stirred at room temperature for 21 hr, then quenched and worked up as described for unlabeled **2**. The products had the following nmr spectra (CCl_4): **4**, δ 1.05 (s, 3 H), 1.08 (s, 3 H), 1.60 (m, 3 H), 1.72 (m, 3 H), 1.98 (s, 3 H); **14**, δ 0.90, 1.03, 1.25, 1.75, and 1.95, all s, 3 H; **15**, δ 1.21 (s, 3 H), 1.46 (d, 3 H, J = 1.7 Hz), 1.83 (s, 3 H), 4.95 (m, 3 H), 5.30 (br s, 1 H); **16**, δ 1.17 (d, 3 H, J = 7.5 Hz), 1.80 (s, 3 H), 2.70 (q, 1 H, J = 7.5 Hz), 5.10 (br s, 1 H), 5.27 (br s, 1 H).

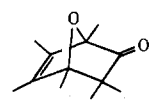
A solution of **2***,† (lacking the signals at δ 2.10 and 1.48) in TFA was allowed to rearrange in the amounts and manner described for **2***. The products had the following nmr spectra (CCl_4): **4**, δ 1.05, 1.08, 1.60, and 1.98 (all s, 3 H); **14**, δ 0.90, 1.03, 1.25, and 1.75 (all s, 3 H); **15**, δ 1.46 (d, 3 H, J = 1.7 Hz), 1.83 (s 3 H), 4.95 (m, 3 H), 5.30 (br s, 1 H); **16**, δ 1.80 (s, 3 H), 2.70 (br s, 1 H), 5.10 (br s, 1 H), 5.27 (br s, 1 H).

Acknowledgment. We are indebted to the National Institutes of Health and the National Science Foundation for their support of this research.

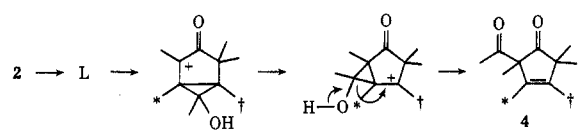
Registry No.—**1**, 40940-60-1; **1**-d_3, 50506-40-6; **1**-d_6, 50506-41-7; **2**, 50506-42-8; **2**-d_3, 50506-43-9; **2**-d_6, 50506-44-0; **3**, 40940-46-3; **3**-d_3, 50506-46-2; **3**-d_6, 50506-47-3; **4**, 50506-48-4; **4**-d_3, 50506-49-5; **4**-d_6, 50506-50-8; **5**, 50506-51-9; **5**-d_3, 50506-52-0; **5**-d_6, 50506-53-1; **6**, 50506-54-2; **7**, 50506-55-3; **11**, 3854-96-4; **12**, 50506-57-5; **12**-d_6, 50506-58-6; **14**, 50506-59-7; **15**, 50506-60-0; **16**, 29765-85-3.

References and Notes

(1) R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 737 (1959); M. S. Malinovskii, "Epoxides and Their Derivatives," Daniel Davey, New York, N. Y., 1965; H. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, p 320.
(2) H. Hart, M. Verma, and I. Wang, *J. Org. Chem.*, **38**, 3418 (1973).
(3) Corresponding respectively to the cyclopentenone and acetyl moieties: K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, San Francisco, Calif., 1962, p 42.
(4) Shown in δ units, with the relative downfield shifts in the presence of Eu(fod)$_3$ given in parentheses; see D. R. Kelsey, *J. Amer. Chem. Soc.*, **94**, 1764 (1972).
(5) All peaks were sharp three-proton singlets except for those at δ 1.60 and 1.72, which were homoallylically coupled (J = 1.5 Hz). The acetyl methyl (δ 1.98), allylic methyls (δ 1.60, 1.72), and aliphatic methyls are readily assigned using chemical shifts. Specific assignments within the last two categories are based on labeling experiments to be described below.
(6) This result also argues against structures **9** and **10** for the hydroxy ketone. The most plausible route to **9** would involve proton loss from B; in this event, product from **1***,† should lack the vinyl protons. The most plausible route to **10** would involve proton loss from D; in this event, product from **1***,† should lack two methyl signals. The label results fit neither of these predictions.
(7) The kinetic experiments require that, when starting from **1**, less than 3% of **4** is produced from **5**; over 97% must be obtained directly from **1**.
(8) One can envision several other plausible mechanisms for the conversion of **1** to **4**. The most attractive of these involved cyclopropylcarbinyl cations derived from participation of the double bond in B. However, none of these fit the observed labeling results.
(9) H. Hart, P. M. Collins, and A. J. Waring, *J. Amer. Chem. Soc.*, **88**, 1005 (1966). (See particularly footnote 16.)
(10) The nucleophile shown is TFA, but may also be water or may even be the hydroxyl group, *via* an intermediate such as



(11) It was from these experiments that **4**, lacking only the singlet at δ 1.27, or lacking both signals at δ 1.27 and 1.72 referred to earlier, was obtained.
(12) Plausible alternative routes from **2** to **4** can be envisioned but can be eliminated as a consequence of the labeling experiments. One example, involving cyclopropylcarbinyl rearrangements, is



(13) Melting points are uncorrected. Analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. Ir spectra were calibrated against a polystyrene film; nmr spectra are referenced against tetramethylsilane.

Notes

Acid-Catalyzed Rearrangement of an Epoxy Ketone by Competitive Protonation at Each Oxygen

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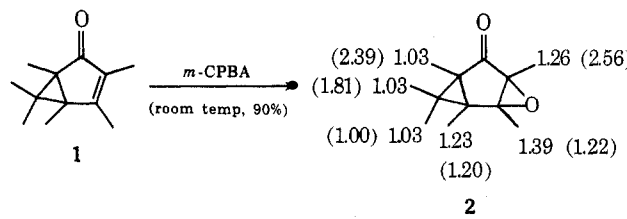
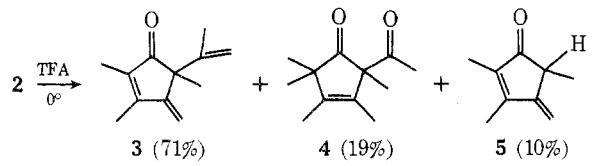
In general, the acid-catalyzed rearrangement of epoxy ketones is initiated by protonation of the epoxide oxygen atom.[1] We describe here the rearrangement of an epoxy ketone to two principal products, one of which appears to arise from protonation of the carbonyl oxygen.

3,4-Epoxy-1,3,4,5,6,6-hexamethylbicyclo[3.1.0]hexan-2-one (**2**) was prepared in good yield from the corresponding unsaturated ketone **1**[2] and *m*-chloroperbenzoic acid. The structure is based on the method of synthesis and spectral properties. The $\nu_{C=O}$ in **2** was at 1715 cm^{-1} (1690 cm^{-1} in **1**). The nmr spectrum[3] showed that all methyl signals were aliphatic ($\delta \leq 1.39$), and europium shift reagent removed the accidental degeneracy of three methyls at δ 1.03 and gave a spectrum with six sharp, equal singlets. Vpc and nmr analysis showed that only a single stereoisomer of **2** was produced; the equal chemical shifts of the two methyl groups at C-6 suggest that the epoxide ring is trans to the cyclopropane ring. Epoxide prepared from **1** with a CD_3 group at C-4 lacked the singlet at δ 1.39 (**2***); epoxide prepared from **1** with CD_3 groups at C-1 and C-4 lacked the singlet at δ 1.39, and that at δ 1.03 was reduced in area to six protons (**2***,†). The labeling and Eu-shift data support the nmr assignments shown in the structure.



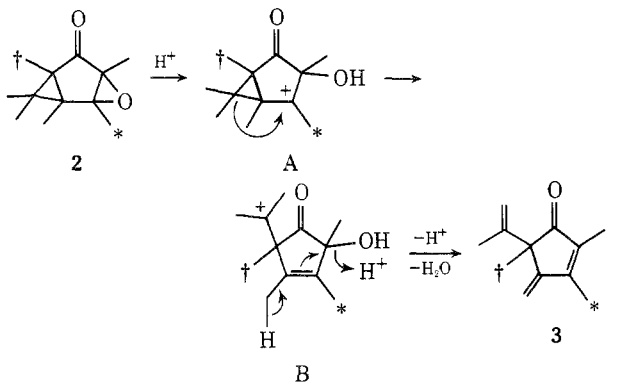
1 **2**

Treatment of **2** with trifluoroacetic acid (TFA) at 0° for 10 min resulted in complete rearrangement to **3** and **4**. Also formed was a small amount of **5** which is known to arise from the dealkylation of **3**.[4] The properties and structure proof of **3**-**5** are described elsewhere.[4]



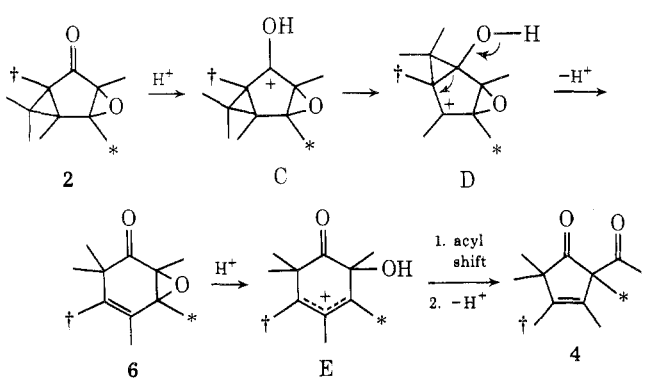
A plausible mechanistic route to **3** is shown in Scheme I. Protonation of the epoxide oxygen by ring opening in a direction which places the positive charge remote from the carbonyl group gives the intermediate cyclopropylcarbinyl cation A. Ring opening gives the homoallyl cation B, or alternatively B may be formed directly from protonated **2** in a concerted process. Proton loss and dehydration gives **3**. Deuterium-labeling results[5] are consistent with this mechanism; **2*** gave **3*** and **2*,†** gave **3*,†**.

Scheme I



A mechanism for obtaining **4** from **2**, consistent with the labeling results, is shown in Scheme II. Protonation at the carbonyl oxygen gives C, which undergoes a cyclopropylcarbinyl rearrangement to D. Such rearrangements are well established and exceedingly facile in the case of protonated **1**.[6] Ring opening and proton loss would lead to the α,β-epoxide of hexamethyl-2,4-cyclohexadienone (**6**). Further rearrangement in a normal manner[4] should lead to **4**. No evidence for the presence of **6** in these solutions was obtained, and we must assume that, if formed, it rearranges to **4** under the reaction conditions.[7]

Scheme II



Experimental Section[8]

3,4-Epoxy-1,3,4,5,6,6-hexamethylbicyclo[3.1.0]hexan-2-one (2). To a solution of 1.2 g (6.75 mmol) of 1,3,4,5,6,6-hexamethylbicyclo[3.1.0]hexen-2-one (**1**)[2] in 20 ml of methylene chloride was added a solution of 1.25 g (7.2 mmol) of *m*-chloroperbenzoic acid in 20 ml of methylene chloride. The mixture was stirred at room temperature for 4 hr (nmr monitoring showed complete reaction at this time), the solvent was removed by rotary evaporation, petroleum ether (bp 30–60°) was added, and the *m*-chlorobenzoic acid was removed by filtration. The filtrate was washed with aqueous $NaHCO_3$ and saturated NaCl solution, dried ($MgSO_4$), and evaporated to give 1.17 g (90%) of **2**. Vpc (5 ft × 0.125 in., 10% FFAP on Chromosorb W, 150°, 30 ml/min N_2) showed only a single peak, retention time 12.5 min: ir (neat) 1715 (s), 1460 (m), 1395 (m), 1080 (w), 1025 (w), 940 (w), 860 cm^{-1} (w); nmr (CCl_4) see structure; mass spectrum (70 eV) *m/e* 194 (M^+).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.20; H, 9.43.

Starting with **1*** (lacking the methyl signal at δ 1.88),[6a] the resulting **2*** had the following nmr spectrum (CCl_4): δ 1.03 (s, 9 H), 1.23 (s, 3 H), 1.26 (s, 3 H). Starting with **1*,†** (lacking the methyl signal at δ 1.88 and having the singlet at δ 1.10 correspond to only 3 H)[2] the resulting **2*,†** had the following nmr spectrum (CCl_4): δ 1.03 (s, 6 H), 1.23 (s, 3 H), 1.26 (s, 3 H).

Rearrangement of 2 in TFA. A solution of **2** (100 mg, 0.517 mmol) in 2 ml of TFA was stirred at 0° for 10 min, then poured into a slurry of aqueous $NaHCO_3$ and ether. The ether layer was separated, washed successively with aqueous $NaHCO_3$ and NaCl solutions, dried ($MgSO_4$), and evaporated to leave 90 mg of a light yellow oil which was analyzed by vpc (5 ft × 0.125 in., 10% FFAP on Chromosorb W, 155°, 30 ml/min N_2). There were three components (retention time, %): 5-isopropenyl-4-methylene-2,3,5-trimethyl-2-cyclopentenone (**3**, 1.9 min, 71), 2-acetyl-2,3,4,5,5-pentamethyl-3-cyclopentenone (**4**, 1.6 min, 19) and 4-methylene-2,3,5-trimethyl-2-cyclopentenone (**5**, 1.3 min, 10). The products were separated by preparative vpc (10 ft × 0.25 in., 20% FFAP on Chromosorb W, 160°, 25 ml/min He) and identified by comparison of their ir and nmr spectra with those of authentic samples.[4]

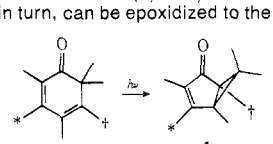
Rearrangement of Labeled 2. The same experimental procedure as described for unlabeled **2** was used. Starting with **2*** the products had the following nmr spectra: **3**, δ 1.21 (s, 3 H), 1.46 (d, 3 H, J = 1.7 Hz), 1.83 (s, 3 H), 4.95 (m, 3 H), 5.30 (br s, 1 H); **4**, δ 1.05, 1.08, 1.98 (s, 3 H each), 1.60, 1.72 (q, 3 H each, J = 1.5 Hz).[9] Starting with **2*,†** the products had the following nmr spectra: **3**, δ 1.46 (d, 3 H, J = 1.7 Hz), 1.83 (s, 3 H), 4.95 (m, 3 H), 5.30 (br s, 1 H); **4**, δ 1.05, 1.08, 1.60, 1.98 (s, 3 H each).

Acknowledgment. We are indebted to the National Institutes of Health for their support of this research.

Registry No.—**1**, 2206-69-1; **1**-d_3, 50507-02-3; **1**-d_6, 50507-03-4; **2**, 50507-04-5; **2**-d_3, 50507-05-6; **2**-d_6, 50507-06-7; **3**, 50506-60-0; **4**, 50506-48-4.

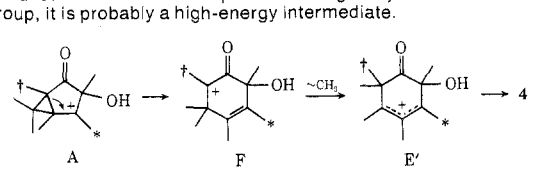
References and Notes

(1) For an example, see House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, p 320.
(2) H. Hart, P. M. Collins, and A. J. Waring, *J. Amer. Chem. Soc.*, **88**, 1005 (1966).
(3) Shown in δ units, with the relative downfield shifts in the presence of $Eu(fod)_3$ given in parentheses; see D. R. Kelsey, *J. Amer. Chem. Soc.*, **94**, 1764 (1972).
(4) H. Hart, I. Huang, and P. Lavrik, *J. Org. Chem.*, **39**, 999 (1974).
(5) Hexamethyl-2,4-cyclohexadienone is labeled selectively at C-3 under mild conditions, or at C-3 and C-5 under more strenous conditions, or (by back exchange of doubly labeled material under mild conditions) at C-5. For proof, see ref 2, particularly footnote 16. Irradiation of the dienone labeled C-3 (*) and/or C-5 (†) gives specifically labeled 1 which, in turn, can be epoxidized to the required labeled **2**.



1

(6) (a) D. W. Swatton and H. Hart, *J. Amer. Chem. Soc.*, **89**, 5075 (1967); (b) H. Hart, T. R. Rodgers, and J. Griffiths, *ibid.*, **91**, 754 (1969).
(7) An alternative route from **2** to **4** which involves initial protonation at the epoxide oxygen (as in Scheme I) is shown. Ring opening of A gives F; a 1,2-methyl shift gives E′ (identical with E in Scheme II, except for the label), which can further rearrange to **4**. This mechanism is inconsistent with the label results and can be unequivocally ruled out. Since F has a positive charge adjacent to the carbonyl group, it is probably a high-energy intermediate.



(8) Analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. Nmr spectra were internally referenced against tetramethylsilane.
(9) Compound **5** was not examined, since the mechanism of its formation from **3** has already been established.[4]