodium chloride, then dried, concentrated, and distilled in a short-path still. The distillate, 0.85 g. (*ca.* 16%) of a colorless liquid boiling at 96° (80 mm.), $n^{25}\mathrm{D}$ 1.4451, contained[23,44] 30% of 2-methylcyclohexanone (**7**, first eluted) and 70% of *cis*-2,6-dimethylcyclohexanone (**16**, second eluted) but no appreciable quantity (*i.e.*, less than 10%) of 2,2-dimethylcyclohexanone (**18**). Each sample was collected and identified with previously described samples by comparison of gas chromatographic retention times, infrared spectra, and mass spectra.[41,45]

Application of the same isolation procedure to a comparable portion of the reaction mixture which had not been heated above room temperature afforded only traces of volatile neutral product. The third portion of the original reaction mixture was extracted with boiling ether to remove the excess methyl *p*-toluenesulfonate. The residue, a viscous liquid, was dried under reduced pressure. The n.m.r. spectrum[46] of this residual material was consistent with the result to be expected for the *p*-toluene sulfonate of N-methyl-1-(1-pyrrolidyl)-6-methylcyclohexene with a series of peaks in the region 2.1–3.0 (4H, aryl C–H), a triplet ($J \sim 4$ c.p.s.) centered at 3.78 (1H, vinyl C–H), a broad peak centered at 6.24 (4H, $-CH_2-\overset{|}{\underset{|}{N}}-^{\oplus}$), a singlet at 6.80 (3H, $CH_3-\overset{|}{\underset{|}{N}}-^{\oplus}$), a singlet at 7.66 (3H, aryl CH_3), broad absorption in the region 7.5–8.7, and a doublet ($J = 6.5$ c.p.s.) centered at 8.82 τ (3H, $CH_3-CH<$).

To a solution of triphenylmethylpotassium,[4] prepared from 47.271 g. (0.193 mole) of triphenylmethane, 7.7287 g. (0.198 g.-atom) of potassium, 100 ml. of 1,2-dimethoxyethane, and 3 ml. of butadiene, was added, dropwise until the red color of the triphenylmethyl anion just disappeared, 19.0878 g. (0.170 mole) of 2-methylcyclohexanone (**7**), corresponding to an 88% yield of triphenylmethylpotassium. To the resulting *suspension* of sodium enolates was added, dropwise with stirring and cooling, 50 g. (0.35 mole) of methyl iodide. After the mixture had been stirred for 15 min., it was filtered and the residual potassium iodide was washed with ether. The combined organic layers were washed with water, dried, concentrated under a Vigreux column and distilled to separate 14.7713 g. of ketonic products, b.p. 89° (130 mm.)–70° (27 mm.) containing[47,48] 2-methylcyclohexanone (**7**, 22%), 2,2-dimethylcyclohexanone (**18**, 41%), *cis*-2,6-dimethylcyclohexanone (**16**, 9%), 2,2,6-trimethylcyclohexanone (**19**, 21%), and 2,2,6,6-tetramethylcyclohexanone (**20**, 6%). Samples of ketones **19** and **20** were collected; the trimethylated derivative **19** has $\bar{\nu}_{C=O}{}^{24}$ 1707 cm.$^{-1}$ with a molecular weight of 140 (mass spectrum) and the tetramethyl ketone **20** has $\bar{\nu}_{C=O}{}^{24}$ 1695 cm.$^{-1}$ with a molecular weight of 154 (mass spectrum). A 10.9-g. sample of the mixture of ketones from this alkylation was allowed to react with ethyl formate and sodium methoxide in benzene and the hydroxymethylene derivatives formed were separated and hydrolyzed[49] to afford a mixture[23] of ketones **7** (40%) and **18** (60%). Fractional distillation through a 40-cm. spinning-band column separated 3.0218 g. of fractions $n^{25}\mathrm{D}$ 1.4330–1.4458, containing from 37% to 83% of the desired ketone **18**. The pure 2,2-dimethylcyclohexanone (**18**), collected by gas chromatography,[23] has $\bar{\nu}_{C=O}{}^{24}$ 1705 cm.$^{-1}$ and peaks at 1365 and 1385 cm.$^{-1}$ [$C(CH_3)_2$] with broad n.m.r. peaks[24] in the regions 7.5–7.9 (2H, CH_2–CO) and 8.0–8.5 (6H) as well as a singlet at 8.92 τ (6H, CH_3–C), and a molecular weight of 126 (mass spectrum). The material formed a 2,4-dinitrophenylhydrazone, m.p. 142.5–143.5°, lit.[50] m.p. 140–142°.

---

(29) Y. I. Denisenko and A. D. Naber, *Bull. acad. sci. URSS Classe sci. chim.*, 35 (1945); *Chem. Abstr.*, **40**, 2801 (1946).

(30) R. Cornubert and C. Borrel, *Bull. soc. chim. France*, [4] **47**, 301 (1930).

(31) B. Shive, W. W. Crouch, and H. L. Lochte, *J. Am. Chem. Soc.*, **63**, 2979 (1941).

(32) H. O. House, E. J. Grubbs, and W. F. Gannon, *ibid.*, **82**, 4099 (1960).

(33) Purchased from the Aldrich Chemical Co.

(34) S. G. Powell. *J. Am. Chem. Soc.*, **46**, 2514 (1924).

(35) F. C. Whitmore, C. I. Noll, and V. C. Meunier, *ibid.*, **61**, 683 (1939).

(36) H. B. Haas, A. G. Susie, and R. L. Heider, *J. Org. Chem.*, **15**, 8 (1950).

(37) H. O. House and J. W. Blaker, *J. Am. Chem. Soc.*, **80**, 6389 (1958).

(38) H. A. Smith, D. M. Alderman, and F. W. Nadig, *ibid.*, **67**, 272 (1945).

(39) K. Mislow and J. Brenner, *ibid.*, **75**, 2318 (1953).

(40) R. B. Carlin, *ibid.*, **67**, 928 (1945).

(41) This experiment was performed by Dr. Max Schellenbaum in our laboratories.

(42) R. Trave and L. Garanti, *Rend. ist. lombardo sci., Pt. I*, **94A**, 405 (1960).

(43) The preparation and composition (85% disubstituted and 15% trisubstituted in the pure liquid) has been described previously. H. O. House and M. Schellenbaum, *J. Org. Chem.*, **28**, 34 (1963).

(44) A column packed with 4-methyl-4-nitropimelonitrile suspended on ground firebrick was employed for this analysis.

(45) From our work, it is clear that the pyrrolidine enamine of 2-methylcyclohexanone reacts at room temperature to give an N-alkylated product which then rearranges at elevated temperature to give a C-alkylated product. The possible generality of this reaction sequence is currently being investigated with other enamines. *Cf.* G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

(46) Determined as a solution in deuteriochloroform.

(47) A 100-ft. capillary column packed with Dow Corning silicone fluid, No. 710, was employed for the analysis.

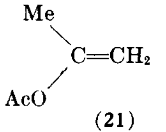
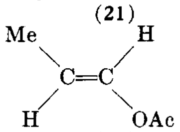
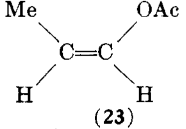
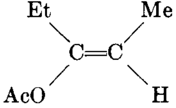
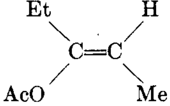
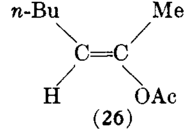
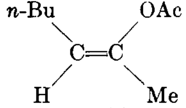
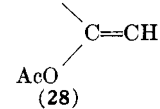
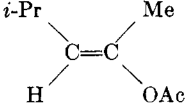
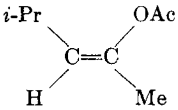
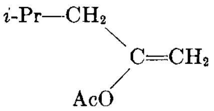
(48) On an ordinary silicone oil column (ref. 23), the mono- and dimethylated cyclohexanones are eluted as follows: first peak, ketone **7**; second peak, ketones **16** and **18**; third peak, ketone **17**. On a nitromethylpimelonitrile column (ref. 44), these compounds are eluted as follows: first peak, ketone **16**; second peak, ketones **7** and **18**; third peak, ketone **17**.

(49) (a) F. E. King, T. J. King, and J. G. Topliss, *J. Chem. Soc.*, 919 (1957); (b) W. S. Johnson and H. Posvic, *J. Am. Chem. Soc.*, **69**, 1361 (1947); (c) W. J. Bailey and M. Madoff, *ibid.*, **76**, 2707 (1954).

(50) P. S. Adamson, A. M. Marlow, and J. L. Simonsen, *J. Chem. Soc.*, 774 (1938).

TABLE III

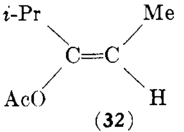
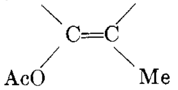
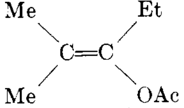
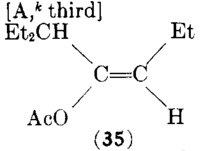
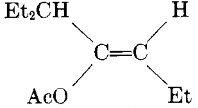
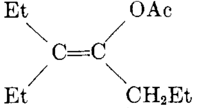
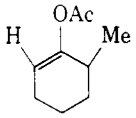
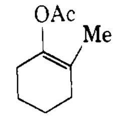
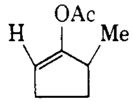
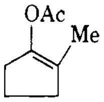
CHARACTERIZATION AND PROPERTIES OF THE ENOL ACETATES

Structure [method of preparation[a] and order of elution on gas chromatography[b]]	Infrared spectrum		N.m.r. spectrum in benzene solution, τ	
	$\tilde{\nu}_{C=O}$ (CCl$_4$), cm.$^{-1}$	$\tilde{\nu}_{C=C}$ (CCl$_4$), cm.$^{-1}$	Vinyl C-H beta to acetoxyl function	Other
 (21)			*cis* 5.31 (multiplet), *trans* 5.50 (multiplet)	8.24 (multiplet, both Me groups)
 (22) [A,[c] second]	1759	1678 (also 930 for *trans* CH=CH)	4.70 (8 lines, J = 7 and 12.5 c.p.s.)[d]	8.31 (singlet, acetyl Me), 8.62 (4 lines, J = 7 and 2 c.p.s., vinyl Me)
 (23) [A,[c] first]	1752	1675	5.29 (5 lines, both J values = 7 c.p.s.)[e]	8.28 (singlet, acetyl Me), 8.44 (4 lines, J = 7 and 2 c.p.s., vinyl Me)
 (24) [A,[f] second]	1750	1690	4.87 (quadruplet, J = 7 c.p.s., long-range coupling, less than 1 c.p.s.)	8.25 (singlet, acetyl Me), 8.58 (quadruplet, J = 7 c.p.s., vinyl Me), 9.04 (triplet, J = 8 c.p.s., Me)
 (25) [A,[f] first]	1755	1699	5.1, (4 triplets, J = 7 and ~1 c.p.s.)	8.19 (singlet, acetyl Me), 8.57 (6 lines, J = 7 and 1 c.p.s. vinyl Me), 9.07 (triplet, J = 7 c.p.s., Me)
 (26) [A[g] and B,[h] third]	1750	1692	4.87 (triplet, J = 7 c.p.s., long-range coupling, ~1 c.p.s.)	8.23 (both acetyl and vinyl Me groups)
 (27) [A[g] and B,[h] first]	1750	1695	5.17 [triplet (J = 7 c.p.s.) of partially resolved multiplets]	8.18 (doublet, J = 1 c.p.s., vinyl Me), 8.22 (singlet, acetyl Me)
 (28) [A[g] and B,[h] second]	1755	1665 (also 885, C=CH$_2$)	5.22 and 5.41 (both partially resolved multiplets)	8.25 (acetyl Me)
 (29) [A[i] and B,[j] third]	1758 and 1744	1690	4.98 (8 lines, J = 9 and 1.5 c.p.s.)	8.20 (doublet, J = 1.5 c.p.s., vinyl Me), 8.26 (singlet, acetyl Me), 9.09 (doublet, J = 7 c.p.s., Me)
 (30) [A[i] and B,[j] first]	1752	1695	5.30 (8 lines, J = 9 and 1.5 c.p.s.)	8.23 (both acetyl and vinyl Me groups), 9.07 (doublet, J = 7 c.p.s., Me)
 (31) [A[i] and B,[j] second]	1756	1665	5.18 and 5.43 (both are partially resolved multiplets)	8.28 (acetyl Me), 9.14 (doublet, J = 7 c.p.s., Me)

[a] Method A is reaction of the carbonyl compound with acetic anhydride and method B is reaction of the carbonyl compound with isopropenyl acetate. [b] See ref. 53. [c] The mixture of enol acetates from this reaction contained 48% of **23** and 52% of **22**. [d] The lower field vinyl proton, obscured by solvent absorption, is found at 2.94 τ (8 lines, J = 2 and 12.5 c.p.s.) in carbon tetrachloride solution. [e] The lower field vinyl proton, obscured by solvent absorption, is found at 2.98 τ (8 lines, J = 2 and 7 c.p.s.) in carbon tetrachloride solution. [f] These enol acetates, prepared as additional spectral models, were only partially characterized. The mixture of enol acetates from this reaction contained 87% of **25** and 13% of **24**. [g] The enol acetate mixture contained 66% of **27**, 4% of **28**, and 30% of

TABLE III

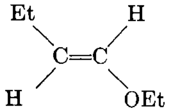
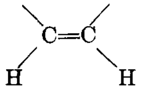
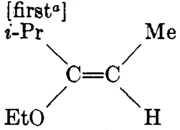
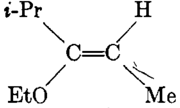
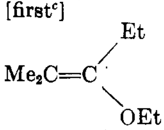
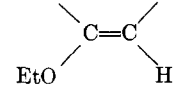
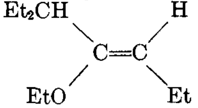
(*continued*)

Structure [method of preparation[a] and order of elution on gas chromatography[b]]	Infrared spectrum		N.m.r. spectrum in benzene solution, τ	
	$\bar{\nu}_{C=O}$ (CCl_4), cm.$^{-1}$	$\bar{\nu}_{C=C}$ (CCl_4), cm.$^{-1}$	Vinyl C–H beta to acetoxyl function	Other
 (**32**) [A,[k] second]	1755	1683	4.92 (quadruplet, J = 7 c.p.s.)	8.19 (singlet, acetyl Me), 8.52 (doublet, J = 7 c.p.s., vinyl Me), 8.98 (doublet, J = 7 c.p.s., Me)
 (**33**) [A,[k] first]	1755	1692	5.03 (quadruplet, J = 7 c.p.s., partially resolved long-range coupling, J ~1 c.p.s.)	8.17 (singlet, acetyl Me), 8.57 (4 lines, J = 7 and 1 c.p.s., vinyl Me), 9.00 (doublet, J = 7 c.p.s., Me)
 (**34**) [A,[k] third]	1748	1693		8.19 (singlet, acetyl Me), 8.51 (singlet, both vinyl Me groups), 9.03 (triplet, J = 7 c.p.s., Me)
 (**35**) [A[l] and B,[m] second]	1755	1675	4.67 (triplet, J = 7.5 c.p.s.)	8.23 (singlet, acetyl Me), 8.8–9.2 (multiplet, 3 Me groups)
 (**36**) [A[l] and B,[m] first]	1755	1685	5.09 (triplet, J = 7 c.p.s.)	8.22 (singlet, acetyl Me), 8.8–9.2 (multiplet, 3 Me groups)
 (**37**) [A[l] and B,[m] third]	1748	1680		8.19 (singlet, acetyl Me), 8.8–9.3 (multiplet, 3 Me groups)
 (**38**)[q] [A[o] and B,[p] ——[n]]	1750	1680[n]	4.80 (6 lines, J = 1.5 and 4 c.p.s.)[n]	7.97 (singlet, acetyl Me), 9.05 (doublet, J = 7 c.p.s.)[n]
 (**39**)[q] [A[o] and B,[p] ——[n]]	1750	1705		7.97 (singlet, acetyl Me), 8.56 (partially resolved multiplet with J < 1 c.p.s., vinyl Me)
 (**40**) [A,[r] first]	1755	1713	4.55 (partially resolved multiplet)	8.31 (singlet, acetyl Me), 9.02 (doublet, J = 7 c.p.s., Me)
 (**41**) [A,[r] second]	1750	1703		8.23 (singlet, acetyl Me), 8.51 (partially resolved multiplet, J < 1 c.p.s., vinyl Me)

26. [h] The enol acetate mixture contained 66% of **27**, 6% of **28**, and 28% of **26**. [i] The mixture of enol acetates contained 67% of **30**, 5% of **31**, and 28% of **29**. [j] The mixture of enol acetates contained 66% of **30**, 16% of **31**, and 18% of **29**. [k] The mixture of enol acetates contained 57% of **33**, 8% of **32**, and 35% of **34**. [l] This enol acetate mixture contained 42% of **36**, 11% of **35**, and 47% of **37**. [m] This enol acetate mixture contained 34% of **36**, 54% of **35**, and 12% of **37**. [n] We were unable to resolve this mixture of enol acetate **38** and **39** by gas chromatography and were forced to work with mixtures of enol acetates whose composition could be estimated from the area under the n.m.r. peak at 9.05 τ in the spectrum of **38**. [o] This mixture of enol acetates, b.p. 82–84.5° (18 mm.), n^{25}D 1.4572, ultraviolet end absorption ε 1830 at 210 mμ in 95% ethanol, was estimated to contain 93% of **39** and 7% of **38**. [p] This mixture of enol acetates, b.p. 84° (18 mm.), n^{25}D 1.4562, ultraviolet end absorption ε 1780 at 210 mμ in 95% ethanol, was estimated to contain 64% of **39** and 36% of **38**. [q] C. Mannich and V. H. Hanau, *Ber.*, **41**, 564 (1908), report b.p. 185–186° for presumably a mixture of enol acetates **38** and **39**. [r] The mixture of enol acetates contained 96% of **41** and 4% of **40**.

TABLE IV

CHARACTERIZATION AND PROPERTIES OF THE ENOL ETHERS

Structure [order of elution on gas chromatography]	$\bar{\nu}_{C=C}$ (CCl$_4$), cm.$^{-1}$	N.m.r. spectrum in benzene solution, τ — Vinyl C-H beta to ethoxyl function	Other
 (**42**) [second[a]]	1652 and 1670[b]	5.31 (6 lines, J = 12 and 7 c.p.s.)	3.85 (doublet, J = 12 c.p.s., vinyl C-H, other coupling not resolved)
 (**43**) [first[a]]	1663	5.69 (quadruplet, both coupling constants = 6 c.p.s.)	4.30 (6 lines, J = 6 and 1 c.p.s., vinyl C-H)
 (**44**) [second[c]]	1673	5.32 (quadruplet, J = 7 c.p.s., long-range coupling not resolved)	8.36 (4 lines, J = 7 and 1.5 c.p.s., vinyl Me), 8.96 (doublet, J = 7 c.p.s., Me)
 (**45**) [first[c]]	1660	5.76 (quadruplet, J = 7 c.p.s.)	8.41 (doublet, J = 7 c.p.s., vinyl Me), 8.83 (doublet, J = 7 c.p.s., Me)
 (**46**) [third[c]]	1680		8.25 and 8.44 (two singlets, vinyl Me), 8.98 (triplet, J = 7 c.p.s., Me)
 (**47**)[e] [second[c]]	1665	. . .[e]	. . .[e]
 (**48**)[e] [first[c]]	1657	5.63 (triplet, J = 7 c.p.s.)	

[a] See ref. 53. [b] This spectrum also has peaks at 937 and 925 cm.$^{-1}$, attributable to a *trans* –CH=CH– function, which are not present in the spectrum of the *cis* isomer **43**. [c] See ref. 59. [d] Some equilibration of **52** and **53** was observed in benzene solution apparently as a result of traces of acidic impurities in the solvent and/or standard. This equilibration was not observed when the samples were run in pyridine solution. The chemical shift values observed in this solvent were 8.35 for **53** and 5.70 and 8.90 τ for **52**. [e] Because of the

Preparation of the Enol Acetates.—The authentic samples of the enol acetates (Table III and V) were prepared by reaction of the ketones with either isopropenyl acetate or acetic anhydride.[51] The following procedures are illustrative.

A mixture of 5.6 g. (0.049 mole) of 2-heptanone (**2**), 10.2 g. (0.10 mole) of acetic anhydride, and 66.1 mg. of *p*-toluenesulfonic acid was heated to boiling under partial reflux, allowing distillate boiling at 118° or less (*i.e.*, acetic acid) to escape.[52] After a reaction period of 5 hr., the reaction mixture was cooled and poured into a cold (0–5°) mixture of saturated, aqueous sodium bicarbonate and pentane. The resulting cold mixture was stirred for 30 min. during which time portions of solid sodium bicarbonate were added periodically until carbon dioxide evolution ceased. The pentane layer, containing[53] 43% of 2-heptanone (**2**) and 57% of the enol acetates (composition: 66% of **27**, 4% of **28**, and 30% of **26**), was dried, concentrated and distilled to separate 4.4 g. of the mixture of ketone and enol acetates, b.p. 132–154°. A mixture of enol acetates **26**, **27**, and **28**, judged by ozonolysis to contain 10% of **28**, has been reported[54] to boil at 63–64° (10 mm.), n^{30}D 1.4200. Samples of each of the enol acetates were collected by gas chromatography.[53] The properties of the materials are listed in Tables III and V.

A mixture of 5.6 g. (0.049 mole) of 2-heptanone (**2**), 10.2 g. (0.102 mole) of isopropenyl acetate, and 53 mg. of *p*-toluenesulfonic acid was refluxed overnight and then the low boiling components (b.p. 54–94°) were separated by fractional distillation. The residual liquid was stirred with a cold pentane–aqueous sodium bicarbonate mixture as described in the previous procedure. The pentane layer, containing[53] 8% of 2-heptanone (**2**) and 92% of the enol acetates (composition: 66% of **27**, 28% of **26**, and 6% of **28**), was dried and concentrated and samples of the pure enol acetates were collected by gas chromatography.[53]

As models for spectral correlations (Table III), commercial isopropenyl acetate (**21**) was employed and samples of *cis* (**23**)- and *trans*-(**22**)-1-acetoxypropene were separated from a mixture,[55] b.p. 92–98°, n^{25}D 1.4102 (lit.[55b] b.p. 104–106°, n^{20}D 1.4122) containing[53] 48% of **23** and 52% of **22**. The footnotes in Table III list the methods of preparation employed for the various enol acetates, the composition of the enol acetate mixtures obtained,

---

(51) For examples, discussion, and leading references, see H. O. House and H. W. Thompson, *J. Org. Chem.*, **26**, 3729 (1961).

(52) With the lower boiling ketones where this procedure was not possible, the reaction mixture was heated under reflux overnight.

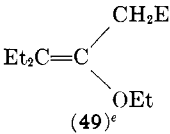
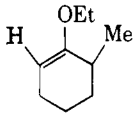
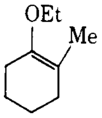
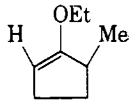
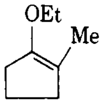
(53) A gas chromatography column packed with Dow Corning silicone fluid, No. 550, suspended on base-washed Chromosorb was employed.

(54) F. G. Young, F. C. Frostick, Jr., J. J. Sanderson, and C. R. Hauser, *J. Am. Chem. Soc.*, **72**, 3635 (1950).

(55) (a) D. Y. Curtin and N. J. Hurwitz, *ibid.*, **74**, 5381 (1952); (b) D. J. Foster and E. Tobler, *J. Org. Chem.*, **27**, 834 (1962).

TABLE IV

(*continued*)

Structure [order of elution on gas chromatography]	$\bar{\nu}_{C=C}$ (CCl_4), cm.$^{-1}$	N.m.r. spectrum in benzene solution, τ: Vinyl C-H beta to ethoxyl function	Other
 (49)[e] [second[c]]	1663		. . .[e]
 (50) [first[a]]	1670	5.61 (triplet, J = 4 c.p.s.)	8.98 (doublet, J = 7 c.p.s., Me)
 (51) [second[a]]	1685		8.45 (multiplet, resolution incomplete, vinyl Me)
 (52) [first[a]]	1640	5.67 (quadruplet, J = 2 c.p.s.)[d]	8.85 (doublet, J = 5.5 c.p.s., Me)[d]
 (53) [second[a]]	1690	. . .[d]	8.31 (partially resolved multiplet with $J < 1$ c.p.s., vinyl Me)[d]

small quantities of enol ethers **47** and **49** in the reaction mixture and the instability of collected samples of these materials, we were unable to obtain sufficient quantities of these materials for analyses and n.m.r. spectra. As a result the structural and stereochemical assignments that were made are based only on gas chromatographic retention times and mass spectra and they should be regarded as tentative.

and the order of elution on gas chromatography.[53] In all cases, including the subsequently described reactions of enolates with acetic anhydride, the identities of the enol acetate samples from various sources were established both by comparison of retention times and by comparison of the infrared spectra of collected samples.

The stereochemical assignments made to the various pairs of geometrical isomers listed in Table III are based on comparison of the n.m.r. spectra of each pair of isomers in benzene solution.[56] For each pair, one isomer exhibited a vinyl proton signal which was at approximately 0.2 to 0.3 p.p.m. lower field than the corresponding peak in the spectrum of the stereoisomer. From these observations alone no firm stereochemical assignment could be made[57] although related measurements of enol ethers[18] suggested that the vinyl proton *cis* to the acetoxy function would have its n.m.r. signal at lower field. We were able to confirm this assignment by examination of the spectra (Table III) of the two isomeric 1-acetoxypropenes **22** and **23** since the stereochemistry of these two isomers was readily apparent both from their infrared spectra and from the magnitudes of the coupling constants between the two vinyl protons.[57] In view of the suggestion[58] that for systems of the type $H_x\text{–}\overset{|}{C}\text{=}\overset{|}{C}\text{–}\underset{|}{\overset{|}{C}}H_a$, $J_{a,x}$ would be slightly larger (*i.e.*, 0.1 to 0.2 c.p.s.) for the *trans* isomer (H_x and CH_a *trans*) than for the *cis* compound, we also considered this possibility for assigning stereochemistry. However, from examination of our spectra it rapidly became apparent that no consistent pattern was being followed as one would conclude if the literature values cited in Fraser's paper[58] are accepted as correct. For this reason as well as the very small differences in coupling constants involved and the lack of understanding of what structural features determine the magnitude of long-range coupling constants, we have abandoned this comparison for making stereochemical assignments and have relied on the aforementioned positions of the vinyl proton signals.

The enol acetate equilibration data listed in Table I were obtained from samples of each set of enol acetates in which approximately 10% (by weight) of *p*-toluenesulfonic acid was dissolved. Each of these solutions, contained in a series of sealed tubes, was heated to 100–140° for periods of time ranging from 24 to 90 hr. and then poured into a pentane–aqueous sodium bicarbonate mixture. The pentane layer was analyzed by gas chromatography.[53]

We were able to reproduce the numbers listed in Table I starting with enol acetate mixtures of varying composition and we were able to demonstrate that neither our isolation procedure nor gas chromatographic analysis was selectively destroying one of the isomers in the enol acetate mixtures.

Preparation of the Enol Ethers.—The ketone enol ethers listed in Tables IV and V were obtained by conversion of the ketones

---

[56] In carbon tetrachloride solution, the n.m.r. signals for the two vinyl protons of isopropenyl acetate (**21**) are superimposed (5.37τ). Although a similar coincidence of peaks was found in deuteriochloroform solution, the peaks were well separated (5.31 and 5.50 τ) in benzene solution.

[57] S. L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, pp. 83–89, 119–121.

[58] R. R. Fraser, *Can. J. Chem.*, **38**, 549 (1960).

TABLE V

ANALYTICAL DATA FOR THE ENOL ACETATES AND ENOL ETHERS

		Analysis				Mol. wt.,
		Calcd.		Found		mass
Structure	Molecular formula	C	H	C	H	spectrum
22	$C_5H_8O_2$					100
23	$C_5H_8O_2$					100
24	$C_7H_{12}O_2$					128
25	$C_7H_{12}O_2$					128
26	$C_9H_{16}O_2$	69.19	10.32	68.90	10.36	156
27	$C_9H_{16}O_2$	69.19	10.32	68.81	10.31	156
28	$C_9H_{16}O_2$	69.19	10.32	69.11	10.36	156
29	$C_8H_{14}O_2$	67.57	9.93	67.13	9.89	142
30	$C_8H_{14}O_2$	67.57	9.93	67.18	9.89	142
31	$C_8H_{14}O_2$	67.57	9.93	67.59	9.97	142
32	$C_8H_{14}O_2$	67.57	9.93	67.16	9.94	142
33	$C_8H_{14}O_2$	67.57	9.93	67.34	9.91	142
34	$C_8H_{14}O_2$	67.57	9.93	67.29	9.91	142
35	$C_{11}H_{20}O_2$	71.69	10.94	71.55	10.89	184
36	$C_{11}H_{20}O_2$	71.69	10.94	71.46	11.11	184
37	$C_{11}H_{20}O_2$	71.69	10.94	71.73	10.98	184
39[a]	$C_9H_{14}O_2$	70.10	9.15	70.21	9.12	154
40	$C_8H_{12}O_2$	68.54	8.63	68.31	8.64	140
41	$C_8H_{12}O_2$	68.54	8.63	68.42	8.78	140
42	$C_6H_{12}O$					100
43	$C_6H_{12}O$					100
44	$C_8H_{16}O$	74.94	12.58	75.14	12.51	128
45	$C_8H_{16}O$	74.94	12.58	74.86	12.49	128
46	$C_8H_{16}O$	74.94	12.58	74.94	12.40	128
47[b]	$C_{11}H_{22}O$					170
48	$C_{11}H_{22}O$	77.58	13.02	77.59	13.02	170
49[b]	$C_{11}H_{22}O$					170
50	$C_9H_{16}O$	77.09	11.50	76.95	11.29	140
51	$C_9H_{16}O$	77.09	11.50	76.91	11.61	140
52	$C_8H_{14}O$	76.14	11.18	76.15	11.25	126
53	$C_8H_{14}O$	76.14	11.18	75.87	11.29	126

[a] The sample of enol acetate **39** was contaminated with approximately 5% of the isomer **38**. See Table III, footnote *n*.
[b] See Table IV, footnote *e*.

5, **6**, **7**, and **8** to their diethyl ketals with ethyl orthoformate followed by either distillation (for the ketals of **5** and **6**) or heating to 190–200° with a catalytic amount of ammonium dihydrogen phosphate (for the ketals of **7** and **8**). The following procedure is illustrative.

A solution of 14.0 g. (0.125 mole) of 2-methylcyclohexanone (**7**), 18.0 g. (0.121 mole) of ethyl orthoformate, and 99.4 mg. of *p*-toluenesulfonic acid in 50 ml. of ethanol was allowed to stand at room temperature for 2 days (a 5-day period was employed for ketones **5** and **6**) and then made basic with ethanolic sodium ethoxide. Distillation afforded 17.2 g. of the crude product containing[53] 85% of the desired ketal. The pure 1,1-diethoxy-2-methylcyclohexane, $n^{25}D$ 1.4395, obtained by collection from a gas chromatograph,[53] has no infrared absorption[24] attributable to a carbonyl or hydroxyl function and only weak end absorption (ϵ 98 at 210 mμ) in the ultraviolet.[25]

Anal. Calcd. for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 71.05; H, 12.12.

A mixture of 18.82 g. (0.101 mole) of this ketal and 1.0 g. of ammonium dihydrogen phosphate was heated to 190–200°. After collection of a forerun, b.p. 74–155°, the mixture of enol ethers (12.41 g. or 88% containing[53] a trace of ethanol, 4% of **7**, 52% of **50**, and 44% of **51**) was collected at 155–165°. Samples of each of the pure enol ethers **50** ($n^{25}D$ 1.4556, ultraviolet end absorption ϵ 2290 at 220 mμ in isooctane) and **51** ($n^{25}D$ 1.4592, ultraviolet end absorption ϵ 7000 at 220 mμ in isooctane) was collected[53] and characterized as summarized in Tables IV and V.

Similarly, 1,1-diethoxy-2-methylcyclopentane, b.p. 68–74° (23 mm.), $n^{25}D$ 1.4281, was prepared from 2-methylcyclopentanone (**8**) in 87% yield.

Anal. Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.76; H, 11.64.

From a mixture of 1-ethoxy-1-butenes, kindly provided by Mr. S. Karady (unpublished work with Professor G. Büchi), samples of the two enol ethers **42** and **43** were collected[43] for spectral measurements. As discussed in the previous section dealing with enol acetates, the stereochemical assignments made for enol ethers **44**, **45**, **47**, and **48** are based on the position of the n.m.r. signal for the vinyl proton beta to the ethoxyl function in benzene solution. Both previous studies[18] and our measurements with enol ethers **42** and **43** are consistent with the idea that the beta vinyl proton will be located at lower field when it is *cis* to the ethoxyl function. Although not listed in Table IV, the n.m.r. spectrum of each of the vinyl ethers exhibited a set of peaks characteristic of an ethoxyl group with a quadruplet in the area 6.4 to 6.6 and triplet in the area 8.8–9.0 τ with J values of 7 c.p.s.

The equilibration data listed in Table I were performed by heating solutions of 1–5% (by weight) of *p*-toluenesulfonic acid in the enol ethers to 100° in sealed tubes for periods of 60–170 hr. The resulting mixtures were poured into mixtures of aqueous sodium bicarbonate and pentane and the organic layer was separated, dried, and analyzed.[53,59]

Reaction of Enolate Mixtures. A. From 2-Methyl-3-pentanone (5) and Triphenylmethylpotassium.—To a solution containing 8.3 mmoles of triphenylmethylpotassium in 10 ml. of 1,2-dimethoxyethane was added a quantity (0.8326 g.) of the ketone **5** such that the red color of the base was discharged and a slight excess of the ketone was present. The resulting solution of enolates was stirred for 30 min. at room temperature and then poured into 67 g. (0.47 mole) of methyl iodide. After the resulting mixture had been stirred for 30 min., it was filtered and the residual potassium iodide was washed with ether. To the combined organic solutions was added 0.8972 g. of ethylbenzene (as an internal standard) and the mixture was analyzed by gas chromatography.[23,44,60] The calculated yields were 68% of monoalkylated products (composed of 93% **9** and 7% **11**), 5% of the starting ketone **5**, and 7% of the dialkylated product **13**. The products were identified both from their retention times and from the infrared spectra of collected samples. From a number of comparable alkylation experiments where the proportions of reactants and isolation procedures were varied, the composition of the monoalkylated product (93% of **9** and 7% of **11**) was essentially unchanged. The alkylation of other potassium enolates, summarized in Table VIII, and the analyses and product identifications were effected in the same manner.

A comparable solution of enolates, prepared from 317.7 mg. (3.18 mmoles) of the ketone **5** in 10 ml. of 1,2-dimethoxyethane, was stirred for 30 min. and then added, dropwise and with stirring, to 4.3 g. (42 mmoles) of freshly distilled acetic anhydride. The resulting mixture was stirred at room temperature for 30 min. and then poured into a cold (0–5°) mixture of pentane and aqueous sodium bicarbonate and again stirred for 30 min. while solid sodium bicarbonate was added until the evolution of carbon dioxide ceased. After the pentane layer had been separated, dried, and concentrated, 215.9 mg. of anisole (as an internal standard) was added and the mixture was analyzed by gas chromatography.[53] The calculated yields were 26% of the ketone **5** and 57% of a mixture of enol acetates containing (average of duplicate runs) 74% of **33**, 14% of **32**, and 12% of **34**. This same procedure was followed for all the enolate acetylation experiments. The results are summarized in Table VI.

A comparable solution of enolates, from 387.2 mg. (3.9 mmoles) of the ketone **5** in 10 ml. of 1,2-dimethoxyethane, was stirred for 30 min. after which a 5-ml. aliquot was quenched by adding it to dilute deuterioacetic acid prepared from 97.9 mg. of acetic anhydride and 10 ml. of deuterium oxide. The resulting solution (pH 5–6) was stirred for not longer than 15 min. and then extracted with ether. The resulting ethereal solution was dried, concentrated, and the ketone **5** was collected by gas chromatography.[23] The recovered ketone **5** was analyzed by mass spectrometry and found to contain 4% of d_0 species and 96% of d_1 species. By the procedure described subsequently, the monodeuterated ketone was found (average of three runs) to be composed of 90% of $(CH_3)_2CHCOCHDCH_3$ and 10% of $(CH_3)_2CDCOCH_2CH_3$. This same procedure was followed for all the potassium enolate quenching experiments. The results are summarized in Table VII. As a control experiment, a 5-ml. aliquot of a solution containing 0.0103 mole of triphenylmethylpotassium in 25 ml. of 1,2-dimethoxyethane was added to a solution of deuterioacetic acid (from 10 ml. of deuterium oxide and

---

(59) A column packed with a mixture of tetraethylene glycol and Carbowax 400 M suspended on base-washed Chromosorb was employed.

(60) The monoalkylated products **9** and **11** were not resolved by our silicone oil column (ref. 23).

TABLE VI

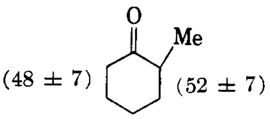
EQUILIBRIA OF 1,2-DIMETHOXYETHANE SOLUTIONS OF POTASSIUM ENOLATES AS DETERMINED BY ACETYLATION OF THE ENOLATE MIXTURES

Ketone, mg. (mmoles)	Solvent, ml.	Ac_2O, g. (mmoles)	Internal standard	Calcd. yield of enol acetate, %[a]	Calcd. recovery of starting ketone, %[a]	Composition of enol acetate mixture (%)[b]
5 317.7 (3.18)	10	4.3 (42)	Anisole	57	26	**33** (74), **32** (14), **34** (12)
2 399 (3.50)	10	5.4 (53)	Anisole	60	19	**27** (39), **28** (51), **26** (10)
3 356 (3.56)	10	4.3 (42)	Anisole	63	15	**30** (18), **31** (75), **29** (7)
6 499.8 (3.51)	10	4.3 (42)	Anisole	58	21	**36** (49), **35** (48), **37** (3)
7 195.9 (1.75)	10	2.16 (21.2)	*m*-Methylanisole	81	6	**38** (~35), **39** (~65)[c]
8 185.4 (1.89)	20	2.16 (21.2)	*m*-Methylanisole	72	7	**40** (30), **41** (70)

[a] Values from a typical experiment. [b] Average values from two or more runs. Unless otherwise noted, the mixture was analyzed by gas chromatography (ref. 53). [c] Since this mixture was not resolved by gas chromatography, its composition was determined from its n.m.r. spectrum. See Table III, footnote *n*.

TABLE VII

EQUILIBRIA OF 1,2-DIMETHOXYETHANE SOLUTIONS OF POTASSIUM ENOLATES AS DETERMINED BY QUENCHING IN BUFFERED DEUTERIUM OXIDE

Ketone, mg. (mmoles)	Solvent, ml.	Deuterium distribution in recovered ketone in a typical experiment, %	Deuterium distribution in monodeuterated ketone (%[a])
5 387.2 (3.9)	10	4 d_0 96 d_1	$Me_2CH—CO—CH_2—Me$ (10) (90)
2 366.5 (3.2)	10	4.5 d_0 95.5 d_1	*n*-$Bu—CH_2—CO—CH_3$ (42) (58)
4 393 (3.48)	10	6 d_0 91 d_1 3 d_2	$Ph—CH_2—CO—CH_3$ (>98) (<2)
3 259.2 (2.6)	10	5 d_0 95 d_1	*i*-$Pr—CH_2—CO—CH_3$ (18) (82)
6 604.7 (4.25)	10	6 d_0 94 d_1	$Et_2CH—CO—CH_2—Et$ (3) (97)
7 187.2 (1.67)	20	17 d_0 83 d_1	

[a] Average values from two or more runs. Unless otherwise indicated individual values agreed with the average value to within 2% or less.

104.3 mg. of acetic anhydride). To this mixture was added 233 mg. (2.3 mmoles) of the ketone **5** and the resulting mixture was stirred for 30 min. and then subjected to the isolation procedure described in the previous experiment. The deuterium content of the recovered ketone **5** did not exceed natural abundance. Comparable control experiments were performed for all of the other enolate quenching experiments described in this paper.

To establish the validity of our procedure for determining the deuterium distribution in the monodeuterated species from our quenching experiments, we required a sample of the ketone **5** in which all of the exchangeable α-hydrogen atoms had been replaced by deuterium. For this purpose a sample of methanol-d_1 was prepared by the following procedure.[61] A mixture of 186 g. (1.57 moles) of freshly distilled dimethyl oxalate, 167 g. (1.57 moles) of anhydrous sodium carbonate, and 31 g. (1.55 moles) of deuterium oxide was heated under reflux for 15 hr. and then distilled to dryness separating 95 g. of distillate, b.p. 35–60°, containing[44] methanol-d_1, deuterium oxide, and methyl formate (identified with an authentic sample by comparison of retention times and infrared spectra). After the distillate had been allowed to react with 0.2 g. of sodium, the resulting solution was refluxed overnight and then fractionally distilled through a 15-cm. Vigreux column to separate 75 g. (73% based on the total amount of deuterium employed) of methanol-d_1, b.p. 64–68°. Throughout this preparation dry apparatus was employed and all of the reactants were protected from atmospheric moisture. The product contained[44] less than 1% of deuterium oxide and was shown by combustion and subsequent falling-drop analysis[62] to be 99.6% methanol-d_1 [*Anal.* Calcd. for CH_3DO: D, 25.00 atom %. Found: 24.91 atom %]. To a solution of sodium methoxide, prepared from 40 ml. of methanol-d_1 and 173.4 mg. (0.0075 g.-atom) of sodium, was added 15 g. (0.15 mole) of 2-methyl-3-pentanone (**5**). The resulting solution was refluxed for 15 hr. under nitrogen and then concentrated. An additional 30-ml. portion of methanol-d_1 and 56 mg. of sodium were added and the exchange was repeated. This procedure was performed a total of eight times after which the concentrated solution was adjusted to pH 5 by the addition of deuterioacetic acid and then poured into 25 ml. of water. The resulting mixture was extracted with ether and the ethereal extract was dried and concentrated. The pure trideuterated ketone **5** was collected by gas chromatography[23] and analyzed by mass spectrometry. The material was found to contain 9% of d_2 species and 91% of d_3 species. Comparison of the relative peak intensities of the molecular ion (*m/e* 100), the isobutyryl fragment [$(CH_3)_2CH—C{\equiv}O^{\oplus}$, *m/e* 71], and the propionyl fragment ($CH_3CH_2C{\equiv}O^{\oplus}$, *m/e* 57)[63] for the nondeuterated and trideuterated ketones **5** established that the fragment peaks did arise entirely from the indicated acyl ions and that the effect of the α-deuterium atoms on the abundance of the fragment ions was negligible. Consequently, after correction for natural isotopic abundance, the intensities of the peaks at *m/e* 57 and 58 provided a measure of the deuterium content at C-4 and the intensities of the peaks at *m/e* 71 and 72 provided a measure of the deuterium content at C-2 in the samples from the enolate quenching experiments.

---

[61] This procedure is a modification of the method described by J. Beersmans and J. C. Jungers, *Bull. soc. chim. Belges*, **56**, 72 (1947).

[62] The analysis was performed by Mr. Josef Nemeth, Urbana, Ill.

[63] The mass spectral data and details of the calculations are available in the Doctoral dissertation of Vera Kramar, Massachusetts Institute of Technology, April, 1963.

TABLE VIII

REACTIONS OF ENOLATES WITH METHYL IODIDE IN 1,2-DIMETHOXYETHANE

Ketone, mg. (mmoles)	Solvent, ml.	Base (mmoles)	Methyl iodide, g. (mmoles)	Internal standard	Calcd. yields, %			Composition of monoalkylated product, %
					Starting ketone	Monoalkylated products	Di(and tri)-alkylated products	
5[a] 832.6 (8.3)	10	Ph_3CK (8.3)	67 (470)	Ph-Et	5	68	7 (of **13**)	**9** (93), **11** (7)
5[a] 871.8 (8.7)	25	NaH (10)	56 (395)	Ph-Et	10	75	<1	**9** (85), **11** (15)
5[b] 992.4 (9.9)	25	NaH (17)	67 (470)	Ph-Et	19	77	4 (of **13**)	**9** (96), **11** (4)
2[a] 987.8 (8.7)	10	Ph_3CK (8.7)	60 (420)	Ph-Et	20	55	22	**10** (26–47),[c] **12** (53–74)[c]
2[a] 251 (2.2)	10	Ph_3CLi (2.2)	18 (130)		25[d]	52[d]	23[d]	**10** (79), **12** (21)
4[a] 1298 (9.8)	10	Ph_3CK (9.8)	57 (400)		4[d]	93[d]	3 or less[d]	**14** (<1), **15** (>99)
7[b] 1128 (10.1)	25	NaH (10.9)	30 (210)	Anisole	43	40	7	**16** (30), **17** (30), **18** (40)

[a] In this experiment the enolates were formed and then added to the methyl iodide. [b] In this experiment the enolates were formed in the presence of methyl iodide. [c] The values quoted are the extremes in the range of values obtained from several runs. [d] These figures are the composition of the product mixture and not the calculated yields.

B. From 2-Methyl-3-pentanone (5) and Sodium Hydride.—Utilizing the quantities indicated in Table VIII, a solution of the ketone in 1,2-dimethoxyethane was heated under reflux with sodium hydride for 21 hr. at which time 210 ml. (91% of the theoretical amount) of hydrogen had been evolved. The resulting solution of enolates was added to methyl iodide. After the resulting mixture had been stirred for 30 min., it was washed with water and the organic product was separated and analyzed as previously described to give the results indicated in Table VIII.[64]

To explore the result of forming the enolates from **5** in the presence of an alkylating agent, the ketone **5** was added with stirring, to a refluxing mixture of sodium hydride, 1,2-dimethoxyethane, and methyl iodide. The resulting mixture was refluxed, with stirring, for 65 hr. and then filtered, concentrated, and analyzed[23,44] (see Table VIII).

A comparable solution of enolates was prepared by refluxing and stirring a mixture of 977.7 mg. (9.8 mmoles) of the ketone **5**, 402.6 mg. (16.7 mmoles) of sodium hydride, and 25 ml. of 1,2-dimethoxyethane for 7 hr. at which time 230 ml. (92.5% of the theoretical amount) of hydrogen had been evolved. A 5-ml. aliquot of this solution was removed, quenched in a deuterioacetic acid–deuterium oxide mixture (pH 5) and the ketone was recovered and analyzed as previously described. The recovered ketone contained 95% of d_1 species and 5% of d_0 species. The monodeuterated ketone was composed (average of two runs) of 82% of $(CH_3)_2CHCOCHDCH_3$ and 18% of $(CH_3)_2CDCOCH_2CH_3$.

C. From 2-Methyl-3-pentanone (5) and the Sodium Salt of Dimethyl Sulfoxide.—A mixture of 241 mg. (10 mmoles) of sodium hydride, several milligrams of triphenylmethane (as an indicator), and 25 ml. of dimethyl sulfoxide (freshly distilled from a mixture containing its sodium salt and triphenylmethylsodium) was heated to 60–70° with stirring under nitrogen for 2 hr.,[65] then cooled, and treated with 820 mg. (8.2 mmoles) of the ketone **5** which just discharged the red color. The resulting blue-green solution was stirred for 30 min. and then a 5-ml. aliquot was quenched in a deuterioacetic acid–deuterium oxide mixture and the ketone was recovered and analyzed as previously described. The recovered ketone contained 94% of d_1 species and 6% of d_0 species. The monodeuterated ketone was composed (average of three runs) of 90% of $(CH_3)_2CHCOCHDCH_3$ and 10% of $(CH_3)_2CDCOCH_2CH_3$.

D. Exchange Experiments with 2-Methyl-3-pentanone (5) and Methanol-d_1.—Orienting experiments established that the ketone **5**, as a 0.3 to 1.0 *M* solution in methanol-d_1, underwent no appreciable hydrogen–deuterium exchanged after 7 hr. in the presence of 0.1 *M* sodium acetate and underwent very rapid exchange (3% d_3, 46% d_2, 42% d_1 and 9% d_0 after 10 min.) in the presence of 0.04 *M* sodium methoxide. Consequently, the following procedure was employed to measure relative rates of hydrogen–deuterium exchange. A solution of 9.7 mg. (0.092 mmole) of anhydrous sodium carbonate and 568.3 mg. (5.68 mmoles) of the ketone **5** in 7 ml. of methanol-d_1 and 3 ml. of deuterium oxide was stirred at room temperature (about 25°) and 1-ml. aliquots were withdrawn and quenched in a pentane–water mixture after 30 sec. and then at 5-min. intervals for a period of 30 min. A suitable control experiment demonstrated the effectiveness of this quenching procedure. The ketone **5** was recovered from the pentane solution in each case and then analyzed for deuterium content and distribution as previously described. After 30 min. the deuterium content of the recovered ketone was 17% d_2 species, 49% d_1 species and 34% d_0 species. From the percentages of material after various times which contain no deuterium at position 4, one can calculate that the rate constant for exchange is 6×10^{-4} sec.$^{-1}$; the corresponding value at position 2 is approximately 3×10^{-5} sec.$^{-1}$. Thus, the ratio of the exchange rate at position 4 to the exchange rate at position 2 is approximately 20 to 1.

E. From 2-Methyl-3-pentanone (5) and Triphenylmethyllithium.—A solution of 1.2416 g. (5.10 mmoles) of triphenylmethane and 6 ml. of an ethereal solution containing approximately 5 mmoles of phenyllithium in 14 ml. of 1,2-dimethoxyethane was stirred for 30 min. at which time the red solution gave a negative Gilman test for phenyllithium. The resulting solution was titrated to a pale pink end point with 444 mg. (4.4 mmoles) of the ketone **5** at which point a 5-ml. aliquot was quenched in a deuterioacetic acid–deuterium oxide mixture. The remaining enolate solution was treated with an additional small quantity of the ketone **5** to completely discharge the red color. The resulting solution was stirred for 1 hr. and then a 5-ml. aliquot was quenched. The recovered ketone from the first quenching process contained 2.5% of d_0 and 97.5% of d_1 species with a distribution in the monodeuterated ketone of 97% MeCHDCOCH-

---

[64] In all of the reactions employing sodium hydride as a base the recovered ketone **5** contained a small amount of 2-methyl-3-pentanol as a contaminant which appeared as a shoulder in the gas chromatogram (ref. 23). The contaminant was identified with an authentic sample by comparison of retention times and infrared spectra. An authentic sample of 2-methyl-3-pentanol, b.p. 127.5° (762 mm.), n^{25}_D 1.4146, was prepared by reduction of the ketone **5** with lithium aluminum hydride in ether solution. F. C. Whitmore and F. Johnston, *J. Am. Chem. Soc.*, **60**, 2265 (1939), report b.p. 125–126° (742 mm.), n^{20}_D 1.4170, for this alcohol.

[65] E. J. Corey and M. Chaykovsky, *ibid.*, **84**, 867 (1962).

Me_2 and 3% $MeCH_2COCDMe_2$. The ketone from the second quenching process contained 4% of d_0 and 96% of d_1 species with a distribution in the monodeuterated ketone of 98% $MeCHDCOCHMe_2$ and 2% $MeCH_2COCDMe_2$.

F. From 2-Heptanone (2) and Triphenylmethylpotassium.—The alkylation experiments are summarized in Table VIII. From the product mixture containing[23] **2** (first eluted), **12** (second eluted), **10** (third eluted), and one or more higher molecular weight ketones[66] (fourth peak eluted) which is presumably a mixture of dialkylated products, each of the monoalkylated products **10** and **12** was identified by comparison of retention times and infrared spectra of collected samples.

The acetylation and deuterium oxide quenching experiments with the potassium enolates from ketone **2** are summarized in Tables VI and VII. 2-Heptanone (**2**) was subjected to eight exchanges with sodium methoxide and methanol-d_1 as previously described to afford a ketone sample containing 1% d_3 species, 10% d_4 species, and 89% d_5 species. The relative intensities of peaks in the mass spectra of the nondeuterated ketone **2** and the pentadeuterated ketone in the region of the molecular ion (m/e 114) and the hexanoyl fragment $CH_3(CH_2)_4C{\equiv}O^{\oplus}$ (m/e 99), established that this fragment could be used to determine the deuterium distribution at C-3 as in the previous case. The acetyl fragment (m/e 43) could not be used in this calculation because of substantial contributions to this fragment peak from the $C_3H_7{}^{\oplus}$ ion. Consequently, the deuterium distribution at C-1 was obtained by subtracting the deuterium content at C-3 from the total deuterium content. The n.m.r. spectrum[24] of the pentadeuterated ketone **2** differs from the spectrum of the nondeuterated ketone in lacking a singlet at 7.96 (CH_3CO) and a triplet (J = 7 c.p.s.) at 7.68 τ (CH_2CO).

An attempt to prepare the enolates of 2-heptanone (**2**) by refluxing a solution of 4.8102 g. (42 mmoles) of the ketone **2** in 25 ml. of 1,2-dimethoxyethane with 1.0824 (45 mmoles) of sodium hydride for 20 hr. resulted in the evolution of 925 ml. (86% of the theoretical amount) of hydrogen. However, after the solution had been poured into water and the organic product separated in the usual way, distillation afforded 2.34 g. of liquid, b.p. 170° (2 mm.), $n^{24}D$ 1.4755, which contained[23] three major components and had infrared absorption[24] at 1715 (C=O), 1665 (conjugated C=O), and 1625 cm.$^{-1}$ (conjugated C=C) with an ultraviolet maximum[25] at 246 mμ (ϵ 5300). This material is presumably a mixture of aldol condensation products derived from the 2-heptanone (**2**).[67]

G. From 2-Heptanone (2) and the Sodium Salt of Dimethyl Sulfoxide.—A solution of enolates, prepared from 381.7 mg. (3.35 mmoles) of the ketone **2** and 10 ml. of a solution prepared from 246.3 mg. (10 mmoles) of sodium hydride and 25 ml. of dimethyl sulfoxide as previously described, was stirred for 30 min. and then a 5-ml. aliquot was quenched in a deuterioacetic acid–deuterium oxide mixture and the ketone recovered as previously described. The recovered ketone, which was typical of several runs, contained 12% d_0 species, 78% d_1 species, 7% d_2 species, and 3% d_3 species indicating that some exchange was occurring during the quenching process. The deuterium distribution in the monodeuterated ketone was approximately 70% of n-$BuCHDCOCH_3$ and 30% of n-Bu-CH_2COCH_2D.

H. Exchange Experiments with 2-Heptanone (2) and Methanol-d_1.—A 1.2-M solution of the ketone **2** in methanol-d_1 underwent no detectable hydrogen-deuterium exchange after 7 hr. in the presence of 0.09 M sodium acetate. The previously described procedure was followed employing a solution of 13.0 mg. (0.123 mmole) of anhydrous sodium carbonate and 533.2 mg. (4.68 mmoles) of the ketone in 7 ml. of methanol-d_1 and 3 ml. of deuterium oxide. Aliquots (1 ml.) were withdrawn and quenched in the usual manner at measured times from 30 sec. to 30 min. after mixing. After 10 min., the recovered ketone sample contained 4% d_0, 19% d_1, 35% d_2, 29% d_3, 11% d_4, and 2% d_5 species and the deuterium content at C-3 was 47% d_0, 43% d_1, and 10% d_2. From the per cent of nondeuterated ketone **2** remaining after various times, the total rate of exchange can be calculated to be 5×10^{-3} sec.$^{-1}$ and from the per cent of material having no deuterium at C-3 after various periods of time, the rate of exchange at position 3 can be calculated to be 1×10^{-3} sec.$^{-1}$. Thus, the ratio of the exchange rate at position 1 to the rate at position 3 is approximately 4 to 1.

I. From Phenyl-2-propanone (4) and Triphenylmethylpotassium.—The results of quenching this enolate mixture are summarized in Table VII. Since the ketone underwent slow hydrogen–deuterium exchange in the inlet system of the mass spectrometer, it was necessary to scan the spectrum several times and then extrapolate to zero time for each analysis. As implied by the formation of some d_2 species in this experiment, some exchange did occur in the quenching. From control experiments of the type previously described, the recovered ketone **4** contained 90–93% of d_0 and 7–10% of d_1 species. Some exchange was also found to occur during the gas chromatographic separation. Since we were unable to find quenching and isolation conditions which prevented some exchange, our data permit us to conclude that the monodeuterated ketone formed on quenching this enolate mixture contains less than 2% of $PhCH_2COCH_2D$ but do not permit us to estimate how much less.

Phenyl-2-propanone (**4**) was subjected to a series of five exchanges with a solution of sodium carbonate in deuterium oxide employing a temperature of 60° and a reaction time of 18 hr. for each exchange. The recovered ketone contained 93% d_5 and 7% d_4 species. From the mass spectra of the nondeuterated and pentadeuterated ketones **4**, the molecular ion (m/e 134) and the acetyl fragment (m/e 43) were found usable for determining deuterium distribution. The n.m.r. spectrum[24] of the pentadeuterated ketone exhibits no absorption at higher field than 3 τ.

The alkylation of a solution of enolates is summarized in Table VIII. The product mixture contained[27] the unchanged ketone **4**, 3-phenyl-2-butanone (**15**), and 3% of a higher boiling component having the same retention time as phenylcyclohexane (*cf.* ref. 4). The alkylated product **15** was identified by its retention time and the infrared spectrum of a collected sample.

J. From 4-Methyl-2-pentanone (3) and Triphenylmethylpotassium.—The reactions of solutions of the enolates with acetic anhydride and buffered deuterium oxide are summarized in Tables VI and VII.

4-Methyl-2-pentanone (**3**) was subjected to a series of seven exchanges with solutions of sodium carbonate in deuterium oxide as previously described. The recovered ketone contained 2% d_3, 15% d_4, and 83% d_5 species. Comparison of peak intensities in the mass spectra of the nondeuterated and pentadeuterated ketones **3** in the regions of the molecular ion (m/e 100), the 3-methylbutyryl fragment $(CH_3)_2CHCH_2C{\equiv}O^{\oplus}$ (m/e 85) and the acetyl fragment (m/e 43) indicates that in the nondeuterated ketone the peak at m/e 85 results from 60% of the fragment $CH_3C^{\oplus}H{-}CH_2COCH_3$ (m/e 90 in the d_5 ketone) and 40% of the fragment $(CH_3)_2CHCH_2C{\equiv}O^{\oplus}$ (m/e 87 in the d_5 ketone). Similarly, the peak at m/e 43 in the nondeuterated ketone results from the fragment $CH_3C^{\oplus}HCH_3$ (approximately 12%, m/e 43 for the d_5 ketone) and the fragment $CH_3C{\equiv}O^{\oplus}$ (approximately 88%, m/e 46 for the d_5 ketone). These correction factors as well as the usual corrections for natural isotope abundance and the amount of nondeuterated ketone were used to calculate the deuterium distribution.

The following control experiment was performed to demonstrate that the conditions used to produce solutions of enolates would suffice to equilibrate the various enolates formed. A solution of enolates, prepared from 285.8 mg. (2.86 mmoles) of the ketone **3** and an equivalent quantity of triphenylmethylpotassium in 10 ml. of 1,2-dimethoxyethane, was treated with 82.5 mg. (0.8 mmole) of the previously described 4-methyl-2-pentanone-d_5 (83% d_5, 15% d_4, and 2% d_3) and the resulting solution was stirred under nitrogen. After 15- and 30-min. periods, 5-ml. aliquots were quenched in aqueous acetic acid and the ketone was recovered and analyzed in the usual way. The ketone recovered after a 15-min. reaction period contained 37% d_0, 41% d_1, 18% d_2, 3.5% d_3, and 0.5% d_4; the sample isolated after a 30-min. reaction contained 39% d_0, 41% d_1, 16% d_2, 3.4% d_3, and 0.6% d_4. Thus equilibration was complete after 15 min.

K. From 4-Methyl-2-pentanone (3) and the Sodium Salt of Dimethyl Sulfoxide.—A solution of enolates, prepared from 310.5 mg. (3.1 mmoles) of the ketone **3**, 107.1 mg. (4.5 mmoles) of sodium hydride, and 10 ml. of dimethyl sulfoxide as previously described, was stirred for 30 min. after which a 5-ml. aliquot was quenched in a solution prepared from 210.8 mg. (2.08 mmoles) of acetic anhydride, 163 mg. (2.0 mmoles) of sodium acetate, and 20 ml. of deuterium oxide. The ketone, recovered and analyzed

---

(66) A collected sample exhibits infrared absorption (see ref. 24) at 1712 cm.$^{-1}$.

(67) J. Colonge, *Bull. soc. chim. France*, [4] **49**, 426 (1931), reports for 8-methyl-7-tridecen-6-one, b.p. 146–149° (30 mm.), $n^{15}D$ 1.4580.

as in previous cases, contained 10% d_0, 89% d_1, and 1% d_2 species. The deuterium distribution in the monodeuterated ketone (average of two runs) was 33% $i\text{-PrCHDCOCH}_3$ and 67% $i\text{-PrCH}_2\text{COCH}_2\text{D}$. A control experiment, as previously described, demonstrated that the conditions used for quenching the enolate solution do not cause hydrogen–deuterium exchange in the ketone **3**.

L. From 3-Ethyl-4-heptanone (6) and Triphenylmethylpotassium.—The reactions of the enolate solutions with acetic anhydride and buffered deuterium oxide are summarized in Tables VI and VII.

A sample of the ketone **6** was subjected to a series of five exchanges with methanol-d_1 in the presence of sodium methoxide as previously described. The recovered ketone contained 1% d_0, 2% d_1, 20% d_2, and 77% d_3 species. The mass spectra of the ketone **6** and its deuterated derivatives in the regions of the molecular ion peak (m/e 142), the 2-ethylbutyryl fragment $\text{Et}_2\text{CHC}{\equiv}\text{O}^{\oplus}$ (m/e 99) and the butyryl fragment $\text{EtCH}_2\text{C}{\equiv}\text{O}^{\oplus}$ (m/e 71) reveal that other fragments contribute to both acyl fragment peaks and that the effect of isotopic substitution on the content of fragmentation is not negligible. Consequently, these data could be used to conclude that at least 90% of the monodeuterated ketone is composed of $\text{Et}_2\text{CHCOCHDEt}$ but did not permit a more reliable calculation.

In order to obtain a more meaningful estimate of the deuterium distribution, the spectra were redetermined in the region of m/e 71 with a CEC, Model 21–110, high resolution mass spectrometer which easily resolves the $\text{C}_5\text{H}_{11}^{\oplus}$ ion (m/e 71.0861) from the $\text{C}_4\text{H}_7\text{O}^{\oplus}$ ion (m/e 71.0497).[7] After suitable correction of the peaks at m/e 73 for natural isotopic abundance and the peaks at m/e 72 for the nondeuterated ketone present in the ketone sample measured, the deuterium distribution in the monodeuterated ketone was calculated to be 95–99% $\text{Et}_2\text{CHCOCHDEt}$ and 1–5% $\text{Et}_2\text{CDCOCH}_2\text{Et}$.

M. From 2-Methylcyclohexanone (7) and Triphenylmethylpotassium.—The reactions of solutions[68] of these enolates, with acetic anhydride and buffered deuterium oxide, are summarized in Tables VI and VII. The average deviations for individual determinations (±7%) in this case were much greater than the deviations (±2% or less) experienced in the previously described experiments. The deviations appeared to be unrelated to the time the enolate mixture was stirred; also, a subsequently described control experiment established that equilibration of the enolates was complete in less than 30 min. The amount of nondeuterated ketone **7** (ranging from 7 to 20%) in the samples recovered from the quenching experiments was also higher than normal for the previously described quenching experiments and suggested that some hydrogen–deuterium exchange was occurring during the gas chromatographic separation[25] of the ketone prior to analysis as had been encountered previously with phenyl-2-propanone (**4**). Unfortunately, our analytical scheme required that the ketone be completely free from other contaminants in the reaction mixture and we were unable to avoid this gas chromatographic separation. As a consequence, our deuterium quenching experiments with enolate solutions derived from this ketone **7** have less quantitative significance than the other measurements reported.

Since the methods previously employed for determining deuterium distribution in the monodeuterated ketones were not applicable to the cyclic ketone **7**, it was necessary to prepare pure samples of both 2-deuterio-2-methylcyclohexanone **54** and 6-deuterio-2-methylcyclohexanone **55**. A solution of 272.7 mg. of the enol ether **50** in 3.5 ml. of methanol-d_1 was mixed with 2.5 ml. of a buffer solution prepared from 5 ml. of deuterium oxide, 53.7 mg. of acetic anhydride, and 89.0 mg. of anhydrous sodium acetate. The resulting solution was stirred at room temperature for a total of 66 hr. Aliquots were removed from the solution at various time intervals and extracted with pentane. Analyses[53] of the various pentane extracts indicated that a negligible concentration of the isomeric enol ether **51** was present throughout the hydrolysis. The half-life of the enol ether **50** in this reaction medium was approximately 19 hr. The ketone **55** resulting from this hydrolysis was collected by gas chromatography.[53] This product **55**, which contained 5% d_0 and 95% d_1 species in one run and 8% d_0, 91% d_1, and 1% d_2 species in a second run, has infrared absorption[24] at 1709 cm.$^{-1}$ (C=O) and at 2190, 2150, and 2120 (shoulder) cm.$^{-1}$ (axial and equatorial C–D)[69] and differs from the spectrum of **54** in the positions and intensities of a number of bands in the fingerprint region. The n.m.r. spectrum[24] of the product has a doublet (J = 6.5 c.p.s.) at 9.03 τ ($\text{CH}_3\text{CH}<$).

The same hydrolysis procedure was applied to 228.3 mg. of the enol ether **51** employing a total reaction time of 84 hr. As in the previous case, the concentration of the isomeric enol ether **50** in the reaction mixture was negligible throughout the hydrolysis. The half-life of the enol ether **51** in the medium was approximately 25 hr. The ketone **54** was collected by gas chromatography and found to contain 8% d_0 and 92% d_1 species in one run and 10% d_0, 88% d_1 and 2% d_2 in a second run. This ketone **54** has infrared absorption[24] at 1709 (C=O) and at 2150 and 2120 cm.$^{-1}$ (axial C–D)[67] as well as an n.m.r. singlet at 9.03 τ ($\text{CH}_3\text{CD}<$).

A series of synthetic mixtures of ketones **54** and **55** were prepared and from the mass spectra of these mixtures and the spectra of the two pure monodeuterated ketones, working curves were prepared plotting the percentage of ketone **54** (or **55**) against the ratios of each of the following pairs of peak intensities: 68/69, 56/57 and 43/44. For analysis of deuterium distribution in ketone samples recovered from quenching experiments, the mass spectrum was first corrected for the amount of nondeuterated ketone in the sample and then the deuterium distribution was determined from each of the three aforementioned intensity ratios.

After a sample of 2-methylcyclohexanone had been subjected to a series of five exchanges with methanol-d_1 and deuterium oxide in the presence of sodium carbonate, the ketone was recovered as previously described. This ketone sample contained 1% d_1, 6% d_2, and 93% d_3 species and had infrared absorption[24] at 1709 cm.$^{-1}$ (C=O) and at 2125 (s), 2160 (shoulder), 2180 (w), and 2220 (s) cm.$^{-1}$ (C–D stretching).[69]

As a control experiment to demonstrate the ability of the enolates derived from the ketone **7** to equilibrate under the conditions of their formation, a solution of the enolates prepared from 187 mg. (1.67 mmoles) of the ketone **7** and triphenylmethylpotassium in 20 ml. of 1,2-dimethoxyethane was treated with 29.4 mg. (0.26 mmole) of the previously described 2,6,6-trideuterio-2-methylcyclohexanone. After the resulting solution had been stirred for 30 min. it was added to an acetic acid–water mixture and the ketone was recovered as previously described. The recovered ketone sample contained 77% d_0, 21% d_1, and 1% d_2 species demonstrating complete hydrogen–deuterium exchange in the solution containing the enolates.

N. From 2-Methylcyclohexanone (7) and Sodium Hydride.—The alkylation of these enolates is summarized in Table VIII. The calculated yields[53] were 43% of recovered **7**, 16% of **18**, 12% of **16**, 12% of **17**, and 7% of **19** corresponding to the following distribution of alkylated products, 36% of **18**, 27% of **16**, 24% of **17**, and 13% of **19**. From a second comparable experiment the distribution of alkylated products was 30% of **18**, 35% of **16**, 25% of **17**, and 10% of **19**.

O. From 2-Methylcyclopentanone (8) and Triphenylmethylpotassium.—The reaction of the solution of enolates with acetic anhydride is summarized in Table VI.

P. Exchange Experiments with 2-Methylcyclohexanone (7) and Methanol-d_1.—A solution of 431.8 mg. (3.95 mmoles) of the ketone **7** and 30.7 mg. of sodium carbonate in a mixture of 3 ml. of deuterium oxide and 7 ml. of methanol-d_1 was stirred at room temperature (about 25°), 1-ml. aliquots being removed and quenched in a pentane–water mixture after time periods ranging from 30 sec. to 21 min. The ketone recovered from each aliquot as previously described was analyzed for deuterium content and distribution in the usual way. The sample recovered after a reaction time of 21 min. contained 39% d_0, 44% d_1, 16% d_2, and 1% d_3 species. The rate constant for total hydrogen deuterium exchange was calculated to be approximately 7×10^{-4} sec.$^{-1}$ and the rate constant for exchange at both the 2 and 6 position were each calculated to be approximately 3×10^{-4} sec.$^{-1}$. Thus, the relative rates of exchange at positions 2 and 6 are approximately 1 to 1.

---

(68) Since the enolates derived from 2-methylcyclohexanone (**7**) were significantly less soluble than the other systems included in this study, it was necessary to work at concentrations of approximately 0.1 to 0.2 M rather than at the approximately 0.4 M concentration used with other compounds in this study.

(69) The stretching frequency for an equatorial C–D bond is reported to be in the range 2155–2162 cm.$^{-1}$ and 2171 and 2177 cm.$^{-1}$, whereas the ranges for an axial C–D bond are 2114–2138 cm.$^{-1}$ and 2139–2164 cm.$^{-1}$. See E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 217; also see ref. 11.

Q. **From 2-Heptanone (2) and Triphenylmethyllithium.**—To a solution containing triphenylmethyllithium (prepared from triphenylmethane and phenyllithium as previously described) in a mixture of 14 ml. of 1,2-dimethoxyethane and 6 ml. of ether was added 500.9 mg. of the ketone **2** which discharged the red color of the triphenylmethyl anion. Aliquots (5 ml.) were removed and quenched in deuterioacetic acid–deuterium oxide mixtures after time periods of *ca.* 30 sec. and 1 hr. In each case the recovered ketone samples contained 4% d_0, 95% d_1, and 1% d_2 species with a deuterium distribution in the monodeuterated ketone of 12% n-BuCHDCOCH$_3$ and 88% of n-BuCH$_2$COCH$_2$D. The 10 ml. of enolate solution remaining from the quenching experiments was added, dropwise and with stirring, to 18 g. (0.13 mole) of methyl iodide. The resulting mixture was stirred for 2 hr., allowed to stand overnight, diluted with water, extracted with pentane, and analyzed[27] (see Table VIII).

Although both the constancy of the composition of the enolate mixture and the formation of dialkylated products with excess methyl iodide indicated that these lithium enolates were equilibrating in the reaction medium, it seemed advisable to verify this point. Accordingly, a solution of triphenylmethyllithium in 7 ml. of 1,2-dimethoxyethane and 3 ml. of ether was treated with a mixture of 182.3 mg. (1.60 mmoles) of the ketone **2** and 76.6 mg. (0.64 mmole) of 2-hepanone-d_5 (composition 88% d_5, 10% d_4, 1% d_3) which served to discharge the red color of the triphenylmethyl anion. Aliquots (5 ml.) were removed and quenched in aqueous acetic acid after time periods of 30 min. and 60 min. The ketone sample recovered from the first quenching experiment (after 30 min.) contained 53% d_0, 11% d_1, 5% d_2, 13% d_3, 16% d_4, and 2% d_5 species. The ketone from the second quenching experiment (after 60 min.) contained 56% d_0, 18% d_1, 10% d_2, 8% d_3, 7% d_4, and 1% d_5. Thus, equilibration of the lithium enolates, although slower than equilibration of the potassium enolates, is clearly occurring in 1,2-dimethoxyethane solution at room temperature and appears to be nearly complete after 60 min.

Dialkoxyphthalocyaninosilicon Derivatives[1a]

PAUL C. KRUEGER AND MALCOLM E. KENNEY

Case Institute of Technology, Cleveland 6, Ohio

Received March 27, 1963

The preparations and reactions of a series of dialkoxyphthalocyaninosilicon complexes are described. The results obtained suggest that siliconium ions may be intermediates in some of the reactions discussed.

A variety of silicon phthalocyanines with groups oxygenbridged to the silicon have been described previously.[2–6] However the only representative of the dialkoxy series reported up to now has been the incompletely characterized but useful intermediate, bis(benzyloxy)phthalocyaninosilicon, PcSi(OCH$_2$C$_6$H$_5$)$_2$.[1b]

The series of dialkoxides described in this paper, together with the silicon phthalocyanines previously described, serve to illustrate the way in which the properties of ring unsubstituted trivalent and tetravalent metal phthalocyanines vary with the nature of the groups attached to the metal. Thus, for example, (PcSiO)$_x$ is thermally stable and insoluble in organic solvents,[2] PcSiF$_2$ is chemically inert,[7] PcSi(OH)$_2$ is chemically reactive,[2–5] and PcSi(OC$_{18}$H$_{37}$)$_2$ is benzene soluble. Ordinary melting point behavior is shown both by PcSi[OSi(C$_6$H$_5$)$_2$(CH$_3$)]$_2$, an interesting species recently reported by Weyenberg and Cekada,[6] and by PcSi(OC$_{18}$H$_{37}$)$_2$.

In all these cases the properties can be accounted for in terms of the nature of the side chain or group and the properties of the macrocyclic ring. Thus, to take the case of the dialkoxides in more detail, in the series PcSi(OC$_2$H$_5$)$_2$, PcSi(OC$_8$H$_{17}$)$_2$, and PcSi(OC$_{18}$H$_{37}$)$_2$ the increase in solubility is attributable to the decrease in molecular symmetry and the increase in molecular flexibility as the side chains are lengthened. Similarly accounted for is the fact that PcSi(OC$_2$H$_5$)$_2$ does not melt up to 360° in a vacuum, PcSi(OC$_8$H$_{17}$)$_2$ melts with decomposition at 260°, and PcSi(OC$_{18}$H$_{37}$)$_2$ melts at 152° without decomposition. In the same vein the changes of infrared spectra due to the presence of the side chains are as expected. For example, bands are shown which are characteristic of C–Cl in PcSi(OCH$_2$CCl$_3$)$_2$ at 842 cm.$^{-1}$, of monsubstituted benzene in PcSi(OCH$_2$C$_6$H$_5$)$_2$ at 696 cm.$^{-1}$, of aliphatic C–H in PcSi(OC$_5$H$_{11}$)$_2$ at 2946, 2898, 2860, 1473, and 1393 cm.$^{-1}$, in PcSi(OC$_8$H$_{17}$)$_2$ at 2926, 2854, 1466, and 1383 cm.$^{-1}$, and in PcSi(OC$_{18}$H$_{37}$)$_2$ at 2922, 2848, 1468, and 1385 cm.$^{-1}$.

Some properties of the dialkoxides, and in fact of the silicon phthalocyanines in general, which are properties of the macrocycle are little influenced by changes in the nature of the side groups. Thus the infrared absorptions attibutable to the macrocycle in the 1150–650-cm.$^{-1}$ range remain essentially unchanged[8] and the compounds all retain the characteristic blue to green color by transmitted light. The degree of constancy of the visible spectra of the dialkoxides is shown by the fact that the strongest band in benzene solutions is at 679 mμ in PcSi(OCH$_2$CCl$_3$)$_2$, 673 mμ in PcSi(OC$_5$H$_{11}$)$_2$, 674 mμ in PcSi(OC$_8$H$_{17}$)$_2$, and 674 mμ in PcSi(OC$_{18}$H$_{37}$)$_2$.[8] The slight blue shift for the band in PcSi(OCH$_2$CCl$_3$)$_2$ is probably due to the electron-withdrawing power of the side groups making the π–π^* transition in the ring more difficult.

It is evident that enough information is available about the characteristics imparted by various sorts of groups on the metal and the methods for attaching them to the metal so that ring unsubstituted phthalocyanines with specified physical and chemical properties can now be made on a rational basis.

In earlier work it was found that PcSi(OH)$_2$ condenses with itself,[2] and with PcAlOH·H$_2$O,[5] (C$_6$H$_5$)$_3$SiOH,[3] C$_6$H$_5$OH,[4] and C$_6$H$_5$CH$_2$OH.[3] Now it has been found that it condenses with simple aliphatic alcohols as well. These findings lead to the conclusion that the reaction

$$\mathrm{PcSi(OH)_2 + 2HOR \longrightarrow PcSi(OR)_2 + 2H_2O}$$

---

[1] (a) This paper is based on the Ph.D. thesis of P. C. K., University Microfilms. The work was made possible by the National Science Foundation Grant NSF-G15833; (b) Pc = phthalocyanino ligand.

[2] R. D. Joyner and M. E. Kenney, *Inorg. Chem.*, **1**, 717 (1962).

[3] R. D. Joyner and M. E. Kenney, *ibid.*, **1**, 236 (1962).

[4] R. D. Joyner, J. Cekada, R. G. Linck, and M. E. Kenney, *J. Inorg. Nucl. Chem.*, **15**, 387 (1960).

[5] J. E. Owen and M. E. Kenney, *Inorg. Chem.*, **1**, 334 (1962).

[6] D. R. Weyenberg and J. Cekada, *Chem. Eng. News*, **40**, No. 51, 39 (1962).

[7] P. C. Krueger, Ph.D. thesis, University Microfilms, p. 13.

[8] Reproductions of the spectra are given in ref. 7, p. 105.