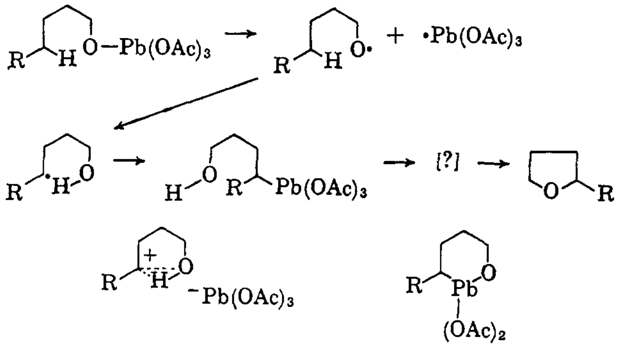
of intermediates follow; however, two possibilities are shown in structures II and III.

Conclusion

Although the results that are reported here by no means prove the mechanism of alcohol oxidation by lead tetraacetate, they highly suggest, at least in part, a free-radical process. It is important to note that the product ratios indicate that ether and aldehyde formation are equally probable. Aldehydes are not intermediates in the ring closure as they are unchanged in control experiments (solvent type). One fact has been established; namely, a prerequisite for ether formation is not one of molecular rigidity holding the alcohol and δ-carbon functions in close proximity. It can hardly be questioned, however, that any structure having rigid proximity of these groups would give rise to higher yields of the THF derivatives.

SCHEME IV



II III

Acknowledgment.—This work was supported by the Research Corporation, to which the author extends his thanks. Helpful comments from Drs. Marmor, Small, and Stuckwisch are gratefully appreciated.

The Chemistry of Carbanions. X. The Selective Alkylation of Unsymmetrical Ketones[1]

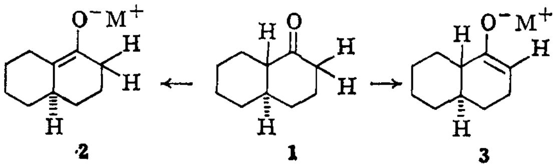
HERBERT O. HOUSE AND BARRY M. TROST[2]

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Received March 19, 1965

Solutions of enolate anions which retain their structural and stereochemical integrity can be prepared by reaction of the corresponding enol acetates with 2 equiv. of methyllithium in 1,2-dimethoxyethane. By use of this procedure it is possible to effect the selective alkylation of unsymmetrical ketones at either the more or less highly substituted α-position, utilizing the appropriate enol acetate derivative of the ketone. Selective alkylations of 2-heptanone, 2-methylcyclopentanone, 2-methylcyclohexanone, and 1-decalone are described. The proportion of *cis*-fused 9-methyl-1-decalone obtained from alkylation of 1-decalone can be significantly enhanced by use of the very reactive alkylating agent, trimethyloxonium 2,4,6-trinitrobenzenesulfonate.

Because the alkylation of unsymmetrical ketones[3] usually leads to mixtures of structurally isomeric alkylated products, methods have been developed for selective alkylation which involve either blocking one α-position[4] or adding an activating group at one α-position.[3,5] In some cases, conversion of the ketone to an enamine[6] or imine[7] derivative prior to alkylation has been reported to give predominantly one structural isomer of the product. An alternative solution to the problem of selectively alkylating an unsymmetrical ketone would be the conversion of the ketone (*e.g.*, **1**) to one of the structurally isomeric enolate anions (*e.g.*, **2**) with reaction conditions which do not permit subsequent interconversion of the isomeric enolate anions (*e.g.*, **2** ⇌ **3**).



2 **1** **3**

In a previous paper[8] we provided direct experimental evidence for the hypothesis that solutions of structurally isomeric enolate anions such as **2** and **3** are interconverted rapidly only when a proton-donating material, such as a protonic solvent or the un-ionized ketone **1**, is present in the solution. In particular, solutions of lithium enolate anions in 1,2-dimethoxyethane (DME) were found not to interconvert over periods of several hours at room temperature unless a substantial amount (10–100 mole %) of un-ionized ketone was present in the solution to serve as a proton donor. Evidence supporting this hypothesis is also derived from selective alkylation experiments in which solutions of particular enolate anions, apparently free of structural isomers, have been generated by reductions, with alkali metals in liquid ammonia, of α,β-unsaturated ketones,[9] of α-halo or α-acyloxy ketones,[10] or

---

[1] This research has been supported by Grant No. AF-AFOSR-573-64 from Directorate of Chemical Sciences, Air Force Office of ScientificResearch.

[2] National Science Foundation Predoctoral Fellow, 1963–1965.

[3] (a) J. M. Conia, *Record Chem. Prog.* (Kresge-Hooker Sci. Lib.), **24,** 43 (1963); (b) J. M. Conia, *Bull. soc. chim. France*, 1040 (1956); (c) J. M. Conia, *ibid.*, 1392 (1956); (d) J. M. Conia and P. Gosselin, *ibid.*, 836 (1961).

[4] (a) A. J. Birch and R. Robinson, *J. Chem. Soc.*, 501 (1944); (b) W. S. Johnson and H. Posvic, *J. Am. Chem. Soc.*, **69**, 1361 (1947); (c) R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives, and R. B. Kelly, *J. Chem. Soc.*, 1131 (1957); (d) R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, **27**, 1615, 1620 (1962); (e) S. Boatman, T. M. Harris, and C. R. Hauser, *J. Am. Chem. Soc.*, **87**, 82 (1965).

[5] (a) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. McLamore, *ibid.*, **74**, 4223 (1952); (b) Y. Mazur and F. Sondheimer, *ibid.*, **80**, 5220, 6296 (1958).

[6] (a) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *ibid.*, **85**, 207 (1963); (b) J. Szmuszkovicz in "Advances in Chemistry, Methods and Results," Vol. 4, R. A. Raphael, E. C. Taylor, and H. Wynberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, pp. 1–113.

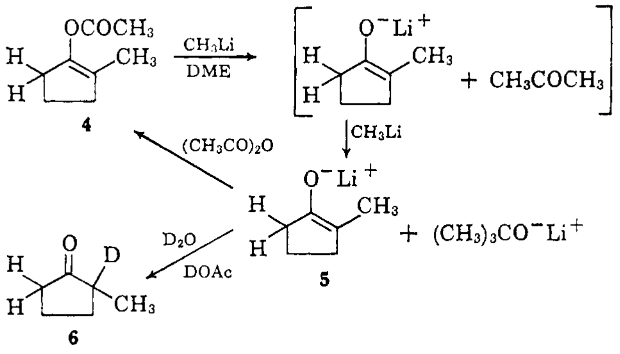
[7] G. Stork and S. R. Dowd, *J. Am. Chem. Soc.*, **85**, 2178 (1963).

[8] H. O. House and B. M. Trost, *J. Org. Chem.*, **30**, 1341 (1965).

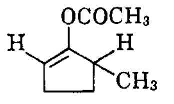
[9] G. Stork, P. Rosen, N. Goldman, R. V. Coombs, and J. Tsuji, *J. Am. Chem. Soc.*, **87**, 275 (1965).

[10] M. J. Weiss, *et al.*, *Tetrahedron*, **20**, 357 (1964).

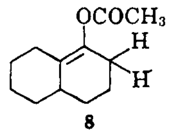
of α-chloromercuric ketones.[11,12] The reaction of α-bromo ketones with methyl Grignard reagents has also been reported to form an enolate which gives a single alkylated product.[13]



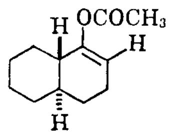
We examined the use of enol acetates (*e.g.*, **4**) as precursors for specific lithium enolate anions (*e.g.*, **5**) because earlier work[8,14] indicated that each of the possible structural and stereochemical enol acetate isomers could be readily prepared and the structure of each isomer could be established by simple physical measurements. In practice, addition of 1 equiv. of the enol acetate (*e.g.*, **4**) to a solution of methyllithium in 1,2-dimethoxyethane resulted in the immediate consumption of 2 equiv. of the organolithium reagent as indicated in the accompanying equations. By the use of a few milligrams of triphenylmethane (present in the organolithium solution as the red triphenylmethyllithium) as an indicator, the addition of the enol acetate could be performed as a titration, the addition being stopped when the solution was a pale pink color. In this way the absence of excess ketone (or other proton-donating materials) in the reaction solution could be ensured. The presence of a single enolate ion (*e.g.*, **5**) in the reaction solution was demonstrated[8,14d] by quenching the anion either in excess acetic anhydride to form a single enol acetate (*e.g.*, **4**) or in buffered deuterium oxide to form a monodeuterio ketone (*e.g.*, **6**). By use of this procedure we have been able to convert each of the cyclic enol acetates **7**–**10** to the corresponding lithium enolate anions **11**–**14**.[15] Interestingly, each of the stereoisomeric, acyclic enol acetates **15** or **16** could be converted to the corresponding lithium enolate **17** or **18** without loss of either structural or stereochemical integrity. In fact, solutions of each of the enolate anions **17** and **18** could be heated to 73° for 40 min. without detecting interconversion of the two anions. These results indicate that the activation energy for interconversion (*e.g.*, by rotation about the enolate C–C bond as in structure **19**) of the two lithium enolate anions must be substantial.[16] It is not clear how much of this activation energy is to be attributed to loss of the resonance stabilization in the free enolate anion (as in structure **19**)[17] rather than to the presence of a partially covalent lithium–oxygen bond which would enhance the double-bond character of the carbon–carbon bond in the lithium enolate. Our efforts to prepare stereoisomeric enolate anions with counterions other than lithium have, thus far, given equivocal results.



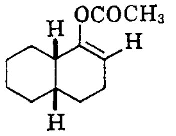
7



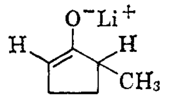
8



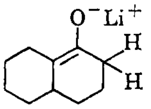
9



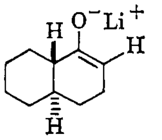
10



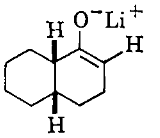
11



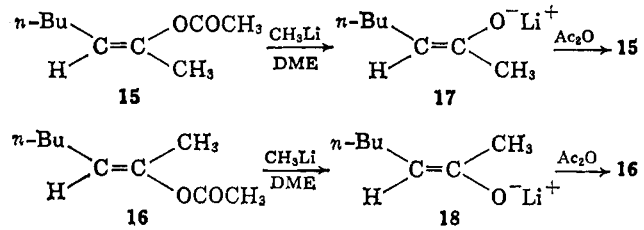
12

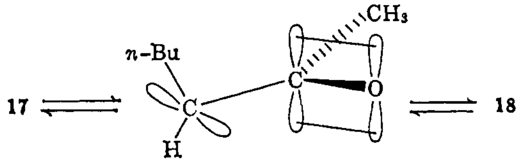


13



14





19

With a procedure for the conversion of an enol acetate to the corresponding lithium enolate anion in hand, we were prompted to consider the procedures for preparing a single enol acetate from an unsymmetrical ketone. Previous experiments have indicated that reaction of an unsymmetrical ketone with acetic anhy-

---

(11) D. Caine, *J. Org. Chem.*, **29**, 1868 (1964).

(12) To examine the question of whether α-chloromercuric ketones possess a C–Hg bond or an O–Hg bond, Mr. W. Larry Respess in our laboratories prepared a pure sample of α-chloromercuriacetone, m.p. 102–103°; A. N. Nesmeyanov, I. F. Lutsenko, and Z. M. Termanova [*Isv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 601 (1949)] reported m.p. 103–104°. The sample has infrared absorption (Nujol mull) at 1650 cm.$^{-1}$(C=O) with n.m.r. (solution in perdeuteriodimethylformamide) singlets at δ 2.80 (2H, $HgCH_2CO-$) and 2.17 (3H, CH_3CO-). In the fraction of the molecules containing the ^{199}Hg isotope, each of these n.m.r. peaks appears as doublet with $J_{^{199}Hg-H}$ values of 317 and 14 c.p.s., respectively. Consequently, we conclude that this derivative has a C–Hg bond.

(13) (a) R. E. Beyler, F. Hoffman, L. H. Sarett, and M. Tishler, *J. Org. Chem.*, **26**, 2426 (1961); (b) S. Binns, J. S. G. Cox, E. R. H. Jones, and B. G. Ketcheson, *J. Chem. Soc.*, 1161 (1964); E. R. H. Jones and D. A. Wilson, *ibid.*, 2933 (1965).

(14) (a) C. W. Marshall, T. H. Kritchevsky, S. Lieberman, and T. F. Gallagher, *J. Am. Chem. Soc.*, **70**, 1837 (1948); (b) A. H. Soloway, W. J. Considine, D. K. Fukushima, and T. F. Gallagher, *ibid.*, **76**, 2941 (1954); (c) H. O. House and H. W. Thompson, *J. Org. Chem.*, **26**, 3729 (1961); (d) H. O. House and V. Kramar, *ibid.*, **28**, 3362 (1963); (e) F. Bohlman, C. Arndt, and J. Starnick, *Tetrahedron Letters*, **No. 24**, 1605 (1963).

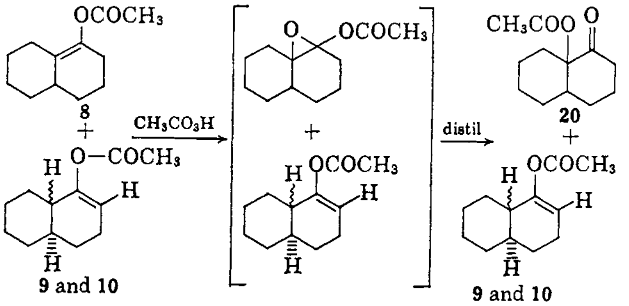
(15) The conversions **9** → **13** and **10** → **14** were described in our previous paper.[8]

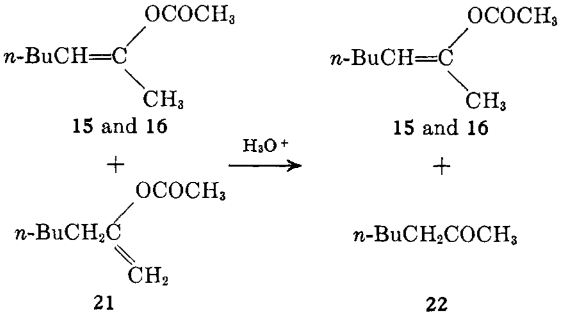
(16) We were unable to explore more vigorous reaction conditions in a meaningful way because attack of methyllithium or triphenylmethyllithium on the solvent destroyed the excess base when longer reaction times (and presumably higher temperatures) were employed. However, it would appear that the free energy of activation for this isomerization is in excess of 20 kcal./mole: see A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1961.

(17) (a) Previous arguments based on kinetic data have indicated a substantial barrier to the interconversion of stereoisomeric allyl carbanions: D. H. Hunter and D. J. Cram, *J. Am. Chem. Soc.*, **86**, 5478 (1964). (b) The products of free-radical substitution reactions indicate a substantial barrier to rotation also exists for the allyl free radical: C. Walling and W. Thaler, *ibid.*, **83**, 3877 (1961).

dride in the presence of p-toluenesulfonic acid[8,14] or perchloric acid[18] usually leads to an equilibrium mixture of enol acetates in which the more highly substituted isomer predominates. This is especially true when long reaction times and an excess of the acid catalyst are employed. Reaction of an unsymmetrical ketone with isopropenyl acetate in the presence of a catalytic amount of p-toluenesulfonic acid[14] frequently yields a mixture of enol acetates in which the less highly substituted isomer is the more abundant component. This result reflects the fact that acid-catalyzed equilibration of the enol acetates occurs relatively slowly under the conditions of the isopropenyl acetate procedure; the mixture obtained apparently approaches the composition to be expected from the kinetically controlled formation of enol acetates from the ketone.

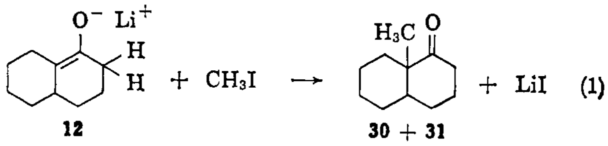
Although several standard physical methods[14] can be applied to the separation of enol acetate mixtures, these methods may become tedious on a preparative scale especially for the isolation of the pure less highly substituted enol acetate. We found that the more highly substituted enol acetate **8** could be selectively epoxidized[19] in the presence of the less highly substituted isomers **9** and **10** to yield a mixture from which the enol acetates **9** and **10** were readily separable by distillation. Alternatively, small amounts of the less highly substituted enol acetate **21** could be removed from the more highly substituted isomers **15** and **16** by partial hydrolysis with aqueous acid. Consequently, it appears that an appropriate choice from among the above procedures will, in general, permit the preparation of either structurally isomeric enol acetate from an unsymmetrical ketone.





Returning to our original objective, the selective alkylation of unsymmetrical ketones, we examined the reactions of each of the enolate ions **5**, **12**, and **13** with methylating agents as well as the reaction of a mixture of stereoisomeric anions **17** and **18** with n-butyl iodide and the reaction of the enolate mixture **23** and **24**[20] with methyl bromoacetate. The results, summarized in the accompanying equations, indicate that selective alkylations can be accomplished without concurrent isomerization of the starting enolate anion. In particular, the methylated products from anions **5**, **12**, and **13** were shown to be free of methylated products **27**, **28**, and **30**, respectively, demonstrating the lack of significant equilibration (*e.g.*, **12** $\rightleftharpoons$ **13**) prior to and during the alkylation reaction[21] (see Scheme I).

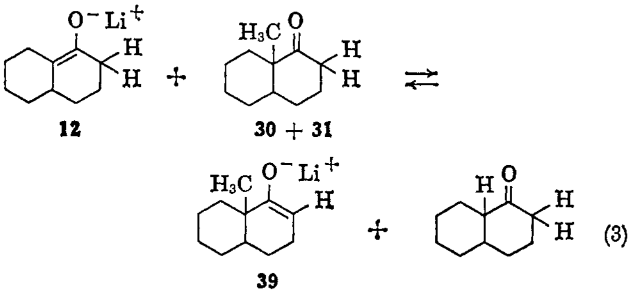
Although the previously cited data provide ample reason to expect no isomerization of enolate anions prior to alkylation, the observed lack of isomerization during the alkylation reaction is by no means inevitable. The accompanying eq. 1–7 illustrate the fact that, during alkylation of a particular enolate anion **12**, a proton-donating product **30** + **31** is formed which can enter into equilibria (eq. 3–5) forming two new enolate anions **13** + **14** and **39** and, subsequently, two new alkylated products **28** and **37**. The alkylation reactions 1 and 2 are relatively rapid having half-lives, under our reaction conditions, of about 1 min. and 20 min., respectively. Both our product studies (*i.e.*, no dialkylated product from the alkylation of **13** with methyl iodide) and earlier kinetic measurements[3,22]



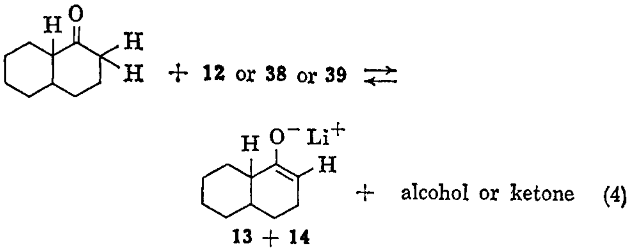
(1)

$$(CH_3)_3CO^-Li^+ + CH_3I \longrightarrow (CH_3)_3COCH_3 + LiI \quad (2)$$

38



(3)



(4)

---

[18] (a) D. H. R. Barton, R. M. Evans, J. C. Hamlet, P. G. Jones, and T. Walker, *J. Chem. Soc.*, 747 (1954); (b) R. Villoti, H. J. Ringold, and C. Djerassi, *J. Am. Chem. Soc.*, **82**, 5693 (1960); (c) M. P. Hartshorn and E. R. H. Jones, *J. Chem. Soc.*, 1312 (1962); (d) B. Berkoz, E. P. Chavez, and C. Djerassi, *ibid.*, 1323 (1962); (e) D. K. Banerjee, V. Paul, S. K. Balasubramanian, and P. S. Murphy, *Tetrahedron*, **20**, 2487 (1964).

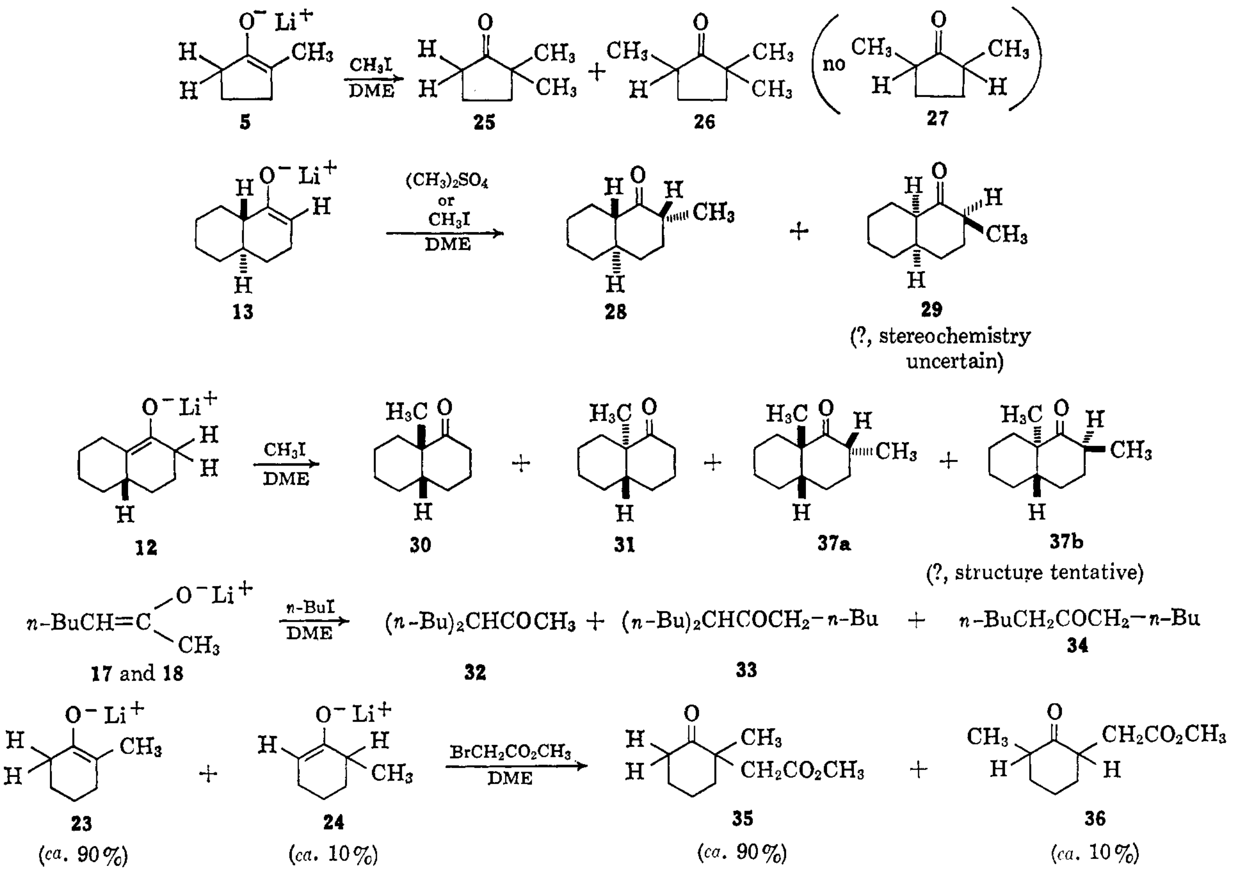
[19] This selectivity is to be expected from the facts that reaction of a peracid with an olefin is not seriously retarded by steric hindrance and is markedly accelerated by the presence of electron-donating substituents: D. Swern, *Chem. Rev.*, **45**, 1 (1949); D. Swern, *Org. Reactions*, **7**, 378 (1953).

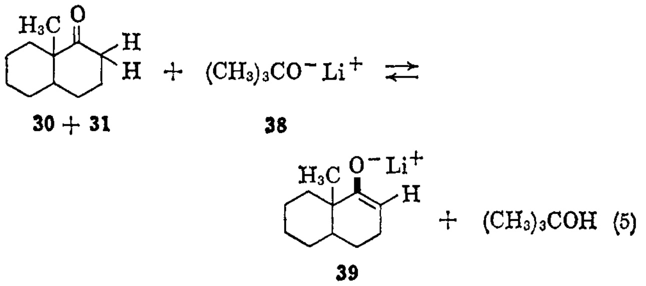
[20] As noted earlier,[11,14d] we have been unable to separate the mixture of enol acetates from 2-methylcyclohexanone by gas chromatography and were forced to determine the approximate composition of the enol acetate mixture from its n.m.r. spectrum. For this reason, a mixture of enolate anions **23** and **24** was generated; the composition of the product mixture corresponded to the enol acetate composition indicating the absence of equilibration among the enolate anions during alkylation.

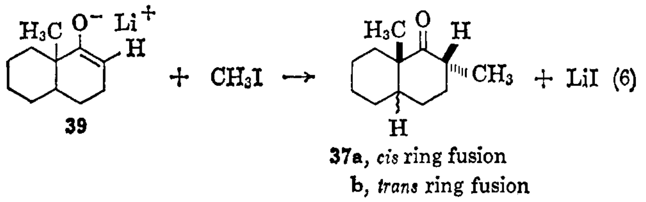
[21] The same degree of structural specificity has been observed in several unrelated alkylation reactions performed in our laboratory by this procedure.

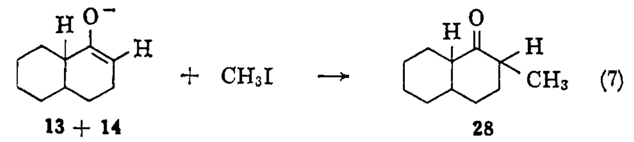
[22] H. Zook and W. L. Rellahan, *J. Am. Chem. Soc.*, **79**, 881 (1957).

SCHEME I









suggest that, at comparable concentrations, alkylation of the less highly substituted enolate anions **13** + **14** (eq. 7) and **39** (eq. 6) will be at least as rapid as reaction 1. Consequently, our failure to find alkylated product **28** in this reaction indicates that no appreciable concentration of enolate anions **13** or **14** was produced and, accordingly, that the rate of the forward reaction in equilibrium 3 and/or 4 must be slower than alkylation.

An approximate measure of the rate of reaction 4 was obtained by determining the rate of hydrogen–deuterium scrambling when a mixture of 1-decalone and 2,2,9-trideuterio-1-decalone was added to a solution of lithium *t*-butoxide in 1,2-dimethoxyethane. At comparable concentrations of reactants, reaction 1 is about four times as rapid as reaction 4. Consequently, it is primarily the slow rate of the ketone–enolate anion equilibration (eq. 3) which accounts for the failure to find any significant quantity of the wrong alkylated product, ketone **28**.

At relatively high enolate anion concentrations (0.5 *M* or greater), the dialkylation product **37** (eq. 6) becomes a significant by-product of the alkylation of the enolate anion **12** in agreement with the fact that the rate of reaction 4 (and, presumably, also reaction 5) is greater than the rate of consumption of the lithium *t*-butoxide (eq. 2). The presence of equimolar concentrations of the enolate anion (*e.g.*, **12**) and lithium *t*-butoxide (**38**) in our reaction mixtures is, of course, an undesirable but necessary consequence of the reaction used to form the enolate anion. In any event, this dialkylation side reaction (eq. 5 and 6) can be effectively minimized by use of short reaction times and solutions in which the concentration of enolate anion and *t*-butoxide anion are in the range 0.1–0.2 *M* as is illustrated in Table I.[23]

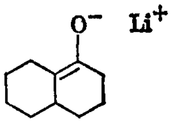
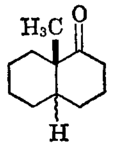
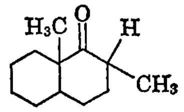
As part of our study of the alkylation of the 1-decalone enolate **12**, we examined the effect of the alkyl-

---

[23] This ability to decrease the proportion of dialkylation by lowering the initial enolate ion **12** (and *t*-butoxide anion **38**) concentration is to be expected if the reactions 3 and 4 are relatively slow since the rates of the initial alkylation reactions 1 and 2 are proportional to the first power of the concentrations of anions **12** and **38**, whereas the formation of the dialkylation precursor **39** is indirectly dependent on the square of the concentration of one or both of the anions **12** and **38**. Of course, this concentration effect also serves to repress the formation of the unwanted monoalkylated product **28** for the same reasons.

TABLE I

CONCENTRATION AND REACTION TIME DEPENDENCE IN THE ALKYLATION OF 1-DECALONE

Reactants, molar concn.			Products, % yield	
 **12**	CH_3I	Reaction time, min.	 **30** + **31**	 **37** + **1-decalone (1)**
0.155	0.47	5.0	86	7
0.145	0.46	10.0	54	39
0.467	1.40	10.0	38	59
0.37	1.84	*ca.* 0.5	51	15

ating agent reactivity of the proportions of *cis*- (**30**) and *trans*-alkylated (**31**) products (Table II). The proportion of the *cis* isomer **30** appeared to increase as the reactivity of the alkylating agent increased[24] and was particularly striking when the trimethyloxonium salt was used. These results may be interpreted in terms of the transition state for alkylation resembling the starting materials (*e.g.*, **40** in which steric factors favor the approach of the alkylating agent to give the *cis* product **30**) rather than the products (*e.g.*, **41** in which thermodynamic and stereoelectronic factors favor the *trans* product **31**).[25] If one accepts this idea, the prediction follows that increasing the reactivity of the alkylating agent would cause the transition state to resemble the reactants[26] even more closely and would enhance the proportion of the *cis* product **30**. Unfortunately, it does not appear practical to utilize the reverse strategy in which an alkylating agent of sufficiently low reactivity is employed that the *trans* ketone **31** (from **41**) will become the major product.

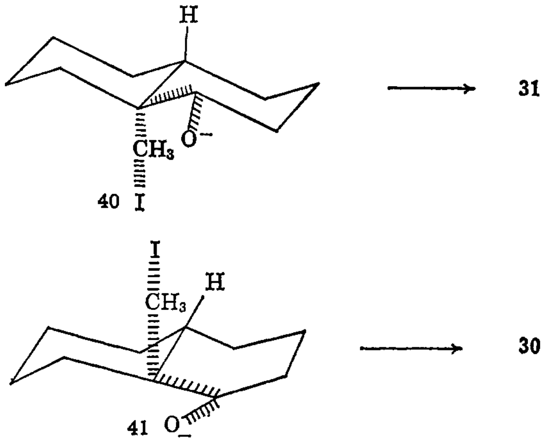


TABLE II

STEREOCHEMICAL OUTCOME OF THE ALKYLATION OF 1-DECALONE

Methylating agent	Approximate half-life for reaction, min.	Composition of 9-methyl-1-decalone *cis* (**30**), %	*trans* (**31**), %
CH_3OTs	30	*ca.* 87[a]	*ca.* 13[a]
CH_3I	1	83	17
$CH_3OSO_2OCH_3$	<0.5	86	14
$CH_3{-}^{+}O(CH_3)_2\ ArSO_3^{-}$	<0.5	>95	<5

[a] Because of the low percentage of reaction, these values are only approximate.

From the foregoing discussion of the relative rates of the various competing processes in the alkylation reaction mixtures, it will be apparent that use of a less reactive alkylating agent will retard the rate of consumption of the initial enolate and the lithium *t*-butoxide (*cf.* eq. 1 and 2) with the result that both dialkylation and equilibration of initial enolate anion prior to reaction (*cf.* eq. 3–7) can be expected to become a serious problem. We found that this difficulty began to become apparent in the reaction of the 2-heptanone enolate anions **17** and **18** with *n*-butyl iodide, an alkylating agent which would appear to be about 50–100 times less reactive than methyl iodide.[3] In this case, reaction conditions which produced 50–55% of the expected monoalkylated ketone **32** also yielded 12–14% of dialkylated product **33** and 6–10% of the structurally isomeric monoalkylated ketone **34**. For comparison, the alkylation of 2-heptanone was effected by treatment of the ketone with *n*-butyl iodide and potassium *t*-butoxide in *t*-butyl alcohol. The yields of the monoalkylated ketones **32** and **34** were 11 and 6%, respectively; other products included unchanged 2-heptanone, the dialkylated ketone **33**, and a large amount of less volatile material, believed to have resulted from an aldol condensation of 2-heptanone with itself.[8] This result, which differs from Conia's generalization[8] that ketones of the type RCH_2COCH_3 are alkylated very largely if not exclusively at the methylene position, leads us to conclude that our alkylation procedure is advantageous even for alkylation with relatively sluggish alkylating agents where complete structural specificity is not maintained.

A feature of incidental interest was noted in certain alkylation reactions with dimethyl sulfate. With solutions of either lithium *t*-butoxide (**38**) alone or equimolar mixtures of the alkoxide **38** and the 1-decalone enolate **12**, in 1,2-dimethoxyethane, reaction with dimethyl sulfate was very rapid (half-lives of ap-

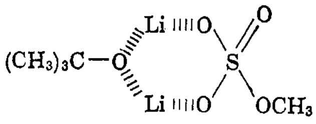
---

(24) J. M. Conia [*Bull. soc. chim. France* 533 (1950)] reported the relative reactivities of methyl iodide, methyl benzenesulfonate, and methyl sulfate to be 1, 4, and 60, respectively, for reaction with a solution prepared from sodium *t*-amylate, 2-methylcyclohexanone, and toluene. Similar studies with ethyl benzenesulfonate and ethyl *p*-toluenesulfonate indicated that the benzenesulfonate esters should be about twice as reactive as the *p*-toluenesulfonate esters suggesting that methyl *p*-toluenesulfonate would be more reactive than methyl iodide. However, it is clear that, for the reaction system we are studying, methyl iodide reacts more rapidly than methyl *p*-toluenesulfonate.

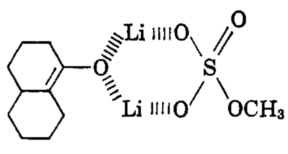
(25) For recent discussions of the stereochemistry of alkylation of cyclohexanone derivatives, see ref. 4a and (a) W. S. Johnson, D. S. Allen, Jr., R. R. Hindersinn, G. N. Sausen, and R. Pappo, *J. Am. Chem. Soc.*, **84**, 2181 (1962); (b) C. Djerassi, J. Osiecki, and E. J. Eisenbraun, *ibid.*, **83**, 4433 (1961); (c) F. J. McQuillin and P. L. Simpson, *J. Chem. Soc.*, 4726 (1963); (d) J. M. Conia and P. Briet, *Tetrahedron Letters*, **No. 39**, 2797 (1964).

(26) G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).

proximately 30 sec.) until one-half of the total base was consumed at which time the reaction rate dropped markedly. In reactions with the alkoxide, a precipitate separated from the reaction solution in less than 1 minute, whereas a significant precipitate was not apparent in the alkoxide–enolate mixture reactions until a reaction time of 20–30 min. had elapsed. These results suggest that the lithium methyl sulfate ($Li^+O^-SO_2OCH_3$) formed during alkylation complexes with the lithium *t*-butoxide or lithium enolate anion to form complexes such as structures **42** and **43** which are either insoluble or are much less nucleophilic than the original anions.



42



43

Experimental[27]

Preparation of Starting Materials.—The preparation of *trans*-1-decalone, 2-methylcyclopentanone, 2-methylcyclohexanone, and 2-heptanone and the preparation and characterization of the corresponding enol acetates have been described previously.[8,14c,14d] Two additional methods were used to obtain the enol acetates of 1-decalone. To a solution of 147 mg. (0.968 mmole) of *trans*-1-decalone (**1**) and 1.0 g. (9.8 mmoles) of acetic anhydride in 3 ml. of carbon tetrachloride was added 0.005 ml. of 70% aqueous perchloric acid.[18,28] The resulting mixture was stirred for 15 min. at room temperature and then diluted with ether, washed with aqueous sodium bicarbonate, dried, and concentrated. The residual liquid contained,[29] in order of elution, *trans*-1-decalone (**1**, 5%), the $\Delta^{1,9}$-enol acetate **8** (78%), the *trans*-$\Delta^{1,2}$-enol acetate **9** (13%), and the *cis*-$\Delta^{1,2}$-enol acetate **10** (4%). From a comparable reaction employing 0.895 mmole of 1-decalone, 9.8 mmoles of acetic anhydride, 0.005 ml. of 70% aqueous perchloric acid, and 3 ml. of carbon tetrachloride in which a reaction period of 24 hr. at room temperature was employed, the composition[29] of the enol acetate mixture was 98% of **8** and 2% of **9**. The calculated[30] yield of the enol acetate mixture was 78%, 5% of 1-decalone also being recovered.

A mixture of enol acetates (40% of **8**, 42% of **9**, and 18% of **10**),[29] b.p. 66–69° (0.2 mm.), was obtained in 82% yield from the reaction of 5.225 g. (34.4 mmoles) of *trans*-1-decalone with 6.948 g. (69.5 mmoles) of isopropenyl acetate containing a few milligrams of *p*-toluenesulfonic acid at 110° for 6 hr. as previously described.[14c,31] A solution of 2.25 g. (11.7 mmoles) of this enol acetate mixture in 250 ml. of petroleum ether (b.p. 30–60°) was stirred at room temperature for 48 hr. with a mixture of 2.5 g. of sodium acetate, 3.75 ml. of water, and 6.0 g. of an acetic acid solution containing 23.6 mmoles of peracetic acid.[32] The resulting reaction mixture was stirred with excess solid sodium bisulfite for 1 hr. and then the organic layer was separated, dried, and concentrated. The residual pale yellow liquid, which no longer contained[29] the enol acetate **8**, was distilled through a 30-cm. spinning-band column to separate 1.008 g. (75% recovery) of the $\Delta^{1,2}$-enol acetates (70% of **9** and 30% of **10**), b.p. 58–61° (0.2 mm.), and 1.221 g. of 9-acetoxy-1-decalone (**20**), b.p. 65–70° (0.2 mm.). The latter product **20** (presumably a mixture of *cis* and *trans* isomers) was identified with a previously described[14c] sample by comparison of infrared spectra.

The reaction of 28.0 g. (0.245 mole) of 2-heptanone, 50.5 g. (0.505 mole) of isopropenyl acetate, and 200 mg. of *p*-toluenesulfonic acid at reflux with continuous distillation of acetone yielded, after the previously described isolation,[14d] 35.2 g. (93%) of a mixture of 2-heptanone (6%), the *trans*-$\Delta^{2,3}$-enol acetate **15** (47%), the $\Delta^{1,2}$-enol acetate **21** (28%), and the *cis*-$\Delta^{2,3}$-enol acetate **16** (19%), b.p. 155–163°. A solution of 2.50 g. (16.4 mmoles) of this mixture in 30 ml. of carbon tetrachloride was added to a solution of 0.020 ml. of 70% aqueous perchloric acid in 5.0 g. of acetic anhydride. The resulting mixture was stirred for 6 hr. and then diluted with ether and washed with aqueous sodium bicarbonate. After the organic layer had been dried, concentrated, and distilled, the distillate (2.50 g., b.p. 145–170°, containing 21% of 2-heptanone, 59% of **15**, and 20% of **16**) was fractionally distilled through a 40-cm. spinning-band column to separate 1.95 g. (78% recovery) of a mixture, b.p. 160–165°, containing 2% of 2-heptanone, 73% of **15**, and 25% of **16**.

Ethereal solutions of methyllithium were prepared from lithium and either methyl bromide or methyl iodide in the usual way. The methyllithium solutions were standardized either by use of a double acid–base titration employing ethylene dibromide or by reaction with chlorodimethylphenylsilane and subsequent gas chromatographic analysis.[33] 1,2-Dimethoxyethane was purified by refluxing over sodium or potassium followed by distillation from lithium aluminum hydride. All organometallic and enolate anion reactions were carried out under a nitrogen atmosphere and either siphons, nitrogen-filled pipets, or nitrogen-filled syringes were used for all transfers. All alkylating agents except the trimethyloxonium salt were distilled immediately before use. Trimethyloxonium 2,4,6-trinitrobenzenesulfonate, m.p. 110–125° dec., resolidified and melted at 181–183° (lit.[34] 115–125° dec., then melts 181–183°), was prepared as previously described.[34]

Preparation of the Enolate Anions. A. From 2-Methylcyclopentanone.—After an ethereal solution containing 1.5 mmoles of methyllithium had been concentrated to dryness under reduced pressure, 1.5 ml. of 1,2-dimethoxyethane containing a few milligrams of triphenylmethane was added.[35] To the resulting red solution was added, dropwise and with stirring, 98 mg. (0.70 mole) of 1-acetoxy-2-methylcyclopentene (**4**) at which point the reaction solution retained a light red color. This solution was stirred for 0.75 hr. and then a 1.0-ml. aliquot was added to deuterium oxide containing sufficient acetic acid-d_1 that the final solution had a pH of 5. This solution was stirred for 5 min. and then partitioned between ether and aqueous sodium carbonate. After the organic layer had been dried and concentrated, the monodeuterated ketone **6** was collected[29] from the residual liquid (which contained[29] no enol acetate **4** or **7**) and found to contain 3% d_0 species, 96% d_1 species, and 1% d_2 species. The mass spectrum of the monodeuterated ketone **6** has abundant peaks at m/e 99, 84, 71, 70, 69, 56, 55, 43, 42, 41, 40, and 39; the corresponding peaks in the nondeuterated ketone are at m/e 98, 83, 70, 69, 55, 42, and 39. The infrared spectrum[36] of the monodeuterio ketone **6** differs from the spectrum of 2-methylcyclopentanone in having a band at 2110 cm.$^{-1}$ (C–D) and in several bands in the fingerprint region.

A comparable solution, prepared from 1.0 mmole of methyllithium and 0.498 mmole of the enol acetate **4** in 1.0 ml. of 1,2-dimethoxyethane, was stirred for 30 min. at room temperature

---

[27] All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin Elmer, Model 237, infrared recording spectrophotometer fitted with a grating. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14. The 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.

[28] The use of larger quantities of perchloric acid led to the formation of high molecular weight by-products.

[29] A gas chromatography column packed with Carbowax 20M suspended on Chromosorb P was employed.

[30] A weighed quantity of acenaphthalene was added to the crude product and the yield was determined by gas chromatography.[29]

[31] No reaction was observed when the *p*-toluenesulfonic acid was omitted.

[32] The use of less peracetic acid for a shorter reaction time resulted in incomplete oxidation of the enol acetate **8**.

[33] (a) H. Gilman and F. K. Cartledge, *J. Organometal. Chem.*, **2**, 447 (1964); H. O. House and W. L. Respess, *ibid.*, in press.

[34] D. J. Pettit and G. K. Helmkamp, *J. Org. Chem.*, **29**, 2702 (1964).

[35] We found it impractical to prepare a stock solution of methyllithium in 1,2-dimethoxyethane because this solvent is attacked by the organolithium reagent at a significant rate. Consequently, solutions of methyllithium in 1,2-dimethoxyethane were always prepared immediately before use. The removal of ether from the ethereal methyllithium solution was necessary because several of the lithium enolates were found to be soluble in 1,2-dimethoxyethane but insoluble in mixtures of ether and 1,2-dimethoxyethane.

[36] Determined as a solution in carbon tetrachloride.

and then poured into 2.0 g. (13.2 mmoles) of acetic anhydride. The resulting mixture was stirred for 30 min. and then diluted with pentane and aqueous sodium carbonate. The organic layer was separated, combined with a pentane extract of the aqueous phase, and then dried, concentrated, and mixed with 44.8 mg. of an internal standard.[37] The crude product contained[38] the enol acetate **4** in which none of the isomeric ester **7** was detected; the calculated yield of **4** was 86%. The product from a corresponding experiment was identified with an authentic sample[14d] of the enol acetate **4** by comparison of retention times and infrared spectra.

Similarly, an enolate solution prepared from 2.0 mmoles of methyllithium and 127.7 mg. (0.911 mmole) of the enol acetate **7** in 2.0 ml. of 1,2-dimethoxyethane was stirred at 25° for 1 hr. and then quenched in 3.0 g. (29.5 mmoles) of acetic anhydride. The crude enol acetate, recovered as in the previous case, contained[38] the enol acetate **7**, but none of the isomer **4** was observed. The calculated[37] yield of the ester **7** was 86%.

B. **From 1-Decalone.**—A solution of the enolate anion **13**, prepared from 0.55 mmole of methyllithium and 33.7 mg. (0.174 mmole) of the *trans*-$\Delta^{1,2}$-enol acetate **9** in 1.0 ml. of 1,2-dimethoxyethane, was stirred for 1 hr. at 25° and then quenched in excess acetic anhydride and processed as in previous cases. The crude product contained[29] the enol acetate **9** (calculated yield[30] was quantitative), but neither of the enol acetates **8** or **10** were detected.

Similarly, the enolate solution obtained from 1.0 mmole of methyllithium and 89.9 mg. (0.464 mmole) of the $\Delta^{1,9}$-enol acetate **8** in 1.0 ml. of 1,2-dimethoxyethane was stirred for 1 hr. and then added to 3.0 g. (29.5 mmoles) of acetic anhydride. The crude product contained[29] the enol acetate **8** but neither of the isomers **9** or **10** was detected.

C. **From 2-Heptanone.**—A solution of the enolate anion **18**, prepared from 1.0 mmole of methyllithium and 30.0 mg. (0.192 mmole) of the enol acetate **16** in 1.0 ml. of 1,2-dimethoxyethane was heated to 73° for 45 min. at which time the solution no longer retained the red color of the triphenylmethyl anion. After the reaction mixture had been poured into acetic anhydride and the crude product had been separated in the usual way, the crude product contained[29] the *cis*-enol acetate **16** (calculated[39] yield 76%), but none of the isomeric enol acetate **15** was detected. A collected sample of the product **16** was identified with an authentic sample[8,14d] by comparison of retention times and infrared spectra.

Similarly a solution of the enolate anion **17**, from 1.0 mmole of methyllithium and 43.0 mg. (0.276 mmole) of the enol acetate **15**, in 1.0 ml. of 1,2-dimethoxyethane was heated to 73° for 40 min. and then subjected to the usual quenching and isolation procedure. The crude product contained[29] the *trans*-enol acetate **15** (calculated[39] yield 99%), but the stereoisomer **16** was not detected.

Preparation of Alkylated Products. A. The Polymethylcyclopentanones.—Following previously described procedures,[40] a solution of 2.00 moles of sodium *t*-amylate in 824 ml. of benzene was added to a solution of 84 g. (1.0 mole) of cyclopentanone and 277 g. (2.20 moles) of dimethyl sulfate in 2.0 l. of ether. The crude product, 52.06 g. of colorless liquid, b.p. 120–145°, was stirred with excess aqueous sodium bisulfite to remove the cyclopentanone and 2-methylcyclopentanone and then treated with 57 g. (0.77 mole) of ethyl formate and 2.70 moles of sodium methoxide in 375 ml. of benzene. The crude 2-formyl-5,5-dimethylcyclopentanone was separated and cleave with 5% aqueous potassium hydroxide to yield 17.59 g. of pure[29] **2,2-dimethylcyclopentanone (25)**, b.p. 142–144°, $n^{25}\mathrm{D}$ 1.4317 (lit.[40] b.p. 143°, $n^{20}\mathrm{D}$ 1.4332), $\nu_{\max}$[36] 1740 (C=O) and 1355 and 1375 cm.$^{-1}$ [$C(CH_3)_2$]. The product has an n.m.r.[36] singlet at δ 1.02 (6H, CH_3C) with a multiplet in the region 1.6–2.4 (6H, aliphatic CH_2), and abundant peaks in the mass spectrum at *m/e* 112 (molecular ion), 97, 79, 69, 56, 41, and 39.

The benzene solution remaining after separation of the formyl derivative was concentrated and the residual yellow oil (19.2 g.) was heated on a steam bath with 20 g. of semicarbazide hydrochloride and 25 g. of sodium acetate in aqueous ethanol for 15 min. The resulting mixture was extracted with ether, and the extract was concentrated. Successive recrystallization of the residue from water and from aqueous ethanol afforded 10.0 g. of the crude semicarbazide of 2,2,5-trimethylcyclopentanone, m.p. 131–135°. A 3.38-g. portion of this derivative was heated under reflux with 26 g. of oxalic acid in 124 ml. of water for 3 hr. and then extracted with ether. The ethereal extract was washed successively with 5% aqueous sodium hydroxide and aqueous sodium chloride and then concentrated and distilled to separate 937 mg. of a colorless liquid, b.p. 149° (lit.[40] b.p. 151°), containing[29] *ca.* 90% of **2,2,5-trimethylcyclopentanone (26)**. A collected[29] sample of the pure ketone **26**, $n^{24}\mathrm{D}$ 1.4275, has infrared absorption[36] at 1735 (C=O) and at 1360 and 1380 cm.$^{-1}$ [$C(CH_3)_2$] with n.m.r.[36] singlets at δ 0.97 and 1.04 (6H, CCH_3), a doublet (J = 6.5 c.p.s.) at 1.07 (3H, methyl group of CH_3CH), and a multiplet in the region 1.4–2.4 (5H, aliphatic CH). The mass spectrum of this product has abundant peaks at *m/e* 126 (molecular ion), 111, 83, 69, 56, 41, and 39.

A mixture of 980 mg. (10 mmoles) of 2-methylcyclopentanone and 4.02 g. (54.3 mmoles) of ethyl formate was added, dropwise and with stirring, to a slurry of 5.95 g. (52.2 mmoles) of sodium methoxide in 62 ml. of benzene. The resulting slurry was stirred overnight and then mixed with 100 g. of ice. After the benzene layer had been separated, the aqueous phase was washed with benzene, cooled, acidified with hydrochloric acid, and extracted with ether. Concentration of the ethereal solution left 1.85 g. of crude 2-formyl-5-methylcyclopentanone as a yellow oil which was taken up in 70 ml. of methanol containing 2 ml. of 10% aqueous hydrochloric acid and hydrogenated at 25° and atmospheric pressure over 1.25 g. of a 5% palladium-on-carbon catalyst. The hydrogen uptake (370 ml. or 14.9 mmoles) ceased after 2 days, the first half of the hydrogen uptake being relatively rapid. The mixture was filtered, concentrated, and taken up in ether. The ethereal solution was washed successively with 5% aqueous potassium hydroxide and water and then dried and concentrated. Distillation of the residue afforded 577 mg. (51.5%) of **2,5-dimethylcyclopentanone (27)** as a colorless liquid, b.p. 149–153°, $n^{25}\mathrm{D}$ 1.4292 (lit.[40] b.p. 149–149.5°, $n^{20}\mathrm{D}$ 1.4310). The product **27**, a mixture of *cis* and *trans* isomers was only partially resolved on our gas chromatograph.[29] This mixture has infrared absorption[36] at 1740 cm.$^{-1}$ (C=O) with abundant peaks in the mass spectrum at *m/e* 112 (molecular ion), 97, 69, 55, 42, 41, and 39. The n.m.r. spectrum[36] of the mixture has a broad multiplet in the region δ 1.2–2.4 (6H, aliphatic C-H) as well as a multiplet in the region 0.9–1.2 (6H, CH_3). The latter multiplet appears to consist of a doublet (J = 6 c.p.s.) at δ 1.07 and a less intense doublet (J = 6.5 c.p.s.) at 1.02.

B. **Preparation of 2-Methyl-1-decalone.**—A mixture of 1.52 g. (10.0 mmoles) of *trans*-1-decalone and 4.02 g. (54.3 mmoles) of ethyl formate was added, dropwise and with stirring at 25°, to a suspension of 5.95 g. (50.5 mmoles) of sodium methoxide in 62 ml. of benzene. The resulting slurry was stirred for 15 hr. and then mixed with ice. The resulting aqueous phase was separated, washed with benzene, acidified with hydrochloric acid at 0°, and then extracted with ether. After the ethereal extract had been dried and concentrated, the remaining crude 2-formyl-1-decalone, a yellow liquid, was taken up in 70 ml. of methanol containing 2 ml. of 10% aqueous hydrochloric acid and hydrogenated at 25° and atmospheric pressure over 1.25 g. of a 5% palladium-on-carbon catalyst. After the hydrogen uptake (465 ml., 19.0 mmoles) ceased, the mixture was filtered, concentrated, and taken up in ether. The ethereal extract was washed with aqueous sodium carbonate, dried, and concentrated. Distillation of the residual yellow oil (1.173 g.) separated 1.165 g. (70%) of **2-methyl-1-decalone (28)**, b.p. 93–95° (2 mm.), $n^{16}\mathrm{D}$ 1.4832 [lit. b.p. 96–99° (4 mm.),[41a] $n^{17.7}\mathrm{D}$ 1.4812[41b]]. This product is an equilibrium mixture of epimers exhibiting two peaks on gas chromatography.[29] The larger peak (94% of area, first eluted) is believed to be the most stable epimer **28** with a *trans* ring fusion and an equatorial methyl group, while the peak eluted second (6% of area) is tentatively assigned the configuration **29** with an equatorial methyl group and a *cis* ring fusion. The material has infrared absorption[36] at 1715 cm.$^{-1}$ (C=O) but lacks absorption attributable to a $-CH_2CO-$ function at 1400–1420 cm.$^{-1}$. The n.m.r. spectrum[36] has a doublet (J = 6 c.p.s.) at δ 0.93 (3H, methyl group of CH_3CH) as well as

---

(37) *m*-Diisopropylbenzene was employed as an internal standard for this experiment.

(38) A gas chromatography column packed with silicone fluid, no. 710, suspended on Chromosorb P was employed.

(39) Anisole was employed as an internal standard for this experiment.

(40) (a) J. M. Conia, *Bull. soc. chim. France*, 537 (1950); (b) J. M. Conia, *ibid.*, 1064 (1957); (c) M. Muhlstadt, *Chem. Ber.*, **93**, 2638 (1960).

(41) (a) W. J. Bailey and M. Madoff, *J. Am. Chem. Soc.*, **76**, 2707 (1954); (b) J. W. Cook and C. A. Lawrence, *J. Chem. Soc.*, 817 (1937).

TABLE III

METHYLATION OF THE ENOLATE ANION **5** FROM 2-METHYLCYCLOPENTANONE

Enol acetate **4**, mg. (mmoles)	1,2-Dimethoxyethane, ml.	Methyl iodide, mg. (mmoles)	Reaction temp., °C.	Reaction time, min.	Composition of methylated cyclopentanone mixture, % 2-Methyl	2,2-Dimethyl	2,2,5-Trimethyl	2,2,5,5-Tetramethyl
113.5 (0.81)	2.0	116.1 (0.81)	0	<0.5[a]	55	45	..	..
96.7 (0.69)	2.0	336.6 (2.40)	0	<0.5[a]	..	70	30	..
148.4 (1.06)	1.6	565.1 (3.95)	−5	2.0[b]	3	53	28	16
163.2 (1.17)	2.0	1303.1 (9.12)	25	<0.5[b]	..	10	30	60
141.8 (1.01)	2.2	6850 (48.2)	25	5.0[a,c]	..	31	69	..
123.7 (0.88)	2.0	8900 (62.6)	25	120[a]	..	..	48	52
152.0 (1.08)	2.0	283.5[d] (2.25)	25	2.0[b,d]	17	63	16	4

[a] The enolate anion solution was added to the alkylating agent. [b] The alkylating agent was added to the enolate anion solution. [c] The calculated material balance[37] in this case was 64%. [d] Dimethyl sulfate was the alkylating agent for this experiment. The calculated[37] material balance was 99%.

complex absorption in the region 1.0–2.5 (15H, aliphatic CH). The mass spectrum has abundant peaks at *m/e* 166 (molecular ion), 124, 109, 81, 67, 55, 41, and 39.

Alkylation of 2-Methylcyclopentanone.—As described previously and summarized in Table III, the enol acetate **4** was added to a solution of methyllithium in 1,2-dimethoxyethane until the red color of the indicator (triphenylmethyllithium) was just discharged. The resulting solution of the enolate anion **5** was mixed with methyl iodide (or dimethyl sulfate); after the mixture had been stirred for the specified time, it was poured into dilute, aqueous hydrochloric acid and extracted with ether. The ethereal solution was washed with aqueous sodium carbonate, dried, concentrated, and analyzed by gas chromatography.[29,38] In certain cases, a weighed amount of an internal standard[37] was added prior to analysis to permit calculation of yields. Samples of the alkylated products **25** and **26** as well as 2-methylcyclopentanone were collected[38] from certain of the reactions and identified with previously described samples by comparison of retention times, infrared, and mass spectra. The product, 2,2,5,5-tetramethylcyclopentanone (lit.[40a] b.p. 154–155°, $n^{20}D$ 1.4280), was formed in certain of the alkylation reactions. A collected[38] sample of this product has infrared absorption[36] at 1780 (weak) and 1740 (strong) cm.$^{-1}$ (C=O in a 5-membered ring; the doublet appears to arise from Fermi resonance with the overtone of a peak at 880 cm.$^{-1}$) with abundant peaks in its mass spectrum at *m/e* 140 (molecular ion), 72, 69, 57, 56, 41, and 39. The sample has two n.m.r.[36] singlets at δ 1.73 (4H, CH_2) and 1.02 (12H, CH_3). To obtain the analytical data summarized in Table III, calibration curves were prepared from known mixtures of authentic samples. The retention times of the products on our silicone oil column[38] follow: 2-methylcyclopentanone, 6.2 min.; 2,2-dimethylcyclopentanone (**25**), 7.7 min.; 2,2,5-trimethylcyclopentanone (**26**), 8.7 min.; 2,2,5,5-tetramethylcyclopentanone, 11.4 min.; 2,5-dimethylcyclopentanone (**27**, both isomers), 11.8 min. The corresponding values on our Carbowax column[29] follow: 2,2,5,5-tetramethylcyclopentanone, 31.2 min.; 2,2,5-trimethylcyclopentanone (**26**), 36.6 min.; 2,2-dimethylcyclopentanone (**25**), 39.2 min.; 2-methylcyclopentanone, 43.2 min.; and 2,5-dimethylcyclopentanone (**27**), 48.0 min. In no case was 2,5-dimethylcyclopentanone (**27**) detected in the product mixtures.

Alkylation of 1-Decalone. A. At Position 2.—To a solution of the enolate anions **13** and **14**, prepared from 1.50 mmoles of methyllithium and 149.1 mg. (0.777 mmole) of the mixture of stereoisomeric $\Delta^{1,2}$-enol acetates **9** and **10** in 2.0 ml. of 1,2-dimethoxyethane, was added in one portion with stirring 307.7 mg. (2.16 mmoles) of methyl iodide. The reaction was immediately (reaction time <30 sec.) quenched by the addition of 5 ml. of dilute, aqueous hydrochloric acid, and the resulting mixture was extracted with ether. After the resulting mixture had been washed with aqueous sodium carbonate, mixed with a known amount of internal standard,[39] dried, and concentrated, the residual oil contained[29] 98% of the more stable 2-methyl-1-decalone **28** and 2% of the less stable epimer believed to be **29**. The calculated yield was 93% of **28** and 2% of **29**.

In a second experiment the enolate anion solution from 1.90 mmoles of methyllithium and 189.4 mg. (0.976 mmole) of the enol acetates **9** and **10** in 2.0 ml. of 1,2-dimethoxyethane was treated with 330 mg. (2.62 mmoles) of dimethyl sulfate after which the reaction and isolation procedure described above was followed. The crude product contained[29] 91% of **28**, 2% of **29**, and 7% of a dialkylated product believed to be 2,2-dimethyl-*trans*-1-decalone; the calculated yields were 84% of **28**, 2% of **29**, and 6% of the dialkylated product. The major alkylation product was identified with the previously described sample of 2-methyl-1-decalone **28** by comparison of retention times and infrared and mass spectra. A collected[29] sample of the dialkylated product, thought to be 2,2-dimethyl-*trans*-1-decalone, has infrared absorption[36] at 1710 (C=O) and 1385 and 1365 [$>C(CH_3)_2$] but lacks absorption in the region 1400–1420 (—CH_2CO—) cm.$^{-1}$. The mass spectrum of the product has abundant peaks at *m/e* 180 (molecular ion), 109, 82, 67, 55, 41, and 39. Neither of the 9-methyl-1-decalones **30** or **31** was detected in these reaction mixtures. The retention times of the various decalone derivatives on our gas chromatography column[29] follow: 2,2-dimethyl-1-decalone, 24.1 min.; 2-methyl-1-decalone (**28**), 27.0 min.; 2-methyl-1-decalone (**29**), 29.3 min.; *trans*-1-decalone, 38.2 min.; 2,9-dimethyl-*cis*-1-decalone (**37a**), 38.2 min. (not resolved from *trans*-1-decalone); 9-methyl-*cis*-1-decalone (**30**), 42.5 min.; a dialkylation product believed to be 2,9-dimethyl-*trans*-1-decalone (**37b**), 46.3 min.; and 9-methyl-*trans*-1-decalone (**31**), 50.3 min.

B. At Position 9.—Solutions of the enolate anion **12** were prepared from the $\Delta^{1,9}$-enol acetate **8** employing the quantities of reactants listed in Table IV. The resulting solutions were mixed with the methylating agents listed and the crude products were separated by adding dilute, aqueous hydrochloric acid to the reaction mixture and subsequent extraction with ether. The ethereal extracts were washed with aqueous sodium carbonate, dried, concentrated, and analyzed.[29] In certain reactions an internal standard[39] was added to permit yield calculations. A calibration curve for 1-decalone and its monomethylated derivatives was prepared from known amounts of authentic samples. The gas chromatographic retention times[29] for the various decalone derivatives are given in the previous experiment. Collected[29] samples of *trans*-1-decalone (**1**) and the *cis*- (**30**) and *trans*-9-methyl (**31**) derivatives were identified with authentic samples[42] by comparison of retention times and infrared and mass spectra. In addition, reaction of 200 mg. of one of the alkylation product mixtures (containing[29] 79% of the *cis* isomer **30** and 21% of the *trans* isomer **31**) with excess hydroxylamine in aqueous ethanol yielded, after purification, 145.1 mg. of the oxime of 9-methyl-*cis*-1-decalone as colorless plates from aqueous methanol, m.p. 108–110° (lit.[4b] 109–110°). The n.m.r. spectrum[36] of the *cis* isomer **30** has broad absorption in the region δ 1.2–2.5 (aliphatic CH) with a singlet at 1.18 (CH_3); the *trans* isomer **31** has broad absorption[36] in the region δ 1.2–2.5 (aliphatic CH) with a singlet at 1.08 (CH_3). The fact that the n.m.r. peak for the axial methyl group of the *trans* isomer **31** is at 0.10 p.p.m. (6 c.p.s.) higher field that the methyl group of the *cis* isomer **30** was confirmed by measuring the spectrum of a mixture of the two isomers.[43] The ratio of *cis* isomer **30** to *trans* isomer **31** was measured for methyl iodide in five separate reactions in which the amount of dialkylation was small; the average value of this ratio for methyl iodide was *cis/trans* = 5.0 ± 0.2. Similarly, for eight different reactions with dimethyl sulfate, the average value was *cis/trans* = 6.2 ± 0.2. Because of the

---

(42) (a) W. S. Johnson, S. L. Gray, J. K. Crandall, and D. M. Bailey, *J. Am. Chem. Soc.*, **86**, 1966 (1964). (b) We are indebted to Professor W. S. Johnson who supplied authentic samples of the *cis*- and *trans*-9-methyl ketones **30** and **31**.

TABLE IV

METHYLATION OF THE ENOLATE ANION 12 FROM 1-DECALONE

Enol acetate **8**, mg. (mmoles)	1,2-Dimethoxyethane, ml.	Methylating agent, mg. (mmoles)	Reaction temp., °C.	Reaction time, min.	Composition of product mixture, %[a] 1 + **37a**	**30**	**31**	**37b**	Yield %[b]
301 (1.55)	10.0	CH_3I, 635 (4.46)	28	5.0	8	77	15	..	93
142 (0.73)	5.0	CH_3I 330 (2.32)	25	10.0	32	44	14	10	93
451 (2.34)	5.0	CH_3I, 996 (7.02)	25	10.0	47	23	16	14	97
158 (0.82)	1.0	CH_3I, 228 (1.61)	25	<0.5	52	40	8	..	97
1447 (7.46)	20.0	CH_3I, 5267 (36.8)	0	*ca.* 0.5	14	66	13	7	69[c]
147 (0.76)	1.0	CH_3OTs, 158 (0.85)	25	2.0	64	31	5	..	96
156 (0.80)	1.0	CH_3OTs, 588 (3.15)	25	<0.5	78	19	3	..	98
301 (1.55)	10.0	$(CH_3)_2SO_4$, 571 (4.53)	28	5.0	60	35	5	..	96
124 (0.64)	1.0	$(CH_3)_2SO_4$, 157 (1.24)	25	5.0	45	43	12	..	..
211 (1.08)	2.0	$(CH_3)_2SO_4$, 545 (4.33)	25	<0.5	51	42	7	..	91
170 (0.88)	1.1	$(CH_3)_2SO_4$, 229 (1.82)	25	30	38	49	10	3	94
208 (1.07)	7.0	$(CH_3)_3O^+$,[d] 1165 (3.30)	25	<0.5	3	97	..	..	68[e]

[a] These compositions were determined by gas chromatography.[29] Since our column did not resolve 1-decalone (**1**) and 2,9-dimethyl-*cis*-1-decalone (**37a**), the combined percentage of these two substances is listed. [b] The total calculated yields of products including 1-decalone. These values were obtained from gas chromatograms in which anisole was employed as an internal standard unless otherwise noted. [c] This yield was determined by the isolation of 866 mg. of product, b.p. 65-67° (0.35 mm.), which has the composition indicated. [d] In this experiment the solution of the enolate anion was added to a slurry of trimethyloxonium 2,4,6-trinitrobenzenesulfonate in 1,2-dimethoxyethane. [e] In addition to the products listed approximately 10% of other unidentified materials were present. The possibility that one of these unidentified products is the O-methyl derivative is being investigated.

low yields of alkylated products, a reliable value was not obtained for methyl *p*-toluenesulfonate; the value obtained was *cis*/*trans* ~ 7. Although a reliable value was also not obtained for alkylation with the trimethyloxonium salt, it is clear that the ratio, *cis*/*trans*, is greater than 20.

In order to obtain samples of the dialkylated products, a mixture of 295 mg. of the crude product from an alkylation experiment (third entry in Table IV) with 0.55 g. (7.4 mmoles) of ethyl formate was added to a suspension of 1.00 g. (18.5 mmoles) of sodium methoxide in 2.0 ml. of benzene. After this mixture had been stirred for 15 hr. at 25°, it was diluted with ice-water. The benzene layer was separated, combined with the benzene extract of the aqueous phase, dried, and concentrated. The residual liquid, which contained[29] one major component (**37a**) and two minor constituents, was dissolved in 10 ml. of *t*-butyl alcohol containing 50 mg. of potassium *t*-butoxide, and the resulting solution was stirred for 2 hr. at room temperature to epimerize any unstable stereoisomers present. After this solution had been diluted with water and extracted with ether, the organic extract was dried and concentrated. The residual liquid contained[29] the *cis*-2,9-dimethyl ketone **37a** (79%) and a component believed to be the *trans* isomer **37b** (21%). A collected[29] sample of the *cis* isomer **37a**[42a] has infrared absorption[36] at 1710 cm.$^{-1}$ (C=O) with a molecular ion peak in the mass spectrum at *m/e* 180 as well as abundant fragment peaks at 125, 109, 95, 81, 68, 67, 55, 41, and 39. A 20-mg. sample of the ketone **37a** was treated with 75 mg. of hydroxylamine hydrochloride in a refluxing mixture of 0.25 ml. of ethanol and 0.25 ml. of pyridine for 2.5 hr. The crude product was recrystallized from an ether-petroleum ether (b.p. 30-60°) mixture to separate 10 mg. of the **oxime of the *cis* ketone 37a** as white needles, m.p. 173-175° (lit.[42a] m.p. 175-176°). A collected[29] sample of the second product, believed to be the *trans* ketone **37b**,[42a] has infrared absorption[36] at 1710 cm.$^{-1}$ (C=O) with a molecular ion peak in the mass spectrum at *m/e* 180 as well as abundant fragment peaks at 95, 82, 68, 67, 55, 41, and 39. The mass spectrum also has low intensity peaks at *m/e* 194 and 178 attributable to contaminants in this sample. A collected sample[29] of this same gas chromatographic peak from a reaction (fifth entry, Table IV) where less dialkylation was observed has a very similar mass spectrum but lacks peaks at *m/e* 194 and 178. The peak at *m/e* 194 is presumably attributable to one of the stereoisomeric 2,2,9-trimethyl-1-decalones as a contaminant; the nature of the contaminant responsible for the peak at *m/e* 178 is unknown.

C. Rates of Reaction.—A 1,2-dimethoxyethane solution of the enolate anion **12** and lithium *t*-butoxide was prepared from the enol acetate **8** in the usual way. Aliquots (10.00 ml.) were held at 28.0° under a nitrogen atmosphere and the alkylating agents listed in Table V were added in one portion to each reaction vessel. Aliquots (1.00 ml.) of each reaction mixture were removed after the time periods indicated, quenched in 5.00 ml. of 0.101 *M* aqueous hydrochloric acid, and titrated to a phenolphthalein end point with standard sodium hydroxide. Duplicate runs were made for each alkylating agent. The average percentage of total base (enolate anion and *t*-butoxide anion) consumed are summarized in Table V. The reaction with dimethyl sulfate became turbid after 20-30 min.

To learn what fractions of the above reactions were attributable to reaction of the alkoxide with the methylating agents, a solution of lithium *t*-butoxide was prepared by the addition of *t*-butyl alcohol to a solution of methyllithium in 1,2-dimethoxyethane until the color of the triphenylmethyllithium indicator was just discharged. Aliquots of the solution were held at 28.0° and the methylating agents indicated in Table V were added. Aliquots (1.00 or 2.00 ml.) of the reaction mixtures were removed after the specified times, quenched in 5.0 ml. of water, and titrated to a phenolphthalein end point with standard hydrochloric acid. The percentages of base consumed are indicated in Table V. The reaction with methyl *p*-toluenesulfonate became turbid after approximately 30 min.; in both reactions with dimethyl sulfate, a precipitate formed in less than 30 sec. A mixture of 1.69 mmoles of lithium *t*-butoxide and 5.12 mmoles of dimethyl sulfate in 10 ml. of 1,2-dimethoxyethane was allowed to stand for 0.5 min. and then centrifuged for 15 min. to separate the precipitate from the supernatant liquid. The supernatant liquid was neutral. The precipitate was washed with 1,2-dimethoxyethane; the n.m.r. spectrum of a solution of the strongly basic residue in deuterium oxide exhibited single peaks at δ 3.72 (CH_3OSO_2-) and 1.25 (CH_3 of the *t*-butyl alcohol).

To examine the product distributions, 10.00-ml. aliquots of a 1,2-dimethoxyethane solution which was 0.155 *M* in the enolate anion **12** and 0.155 *M* in lithium *t*-butoxide (0.311 *M* in total base by titration) were held at 28° and treated with 570.7 mg. (4.53 mmoles) of dimethyl sulfate or 634.9 mg. (4.46 mmoles) of methyl iodide. After the solutions had been stirred for 5.0 min., 1.00-ml. aliquots were quenched in excess standard acid and back-titrated with base; the remaining 9.0 ml. of solution was quenched with dilute aqueous hydrochloric acid, and the crude product was separated and analyzed[29] as described previously. In the dimethyl sulfate reaction 49% of the total base had been consumed, and the calculated yields of products follow: 1-decalone (**1**), 57%; 9-methyl-*cis*-1-decalone (**30**), 34%; 9-methyl-*trans*-1-decalone (**31**), 5%. In the methyl iodide reaction 54% of the total base had been consumed, and the cal-

---

(43) This chemical shift difference is in agreement with the previous generalization of J. I. Musher [*J. Am. Chem. Soc.*, **83**, 1146 (1961)] that the 9-methyl group of a *trans*-fused decalin derivative has an n.m.r. peak at 0.14 p.p.m. highfield than the corresponding *cis*-fused isomer. Our results suggest that this generalization remains valid for decalin systems which contain a 1-keto group unlike the reversal observed for the axial and equatorial protons of α-halo ketones: A. Nickon, M. A. Castle, R. Harada, C. E. Berkoff, and R. O. Williams, *ibid.*, **85**, 2185 (1963).

TABLE V

REACTION OF THE ENOLATE ANION 12 AND LITHIUM *t*-BUTOXIDE WITH METHYLATING AGENTS IN 1,2-DIMETHOXYETHANE AT 28°

Concn., *M*			Amount of base consumed after various times (min.), %[a]						
Enolate anion	Lithium *t*-butoxide	Methylating agent	0.5[b]	2.0[b]	5.0	15.0	30.0	60.0	90.0
0.173	0.173	CH_3I,[c] 0.518	28	45	60	73	77	82	85
. . .	0.181	CH_3I, 0.543	4	13	21	39	58	70	76
0.173	0.173	CH_3OTs,[c] 0.518	5	11	19	33	42	47	52
. . .	0.181	CH_3OTs, 0.543	14	18	20	26	36	40	48
0.173	0.173	$(CH_3)_2SO_4$,[c] 0.518	46	48	49	50	53	59	59
. . .	0.181	$(CH_3)_2SO_4$, 0.543	32	36	42	44	46	47	48
	0.181	$(CH_3)_2SO_4$,[d] 0.543	15	39	42	44	47	50	50

[a] The numbers refer to the percentage of the total base consumed. Consequently, complete consumption of only the enolate anion 12 would give a value of 50%. [b] Since no special provisions were made for instant mixing, the numbers in these columns are only approximate. [c] The data listed are average values from duplicate runs. [d] In this run the dimethyl sulfate was mixed with an equimolar quantity of *trans*-1-decalone, and the mixture was added.

culated yields follow: 1-decalone (**1**), 7%; 9-methyl-*cis*-1-decalone (**30**), 72%; 9-methyl-*trans*-1-decalone (**31**), 14%.

It is apparent from the foregoing data that the initial rates of reaction of dimethyl sulfate with both the enolate anion **12** and lithium *t*-butoxide are very rapid. More than 50% of the enolate anion **12** had reacted in less than 0.5 min. However, both reactions became very slow after approximately 50% of the bases had been consumed, presumably because of complex formation and/or precipitation of mixtures of the bases and the lithium salt of methyl hydrogen sulfate. It is not clear whether similar complex formation retards the reaction with methyl *p*-toluenesulfonate but in any case the reaction is relatively slow. About 80 min. was required for the consumption of 50% of the total base and approximately 30 min. for consumption of 50% of the enolate anion **12**. The corresponding half-life for the reaction of methyl iodide with a mixture of the enolate anion **12** and the *t*-butoxide anion was about 2.5 min. and the separate half-lives for the reaction of methyl iodide with the enolate anion **12** and with lithium *t*-butoxide are estimated to be 1 and 22 min., respectively.

To obtain a measure of how rapidly a solution of lithium *t*-butoxide reacts with 1-decalone, a solution containing 1.69 mmoles of lithium *t*-butoxide in 10 ml. of 1,2-dimethoxyethane was treated with a mixture of 130.9 mg. (0.861 mmole) of *trans*-1-decalone and 138.6 mg. (0.894 mmole) of 2,2,9-trideuterio-*trans*-1-decalone (86% d_3 species and 14% d_2 species).[8] The resulting solution, which was 0.169 *M* in lithium *t*-butoxide and 0.176 *M* in *trans*-1-decalone (mixture of deuterated and nondeuterated), was stirred under a nitrogen atmosphere at 25° and 2.00-ml. aliquots were removed after the times specified (Table VI) and quenched in aqueous acetic acid (final pH 5). After the resulting mixtures had been extracted with ether, the extracts were washed with aqueous sodium bicarbonate, dried, and concentrated. The samples of *trans*-1-decalone were collected[29] and analyzed for deuterium content by mass spectrometry to give the data summarized in Table VI. From these data we estimate the half-life for equilibration of the nondeuterated and deuterated 1-decalones to be about 4 min. at the concentrations used.

TABLE VI

EQUILIBRATION OF 1-DECALONE-d_0 (0.0861 *M*) AND 1-DECALONE-d_3 (0.0894 *M*) IN A 0.169 *M* SOLUTION OF LITHIUM *t*-BUTOXIDE IN 1,2-DIMETHOXYETHANE

	Deuterium distribution, %			
Reaction time, min.	d_0	d_1	d_2	d_3
0	49	0	7	44
0.5	41	3	15	41
5.0	31	20	28	21
15.0	23	35	30	12
60.0	19	41	32	8

Alkylation of 2-Methylcyclohexanone.—Reaction of 2-methylcyclohexanone with acetic anhydride and *p*-toluenesulfonic acid as previously described[14d] afforded a mixture of enol acetates corresponding to enolates **23** and **24**, b.p. 80° (10 mm.). Although we were unsuccessful in resolving this mixture by gas chromatography, the n.m.r. spectrum[36] of the mixture allowed us to estimate[14d] the composition as 90% of the acetate of **23** and 10% of the acetate of **24**. The addition of 2.4112 g. (15.45 mmoles) of this enol acetate mixture to 31.0 mmoles of methyllithium in 30 ml. of 1,2-dimethoxyethane just discharged the color of the indicator to give a yellow, slightly cloudy solution of the enolate anion. The solution was cooled to 0° and 5.107 g. (33.4 mmoles) of methyl bromoacetate was added in one portion with swirling. After 30 sec. dilute, aqueous hydrochloric acid was added, and the mixture was extracted with ether. This extract was washed with aqueous sodium carbonate, dried, concentrated, and distilled to separate 1.73 g. (60%) of a mixture of ketones **35** and **36**, b.p. 59–61° (0.10 mm.). A collected[44] sample of this mixture, $n^{26}\text{D}$ 1.4643, exhibits a single peak on gas chromatography.[29,38,44] The infrared spectrum[36] of this material has peaks at 1740 (ester C=O) and 1715 cm.$^{-1}$ (C=O); the mass spectrum exhibits a weak molecular ion peak at *m/e* 184 with abundant fragment peaks at 153, 152, 140, 112, 96, 95, 82, 81, 74, 69, 68, 67, 59, 55, 43, and 41. The n.m.r. spectrum[36] of the product has a large singlet at δ 3.58 (CH_3O of **35**) as well as two weak singlets at 3.73 and 3.76 (CH_3O of the two diastereoisomers of **36**). From the relative areas of these peaks, we estimate the composition of the mixture to be 90% of **35** and 10% of **36**. The spectrum also has broad absorption in the region δ 1.5–2.6 (aliphatic CH) upon which are superimposed two doublets (J = 15 c.p.s.) centered at 2.32 and 2.53 (AB pattern for $\geqslant CCH_2CO_2R$ of **35**) as well as a singlet at 1.16 (CCH_3 of **35**) and a weak doublet (J = 6 c.p.s.) at 0.96 (CCH_3 of **36**).

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.93; H, 8.77.

Alkylation of 2-Heptanone.—A mixture of $\Delta^{2,3}$-enol acetates (74% of **15** and 26% of **16**) was employed, and the solutions of enolate anions **17** and **18** in 1,2-dimethoxyethane were generated in the usual way employing the quantities specified in Table VII. After the *n*-butyl iodide had been added in one portion, the reaction mixtures were stirred at 25° for the specified times and then diluted with aqueous hydrochloric acid and extracted with ether. The ethereal extracts were washed with aqueous sodium bicarbonate, dried, concentrated, mixed with a known weight of anisole (an internal standard), and analyzed.[29] Collected[29] samples of alkylated ketones **32** and **33** were used to prepare a calibration curve. Because of the large differences in retention times, a column temperature of 120° was used to elute 2-heptanone (first eluted), the ketone **32** (second eluted), an unknown component (eluted third), and the ketone **34** (eluted fourth), after which the column temperature was raised to 150° to elute the dialkylated product **33**. The retention times[29] at 150° of the products follow: **32**, 9.0 min.; the unknown component, 10.8 min.; **34**, 12.6 min.; **33**, 32.4 min. A collected[29] sample of the ketone **32** has infrared absorption[36] at 1715 cm.$^{-1}$ (C=O) with peaks in its mass spectrum at *m/e* 170 (very weak molecular ion) and at 127 (weak, M − $COCH_3$), as well as abundant peaks at 114, 71, 58, 57, and 43. A 12-mg. sample of the collected ketone **32** was allowed to react with excess semicarbazide in boiling aqueous ethanol. Recrystallization of the crude product from aqueous ethanol afforded 8 mg. of the **semicarbazone of 3-butyl-2-heptanone**, m.p. 108–109° (lit.[45] 109°). The n.m.r. spectrum[36] of our ketone **32** has a multiplet centered at δ 2.27 (1H, CHCO), a singlet at 2.00 (3H, CH_3CO), a multiplet in the

---

[44] A gas chromatography column packed with LAC, No. 728, liquid phase suspended on Chromosorb P was employed.

[45] W. B. Renfrow, Jr., *J. Am. Chem. Soc.*, **66**, 144 (1944).

region 1.0–1.6 (12H, aliphatic CH_2), and a multiplet in the region 0.8–1.0 (6H, CH_3).

TABLE VII

ALKYLATION OF THE ENOLATE ANIONS **17** AND **18** FROM 2-HEPTANONE

Enol acetates **15** and **16**, mg. (mmoles)	*n*-Butyl iodide, mg. (mmoles)	1,2-Dimethoxyethane, ml.	Reaction time, min.	Yield of products, %[a] 2-Heptanone	**32**	**33**	**34**
120.2 (0.78)	420.2 (2.26)	3.0	30	50	33	. .	6
191.0 (1.23)	675.0 (3.63)	5.0	120[b]	20	55	12	6

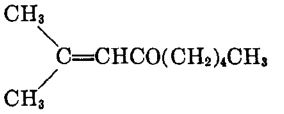
[a] Unless otherwise noted, the yields listed have been calculated from the gas chromatographs of mixtures of the products and a known amount of internal standard. [b] In a duplicate run, the yields were 20% of 2-heptanone, 51% of **32**, 14% of **33**, and 10% of **34**.

In a preparative run, a solution of 78 mmoles of methyllithium in 200 ml. of 1,2-dimethoxyethane was treated with 6.053 g. (38.8 mmoles) of the mixture of enol acetates **15** and **16**. Sufficient heat was generated during the addition to cause the solution to reflux. Titration of a 2.00-ml. aliquot of the enolate solution with standard acid indicated that the total amount of base present was 77.6 mmoles. *n*-Butyl iodide (21.50 g., 13.3 ml., or 118 mmoles) was added, and the mixture was stirred at room temperature. Aliquots (2.00 ml.) were removed at 30-min. intervals and titrated; after 30 min. (when 19% of the total base present had been consumed) a white precipitate began to separate from the reaction mixture. A total reaction time of 2.5 hr. was employed at which time 35% of the total base present had been consumed. The crude product, separated as in the previous cases, was distilled to separate the following fractions: (1) one of b.p. 135–160° containing 2-heptanone and other low-boiling components; (2) 3.250 g. (49%) of a fraction [b.p. 90–105° (8 mm.)] containing[29] 2-heptanone (4%), the ketone **32** (85%) [lit.[45] b.p. 104–107° (22 mm.)], an unknown component (5%), and the ketone **34** (6%); (3) 1.496 g. (17%) of a fraction [b.p. 130–138° (8 mm.)] containing[29] the ketone **32** (4%), the ketone **34** (4%), the dialkylated ketone **33** (67%), and 21% of at least three other high-boiling components of unknown constitution.

Samples of the ketone **34** collected[29] from both this reaction and a small-scale reaction were identified with a commercial[46] sample of the ketone **34**. A collected[29] sample of the dialkylated ketone **33** has infrared absorption[36] at 1715 cm.$^{-1}$ (C═O) with a very weak molecular ion peak at *m/e* 226 and abundant fragment peaks at 99, 71, 57, and 43. The sample has n.m.r. multiplets[36] in the regions δ 2.0–2.5 (3H, $-CH_2COCH<$) and 0.8–1.9 (27H, aliphatic C–H).

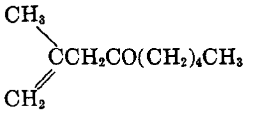
Anal. Calcd. for $C_{15}H_{30}O$: C, 79.57; H, 13.36. Found: C, 79.41; H, 13.31.

A collected[29] sample of the minor unknown component, eluted just after ketone **32**, was identified with a subsequently described sample of the unsaturated ketone **44** by comparison of retention times and infrared and mass spectra.



$$(CH_3)_2C{=}CHCO(CH_2)_4CH_3$$

44



$$CH_2{=}C(CH_3)CH_2CO(CH_2)_4CH_3$$

45

An ethereal solution of *n*-amyllithium was prepared as previously described[47] and found to be 1.2 *M* by a double titration procedure[33a] employing ethylene dibromide. A 50-ml. (60-mmole) portion of this *n*-amyllithium solution was added, dropwise and with stirring and external cooling (ice bath), to a solution of 2.0 g. (20 mmoles) of β,β-dimethylacrylic acid in 5 ml. of ether. The resulting mixture was stirred for 3.5 hr. and then poured into cold, dilute, aqueous hydrochloric acid, and extracted with ether. The ethereal extract was washed with aqueous sodium bicarbonate, dried, concentrated, and distilled to separate 2.55 g. (83%) of a yellow liquid, b.p. 80–84° (8 mm.). This product contained[29] 30% of the unconjugated isomer **45** (first eluted) and 70% of the conjugated ketone **44** (second eluted). A collected sample[29] of the **conjugated ketone 44** has infrared absorption[36] at 1690 (conjugated C═O) and 1625 cm.$^{-1}$ (conjugated C═C) with an ultraviolet maximum[48] at 237 mμ (ϵ 12,500) and an n.m.r.[36] multiplet at δ 6.02 (1H, vinyl CH) as well as two doublets (J = 1 c.p.s. for each) at 2.10 and 1.85 [6H, $C{=}C(CH_3)_2$] superimposed on complex absorption in the region 1.8–2.5 (11H, aliphatic CH).

Anal. Calcd. for $C_{10}H_{18}O$: C, 77.86; H, 11.76; mol. wt., 154. Found: C, 78.08; H, 12.09; mol. wt., 154 (mass spectrum).

A collected sample[29] of the unconjugated isomer **45** has infrared absorption[36] at 1720 (C═O), 1650 (C═C), and 895 cm.$^{-1}$ ($C{=}CH_2$) with an ultraviolet maximum[48] at 287 mμ (ϵ 96) and ϵ 1780 at 210 mμ. The sample has n.m.r. multiplets[36] at δ 4.81 and 4.90 (2H, vinyl CH) with a peak (no splitting resolved) at 3.02 (2H, $C{=}CCH_2CO-$) and a partially resolved multiplet at 1.74 (3H, $CH_3C{=}C$) superimposed on complex absorption in the region 1.8–2.5 (11H, aliphatic CH).

Anal. Calcd. for $C_{10}H_{18}O$: C, 77.86; H, 11.76; mol. wt., 154. Found: C, 77.98; H, 11.97; mol. wt., 154 (mass spectrum).

To learn the product distribution in a direct alkylation of 2-heptanone, a solution of 570 mg. (5.00 mmoles) of 2-heptanone and 1.00 g. (5.43 mmoles) of *n*-butyl iodide in 10 ml. of *t*-butyl alcohol containing 5.00 mmoles of potassium *t*-butoxide was stirred at 25° under a nitrogen atmosphere for 7 hr. A white precipitate began to separate from the reaction mixture after approximately 30 min. After the 7-hr. reaction period, the mixture, which was still basic, was diluted with aqueous hydrochloric acid and extracted with ether. The ether extract was washed with aqueous sodium carbonate, dried, concentrated, mixed with an internal standard,[39] and analyzed. The calculated yields follow: 2-heptone, 11%; the monoalkylated ketone **32**, 11%; the monoalkylated ketone **34**, 6%; the dialkylated ketone **33**, 1%. In addition, the crude product contained several minor components (estimated yield *ca.* 1%) with retention times similar to the dialkylated ketone and two (or more) components (estimated yield *ca.* 60%) with longer retention times which are believed to arise from aldol condensation of 2-heptanone with itself.[8]

---

[46] Aldrich Chemical Co., Inc., Milwaukee, Wis.

[47] H. W. Gilman, F. W. Moore, and D. Baine, *J. Am. Chem. Soc.*, **63**, 2479 (1941).

[48] Determined as a solution in 95% ethanol.