Registry No.—**1**, 13066-51-8; **2**, 26532-23-0; **2a**, 30346-27-1; **3**, 26532-24-1; **4**, 26532-25-2; (*E*)-**6**, 4698-08-2; (*Z*)-**6**, 4613-38-1; (*E*)-**6a**, 1189-09-9; (*Z*)-**6a**, 1862-61-9; **9**, 55298-92-5; **10**, 55298-93-6; **11**, 55298-94-7; **12**, 55298-95-8; **13**, 55298-96-9; **14**, 28043-10-9; **15**, 30346-23-7; **16**, 30346-25-9; **18**, 36866-77-0; **19**, 55298-72-1.

References and Notes

(1) Presented in part at the VI International Congress of Essential Oils, San Francisco, Calif., Sept 1974.
(2) J. H. Tumlinson, R. C. Gueldner, D. D. Hardee, A. C. Thompson, P. A. Hedin, and J. P. Minyard, "Chemicals Controlling Insect Behavior", M. Beroza, Ed., Academic Press, New York, N.Y., 1970.
(3) For the isolation, identification, and synthesis of **2**, **3**, **4**, and **5** see J. H. Tumlinson, D. D. Hardee, R. C. Gueldner, A. C. Thompson, P. A. Hedin, and J. P. Minyard, *Science*, **166**, 1010 (1969); J. H. Tumlinson et al., *J. Org. Chem.*, **36**, 2616 (1971).
(4) For syntheses of grandisol (**5**) see (a) R. C. Gueldner, A. C. Thompson, and P. A. Hedin, *J. Org. Chem.*, **37**, 1854 (1972); (b) R. Zurflüh, L. L. Dunham, V. L. Spain, and J. B. Siddal, *J. Am. Chem. Soc.*, **92**, 425 (1970); (c) W. E. Billups, J. H. Cross, and C. V. Smith, *ibid.*, **95**, 3438 (1973); (d) G. Stork and J. F. Cohen, *ibid.*, **96**, 5270 (1974).
(5) Geranic acid is available from Fritzsche D & O, or can be synthesized by silver oxide oxidation of citral.[6]
(6) K. Bernhauer and R. Forster, *J. Prakt. Chem.*, **147**, 199 (1936).
(7) For earlier syntheses of γ-geraniol, see (a) H. C. Brown, K. Singh, and B. J. Garner, *J. Organomet. Chem.*, **1**, 2 (1963); (b) S. Watanabe and K. Suga, *Bull. Chem. Soc. Jpn.*, **36**, 1495 (1963); (c) A. I. Lebedeva and L. V. Kukhareva, *Zh. Obshch. Khim.*, **28**, 2782 (1958).
(8) Y. Iwakura, F. Toda, R. Iwata, and Y. Torii, *Bull. Chem. Soc. Jpn.*, **42**, 841 (1969).
(9) Geranic acid is a mixture of *E* and *Z* isomers.
(10) The reaction of geranic acid with thionyl chloride resulted in the addition of the by-product HCl to the $\Delta^{6,7}$ double bond.
(11) The nonconjugated ester **9** most likely forms by way of a vinyl ketene intermediate, as suggested by Iwakura.[8]
(12) Typical runs on a small scale yield 65% **9**.
(13) Compound **14** arises by cyclization of methyl geranate (**6a**), which was present in the sample of **9**.
(14) H. C. Brown, J. H. Brewster, and H. Shechter, *J. Am. Chem. Soc.*, **76**, 467 (1954); G. A. R. Kon and R. P. Linstead, *J. Chem. Soc.*, 1269 (1929).
(15) For examples of analogous 1,5-hydrogen transfers involving β,γ-unsaturated aldehydes, ketones, and esters see (a) G. Ohloff, *Tetrahedron Lett.*, **11**, 10 (1960); (b) G. Ohloff, J. Osiecki, and C. Djerassi, *Chem. Ber.*, **95**, 1400 (1962); (c) D. E. McGreer and N. W. K. Chiu, *Can. J. Chem.*, **46**, 2225 (1968).
(16) All boiling points are uncorrected. GLC analyses were performed using a 12 ft × 0.375 in. Carbowax 20M column at 175° except as otherwise noted. NMR spectra were determined with a Varian Associates A-60 spectrometer. Infrared spectra were recorded on a Perkin-Elmer Infracord spectrometer. Mass spectra were determined at 70 eV with a Hitachi RMU-6A mass spectrometer. Microanalyses were performed by Dr. C. S. Yeh and associates.

Regiospecific Alkylation of Enolate Ions in Liquid Ammonia–Tetrahydrofuran

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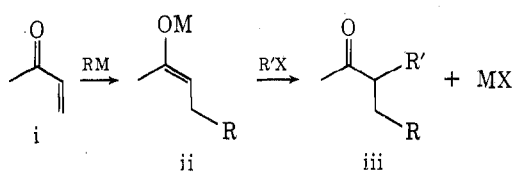
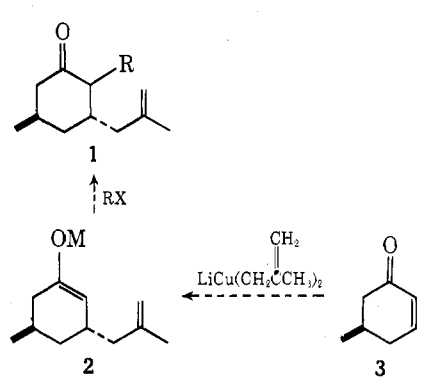
Specific cyclohexanone enolates are generated by cleaving the corresponding trimethylsilyl enol ethers with lithium amide in liquid ammonia. Butylation proceeds in high yield in this solvent, with little enolate equilibration. With corresponding sodium and potassium enolates, alkylation and enolate equilibration proceed at comparable rates.

Vicinal dialkylation of enones, by conjugate addition[1] and alkylation of the resulting specific enolate (i → ii → iii), is an important synthetic process which has received considerable recent attention.[2] The main problem is the



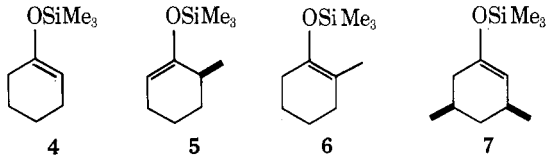
matter of proton exchange vs. alkylation. With very reactive electrophiles such as benzylic and allylic halides, alkylation is significantly more rapid than proton exchange, and regiospecific vicinal alkylation results.[2a,b,d] Coates found dimethoxyethane (DME) to be an effective solvent for promoting alkylation vis-à-vis proton transfer, although he still encountered substantial proton transfer in some cases.[2f]

In connection with a projected alkaloid synthesis, we required 2-alkyl-3-methallyl-5-methylcyclohexanones, in which the C-3 and C-5 substituents are trans (1). Since the conjugate addition of dialkylcuprates to 5-methylcyclohex-2-en-1-one is known to occur with good trans stereoselectivity,[3] the vicinal dialkylation process is an attractive route to **1**.

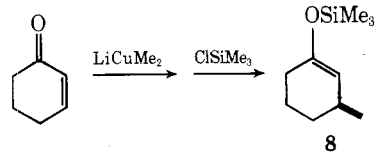


In the process of this study, we discovered that specific lithium enolates undergo alkylation in a mixture of liquid ammonia–tetrahydrofuran under conditions where proton transfer is an insignificant side reaction.[4] In this paper, we report the results of a limited study of this phenomenon.

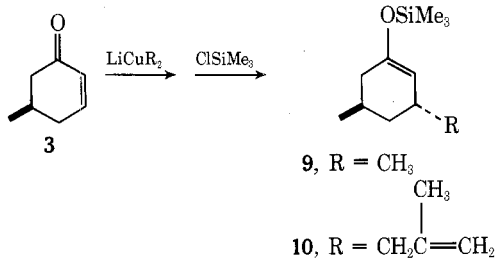
Preparation of Alkylation Substrates. The ketone enolates which we have studied were prepared by cleavage of the appropriate silyl enol ether with methyllithium in the appropriate ether[4] or with lithium amide in liquid ammonia.[5] Silyl enol ethers **4**, **5**, and **6** were prepared by literature procedures.[6] Ether **7** was prepared in a similar manner from *cis*-3,5-dimethylcyclohexanone. This ether was contaminated with 10% of the *trans*-3,5-dimethyl isomer **9**,



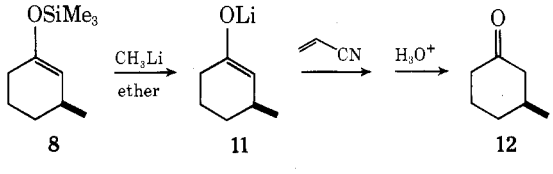
owing to the method by which it was prepared (see Experimental Section). Ether 8 was prepared in 69% yield by conjugate addition of lithium dimethylcuprate to cyclohex-2-en-1-one, followed by addition of chlorotrimethylsilane.[7]



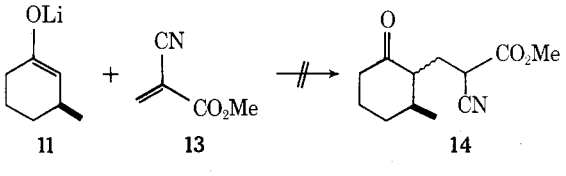
Ethers 9 and 10 were prepared from enone 3 in yields of 71 and 86%, respectively, using the corresponding dialkylcuprates. Ether 9 was contaminated by 7% of the *cis*-3,5-dimethyl isomer 7.



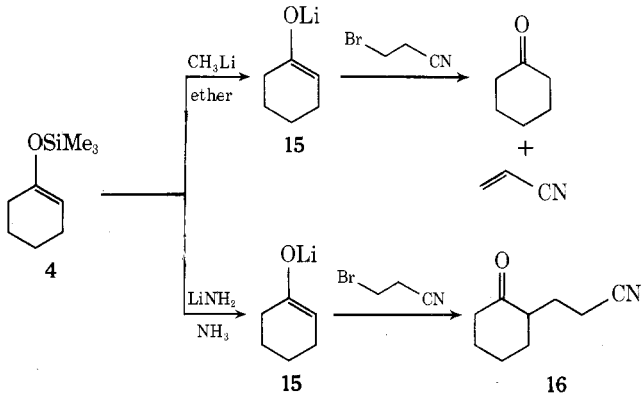
Alkylation Results. We had hoped to alkylate enolate 2 with acrylonitrile or its equivalent. In our initial experiment toward this end, we treated enolate 11, prepared in ether solution by treating 8 with methyllithium, with acrylonitrile. Not surprisingly, the reaction yielded no adduct but instead resulted in complete polymerization of the acrylonitrile; 3-methylcyclohexanone was the only product,



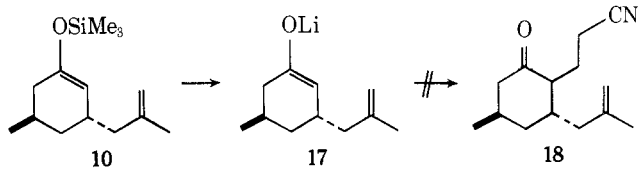
obtained in 80% yield. Enolate 11 also catalyzed the polymerization of methyl 2-cyanoacrylate (13). None of the desired product 14 could be detected.



Having been thwarted in attempts to carry out Michael reactions on our specific enolates, we turned our attention to alkylation with 3-halopropionitriles. Enolate 15, prepared in ether by treating silyl ether 4 with methyllithium, is not alkylated by 3-bromopropionitrile. The only products obtained are cyclohexanone and polyacrylonitrile. Because the C-2 protons in 3-bromopropionitrile are fairly acidic, E2 elimination predominates, and no alkylation is achieved. However, if the alkylation is carried out in liquid ammonia with excess β-bromopropionitrile, cyano ketone 16 is obtained in 48% yield. Unfortunately, we were unable to extend this result to the 3-methallyl-5-methyl system.



Enolate 17, prepared by lithium amide cleavage of silyl ether 10, failed to react with 3-bromopropionitrile or 3-iodopropionitrile. Apparently, the E2/SN2 ratio is lower in liquid ammonia than it is in ether. However, even in this solvent, the more hindered enolate 17 gives complete elimination of the 3-halopropionitrile.



The efficacy of liquid ammonia in reducing the proton-transfer process in the alkylation of 15 by 3-bromopropionitrile seemed interesting and worthy of further study. Consequently, we examined the butylation of enolate 17 and its sodium and potassium analogs in this medium. With the lithium enolate, the corresponding 2-butyl product 19 was obtained in 91% yield. With the sodium and potassium enolates, complex product mixtures were obtained. Representative data are shown in Table I.

Table I
Butylation of 17 in THF–NH_3[a]

	Product composition, %					
Cation	19	20	21	22	23	24
Li^{+c}	5.5	94.5	0	0	0	0
Na^{+b}	33.8	34.6	31.6	0	0	0
K^{+b}	7.7	49.0	13.7	5.5	8.3	15.8
$K^{+c,d}$	12.2	55.5	32.2	0	0	0

[a] Enolates were prepared by treating ether 10 with $LiNH_2$, $NaNH_2$, or KNH_2 in THF–NH_3 (40% THF, 60% NH_3). A fourfold excess of *n*-butyl iodide was added. Alkylation was allowed to proceed for 2 hr for M = Na and K and 6 hr for M = Li. [b] In these experiments, a 20% excess of the metal amide was used. [c] Only 1 molar equiv of MNH_2 was used. [d] Eight molar equivalents of *n*-butyl iodide.

Solvent systems containing hexamethylphosphoramide (HMPT) are also reported to be efficacious in promoting alkylation relative to proton transfer reactions.[8] We therefore studied the alkylation of 17 (M = Li) in a mixture of 80% THF and 20% HMPT at two different temperatures. The data are summarized in Table II. While this system provides up to 66% of the desired product 20 (after hydrolysis of the O,C-dialkylated product 24), substantial amounts of the C-6 butyl product 21 and dibutylated products 22 and 23 are also produced. Clearly, with lithium enolates, the liquid ammonia–THF mixture is more effective in suppressing enolate equilibration than is HMPT–THF.

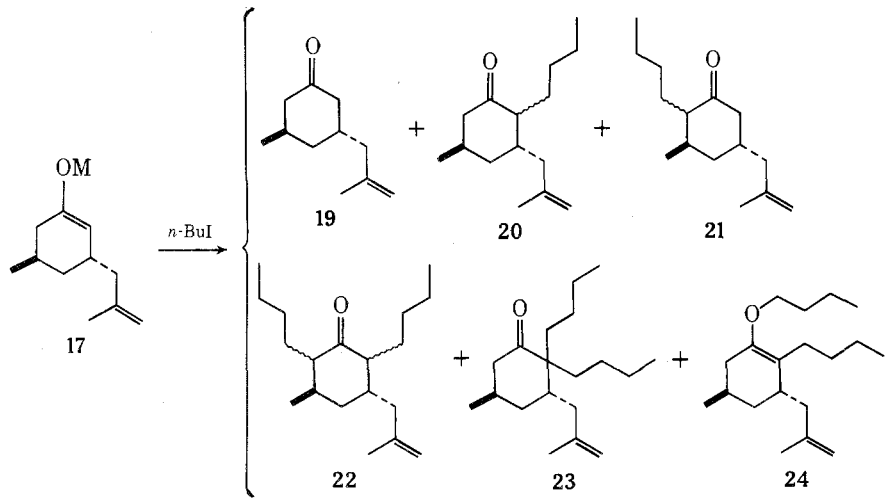


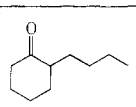
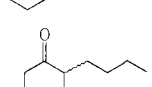
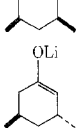
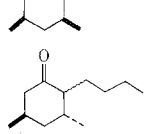
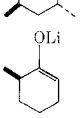
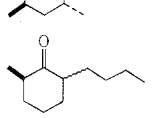
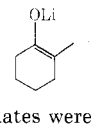
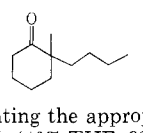
Table II
Butylation of 17 (M = Li) in THF–HMPT[a]

	Product composition, %					
Temp, °C	19	20	21	22	23	24
25	5.9	51.5	14.0	6.9	6.8	14.9
25[b]	5.9	66.4	14.0	6.9	6.8	0
55	10.9	42.5	23.1	5.6	5.6	12.3
55[b]	10.9	54.8	23.1	5.6	5.6	0

[a] The enolate was prepared by treating ether **10** with CH_3Li in THF. HMPT was added (20%), along with 4 molar equiv of *n*-butyl iodide. Alkylations were allowed to proceed for 10 hr. [b] After treating the total product with 5% aqueous HCl for 1 hr.

In order to establish the generality of the procedure, we have also carried out butylations of cyclohexanone enolates **15, 25, 26, 27,** and **28.** In all cases, the C-2 butylated product was obtained in high yield, uncontaminated by C-6 butylated or dibutylated products (Table III). Ketones **30, 31,** and **32** were each obtained as a mixture of C-2 epimers. In each case, the individual epimers were collected by preparative GLC and shown to be interconvertible under basic conditions (see Experimental Section).

Table III
Butylation of Lithium Enolates in NH_3–THF[a]

No.	Enolate	No.	Product	Yield,[b] %
15		29		74
25		30		70
26		31		83
27		32		90
28		33		92

[a] Enolates were prepared by treating the appropriate trimethylsilyl ether with $LiNH_2$ in THF–NH_3 (40% THF, 60% NH_3). A fourfold excess of *n*-butyl iodide was used. [b] Yield of distilled product, often contaminated with a small amount of the appropriate unbutylated ketone.

Experimental Section

Preparation of 1-Trimethylsiloxycyclohexane (4).[6] To a slurry of 10.5 g (0.25 mol) of 56.8% NaH oil dispersion in 200 ml of anhydrous DME was added 9.8 g (0.1 mol) of cyclohexanone. The resulting mixture was refluxed for 3 hr. At the end of this time the reaction mixture was cooled and 15 ml of both trimethylchlorosilane and triethylamine (50% excess of each) was added. After stirring for 15 min at room temperature, the reaction mixture was diluted with 400 ml of pentane and carefully quenched with 5% HCl. After the excess NaH was consumed the organic layer was washed with 200 ml of 5% HCl and 200 ml of 5% $NaHCO_3$ and dried over K_2CO_3. After solvent removal and distillation, 10.8 g (63%) of **4** was collected at 89–90° (20 Torr): ^1H NMR (CCl_4) τ 5.30 (m, 1, vinyl H), 9.85 (s, 9, $SiMe_3$).

Preparation of 1-Trimethylsiloxy-*cis*-3,5-dimethylcyclohexene (7). The silyl enol ether of *cis*-3,5-dimethylcyclohexanone was prepared using the procedure described above. Starting with 5.04 g (40 mmol) of ketone, obtained by the lithium–ammonia reduction of 3,5-dimethylcyclohex-2-en-1-one,[8] and 4.23 g (100 mmol) of 56.8% NaH oil dispersion in 40 ml of DME, 4.45 g (56%) of **7** was obtained, bp 96° (20 Torr). GLC analysis (6 ft × 0.25 in. 15% NPGS, 150°, 120 ml/min) indicated two components: 90% **7** (retention time 6.5 min) and 10% **9** (retention time 7.25 min). The trans isomer **9** arises from a comparable amount of *trans*-3,5-dimethylcyclohexanone produced in the lithium–ammonia reduction: ir (neat) 1665 cm^{-1} (enolate double bond stretching); ^1H NMR (CCl_4) τ 9.87 (s, 9, $SiMe_3$), 9.05 (d, 6, ring Me), 5.30 (broad s, 1, enolate vinyl H). Anal. Calcd for $C_{11}H_{22}SiO$: C, 66.58; H, 11.18. Found: C, 66.49; H, 10.83.

Preparation of 1-Trimethylsiloxy-2-methylcyclohexene (6). A 7:3 mixture of **6** and **5** was prepared in 85% yield from 2-methylcyclohexanone as described above. A 96.5% pure sample of **6,** bp 91–92° (20 Torr), was obtained by spinning band distillation: GLC (6 ft × 0.25 in. 15% NPGS, 100°, 120 ml/min) retention time 3.1 min; ^1H NMR (CCl_4) τ 8.40 (s, 3, vinyl Me), 9.80 (s, 9, $SiMe_3$).

Preparation of 1-Trimethylsiloxy-*trans*-3-methallyl-5-methylcyclohexene (10). To 14.6 g (100 mmol) of freshly distilled di-*n*-butyl sulfide was added with stirring 9.5 g (50 mmol) of purified copper(I) iodide,[9] and the resulting clear orange liquid complex was filtered and stored. A solution of 9.65 g (20 mmol) of this copper(I) iodide complex and 10 ml of dry ether was cooled to −78° under nitrogen and 80 ml (40 mmol) of a 0.5 *M* methallyllithium–ether solution[10] was slowly added. After 1 equiv of methallyllithium–ether solution had been introduced, the reaction mixture was a bright red slurry, which changed to a clear pale yellow solution upon addition of the second equivalent. This resulting lithium dimethallylcuprate solution was allowed to stir for an additional 15 min at −78°, and then a mixture of 1.84 g (16.7 mmol) of 5-methylcyclohex-2-en-1-one (**3**)[11] in 10 ml of dry ether was added dropwise. After the addition was complete, the mixture was stirred for an additional 15 min at −78° and then warmed to 0°. At this point, 6.1 ml of chlorotrimethylsilane was rapidly added, followed immediately by 7.6 ml of freshly distilled triethylamine and 3.8 ml of dry HMPT, and the resulting reaction mixture was stirred at room temperature for 1 hr. At the end of this time, the reaction mixture was diluted with 150 ml of pentane and the liquid layer was decanted from the insoluble copper salts. After this solid material

was washed with more pentane, the combined organic portions were washed successively with two 50-ml portions each of 5% HCl and 5% $NaHCO_3$, and then dried over magnesium sulfate. Solvent removal followed by distillation yielded 3.41 g (86% yield) of product which was collected at 74° (0.9 Torr): ir (neat) 1665 cm^{-1} (enolate double bond stretching); ^1H NMR (CCl_4) τ 9.83 (s, 9, $SiMe_3$), 9.03 (d, 3, ring Me), 8.30 (s, 3, vinyl Me). Anal. Calcd for $C_{14}H_{26}OSi$: C, 70.52; H, 10.99. Found: C, 70.26; H, 11.07.

Preparation of 1-Trimethylsiloxy-3-methylcyclohexene (8). To a cold (0°) slurry of 7.6 g (40 mmol) of copper(I) iodide in 92 ml of anhydrous ether was added 48 ml (72 mmol) of a 1.5 *M* methyllithium–ether solution. After the addition was complete, 1.92 g (20 mmol) of cyclohex-2-en-1-one in 18 ml of ether was added, the resulting mixture was stirred for 15 min at 0°, and 6.1 ml of trimethylchlorosilane, 7.6 ml of triethylamine, and 3.8 ml of HMPT were added. The mixture was then stirred at room temperature for 1 hr, after which time it was diluted with an equal volume of pentane. The resulting mixture was washed successively with two 50-ml portions each of 5% HCl and 5% $NaHCO_3$ and dried over $MgSO_4$. Solvent removal and distillation yielded 2.54 g (69%) of **8**: bp 35° (1.4 Torr); ^1H NMR (CCl_4) τ 5.37 (m, 1, vinyl H), 9.17 (d, 3, ring Me), 9.83 (s, 9, $SiMe_3$); ir (neat) 1660 cm^{-1} (enol ether).

Preparation of 1-Trimethylsiloxy-*trans*-3,5-dimethylcyclohexene (9). This silyl enol ether was prepared from 5-methylcyclohex-2-en-1-one **3**[11] using the above procedure. After distillation, **9** was collected in a yield of 70.5%, over a range of 43–44° (2.0 Torr). GLC analysis (6 ft × 0.25 in. 15% NPGS, 150°, 120 ml/min) indicated that 93% of the product was the desired trans material **9**, and that 7% of the cis isomer **7** was present: ir (neat) 1665 cm^{-1} (enolate double bond stretching); ^1H NMR (CCl_4) τ 9.85 (s, 9, $SiMe_3$), 9.03 (d, 6, ring Me), 5.33 (broad d, 1, enolate vinyl H). Anal. Calcd for $C_{11}H_{22}SiO$: C, 66.58; H, 11.18. Found: C, 66.55; H, 11.20.

Preparation of 2-Butyl-3-methallyl-5-methylcyclohexanone (20). A. A solution of 0.6 g (2.5 mmol) of **10** in 10 ml of dry tetrahydrofuran was slowly added to a slurry of lithium amide, formed from 0.0175 g (2.5 mg-atoms) of lithium, a crystal of ferric nitrate, and 13 ml of anhydrous ammonia. After stirring for 30 min at the reflux temperature of ammonia, a solution of 1.84 g (10 mmol) of butyl iodide in 5 ml of THF was added rapidly and the resulting mixture was stirred for 6 hr. At the end of this time solid ammonium chloride was added to quench any unalkylated enolate and the ammonia was allowed to evaporate. The resulting material was dissolved in 100 ml of ether and washed with two 50-ml portions of water and 50 ml of saturated NaCl solution and dried over magnesium sulfate. Solvent removal yielded 1.0 g of liquid. GLC analysis (6 ft × 0.25 in. 15% NPGS, 200°, 120 ml/min) indicated that two ketone components were present in addition to excess butyl iodide: 5.5% **19** (retention time 4.7 min) and 94.5% **20** (retention time 8.7 min). The above assignments were based on mass spectra,[12] ir, and ^1H NMR data. Excess butyl iodide was removed at reduced pressure to give 0.535 g of a mixture of **19** and **20**. Using the above composition, this corresponds to a 91% yield of **20**. An analytical sample of **20** was obtained by preparative glpc using the conditions described above: ir (neat) 1710 (carbonyl stretching), 892 cm^{-1} (methallyl double bond); ^1H NMR (CCl_4) τ 9.03 (d, 6, ring and butyl Me), 8.33 (s, 3, vinyl Me), 5.33 (d, 2, vinyl H). Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.09; H, 11.60.

B. The above reaction was repeated, using $NaNH_2$, rather than $LiNH_2$, to form the enolate. The enolate was prepared from 69 mg (3.0 mg-atoms) of sodium. Silyl ether **10** (600 mg, 2.5 mmol) was added, followed by 1.84 g (10 mmol) of butyl iodide. After 2 hr, the reaction was processed as above to obtain 470 mg of a ketone mixture, which was assigned (GLC) the following composition: 33.8% **19**, 34.6% **20**, and 31.6% **21** (equal amounts of two epimers). The two epimers of **21** were collected separately and shown to be interconvertible in a KOH–methanol solution.

C. 1. The butylation described above was repeated using 0.117 g (3.0 mg-atoms) of potassium. A yellow oil (615 mg) was isolated, which, upon GLC analysis (6 ft × 0.25 in. 15% NPGS column, 200°, 120 ml/min), was found to consist of seven components: 7.7% **19** (retention time 4.8 min), 15.8% **24** (retention time 6.0 min), 49.0% **20** (retention time 8.7 min), 13.7% **21** (both epimers in equal amounts with retention times of 9.8 and 11.0 min), 5.5% **22** (retention time 14.2 min), and 8.3% **23** (retention time 16.4 min). The two epimers of **21** were collected separately and shown to be interconvertible in a KOH–methanol solution.

2. The foregoing procedure was repeated using only 97.7 mg (2.5 mg-atoms) of potassium. After formation of the potassium enolate, 3.68 g (20 mmol) of butyl iodide was added. Upon normal work-up, there was obtained 490 mg of material which was shown by GLC to consist of 12.2% **19**, 55.5% **20**, and 32.2% **21**. No dialkylated material was detected.

D. 1. To a solution of 0.6 g (2.5 mmol) of **10** in 10 ml of anhydrous tetrahydrofuran at room temperature was added 1.25 ml (2.5 mmol) of a 2.0 *M* methyllithium–ether solution. The reaction was checked periodically by TLC (10% ether–hexane), which indicated that all of **10** had been converted to the lithium enolate **17** after 2 hr. At this point 1.84 g (10 mmol) of butyl iodide dissolved in 3 ml of anhydrous HMPT was added all at once and the resulting mixture was allowed to stir at room temperature for 10 hr. At the end of this time, the reaction mixture was added to a saturated NH_4Cl–water solution and extracted with two 100-ml portions of ether. The combined ether layers were washed with 100 ml of water and dried over $MgSO_4$. After solvent removal the resulting 600 mg of orange liquid was analyzed by GLC (6 ft × 0.25 in. 15% NPGS, 200°, 120 ml/min) and found to have the following composition: 5.9% **19**, 14.9% **24**, 51.5% **20**, 14.0% **21**, 6.9% **22**, and 6.8% **23**. After treatment with 5% HCl for 1 hr, all of **24** was converted to **20**, bringing its total up to 66.4%.

2. The foregoing experiment was repeated, only the enolate was allowed to alkylate for 10 hr at 55°. The GLC composition was found to be 10.9% **19**, 12.3% **24**, 42.5% **20**, 23.1% **21**, 5.6% **22**, and 5.6% **23**. Treatment with HCl increased the proportion of **20** to 54.8%.

Preparation of 2-Butylcyclohexanone (29). The silyl enol ether **4** (1.7 g, 10 mmol) was converted to its lithium enolate with a solution of $LiNH_2$ prepared from 84.8 mg (12 mg-atoms) of lithium and alkylated with butyl iodide using the same procedure developed for **20**, part A. The alkylation was allowed to proceed for only 2 hr. The product was distilled to obtain **29** in a yield of 74%. The product was collected at 65° (1.8 Torr) [lit. 70° (2.0 Torr)]. No dialkylated or unalkylated ketones were isolated. The structure of the product was confirmed by its mass spectrum:[13] major mass spectral peaks at *m/e* 154 (M^+), 98 ($M^+ - C_4H_8$, McLafferty), 70 ($M^+ - C_4H_8 - C_2H_4$), 55 ($M^+ - C_7H_{15}$, α cleavage); ir (neat) 1715 cm^{-1} (carbonyl); ^1H NMR (CCl_4) τ 9.06 (t, 3, butyl Me).

Preparation of 2-Butyl-*cis*-3,5-dimethylcyclohexanone (30). Compound **7** (1.0 g, 5 mmol) was converted into its lithium enolate (41.8 mg of lithium, 6 mg-atoms) and alkylated with butyl iodide as described in the foregoing preparation of **29**. The resulting product was distilled to obtain a mixture of unalkylated and butylated ketone in a ratio of 8:92. The butylated fraction was collected at 69° (3.0 Torr) in a yield of 70%. GLC analysis of this fraction (6 ft × 0.25 in. 15% NPGS, 150°, 120 ml/min) revealed the presence of three components: 90% **30** (two epimers, retention times 12.5 and 13.8 min) and 10% **31** (retention time 15.6 min). An analytical sample was obtained by preparative GLC using the above described conditions: ir (neat) 1700 cm^{-1} (carbonyl); ^1H NMR (CCl_4) τ 9.15 (d, 9, Me); major mass spectral peaks[13] at *m/e* 182 (M^+), 126 ($M^+ - C_4H_8$, McLafferty), 111 ($M^+ - C_4H_8 - CH_3$), 84 ($M^+ - C_4H_8 - C_3H_6$), 69 ($M^+ - C_8H_{17}$, α cleavage), 55. Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.12. Found: C, 79.13; H, 12.07.

The two epimers of **30** were collected separately and equilibrated using KOH–MeOH solution. At equilibrium the two epimers were present in a ratio of 89 (retention time 12.5 min) to 11 (retention time 13.8 min).

Preparation of 2-Butyl-*trans*-3,5-dimethylcyclohexanone (31). The silyl enol ether **9** was alkylated as described above, using 1.0 g (6 mmol) of **9**, 41.8 mg (6 mg-atoms) of lithium, and 3.68 g (20 mmol) of butyl iodide. The product was distilled and two fractions were collected, one boiling at 40° (0.5 Torr) and the second at 66° (0.5 Torr). The first fraction weighed 83 mg and was identified as *trans*-3,5-dimethylcyclohexanone by its mass spectrum. GLC analysis (6 ft × 0.25 in. 15% NPGS, 150°, 120 ml/min) of the second fraction (750 mg, 83% yield) revealed the presence of three components: 5.6% **30** (retention time 12.0 min) and 94.4% **31** (two epimers, retention time 14.5 and 16.0 min). An analytical sample was obtained by preparative GLC: ir (neat) 1690 cm^{-1} (carbonyl); ^1H NMR (CCl_4) τ 9.16 (d, 9, Me); major mass spectral peaks at *m/e* 182 (M^+), 126 ($M^+ - C_4H_8$, McLafferty), 111 ($M^+ - C_4H_8 - CH_3$), 84 ($M^+ - C_4H_8 - C_3H_6$), 69 ($M^+ - C_8H_{17}$, α cleavage), 55. Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.12. Found: C, 79.23; H, 12.19. The epimer percentages at equilibrium were obtained as before. This ratio was found to be 49.8 (retention time 14.5 min) to 50.2 (retention time 16.0 min).

Preparation of 2-Butyl-6-methylcyclohexanone (32). A 0.46-g (2.5 mmol) sample of **5**[4] was converted to its lithium enolate with a solution of $LiNH_2$ prepared from 17.5 mg (2.5 mg-atoms) of lithium and then alkylated with 10 mmol of butyl iodide, using the

procedure described above. After solvent and excess butyl iodide removal the resulting ketone mixture (90% recovery) was analyzed by GLC (6 ft × 0.25 in. 15% NPGS, 175°, 120 ml/min) and found to consist of 17% unalkylated ketone (retention time 2.5 min) and 83% **32** (two interconvertible epimers, retention times 8.75 and 9.3 min). Product identification was made from comparative GLC with **33** and mass spectral results.[13]

Preparation of 2-Butyl-2-methylcyclohexanone 33. The silyl enol ether **6**[4] was butylated exactly as described above. The product ketones were obtained in a yield of 92% and found to have the following compositions by GLC: 2.5% unalkylated ketone (retention time 3.8 min) and 97.5% **33** (retention time 9.5 min).

Preparation of 2-(2-Cyanoethyl)cyclohexanone (16). Using the procedure developed for **20**, part A, 1.7 g (10 mmol) of **4** was converted to its lithium enolate with a $LiNH_2$ solution prepared from 91.0 mg (13 mg-atoms) of lithium and then treated with 5.35 g (40 mmol) of 3-bromopropionitrile. After solvent removal, the resulting product was distilled, yielding 200 mg of cyclohexanone and 500 mg of **16** (48%), boiling at 118° (1.8 Torr): ir (neat) 1700 (carbonyl), 2230 cm^{-1} (-C≡N).

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Registry No.—**3**, 7214-50-8; **4**, 6651-36-1; **5**, 19980-33-7; **6**, 19980-35-9; **7**, 55373-57-4; **8**, 55373-58-5; **9**, 55373-59-6; **10**, 55373-44-9; **15**, 21300-30-1; **16**, 4594-78-9; **20**, 55373-32-5; **25**, 55373-60-9; **26**, 55373-61-0; **27**, 13670-83-2; **28**, 13670-84-3; **29**, 1126-18-7; **30** epimer 1, 55373-62-1; **30** epimer 2, 55373-63-2; **31** epimer 1, 55373-64-3; **31** epimer 2, 55373-65-4; *cis*-3,5-dimethylcyclohexanone, 7214-52-0; *trans*-3,5-dimethylcyclohexanone, 7214-49-5; lithium dimethallylcuprate, 55373-66-5; chlorotrimethylsilane, 75-77-4; lithium dimethylcuprate, 15681-48-8; cyclohex-2-en-1-one, 930-68-7; lithium amide, 7782-89-0; butyl iodide, 542-69-8; sodium amide, 7782-92-5; potassium amide, 17242-52-3; 3-bromopropionitrile, 2417-90-5.

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Mass Spectra of Some 2,3,5-Trialkylcyclohexanones

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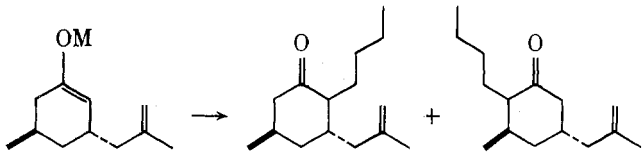
Mass spectra have been obtained for several pairs of isomeric 2,3,5-trisubstituted cyclohexanones. In all cases, the principle mode of fragmentation involves McLafferty rearrangement, followed by decomposition of the initial McLafferty ion. When there is an allylic group at C-3, the initial McLafferty ion simply loses allyl radical. When the allylic group is at C-5, the base peak corresponds to loss of the allylic substituent plus two hydrogens. A mechanism is proposed to rationalize the results.

In the accompanying paper, we report a study of the site-specific alkylation of enolate **1** and related enolates.[1] Under some conditions, enolate equilibration occurs and isomers **2** and **3** are produced. In searching for a method to assign

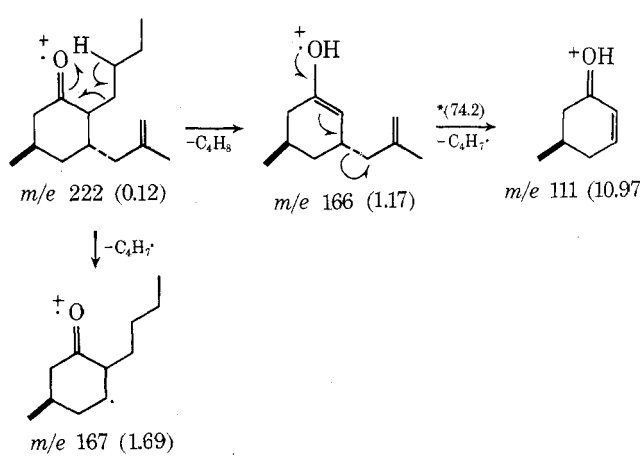


1 **2** **3**

structures to such isomers, we examined the mass spectra of **2** and **3**. We were gratified to find that the two isomers differ markedly in their fragmentation patterns, and that structures may be readily assigned on this basis.

The 70-eV mass spectra of **2** and **3** are plotted in Figures 1 and 2. The base peak in the spectrum of **2** is *m/e* 111, at 10.97% of the total ion current (% TIC). The *m/e* 109 peak has an intensity of 3.19% TIC. For isomer **3**, the relative intensities of the *m/e* 109 and 111 peaks is reversed, with *m/e* 111 being 1.50% TIC and *m/e* 109 being 10.77% TIC. In addition to the *m/e* 109 and 111 fragments, both isomers show significant peaks at *m/e* 167 (loss of methallyl radical) and *m/e* 166 (McLafferty rearrangement). A rationale

Scheme I



for the principal fragmentations of compound **2** is outlined in Scheme I. A high-resolution spectrum of compound **2** confirmed that the *m/e* 111 fragment has the composition $C_7H_{11}O$. That this ion arises directly from a *m/e* 166 ion is shown by a significant metastable peak at *m/e* 74.2 (calcd, *m/e* 74.22).