Lewis Acid Rearrangement of 2,3-Epoxycarane. Formation of a Novel *m*-Menthenone

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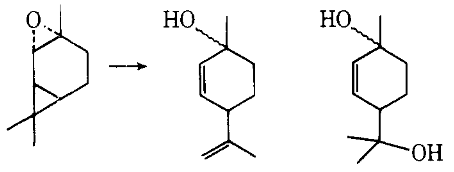
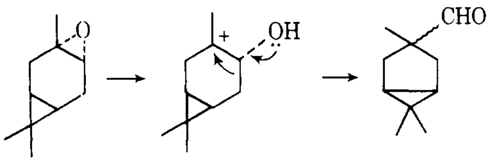
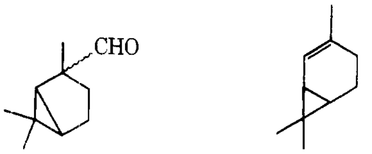
Rearrangement of 2,3-epoxycarane (**1**) employing metatitanic acid has been previously studied[1] and found to yield predominately alcohol **2**. It has also been reported[2] that epoxidation of 2,3-carene with peracetic acid leads directly, after saponification of acetates, to **2** and diol **3**. Recent work,[3] consistent with earlier results, has shown that epoxide **1** undergoes rearrangement to **2** and a series of allylic alcohols and hydrocarbons derived most likely from **2**. This latter work employed a wide range of solid acids and bases SiO_2–Al_2O_3, Al_2O_3, $FeSO_4$, TiO_2–ZrO_2, and CAO, and in no case were carbonyl and/or ring-contraction products identified. Conversely, it has been found that 3,4-epoxycarane (**4**), using the above solid catalysts[3] and also zinc bromide ($ZnBr_2$),[4] gave relatively good yields of the ring-contraction product aldehyde **5** along with ketones and allylic alcohols, almost all of which could be derived from an intermediate of type **6**.



1 **2** **3**



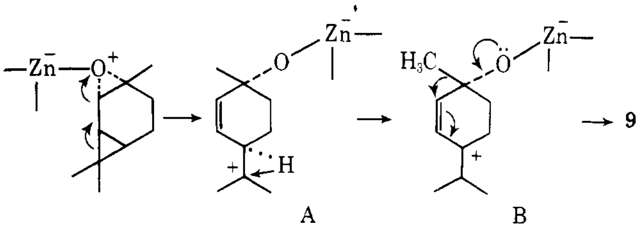
4 **6** **5**



7 **8**

We had a need for aldehyde **7** which, in principle, could be formed from epoxide **1** by an analogous route using the strong Lewis acid $ZnBr_2$. Accordingly, epoxide **1** was prepared essentially quantitatively from 2,3-carene (**8**) using *m*-chloroperbenzoic acid in a two-phase system reported[5] to be useful for very labile epoxide preparation. The NMR of **1** compared well to a published spectrum.[6] A conventional procedure using monoperphthalic acid gave considerable rearrangement to **2** and **3**.

Scheme I



A B

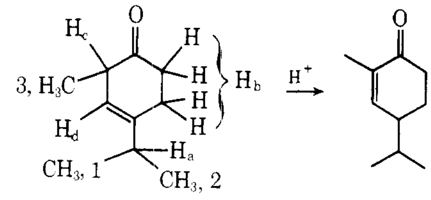
Only a very small amount of an aldehyde was produced (see Table I). The aldehyde had a MS almost identical to **5**, which as previously discussed is formed from 3,4-epoxycarane (**4**). The yield could not be increased and not enough material could be isolated to determine if the aldehyde was the desired compound **7** or the known **5**. It is almost certain that the aldehyde in question is **5** derived from 3,4-epoxycarane (**4**), present as an approximately 2% impurity in the starting epoxide. *cis*-3-Caranone (**11**), the major product of $ZnBr_2$ rearrangement of **4**, was also detected. Production of **7** would require epoxide opening without cyclopropyl participation, which apparently does not occur to any detectable extent. Rearrangement of **1** employing stannic chloride ($SnCl_4$) led to lower yields of ketone; results are included in Table I along with the products of the $ZnBr_2$ rearrangement in benzene.

Treatment of epoxide **1** with $ZnBr_2$ in refluxing toluene yielded a number of terpene hydrocarbons. The reaction products and amounts are given in Table I and are listed as they elute from the VPC. α-Terpinene, limonene, and β-phellandrene are reported for the first time as products of acid rearrangement of 2,3-epoxycarane (**1**). Of considerably more interest was the major product, a *m*-menthenone, shown to be 2-methyl-4-isopropylcyclohex-3-en-1-one (**9**) amounting to 40% of the volatile products. The IR of **9** showed it to contain a nonconjugated carbonyl (ν = 1720 cm^{-1}). The 100-MHZ NMR spectrum was in accord with **9** and exhibited a sharp six-proton doublet at δ 1.04 (J = 7 Hz; CH_3, 1 and 2), a three-proton doublet at 1.14 (J = 7 Hz, CH_3, 3), a one-proton quintet centered at 2.3 (J = 7 Hz, H_a), a four-proton narrow multiplet at 2.46 (H_b), a broad one-proton quartet with additional splitting at 2.88 (J = 7 Hz, H_c), and a one-proton doublet with additional splitting at 5.37 (J = 3 Hz, H_d). Proton

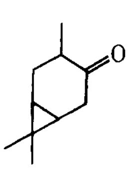
Table I. 2,3-Epoxycarane Rearrangement Products

Compound	Registry no.	Structure determined by	Area, %[a] b	c	d
α-Terpinene	99-86-5	MS	0.1	0.4	0.4
Limonene	138-86-3	MS	1.9	0.4	1.1
A *p*-menthatriene—possibly 1,4,8-*p*-menthatriene	28233-65-0	MS	0.2	0.4	<0.1
β-Phellandrene and a *p*-menthatriene	555-10-2	MS	0.6	0.4	<0.1
p-Cymene	99-87-6	IR, MS	17.0	17.0	24.2
Terpinolene	586-62-9	IR, MS	6.0	0.5	0.1
Aldehyde (probably aldehyde **5**)	13124-67-9	MS	0.7	<0.1	<0.1
p-α-Dimethylstyrene	1195-32-0	IR, NMR, MS	7.7	22.7	<0.5
2-Methyl-4-isopropylcyclohex-3-en-1-one (**9**)	63028-18-2	See Exptl Sect	40.4	29.1	17.1
% total volatiles identified			74.4	70.9	43.4

[a] VPC peak area as a percent of total peak area. [b] $ZnBr_2$–refluxing toluene. [c] $ZnBr_2$–refluxing benzene. [d] ≃2% $SiCl_4$ in benzene cooled in ice bath.



9 10

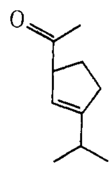


11

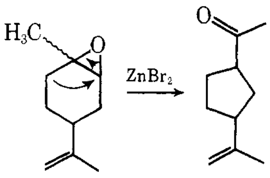
H_a exhibited five lines of the theoretical septet due to the very low intensity of outer septet lines and low S/N ratio encountered in microcell techniques. Structure **9** was further confirmed by isomerization with *p*-toluenesulfonic acid to the known ketone **10**.[7]

Formation of the major product, ketone **9**, can be postulated by a mechanism outlined in Scheme I. Anti-Markovnikov opening of the epoxide ring with cyclopropyl participation could yield carbonium ion A. In the previous studies,[1–3] this ion could account for the reported products without carbon rearrangement. However, by employing conventional Lewis acids ($ZnBr_2$ and $SiCl_4$), it appears that a fundamental rearrangement involving both a hydride and methyl shift takes place (A → B → **9**). The stereochemistry of the oxide and resulting carbonium ions is most likely as shown, since the stereochemistry of the starting oxide, prepared with peracid, has been shown to be *trans*-**1**.[6]

The methyl ketone **12**, which could be formed from ion B by ring migration, was not detected in the reaction mixture. In contrast, a mixture of *cis*- and *trans*-limonene oxide (**13**) was found[8] to undergo rearrangement without methyl migration but with ring contraction (**13** → **14**).[9] Models show that these results can be explained by stereochemical differences, since the axial methyl group is ideally disposed for migration (axial and parallel to the p orbitals of the double bond) in intermediates (A, B) leading to ketone **9**.



12



13 14

For limonene oxide (**13**), both the methyl group and ring carbon are equally disposed stereochemically to migration. If it is assumed that the transition state resembles the ground state, then the group with the highest migratory aptitude (the secondary ring carbon) will undergo rearrangement.

Experimental Section

Analyses by VPC were performed on a Perkin-Elmer 900 equipped with dual 12 ft, ⅛ in. i.d. glass columns, modified for on-column injection and packed with 5% Triton X-305 on Chromosorb W. H.P. 80–100 mesh. The oven temperature was programmed from 70 to 170 °C at 2 °C/min. A flow rate of 35 mL/min of helium was employed. Compounds were purified as clear liquids by collection in glass capillaries or ⅛-in. glass tubing from an F&M 810 GC equipped with a TC detector, ¼-in. glass column, and generally operated as above. IR spectra were determined using a PE-221 or PE-281; MS were determined using a Hitachi-RMU-6L. NMR were determined on a Varian T-60-A or JEOL-MH-100 in $DCCl_3$ using Me_4Si as an internal standard. Microanalysis was performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

2,3-Epoxycarane (1). *m*-Chloroperbenzoic acid (1.28 g, 6.3 mmol) was added over 1.5 h to a mixture of 0.75 g (5.5 mmol) of 2,3-carene (**8**),[10] 18 mL of 0.5 M $NaHCO_3$, and 60 mL of CH_2Cl_2, and stirred in an ice bath. The ice bath was then removed and the mixture was stirred an additional 2 h. The solution was washed with saturated $NaHCO_3$ (2 × 20 mL), H_2O (1 × 20 mL), and saturated NaCl (1 × 20 mL), dried over anhydrous potassium carbonate, and concentrated under reduced pressure to yield epoxide **1** (0.8 g). VPC analysis showed the material to be >95% pure and it was used without further purification:[11] IR (neat) 2940, 1450, 1372, and 855 cm^{-1}; NMR δ 0.6 (br m, 1 H) and 1.0 (n, m, 1 H) (cyclopropyl protons), 1.07 (s, 6 H, CH_3CCH_3), 1.27 (s, 3 H, CH_3CO), 1.67 (t, 2 H superimposed on br m, 2 H, CH_2CH_2), 3.0 (d, 1 H, $J = 2$ Hz, HCO); MS *m/e* (rel intensity) 152 (7), 134 (73), 132 (19), 120 (20), 119 (100), 117 (34), 91 (67), 79 (15), 77 (23).

Rearrangement of Epoxide 1 with Zinc Bromide. Approximately 20 mg of $ZnBr_2$ (Fisher certified, not fused) was added to 3 mL of toluene which had been distilled and stored over molecular sieves. The mixture was brought to reflux with vigorous stirring in an apparatus which had been well flushed with nitrogen and equipped with a drying tube. Three-quarters of a mixture of epoxide **1** (150 mg, 0.98 mmol) and 3 mL of toluene was added immediately. After 10 min the remaining one-quarter was added over a 10-min period. Forty minutes after initial oxide addition, the reaction mixture was cooled, taken up in 30 mL of ether, washed successively with water (2 × 10 mL), saturated $NaHCO_3$ (1 × 10 mL), and saturated NaCl (1 × 10 mL), and dried over anhydrous Na_2SO_4. Partial removal of solvent under reduced pressure afforded an oily residue from which 2-methyl-4-isopropylcyclohex-3-en-1-one (**9**)[15] was isolated by preparative VPC: IR (CCl_4) 2975, 1720, 1360, 1200, 1180 (d), 970 and 930 cm^{-1}; UV (95% EtOH) λ_{max} 290 nm (Σ = 90.9); NMR δ 1.04 (d, 6 H, $J = 7$ Hz, CH_3CCH_3), 1.14 (d, 3 H, $J = 7$ hz, CH_3C–), 2.3 (quintet, 1 H, $J = 7$ Hz), 2.46 (n, m, 4 H), 2.88 (br q with additional splitting HCC=O), 5.37 (n, m, 1 H, HC=C); MS *m/e* (rel intensity) 153 (4), 152 (42), 135 (5), 100 (65), 109 (10), 96 (11), 95 (100), 81 (30), 68 (10), 67 (25), 55 (11). Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 79.08; H, 10.41.

2-Methyl-4-isopropylcyclohex-2-en-1-one (10). A mixture of ketone **9** (4.4 mg, 2.9 × 10^{-2} mmol), a trace of *p*-toluenesulfonic acid monohydrate, and $CHCl_3$ (3 mL) was refluxed for 30 min, taken up in 30 mL of ether, and worked up as previously described for the $ZnBr_2$ rearrangement to yield an oily residue. One major product (>95% of total volatiles) was isolated by VPC and shown to be ketone **10**: UV (95% EtOH) λ_{max} 227 nm; IR[12] 2950, 1680 (C=O), 1355 and 1375 (d), 1125, 1103, 1072 (d) cm^{-1}; MS[13] *m/e* (rel abundance) 153 (9), 152 (57), 137 (9), 111 (10), 110 (100), 109 (58), 97 (23), 96 (19), 95 (73), 81 (43).

Acknowledgment. We thank Dr. F. Bayer for determination of the 100-MHz NMR Spectra.

Registry No.—**1**, 64130-68-3; **8**, 554-61-0; **10**, 41469-46-9.

References and Notes

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(9) It should be noted that 90% of the products from this reaction are derived from normal opening of the epoxide to yield a tertiary carbonium ion.
(10) Supplied as a gift by Dr. T. F. Sanderson, Hercules, Inc., Wilmington, Del., 95% pure by VPC and contained ≃2.5% 3,4-carene.
(11) The oxide was very sensitive and underwent some rearrangement/decomposition when collected via VPC.
(12) The IR compared well to a spectra of authentic ketone **10** kindly furnished by Dr. J. G. Witteveen of Naarden International, Holland.
(13) MS was identical to authentic **10** generated with levulinic acid[14] from the 2,4-dinitrophenylhydrazone supplied as a gift by Professor T. S. Sorensen, University of Calgary, Calgary, Alberta, Canada.
(14) C. H. DePuy and B. W. Ponder, *J. Am. Chem. Soc.*, **81**, 4629 (1959).
(15) **Note Added in Proof.** After this paper was accepted for publication we became aware of a report of menthenone **9** by W. Kraus and G. Zartner, *Tetrahedron Lett.*, 13 (1977), in which **9** was reported in low but unspecified yield by rearrangement of fenchone. The compound was characterized only by two NMR bands and two IR bands. These spectral data do not appear compatible with **9**. Essentially no experimental was given.