# The Chemistry of Carbanions. XXIV. Comparison of Stereochemistry in Alkylation and the Michael Reaction[1a]

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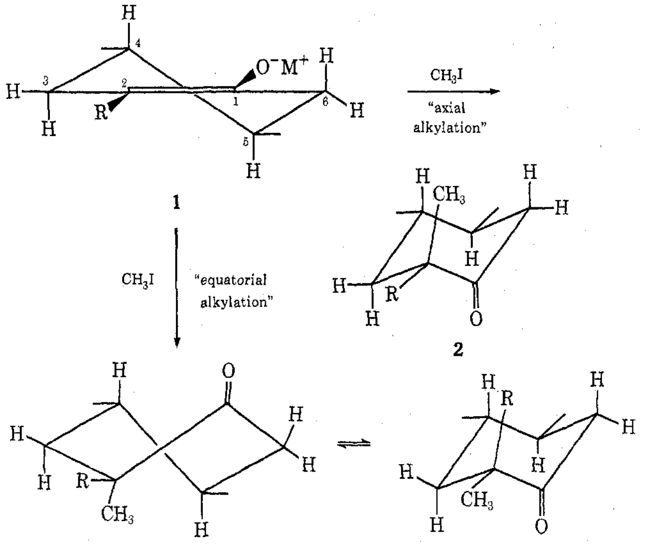
*Received September 12, 1972*

Reaction of the lithium enolate **9** from 2-methyl-5-*tert*-butylcyclohexanone (**4**) with trideuteriomethyl iodide yielded an alkylated product with 83% of the trideuteriomethyl group in an axial position. Reaction of the same ketone **4** with methyl acrylate produced a mixture of keto esters **14** and **15** with 82–86% of the β-methoxycarbonylethyl group in an axial position. These stereochemical results are suggested to result from deformation in the geometry of the starting metal enolate **9** that favors the introduction of a new axial substituent.

In the absence of substantial steric hindrance to attack from one side of an enolate anion **1** derived from a suitably substituted cyclohexanone derivative, the amounts of alkylated products formed with the new alkyl group axial (**2**) or equatorial (**3**) are influenced by the nature of the α substituent R. When this substituent is hydrogen, approximately equal amounts of axial and equatorial products are formed.[2a,b,f] However, when this substituent is alkyl, cyano, or carboalkoxy, the alkylated product is usually composed of 70–90% of the axial product **2** and 10–30% of the equatorial product **3**.

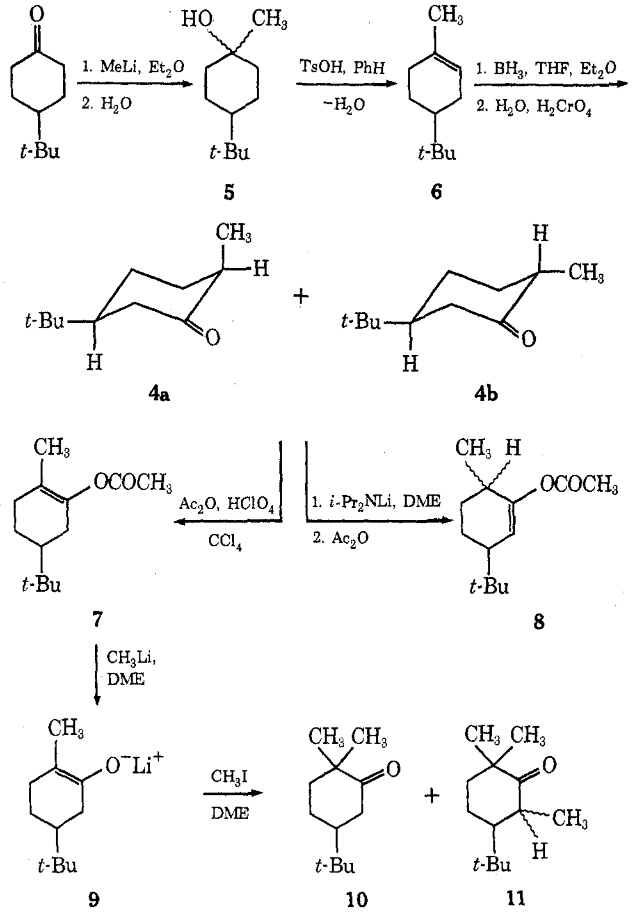
These sterochemical results could be explained in terms of a reactantlike transition state for enolates with hydrogen at the α carbon (**1**, R = H) and a productlike transition state with geometry similar to **2** or **3a** when some larger α substituent R is present. We have described elsewhere[3] evidence indicating that early, reactantlike transition states are generally appropriate for both N- and C-alkylation reactions even though the relative rates of the alkylation reactions may differ by large factors.



**1** **2** **3a** **3b**

In the present study we have compared the stereochemical results in two different reactions of an enolate anion: the alkylation with methyl iodide and the Michael reaction with methyl acrylate. The ketone **4**, selected for study, was prepared by the process summarized in Scheme I and converted into its lithium enolate **9** by way of the appropriate enol acetate **7**. The stereochemical results obtained from reaction of the lithium enolate **9** with trideuteriomethyl iodide and from Michael addition of the potassium enolate from ketone **4** to methyl acrylate are provided in Scheme II. Appropriate control experiments (see Experimental Section) were employed to demonstrate that the Michael products **14** and **15** were formed under conditions of kinetic control and that the proportions of these products were not being altered by further reac-

Scheme I



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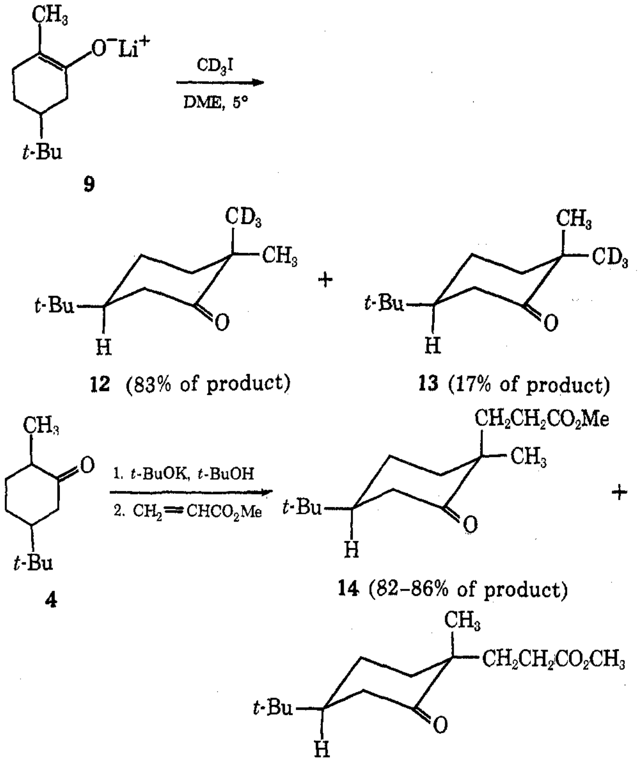
[1] (a) This research has been supported by Public Health Service Grant No. 7-R01-CA-12634 from the National Cancer Institute. (b) This work is part of the Ph.D. Thesis of M. J. Umen done *in absentia* from the Department of Chemistry, Massachusetts Institute of Technology.

[2] (a) H. O. House, B. A. Tefertiller, and H. D. Olmstead, *J. Org. Chem.*, **33**, 935 (1968); (b) B. J. L. Huff, F. N. Tuller, and D. Caine, *ibid.*, **34**, 3070 (1969); (c) M. E. Kuehne and J. A. Nelson, *ibid.*, **35**, 161 (1970); M. E. Kuehne, *ibid.*, **35**, 171 (1970); (e) for a recent review of other examples, see H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, pp 586–615; (f) P. T. Lansbury and G. E. DuBois, *Tetrahedron Lett.*, **No. 32**, 3305 (1972).

[3] (a) H. O. House and T. M. Bare, *J. Org. Chem.*, **33**, 943 (1968); (b) T. M. Bare, N. D. Hershey, H. O. House, and C. G. Swain, *ibid.*, **37**, 997 (1972).

SCHEME II



**9**

**12** (83% of product)

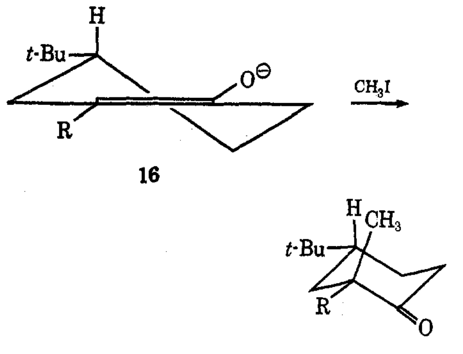
**13** (17% of product)

**4**

**14** (82–86% of product)

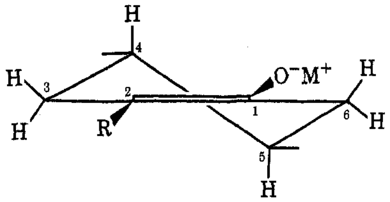
**15** (14–18% of product)

tion. The stereochemical assignments are based on the changes in nmr chemical shift values of the substituents α to the carbonyl group as the solvent was changed from $CCl_4$ to $C_6D_6$.[4] Thus in both of these reactions, one involving the nucleophilic displacement by the enolate anion at a tetravalent carbon and the second involving addition of the enolate to an unsaturated center, the stereochemical results are practically the same, namely *ca.* 85% reaction to introduce a new axial substituent. In a related study of the aldol condensation of the enolate **9** with benzaldehyde in the presence of $Zn^{2+}$,[5] the initially formed aldol product contained 70% of the least stable stereoisomers with the added substituent axial. It is also appropriate to note that, in the methylation of the various enolates **16**[2b,c] with substituents of different character, the proportion of the major alkylated product, the axial isomer **17**, is remarkably similar.

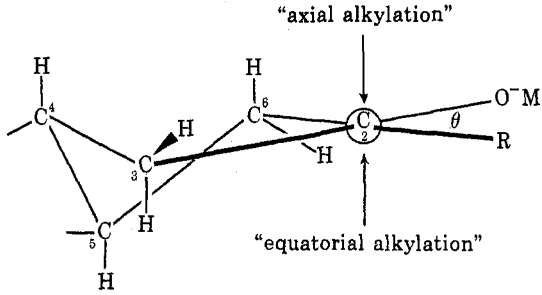


**16**

**17a**, R = $CH_3$ (with $CD_3I$) (~70% of product)
**b**, R = CN (77% of product)
**c**, R = $CO_2CH_3$ (83% of product)



**1a**



**1b**

It seems to us unlikely that the similar stereochemical results obtained in the various reactions studied should be ascribed to a series of productlike transition states, each of which involves approximately the same degree of new carbon–carbon bond formation. An alternative hypothesis, which we find more attractive, is that all of the enolate reactions described involve early reactantlike transition states with stereochemistry being determined primarily by the geometry of the starting enolates. Specifically, we suggest that the dihedral angle defined by $C_1$–$O^-M^+$ and $C_2$–R (angle θ in structure **1b**) is not zero in order to avoid eclipsing of the C-1 and C-2 substituents.[6] This deformation is expected to occur in the direction illustrated in structure **1b** in order to avoid eclipsing the pseudoequatorial hydrogen at C-6 with the substituent $O^-M^+$ and eclipsing the pseudoequatorial hydrogen at C-3 with the substituent R. Furthermore, this deformation of the planar enolate system would be expected to increase as the steric bulk of R (or the negative charge at R) is increased. Since the deformation suggested in structure **1b** would be accompanied by a partial rehydridization of the p orbital at C-2 toward an $sp^3$ orbital, the result of this deformation would be to favor axial attack both by allowing increased orbital overlap and by decreasing steric interference with an entering axial substituent. As has been noted in a different context,[2f] "equatorial alkylation" of the deformed enolate **1b** also will be accompanied by movement of the substituent R in a direction that will increase eclipsing of the substituents R and $O^-M^+$ as the new C–C bond is formed, since the

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(4) (a) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, pp 159–182. (b) Earlier studies of the stereochemistry of alkylation of 2-alkyl-4-*tert*-butylcyclohexanones [J. M. Conia and P. Briet, *Bull. Soc. Chim. Fr.*, 3881, 3888 (1966)] had suggested that the major products resulted from "equatorial alkylation" at C-2 and that the alkylated products did not follow the nmr solvent shift rule. Subsequent study [K. Dawes, N. J. Turro, and J. M. Conia, *Tetrahedron Lett.*, **No. 18**, 1377 (1971)] has established that the original stereochemical assignments were reversed and, in agreement with other studies,[2b] the major products resulted from axial alkylation at C-2 and all products obey the expected nmr solvent shift rule.

(5) H. O. House, D. S. Crumrine, A. Y. Teranishi, and H. D. Olmstead, to be published.

(6) A similar deformation of a carbon–carbon double bond has been suggested to minimize the energy of strained olefins: N. L. Allinger and J. T. Sprague, *J. Amer. Chem. Soc.*, **94**, 5734 (1972). An example of this deformation is provided by an X-ray structure determination for 2,3-bis-(*cis*-4-chloro-1-methylcyclohexyl)-*trans*-2-butene: D. Mootz, *Acta Crystallogr., Sect. B*, **24**, 839 (1968). With polar α substituents (CN, $CO_2CH_3$), the suggested deformation could result in part from electrostatic rather than steric repulsion.

two substituents R and $\mathrm{O^-M^+}$ must move past one another. This problem does not arise in "axial alkylation." Thus, we believe that the suggested deformation of the initial metal enolate can both account for the stereochemical differences observed in the alkylation when the $\alpha$ substituent (R in structure **1**) is changed from hydrogen to an alkyl group and account for apparent increases in the tendency to obtain axial alkylation when bulky substituents (which would increase the enolate deformation) are present in the pseudoequatorial positions at C-3[2f] and C-6.[7]

## Experimental Section[8]

4-*tert*-**Butyl-1-methylcyclohexene (6).**—To a cold (−10°) solution of 0.94 mol of MeLi in 611 ml of $\mathrm{Et_2O}$ was added, dropwise and with stirring over 2 hr, 117.7 g (0.767 mol) of 4-*tert*-butylcyclohexanone in 120 ml of $\mathrm{Et_2O}$. The reaction solution, maintained at −10 to +10° throughout the addition, was stirred for an additional 10 min at 5–10° and then partitioned between $\mathrm{Et_2O}$ and aqueous $\mathrm{NH_4Cl}$. The $\mathrm{Et_2O}$ solution was washed successively with aqueous 1 *M* HCl and with aqueous NaCl and then dried and concentrated to leave the crude mixture of epimeric alcohols **5** as a white solid containing (glpc, silicone fluid 710 on Chromosorb P) the alcohols **5** (retention times 12.2 and 16.2 min) and a small amount of unchanged 4-*tert*-butylcyclohexanone (18.4 min). A solution of this solid and 2.55 g of *p*-toluenesulfonic acid in 1.1 l. of PhH was refluxed with continuous removal of $\mathrm{H_2O}$ for 64 hr at which time analysis (glpc) of an aliquot indicated that dehydration was essentially complete. The resulting PhH solution was washed with aqueous $\mathrm{NaHCO_3}$, stirred with saturated aqueous $\mathrm{NaHSO_3}$ for 2.5 hr, and then washed with aqueous NaCl, dried, and concentrated. Distillation separated 95.3 g (82%) of the olefin **6**, bp 71–72° (9 mm), $n^{25}\mathrm{D}$ 1.4588 [lit. bp 74–75 (11 mm),[9] $n^{25}\mathrm{D}$ 1.4578[10]], as a pale yellow liquid which contained (glpc, silicone fluid 710 on Chromosorb P) the olefin **6** (retention time 5.8 min) accompanied by traces of the starting ketone (17.7 min). A pure sample of this olefin **6** was obtained by collection (glpc): nmr ($\mathrm{CCl_4}$) $\delta$ 5.32 (1 H, m, vinyl CH), 1.0–2.2 (10 H, m, aliphatic CH), and 0.85 (9 H, s, *t*-Bu); mass spectrum, *m/e* (rel intensity), 152 ($\mathrm{M^+}$, 46), 96 (75), 95 (53), 81 (95), 79 (34), 69 (45), 68 (83), 67 (80), 57 (84), 55 (46), 41 (100), and 39 (34).

5-*tert*-**Butyl-2-methylcyclohexanone (4).**—To a solution of 95.02 g (0.625 mol) of the olefin **6** in 300 ml of $\mathrm{Et_2O}$, maintained at 15 to 34°, was added, dropwise and with stirring, 282 ml of a tetrahydrofuran solution containing 0.377 mol of $\mathrm{BH_3}$. The resulting white slurry was stirred for 1 hr and then 100 ml of $\mathrm{H_2O}$ was added followed by the dropwise addition (during 35 min) of a solution of 137.5 g (0.460 mol) of $\mathrm{Na_2Cr_2O_7}$ and 103 ml of concentrated $\mathrm{H_2SO_4}$ in 495 ml of $\mathrm{H_2O}$. The resulting mixture was refluxed with stirring for 1.5 hr and then partitioned between $\mathrm{H_2O}$ and $\mathrm{Et_2O}$. The $\mathrm{Et_2O}$ solution was washed successively with aqueous $\mathrm{NaHCO_3}$ and aqueous NaCl and then dried and concentrated. Distillation separated 66.0 g (63%) of a mixture of the epimeric ketones **4** [glpc, 1,2,3-tris($\beta$-cyanoethoxy)propane on Chromosorb P, retention times 28.2 (major epimer **4b**) and 30.0 min (minor epimer **4a**)]: bp 99–105° (10 mm); $n^{25}\mathrm{D}$ 1.4562 [lit.[10] bp 42–46° (0.3 mm), $n^{25}\mathrm{D}$ 1.4557]; ir ($\mathrm{CCl_4}$), 1711 cm$^{-1}$ (C=O); nmr ($\mathrm{C_6D_6}$) $\delta$ 0.8–2.5 (11 H, m, aliphatic CH) and 0.72 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity), 168 ($\mathrm{M^+}$, 17), 112 (57), 111 (39), 83 (31), 57 (100), 55 (66), and 41 (74).

**Preparation of the Enol Acetate 7.**—A mixture of 18.32 g (0.109 mol) of the ketone **4**, 59.4 g (0.582 mol) of $\mathrm{Ac_2O}$, 0.07 ml of aqueous 70% $\mathrm{HClO_4}$, and 131 ml of $\mathrm{CCl_4}$ was stirred at 25° for 3 hr and then stirred with 100 ml of pentane and 100 ml of cold (0–5°) aqueous $\mathrm{NaHCO_3}$ for 2.5 hr. Additional solid $\mathrm{NaHCO_3}$ was added during this period to complete the neutralization of the HOAc. The pentane layer and pentane extract of the aqueous phase were dried and concentrated. Distillation of the residual liquid separated 20.49 g (89%) of the crude enol acetate **7**, bp 70–76° (0.1 mm), $n^{25}\mathrm{D}$ 1.4609, containing (glpc, silicone fluid $\mathrm{QF_1}$ on Chromosorb P) the desired enol acetate **7** (*ca.* 92%, retention time 9.4 min) and the isomeric enol acetates **8** (*ca.* 8%, 7.2 and 7.6 min). Fractional distillation through a 60-cm spinning band column afforded the pure (glpc) enol acetate **7** as a colorless liquid: $n^{25}\mathrm{D}$ 1.4629; ir ($\mathrm{CCl_4}$), 1752 (enol ester C=O) and 1711 cm$^{-1}$ (enol C=C); uv (95% EtOH), end absorption with $\epsilon$ 1410 at 210 m$\mu$; nmr ($\mathrm{CCl_4}$), $\delta$ 2.02 (3 H, s, $\mathrm{CH_3CO}$), 1.0–2.2 (7 H, m, aliphatic CH), 1.47 (3 H, broad, vinyl $\mathrm{CH_3}$), and 0.87 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity), 210 ($\mathrm{M^+}$, 10), 169 (32), 168 (100), 153 (50), 111 (61), 84 (49), 69 (30), 57 (41), 43 (41), and 41 (34).

*Anal.* Calcd for $\mathrm{C_{13}H_{22}O_2}$: C, 74.24; H, 10.54. Found: C, 74.27; H, 10.59.

**Preparation of the Enol Acetates 8.**—To a cold (−20 to −40°) solution of $\mathrm{(Me_2CH)_2NLi}$ [from 94.2 mmol of MeLi and 9.51 g (94.0 mmol) of $\mathrm{(Me_2CH)_2NH}$] in 200 ml of 1,2-dimethoxyethane was added, dropwise and with stirring, 15.03 g (89.3 mmol) of the ketones **4**. The resulting suspension was warmed to 20° and added to a mixture of 140.6 g (1.37 mol) of $\mathrm{Ac_2O}$ and 200 ml of pentane. The resulting mixture was partitioned between pentane and aqueous $\mathrm{NaHCO_3}$ (excess solid $\mathrm{NaHCO_3}$ added), and the pentane solution was washed successively with cold (5°), aqueous 0.5 *M* HCl and aqueous $\mathrm{NaHCO_3}$. After the organic solution had been dried and concentrated, distillation of the residue separated 14.66 g (78%) of the crude enol acetates **8**, bp 60–68° (0.5 mm), $n^{25}\mathrm{D}$ 1.4580, contaminated (nmr and glpc) with several other components. Successive fractional distillations through a 60- and a 24-cm spinning band column separated a colorless liquid, bp 55–58° (0.5 mm), $n^{25}\mathrm{D}$ 1.4600, which contained [glpc, 1,2,3-tris($\beta$-cyanoethoxyl)propane on Chromosorb P] the epimeric enol acetates **8** (*ca.* 95%, retention times 22.5 and 24.6 min) accompanied by the enol acetate **7** (*ca.* 5%, 30.2 min): ir ($\mathrm{CCl_4}$), 1752 (enol ester C=O), and 1680 cm$^{-1}$ (enol C=C); nmr ($\mathrm{CCl_4}$) $\delta$ 5.25 (1 H, m, vinyl CH) and 2.08 (3 H, s, $\mathrm{CH_3CO}$), and two partially resolved singlets at $\delta$ 0.89 and 0.90 (9 H, *t*-Bu) superimposed on a multiplet at 0.8–2.0 (9 H, aliphatic CH); mass spectrum *m/e* (rel intensity) 210 ($\mathrm{M^+}$, 1), 153 (38), 112 (23), 111 (100), 57 (20), 43 (42), and 41 (20).

*Anal.* Calcd for $\mathrm{C_{13}H_{22}O_2}$: C, 74.24; H, 10.54. Found: C, 74.14; H, 10.51.

**Reaction of the Ketone 4 with Methyl Acrylate.**—To a solution of 6.09 g (36.2 mmol) of the ketones **4** and 0.4 g (4 mmol) of *t*-BuOK in 33 ml of *t*-BuOH was added, dropwise and with stirring and cooling, 3.46 g (40.2 mmol) of methyl acrylate while the reaction mixture was kept at 23–30°. The resulting solution was stirred at 25–28° for 2 hr and then acidified with 25 ml of aqueous 2 *M* HOAc, concentrated, and partitioned between $\mathrm{Et_2O}$ and aqueous $\mathrm{NaHCO_3}$. After the $\mathrm{Et_2O}$ solution had been dried and concentrated, a portion of the residual pale yellow liquid (8.275 g) was mixed with an internal standard (*o*-terphenyl, retention time 6.6 min), and subjected to glpc analysis (silicone fluid $\mathrm{QF_1}$ on Chromosorb P). The calculated yields were 58% of keto ester **14** (retention time 14.8 min) and 9% of keto ester **15** (retention time 18.4 min). A 2.793-g portion of the crude product was fractionally distilled with a 24-cm spinning band column to separate 1.604 g (48%) of fractions, bp 92–99° (0.2 mm), containing (glpc) mixtures of the keto esters **14** and **15** from which pure samples were collected (glpc).

The high-boiling liquid residue remaining after distillation of the keto esters **14** and **15** is believed to be dialkylated material. This crude material exhibits a single major glpc peak (60-cm silicone rubber on Chromosorb P) with ir absorption ($\mathrm{CCl_4}$) at 1740 (ester C=O) and 1695 cm$^{-1}$ (C=O) and prominent high-mass peaks in the mass spectrum at *m/e* 283, 277, and 251.

The major product, keto ester **14**, was obtained as a colorless liquid: $n^{25}\mathrm{D}$ 1.4690; ir ($\mathrm{CCl_4}$) 1740 (ester C=O) and 1705 cm$^{-1}$ (C=O); uv$\lambda_{\mathrm{max}}^{95\%\ \mathrm{EtOH}}$ 290 m$\mu$ ($\epsilon$ 40); nmr ($\mathrm{CCl_4}$) $\delta$ 3.58 (3 H, s,

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(7) An example of the effect of substituents at C-6 is provided by R. E. Ireland, P. S. Grand, R. E. Dickerson, J. Bordner, and D. R. Rydjeski, *J. Org. Chem.*, **35**, 570 (1970).

(8) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated $\mathrm{MgSO_4}$ was employed as a drying agent. The ir spectra were determined with a Perkin-Elmer, Model 257, infrared recording spectrophotometer fitted with a grating. The uv spectra were determined with a Perkin-Elmer, Model 202, recording spectrophotometer. The nmr spectra were determined at 60 MHz with a Varian, Model A-60 or Model T-60, nmr spectrometer. The chemical shift values are expressed in $\delta$ values (ppm) relative to a $\mathrm{Me_4Si}$ internal standard. The mass spectra were obtained with an Hitachi (Perkin-Elmer) or a Varian, Model M-66, mass spectrometer. All reactions involving strong bases or organometallic intermediates were performed under a nitrogen atmosphere.

(9) B. Cross and G. Whitham, *J. Chem. Soc.*, 3892 (1960).

(10) N. LeBel and G. Ecke, *J. Org. Chem.*, **30**, 4316 (1965).

$OCH_3$), 1.0–2.5 (7 H, m, aliphatic CH), and 0.90 (12 H, s, $CH_3$ and *t*-Bu); in benzene-$d_6$ the singlets are found at δ 3.56 ($CH_3O$), 0.95 ($CH_3$), and 0.72 (*t*-Bu) corresponding to a solvent shift, $\delta_{CCl_4} - \delta_{C_6D_6}$, of −3 Hz for the equatorial methyl group;[4] mass spectrum *m/e* (rel intensity) 254 ($M^+$, 2), 168 (27), 137 (33), 109 (31), 95 (37), 69 (37), 67 (24), 57 (64), 55 (53), 43 (27), and 41 (100).

*Anal.* Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 70.54; H, 10.26.

A collected (glpc) sample of the minor product, keto ester **15**, was obtained as a colorless liquid: $n^{25}\text{D}$ 1.4713; ir ($CCl_4$), 1740 (ester C=O) and 1705 $cm^{-1}$ (C=O); uv$\lambda_{max}^{95\%\ EtOH}$ 290 mμ (ε 35); nmr ($CCl_4$), δ 3.60 (3 H, s, $OCH_3$), 1.2–2.5 (7 H, m, aliphatic CH), 1.10 (3 H, s, $CH_3$), and 0.92 (9 H, s, *t*-Bu); in benzene-$d_6$ the singlets are at δ 3.43 ($OCH_3$), 0.83 ($CH_3$), and 0.70 (*t*-Bu) corresponding to a solvent shift, $\delta_{CCl_4} - \delta_{C_6D_6}$, of +16 Hz for the axial methyl group;[4] mass spectrum *m/e* (rel intensity) 254 ($M^+$, 2), 168 (40), 165 (25), 137 (38), 109 (33), 95 (39), 69 (38), 67 (25), 57 (65), 55 (55), 43 (24), and 41 (100).

*Anal.* Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 70.62; H, 10.24.

To demonstrate that keto esters **14** and **15** are not interconverted under the reaction conditions, a solution of 17.8 mg (0.16 mmol) of *t*-BuOK, 305 mg (1.20 mmol) of the keto ester **14**, and 116 mg (1.35 mmol) of methyl acrylate in 1.1 ml of *t*-BuOH was stirred at 25° for 2 hr and then quenched with aqueous 2 *M* HOAc. An $Et_2O$ solution of the crude product was mixed with 121 mg of 1-methylnaphthalene (an internal standard), washed successively with aqueous $NaHCO_3$ and aqueous NaCl, dried, concentrated, and analyzed (glpc). The recovered ketone **14** amounted to 73% and no ketone **15** was detected. A collected (glpc) sample of the ketone **14** was identified with the previously described material by comparison of ir spectra and glpc retention times.

For quantitative studies of the reaction products, the glpc equipment was calibrated with known mixtures of the keto esters **14** (retention time 17.1 min) and **15** (21.5 min), the starting ketones **4** (3.0 min), and the internal standard *o*-terphenyl (7.4 min). A reaction of 1.627 g (9.71 mmol) of the ketones **4** and 115 mg (1.02 mmol) of KOBu-*t* in 6 ml of *t*-BuOH with 285 mg (3.31 mmol) of methyl acrylate at 25–31° was quenched after 57 sec in aqueous 1 *M* $NH_4Cl$. The organic product was extracted with $Et_2O$, mixed with an internal standard and analyzed (glpc). The calculated yields (based on methyl acrylate) were 58% of keto ester **14** and 9% keto ester **15**, and no polyalkylated product was detected (glpc). In a comparable reaction from which aliquots were removed at regular intervals from a reaction time of 45 sec to 19.2 hr, the composition of the alkylated product was within the range 82–86% of keto ester **14** and 14–18% of keto ester **15**, and no polyalkylated material was detected.

**Reaction of the Lithium Enolate 9 with Methyl Iodide and Trideuteriomethyl Iodide.**—A solution of the enolate **9** was prepared by the addition, dropwise and with stirring, of 1.485 g (7.07 mmol) of the enol acetate **7** to a cold (5–11°) solution of 15 mmol of MeLi in 15 ml of DME containing several milligrams of 2,2′-bipyridyl as an indicator to establish the presence of excess MeLi. After the resulting red solution had been treated with 6.26 g (44.2 mmol) of $CH_3I$, it was stirred for 4 min (during which time the temperature rose to 25° and separation of a white solid began after *ca.* 1 min) and then partitioned between pentane and aqueous $NH_4Cl$. The organic solution was washed with aqueous NaCl, dried, concentrated, and analyzed (glpc, TCEP on Chromosorb P) employing *n*-hexadecane as an internal standard and glpc equipment calibrated with known mixtures. The crude product contained *n*-hexadecane (4.4 min), trimethyl ketone **11** (36% yield, 12.0 min), dimethyl ketone **10** (48% yield, 13.7 min), and starting ketone **4** (<1%, 15.7 min). In a subsequent comparable run, performed at 9–15°, aliquots were removed, quenched, and analyzed at regular intervals. The following yields were obtained after the times indicated: 15 sec, <1% **11**, 73% **10**, and 4% **4**; 44 sec, 11% **11**, 62% **10**, and 3% **4**; 121 sec, 23% **11**, 59% **10**, and <1% **4**. Authentic samples of the ketones **10** and **11** were collected by glpc (Apiezon L on Chromosorb P).

The dimethyl ketone **10** was obtained as a colorless liquid: $n^{25}\text{D}$ 1.4567; ir ($CCl_4$) 1705 $cm^{-1}$ (C=O); mass spectrum *m/e* (rel intensity), 182 ($M^+$, 25), 139 (79), 126 (46), 125 (80), 123 (70), 111 (63), 97 (100), 83 (58), 57 (35), and 55 (42); nmr ($CCl_4$) δ 1.2–2.4 (7 H, m, aliphatic CH), 1.09 (3 H, s, axial $CH_3$), 0.97 (3 H, s, equatorial $CH_3$), and 0.90 (9 H, s, *t*-Bu). In $C_6D_6$ solution the high-field singlets are found at δ 1.12 (3 H, s, equatorial $CH_3$, shifted downfield 9 Hz), 0.89 (3 H, s, axial $CH_3$, shifted upfield 20 Hz), and 0.70 (9 H, s, *t*-Bu). The assignments of these peaks in the two solvents were established by measuring the nmr spectrum repeatedly as increments of $C_6D_6$ were added to the $CCl_4$ solution of the ketone **10**. A sample of the ketone **10** crystallized from pentane solution at Dry Ice temperatures as white plates, mp 32.5–34.5° (lit.[11] mp 33–35°).

A sample of the ketone **11** was obtained as a colorless liquid: $n^{25}\text{D}$ 1.4589; ir ($CCl_4$), 1693 $cm^{-1}$ (C=O); mass spectrum *m/e* (rel intensity), 196 ($M^+$, 8), 139 (38), 138 (44), 125 (32), 111 (100), 97 (37), 69 (42), 57 (45), 56 (43), 55 (53), and 41 (65); nmr ($CCl_4$) δ 1.2–2.4 (6 H, m, aliphatic CH), 1.20 (3 H, d, *J* = 7.2 Hz, $CH_3$ at C-6), 1.08 (3 H, s, $CH_3$ at C-2), 1.05 (3 H, s, $CH_3$ at C-2), and 0.91 (9 H, s, *t*-Bu). In $C_6D_6$ solution the high-field peaks are found at δ 1.14 (3 H, d, *J* = 7.2 Hz, $CH_3$ at C-6 shifted upfield 4 Hz),[12] 1.10 (3 H, s, $CH_3$ at C-2), 1.02 (3 H, s, $CH_3$ at C-2), and 0.75 (9 H, s, *t*-Bu).

*Anal.* Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.36; H, 12.30.

The alkylation reaction was repeated with the enolate **9**, prepared from 7.6 mmol of MeLi and 774 mg (3.68 mmol) of the enol acetate **7** in 7.5 ml of DME, and 3.29 g (22.7 mmol) of $CD_3I$. After a reaction period of 30 sec at 5–10°, the reaction mixture was partitioned between aqueous $NH_4Cl$ and pentane. After the organic solution had been dried, concentrated, and mixed with an internal standard, glpc analysis indicated the product yields to be 68% of monoalkylated ketones **12** and **13**, 17% of dialkylated ketone (the $d_6$ analog of **11**), and 4% of the starting ketones **4**. A collected (glpc) sample of the monoalkylated ketones **12** and **13** was subjected to nmr analysis in both $CCl_4$ and $C_6D_6$ solution to measure the areas under the axial and equatorial C-2 methyl peaks. The composition was 83% of the axial deuteriomethyl ketone **12** and 17% of the equatorial deuteriomethyl ketone **13**. The mass spectrum of the mixture of ketones **12** and **13** indicated the presence of only $d_3$ species: *m/e* (rel intensity) 185 ($M^+$, 12), 141 (95), 128 (43), 100 (55), 69 (64), 59 (89), 58 (67), 57 (98), 56 (56), 55 (87), 53 (59), 44 (45), 43 (61), 42 (57), 41 (100), and 39 (51).

The same alkylation reaction was repeated with a reaction time of 11.7 hr at −64°. The cold reaction mixture was quenched in a MeOH–HOAc mixture, and the resulting mixture was neutralized with aqueous $NaHCO_3$ and then extracted with pentane. The crude product contained (glpc) the monoalkylated ketones **12** and **13** (35% yield) and the unalkylated ketones **4** (38% recovery). A collected (glpc) sample of the monoalkylated ketones was subjected to the previously described nmr analysis and found to contain 90% of the axial deuteriomethyl ketone **12** and 10% of the equatorial isomer **13**.

**Registry No.**—**4a**, 5951-22-4; **4b**, 5937-40-6; **6**, 3419-74-7; **7**, 37786-83-7; *cis*-**8**, 37818-69-2; *trans*-**8**, 37786-84-8; **9**, 37786-85-9; **10**, 17359-15-8; **11**, 37786-87-1; **12**, 37786-88-2; **13**, 37786-89-3; **14**, 37818-70-5; **15**, 37786-90-6; 4-*tert*-butylcyclohexanone, 98-53-3.

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[11] J. Sicher and M. Tichy, *Collect. Czech. Chem. Commun.*, **32**, 3687 (1967).

[12] Because of the small magnitude of the upfield shift in a sterically congested molecule, we regard the configuration as uncertain.