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).

Acknowledgment. The authors express their gratitude to the National Science Foundation for support of this research under Grant GP 31321X.

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.

References and Notes

(1) G. H. Posner, *Org. React.*, **19**, 1 (1972).
(2) (a) G. Stork, *Pure Appl. Chem.*, **17**, 383 (1968); (b) R. A. Kretchmer and W. M. Schafter, *J. Org. Chem.*, **38**, 95 (1973); (c) P. A. Grieco and R. Finkelhor, *ibid.*, **38**, 2100 (1973); (d) J. W. Patterson, Jr., and J. H. Fried, *ibid.*, **39**, 2506 (1974); (e) R. K. Boeckman, Jr., *ibid.*, **38**, 4450 (1973); (f) R. M. Coates and L. O. Sandefur, *ibid.*, **39**, 275 (1974); (g) G. H. Posner, J. F. Sterling, C. E. Whitten, C. M. Lentz, and D. J. Brunelle, *J. Am. Chem. Soc.*, **97**, 107 (1975).
(3) H. O. House and W. F. Fischer, *J. Org. Chem.*, **33**, 949 (1968).
(4) G. Stork and P. F. Hudrlik, *J. Am. Chem. Soc.*, **90**, 4464 (1968).
(5) This procedure was developed independently by Dr. John W. Patterson, Syntex Research Laboratories, Palo Alto, Calif., ref 2d.
(6) G. Stork and P. F. Hudrlik, *J. Am. Chem. Soc.*, **90**, 4462 (1968).
(7) This ether has been prepared previously, although full experimental details have not yet been published: R. K. Boeckman, Jr., *J. Am. Chem. Soc.*, **96**, 6179 (1974).
(8) G. Stork and S. D. Darling, *J. Am. Chem. Soc.*, **86**, 1761 (1964).
(9) G. B. Kauffman and L. A. Teter, *Inorg. Synth.*, **7**, 9 (1963).
(10) D. Seyferth and M. A. Weiner, *J. Org. Chem.*, **26**, 4797 (1961); G. M. Whitesides, W. F. Fischer, J. S. Filippo, R. W. Bashe, and H. O. House, *J. Am. Chem. Soc.*, **91**, 4871 (1969).
(11) C. H. Heathcock and J. E. Ellis, *Chem. Commun.*, **1474** (1971).
(12) The mass spectra of these compounds and their interpretation are discussed in the following paper in this issue: E. S. Binkley and C. H. Heathcock.
(13) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds", Holden-Day, San Francisco, Calif., 1967, Chapter 3, pp. 146–150, 158–159.

Mass Spectra of Some 2,3,5-Trialkylcyclohexanones

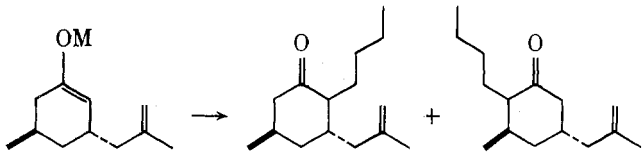
Edward S. Binkley and Clayton H. Heathcock*

Department of Chemistry, University of California, Berkeley, California 94720

Received January 15, 1975

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

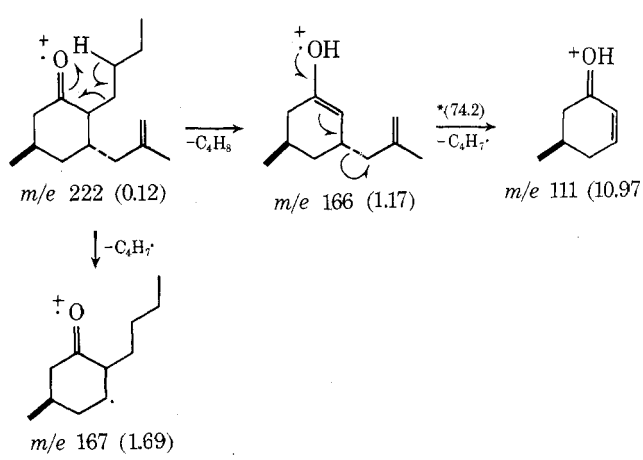


1 **2** **3**

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).

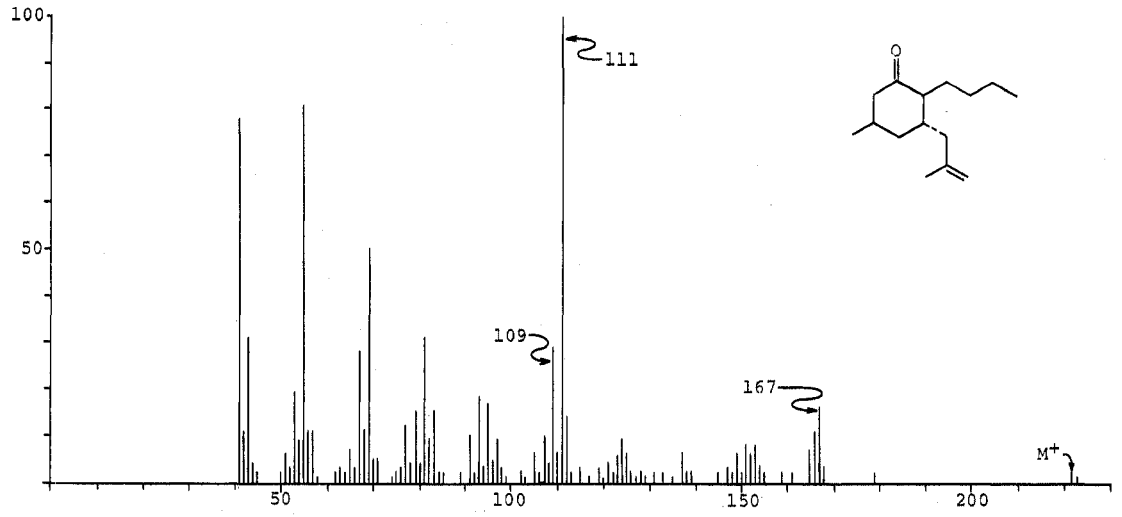


Figure 1. Mass spectrum of compound **2.**

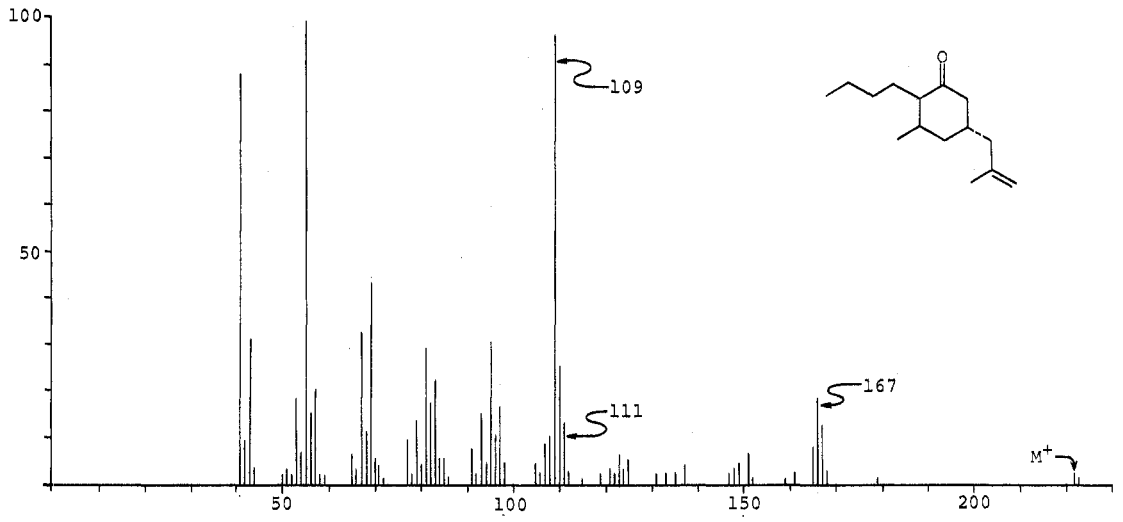
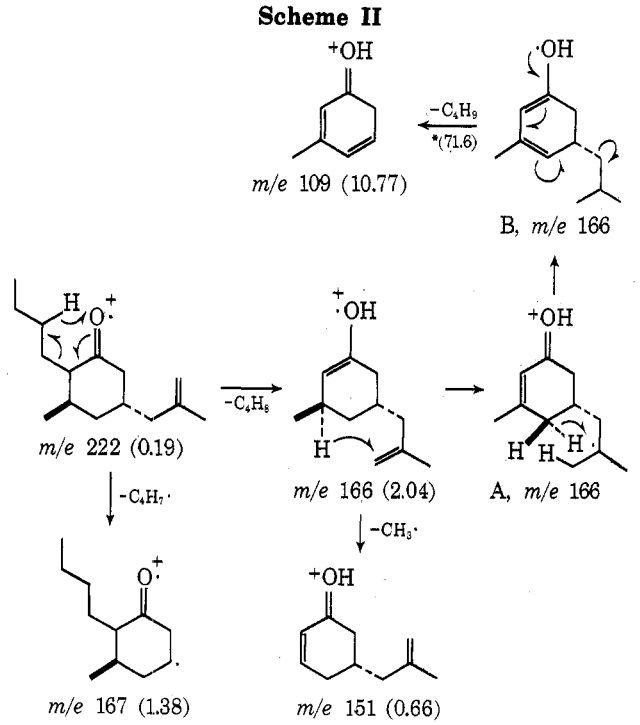


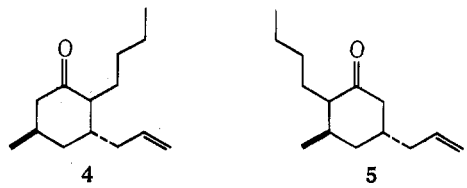
Figure 2. Mass spectrum of compound **3.**

For isomer **3** (Scheme II), the principal primary fragmentations are again loss of the methallyl chain (1.38% TIC) and McLafferty rearrangement (2.04% TIC). In this case, however, the McLafferty ion radical (*m/e* 166) cannot lose methallyl radical to give a stable oxonium ion, analogous to the *m/e* 166 → 111 fragmentation in Scheme I. Loss of methyl radical gives such an oxonium ion (*m/e* 151), but this fragmentation is not significant, probably because of the relatively high energy of CH_3·. Instead, we propose the path outlined in Scheme II. Transfer of the tertiary allylic hydrogen to the side-chain double bond gives a relatively stable oxonium ion A, which transfers a second hydrogen to give ion B. Finally, loss of isobutyl radical from ion B gives the stabilized oxonium ion with *m/e* 109. The *m/e* 109 fragment was shown to have the composition C_7H_9O by high-resolution studies. The observed metastable peak at *m/e* 71.6 (calcd, *m/e* 71.57) confirms the hypothesis that the *m/e* 109 ion arises directly from a fragment with *m/e* 166. Metastable ions corresponding to alternate origins of the *m/e* 109 fragment, which involve loss of the methallyl side chain and two hydrogens from the McLafferty ion, are not observed.

Scheme II

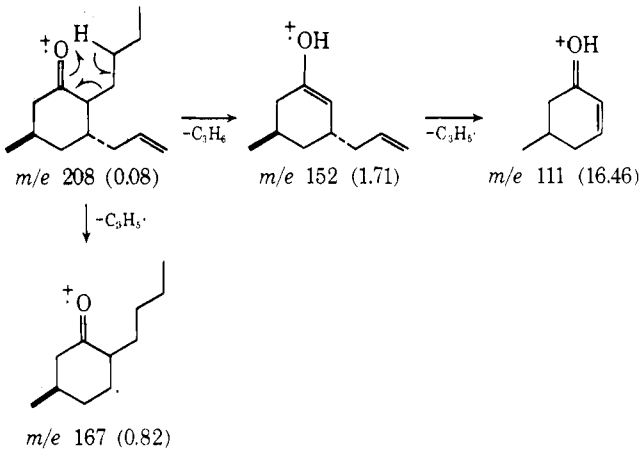


The generality of this fragmentation scheme is shown by the spectra of isomers **4** and **5**, in which the base peaks also

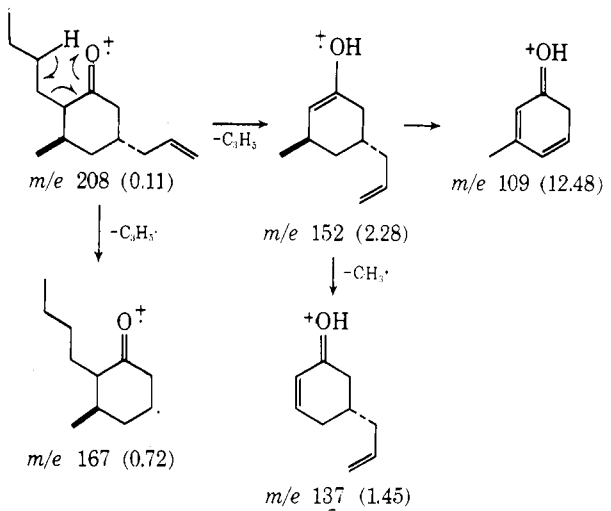


4 **5**

Scheme III

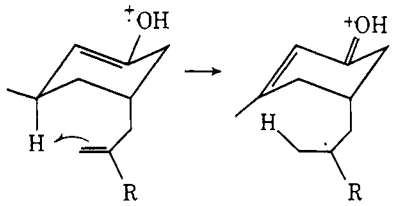


Scheme IV

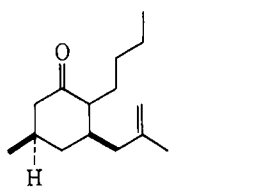


occur at *m/e* 111 and 109, respectively (see paragraph at end of paper regarding supplementary material). Principal fragmentations for the two isomers are shown in Schemes III and IV. Again, the reversal of the *m/e* 111 and 109 intensities is observed. Additionally, the McLafferty ion derived from **5** shows a greater tendency to lose CH_3· to give the *m/e* 137 ion (1.45% TIC). In the case of isomer **4**, the *m/e* 137 ion has only about one-third this intensity (0.45% TIC).

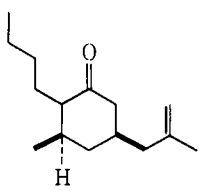
The intramolecular hydrogen transfers which are proposed to be involved in transforming the initial McLafferty ions into the *m/e* 109 ion would require that the allyl substituent be cis to the tertiary allylic hydrogen. To check



this hypothesis, we prepared isomers **6** and **7**, in which the methallyl side chain is trans to the relevent hydrogen. Isomer **6** behaves as expected, with the *m/e* 111 peak being 12.96% TIC, and the *m/e* 109 peak being only 3.68% TIC. However, we were surprised to find that the base peak in the spectrum of **7** is still *m/e* 109 (10.78% TIC), while the *m/e* 151 peak, which would result from loss of CH_3· from the McLafferty ion, is only 0.84% TIC (see paragraph at end of paper regarding supplementary material). These results are understandable in terms of the fragmentation

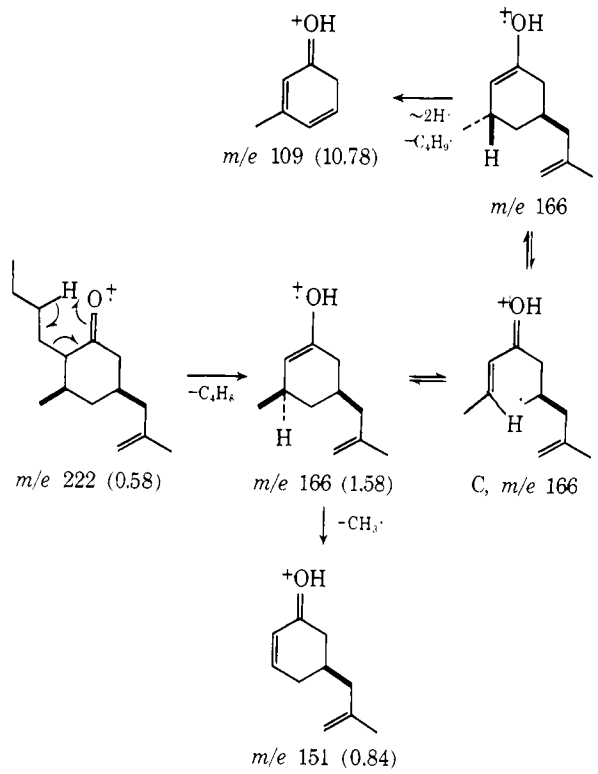


6



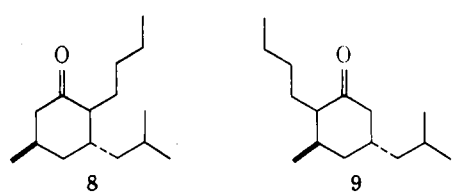
7

Scheme V



pathway in Scheme V. In other words, the cis and trans isomers may equilibrate in the McLafferty ion *via* ring-opened radical cation C.

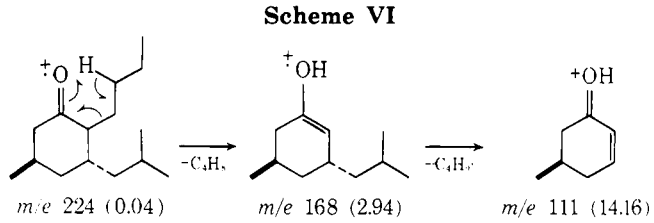
Compounds **8** and **9**, in which the methallyl group has been replaced by an isobutyl group, were prepared to test



8 **9**

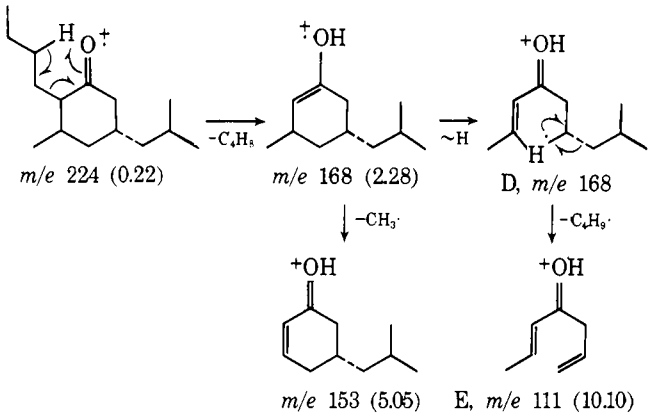
our hypothesis that intramolecular transfer of two hydrogens to the double bond is involved in the genesis of the *m/e* 109 fragments. As expected on the basis of this hypothesis, neither isomer gives a substantial fragment with *m/e* 109. The principal fragmentation path of **8** is McLafferty rearrangement, followed by expulsion of the isobutyl

Scheme VI



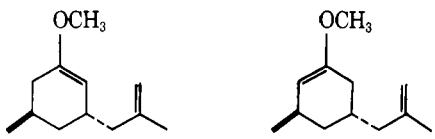
group to give the *m/e* 111 oxonium ion (Scheme VI, see paragraph at end of paper regarding supplementary mate-

Scheme VII



rial). For isomer **9** (Scheme VII), the McLafferty ion loses $CH_3\cdot$ to a significant extent, giving ion *m/e* 153 (5.05% TIC). The corresponding ion in the spectrum of **8** has an intensity of only 0.27% TIC. The *m/e* 111 peak in the spectrum of **9** is still substantial (10.10% TIC), and could arise via the ring-opened radical cation D. Expulsion of isobutyl radical would yield oxonium ion E.

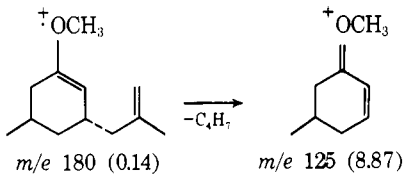
To further confirm the idea that the position of the double bond in the initial McLafferty ion governs the subsequent decomposition of the ion, the isomeric methyl enol



10 **11**

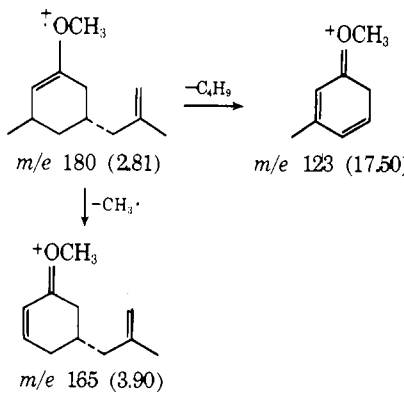
ethers **10** and **11** were prepared. As expected, the base peak in the spectrum of **10** has *m/e* 125, Scheme VIII. The M −

Scheme VIII



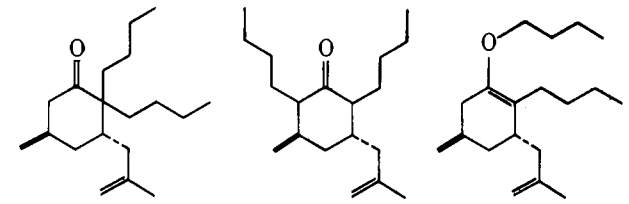
15 peak (*m/e* 165) is very weak, 0.10% TIC. For isomer **11**, the base peak is *m/e* 123, again corresponding to loss of methallyl and H_2 (Scheme IX). Additionally, the M − 15

Scheme IX



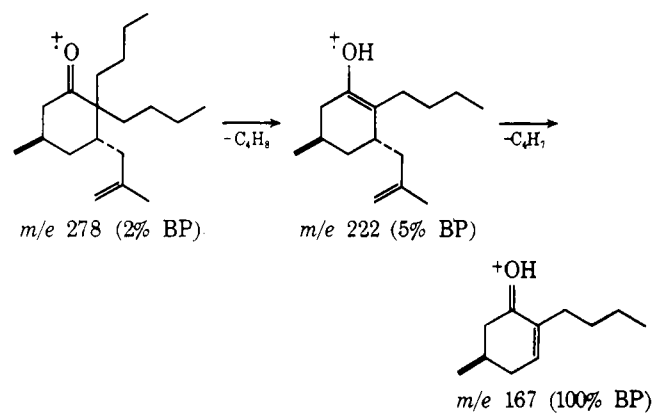
peak is now significant (3.90% TIC). (See paragraph at end of paper regarding supplementary material).

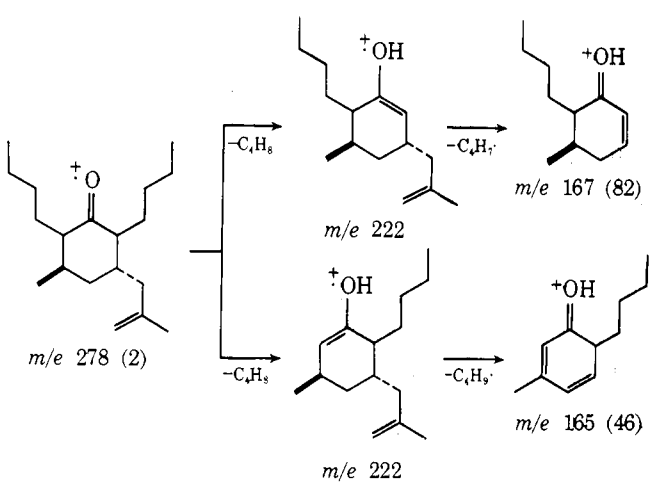
The fragmentation patterns which we have observed have been useful in assigning structure to some more highly alkylated materials prepared in our alkylation studies. For example, butylation of enolate **1**, when M = Na or K, gives three butylated products, **12**, **13**, and **14**, in addition to **2**



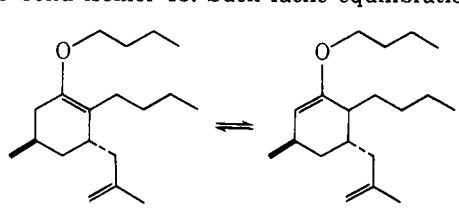
12 **13** **14**

and **3**. The structures of the three isomers were assigned on the basis of their mass spectra. The base peak in the spectrum of isomer **12** has *m/e* 167, corresponding to the fragmentation shown. Isomer **13** can undergo McLafferty rearrangement in either of two ways. Consequently, its spectrum shows ions which *m/e* (rel intensity) 167 (82) and 165 (46).





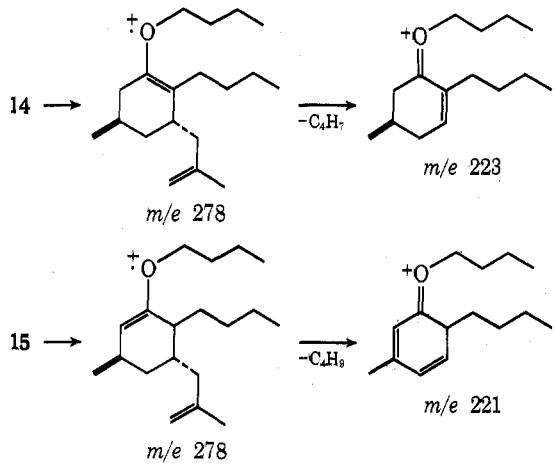
From its ir spectrum isomer **14** was suspected to be an enol ether with a tetrasubstituted double bond (ν 1675 cm^{-1}).[2] However, the double bond equilibrates upon GLC collection, so that the analytically pure material which we isolated by this method was actually a mixture of **14** and its double bond isomer **15**. Such facile equilibration was not



14 **15**

unexpected, since we had also encountered it with the isomeric enol ethers **10** and **11**. Correspondingly, the mass spectrum of the mixture shows fragments with *m/e* 121,

presumably deriving from **15**, and *m/e* 123, presumably deriving from **14**.



Experimental Section

Mass spectra were determined by Sherri Ogden on an MS-12 (low resolution) or CEC 21-110B (high resolution) instrument. Data were acquired with the Incos data acquisition system, Incos Corp., Berkeley, Calif.

Alkylation of Enolate 1. Isolation of Compounds 2, 3, 12, 13, and 14. The potassium enolate 1 (M = K) was alkylated as described in the accompanying communication.[1] Upon work-up, a mixture of butylated ketones was isolated which was shown by GLC (6 ft × 0.25 in. 15% NPGS, 200°, 120 ml/min) to have the following composition: 7.7% unalkylated ketone, 49.0% **2**, 13.7% **3**, 8.3% **12**, 5.5% **13**, and 15.8% **14**. Samples for mass spectral analysis were obtained by preparative GLC using the conditions described above. See Figures 1 and 2 for the spectra of **2** and **3**.

A sample of **14** was examined by ir as well as mass spectroscopy, ir (neat) 1675 cm^{-1} (enol ether). The sample of **14** was converted exclusively to **2** by treatment with 5% HCl.

Preparation of 2-Butyl-*trans*-3-allyl-5-methylcyclohexanone (4) and 2-Butyl-*trans*-3-methyl-5-allylcyclohexanone (5). Using conditions described elsewhere,[1,3] 48 mmol of a 0.98 *M* solution of allyllithium in ether, obtained by treatment of commercial tetraallyltin (Alfa-Ventron, Inc.) with phenyllithium,[4] was combined with 11.6 g (24 mmol) of copper iodide in 40 ml of anhydrous ether at −78° in an inert atmosphere to produce lithium diallylcuprate. This cuprate was in turn combined with 2.2 g (20 mmol) of 5-methylcyclohex-2-en-1-one, followed after 30 min by 6.1 ml of trimethylchlorosilane, 7.6 ml of triethylamine, and 3.8 ml of HMPT. After work-up and distillation, 3.0 g (76%) of 1-trimethylsiloxy-*trans*-3-allyl-5-methylcyclohex-1-ene was obtained: bp 58–60°C (1.0 Torr); ir (neat) 1660 cm^{-1} (enol ether); ^1H NMR (CCl_4) τ 4.33 (m, 1, vinyl H), 4.99 (m, 1, enol ether vinyl H), 5.30 (m, 2, vinyl H), 9.07 (d, 3, ring Me), 9.85 (s, 9, $SiMe_3$). Anal. Calcd for $C_{13}H_{24}OSi$: C, 69.57; H, 10.78. Found: C, 69.50; H, 10.96.

A solution of 560 mg (2.5 mmol) of the above silyl enol ether dissolved in 10 ml of dry tetrahydrofuran was added dropwise to a slurry of potassium amide prepared from 98 mg (2.5 mg-atoms) of potassium metal and 13 ml of ammonia. Following the procedure described earlier,[1] the resulting enolate was treated with 1.84 g (10 mmol) of butyl iodide to yield 550 mg of a ketone mixture upon work-up. GLC analysis (6 ft × 0.25 in. 15% NPGS, 225°, 120 ml/min) indicated that this mixture had the following composition: 7.2% unalkylated ketone (retention time 4.5 min), 54.0% **4** (retention time 7.2 min), 29.4% **5** (both epimers in equal amounts with retention times of 7.8 and 8.7 min), and 9.4% di-C-alkylated ketone (two compounds in equal amounts with retention times of 10.7 and 12.2 min). Samples for mass spectral analysis were again obtained by preparative GLC using the conditions described above. See Figures 3 and 4 (supplementary material) for the spectra of **4** and **5**.

Preparation of 2-Butyl-*cis*-3-methallyl-5-methylcyclohexanone (6) and 2-Butyl-*cis*-3-methyl-5-methallylcyclohexanone (7). Following a previously reported procedure,[5] a sample of 3-methallyl-5-methylcyclohex-2-en-1-one was prepared by treating methallylmagnesium chloride with 3-isobutoxy-5-methylcyclohex-2-en-1-one,[6] followed by hydrolysis of the resulting unsaturated alcohol with dilute HCl. A solution of 1.64 g (10 mmol) of the above unsaturated ketone, 0.7412 g (10 mmol) of *tert*-butyl alcohol, 4.0 ml of dry HMPT, and 5 ml of anhydrous ether was added dropwise to a dark blue solution of 0.153 g (22 mg-atoms) of lithium metal dissolved in 75 ml of anhydrous ammonia. After the addition was complete, the resulting mixture was stirred at the reflux temperature of ammonia for an additional 30 min. At the end of this time, the ammonia was allowed to evaporate under anhydrous conditions. The last traces of ammonia were removed by blowing nitrogen through the reaction flask for 2 hr. The resulting product was then dissolved in 50 ml of ether and treated with 6.1 ml of trimethylchlorosilane and 7.6 ml of triethylamine. The resulting mixture was stirred for 1 hr at room temperature and then diluted with 100 ml of pentane. This solution was 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 1.49 g (62.5% yield) of product which was identified as 1-trimethylsiloxy-*cis*-3-methallyl-5-methylcyclohex-1-ene: bp 73–74° (0.09 Torr); ir (neat) 1665 cm^{-1} (enol ether); ^1H NMR (CCl_4) τ 5.43 (m, 3, enol ether and methallyl vinyl H's), 8.36 (s, 3, vinyl Me), 9.10 (d, 3, ring Me), 9.87 (s, 9, silyl Me). Anal. Calcd for $C_{14}H_{26}OSi$: C, 70.52; H, 10.99. Found: C, 70.56; H, 10.91.

The $\Delta^{1,2}$ potassium enolate of *cis*-3-methallyl-5-methylcyclohexanone, prepared by treating 0.595 g (2.5 mmol) of the above silyl enol ether with 1 equiv of potassium amide, was combined with 1.84 g (10 mmol) of butyl iodide.[1] After work-up and solvent removal 500 mg of a ketone mixture was isolated and shown by GLC (6 ft × 0.25 in. 15% NPGS, 200°, 120 ml/min) to have the following composition: 31.3% unalkylated ketone (retention time 3.3 min), 30.5% **6** (retention time 5.5 min), 33.6% **7** (retention time 6.7 min), and 4.6% di-C-alkylated ketone (retention time 10.0 min). Samples for mass spectral analysis were prepared by preparative GLC. See Figures 5 and 6 (supplementary material) for the spectra of **6** and **7**.

Preparation of 2-Butyl-*trans*-3-isobutyl-5-methylcyclohexanone (8) and 2-Butyl-*trans*-3-methyl-5-isobutylcyclohexanone (9).[7] A solution of 5.5 g (60 mmol) of isobutyl chloride dissolved in 12 ml of anhydrous ether was added dropwise to 0.975 g (40 mg-atoms) of magnesium turnings covered with 25 ml of ether. The reaction was initiated with a crystal of iodine after a few drops of the halide solution had been added. Once the Grignard had begun to form, the addition was continued over a period of 45 min at room temperature, and the resulting mixture was allowed to stir for an additional 12 hr, during which time all of the magnesium was consumed. The resulting solution was then diluted with 25 ml of ether, cooled to 0°, and treated with 0.40 g of copper(I) iodide. To the resulting dark black mixture was slowly added a solution of 2.2 g (20 mmol) of 5-methylcyclohex-2-en-1-one[8] and 15 ml of ether. After the addition was complete, the resulting solution was stirred for an additional 1 hr at 0°. At the end of this time, 6.1 ml of trimethylchlorosilane, 7.6 ml of triethylamine, and 3.8 ml of HMPT was added successively and the resulting mixture was stirred for 1 hr at room temperature. This solution was then diluted with 100 ml of pentane, washed successively with two 50-ml portions each of 5% HCl and 5% $NaHCO_3$, and dried over magnesium sulfate. After solvent removal, the crude product was distilled, yielding 3.4 g (71%) of 1-trimethylsiloxy-*trans*-3-isobutyl-5-methylcyclohex-1-ene: bp 71° (0.9 Torr); ir (neat) 1665 cm^{-1} (enol ether); ^1H NMR (CCl_4) τ 5.30 (d, 1, vinyl H), 9.10 (m, 9, ring and isobutyl Me's), 9.83 (s, 9, silyl Me). Anal. Calcd for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74. Found: C, 70.34; H, 11.38.

The above silyl ether (0.60 g, 2.5 mmol) was then converted to its potassium enolate with 1 equiv of potassium amide and treated with 1.84 g (10 mmol) of butyl iodide. Upon work-up and solvent removal, 500 mg of a ketone mixture was isolated, which was examined by GLC (6 ft × 0.25 in. 15% NPGS, 200°, 120 ml/min) and found to have the following composition: 7.2% unalkylated ketone (retention time 2.5 min), 53.4% **8** (retention time 4.5 min), 32.2% **9** (two epimers in a ratio of 3:2, retention times of 5.1 and 5.7 min), and 7.2% di-C-alkylated ketone (retention time 7.5 min). Spectral samples were obtained by preparative GLC (6 ft × 0.25 in. 15% NPGS, 175°, 120 ml/min). See Figures 7 and 8 (supplementary material) for the mass spectra of **8** and **9**.

Preparation of 1-Methoxy-*trans*-3-methallyl-5-methylcyclohex-1-ene (10) and 1-Methoxy-*trans*-3-methyl-5-methallylcyclohex-1-ene (11). A solution of 1-trimethylsiloxy-*trans*-3-methallyl-5-methylcyclohex-1-ene[1] (0.595 g, 2.5 mmol) in 10 ml of anhydrous THF was treated with 2.5 mmol of a methyllithium–ether solution for 2 hr at room temperature. The resulting lithium enolate solution was transferred by syringe to a clean, dry dropping funnel and added dropwise to a slurry of 1.03 g (5.0 mmol) of trimethyloxonium hexafluorophosphate (Alfa-Ventron, Inc.) in 5 ml of ether. After stirring for 15 min at room temperature, the so-

lution was diluted with 50 ml of ether and washed successively with 50 ml of water and 50 ml of saturated NaCl solution. After drying over potassium carbonate, the solvent was removed, yielding 400 mg of product. Analysis of this crude material by GLC (10 ft × 0.25 in. 15% NPGS, 175°, 120 ml/min) indicated that it consisted of three components: 36.2% **10** (retention time 4.0 min), 34.8% **11** (retention time 4.4 min), and 30.0% C-methylated ketone (retention time 8.2 min). This was rather surprising, since enolate equilibration is not usually encountered under the reaction conditions employed. To check if the observed equilibration was taking place in the chromatograph, the remaining product was purified by column chromatography (15 g of Silicar CC-7, 200–325 mesh, 10% ether–hexane elutant). This was indeed the case as the 200 mg of enol ether obtained from the chromatography column was identified as pure **10**. See Figure 9 (supplementary material) for the mass spectrum of **10**: ir (neat) 1665 (enol ether), 889 cm^{-1} (methallyl double bond); ^1H NMR (CCl_4) τ 5.33 (m, 1, vinyl H), 6.55 (s, 3, enol Me), 8.27 (s, 3, vinyl Me), 9.03 (d, 3, ring Me).

A sample of **11** was obtained by preparative GLC of the initial crude product. See Figure 10 (supplementary material) for the mass spectrum of **11**: ir (neat) 1665 (enol ether), 890 cm^{-1} (methallyl double bond).

Acknowledgment. The authors express their gratitude to the National Science Foundation for support of this research under Grant GP 31321X.

Registry No.—**1**, 55373-31-4; **2**, 55373-32-5; **3**, 55373-33-6; **4**, 55373-34-7; **5**, 55373-35-8; **6**, 55449-02-0; **7**, 55449-03-1; **8**, 55373-36-9; **9** epimer 1, 55373-37-0; **9** epimer 2, 55373-38-1; **10**, 55373-39-2; **11**, 55373-40-5; **14**, 55373-41-6; 1-trimethylsiloxy-*trans*-3-allyl-5-methylcyclohex-1-ene, 55373-42-7; potassium amide, 17242-52-3; butyl iodide, 542-69-8; 1-trimethylsiloxy-*cis*-3-methallyl-5-methylcyclohex-1-ene, 55400-55-0; isobutyl chloride, 513-36-0; 5-methylcyclohex-2-en-1-one, 7214-50-8; trimethylchlorosilane, 75-77-4; 1-trimethylsiloxy-*trans*-3-isobutyl-5-methylcyclohex-1-ene, 55373-43-8; 1-trimethylsiloxy-*trans*-3-methylallyl-5-methylcyclohex-1-ene, 55373-44-9.

Supplementary Material Available. Mass spectra of compounds **4–11** will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.50 for photocopy or $2.50 for microfiche, referring to code number JOC-75-2160.

References and Notes

(1) Preceding paper in this issue: E. S. Binkley and C. H. Heathcock.
(2) H. O. House and V. Kramar, *J. Org. Chem.*, **28**, 3362 (1963).
(3) H. O. House and W. F. Fischer, *J. Org. Chem.*, **34**, 3615 (1969).
(4) D. Seyferth and M. A. Werner, *J. Org. Chem.*, **26**, 4797 (1961); H. O. House et al., *J. Am. Chem. Soc.*, **91**, 4872 (1969).
(5) L. Mandell and J. M. Brodmann, *J. Org. Chem.*, **31**, 591 (1966).
(6) W. F. Gannon and H. O. House, "Organic Syntheses", Collect. Vol. V, Wiley, New York, N.Y., 1973, p 539.
(7) H. O. House, R. A. Latham and C. D. Slater, *J. Org. Chem.*, **31**, 2667 (1966).
(8) C. H. Heathcock and J. E. Ellis, *Chem. Commun.*, 1474 (1971).

A Synthetic Approach to the Dendrobine Skeleton

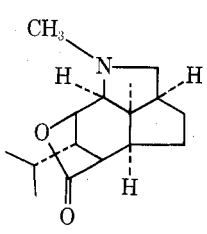
Donald N. Brattesani and Clayton H. Heathcock*

Department of Chemistry, University of California, Berkeley, California 94720

Received February 14, 1975

A possible synthetic route to the alkaloid dendrobine has been explored. Intramolecular Michael cyclization of unsaturated keto nitrile **17** yields only stereoisomer **18**. The stereochemistry of **18** has been established by the synthesis of a compound with the opposite stereochemistry of the cyanomethyl side chain (**28**). A rationale for the stereospecificity of the cyclization reaction is proposed.

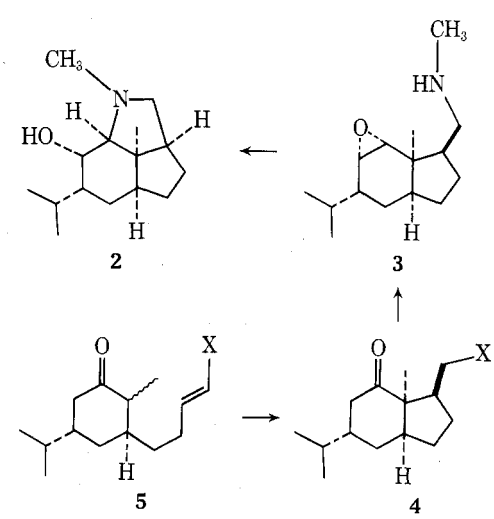
The sesquiterpene alkaloid dendrobine (**1**) occurs as a component of the Chinese drug Chin-Shih-Hu, which is prepared from the ornamental orchid *Dendrobium nobile* (Orchidaceae). It was first isolated from the stem of the



1

plant by Suzuki and coworkers.[1] Recently, the alkaloid, as well as a number of its congeners, has been extensively investigated by Hirata,[2] Inubushi,[3] and Okamoto,[4] who have determined the stereostructure shown in **1**. Dendrobine's interesting structure has elicited considerable attention from synthetic chemists, resulting in three total syntheses of the alkaloid itself[5–7] as well as a synthesis of the basic tricyclic skeleton.[8] In this communication we outline our own approach to the synthesis of the alkaloid.

In our projected synthesis of the basic skeleton, presented below in gross outline, the key step would be the Michael reaction **5** → **4**. The group X must be the synthetic



2 **3** **5** **4**

equivalent of $NHCH_3$, i.e., NO_2, CO_2R, CN, etc. Although the cis fusion of the product hydrindanone **4** could reasonably be expected,[9] the steric disposition of CH_2X in such a reaction is difficult to predict. As will be seen in the sequel, the desired intramolecular Michael reaction does indeed occur readily when X = CN, albeit in precisely the opposite steric sense. Although we were able to invert the stereo-