[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WAYNE STATE UNIVERSITY, DETROIT, MICHIGAN]

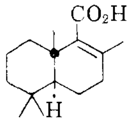
The Cyclization of Epoxyolefins: The Reaction of Geraniolene Monoepoxide with Boron Fluoride Etherate

BY DAVID J. GOLDSMITH

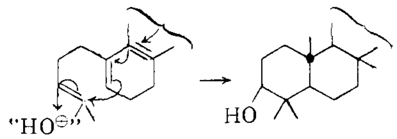
RECEIVED JUNE 21, 1962

Geraniolene monoepoxide has been allowed to react with boron fluoride etherate to yield a variety of products depending on the solvent employed. The formation and interconversion of some of these compounds is discussed in terms of the mechanism of opening of the epoxide ring.

With the discovery of the path of cholesterol biogenesis[1] and the suggestions for the similar natural formation of terpenoids,[2a,b] considerable attention has been turned to the chemical problem of polyene cyclization.[3] Two major areas of this problem have evoked the greatest interest: the feasibility of obtaining terpenoid-like substances by the acid-catalyzed cyclization of polyolefins, and the elucidation of the mechanism of this process. The possibility of the former has been amply demonstrated.[3] Stereochemically, the products so obtained (*e.g.*, bicyclofarnesic acid, **1**) have been shown to possess the presumably more stable *trans* ring fusion. Since this geometry may result either from cyclization through discrete carbonium ions or by a concerted process, the second problem remains unsolved. In connection with both of these aspects it was of interest to examine the possibility of producing hydroxylated terpenoids by catalyzing polyene cyclization with a source of positive oxygen in the manner shown below. A formal equivalent of this process would be the acid-catalyzed cyclization of an epoxy olefin,[4] the epoxide group being derived from a source of the theoretical hydroxyl cation. This report is concerned with the results of an investigation of some aspects of the latter alternative.



1



Geraniolene, **2**, prepared by distillation of geranic acid at atmospheric pressure,[5] was treated with one equivalent of monoperphthalic acid. A single monoepoxide was obtained. The presence of an infrared absorption band at 890 cm.$^{-1}$ indicated that epoxidation had occurred at only the trisubstituted double bond to yield **3**. Having an epoxyolefin of the desired substitution pattern, it was necessary to consider the two routes by which cyclization might occur. Path A, Fig. 1, would lead to the desired cyclohexanol **4**[6] by a concerted opening of the protonated epoxide. Path B, in contrast, would involve the intermediacy of a distinct carbonium ion species. Although no real distinction between concerted and non-concerted cyclization has been possible in the case of polyene cyclization, previous work on the opening of the epoxide ring[7] suggested that both types of mechanisms might be experimentally detectable with epoxyolefins.

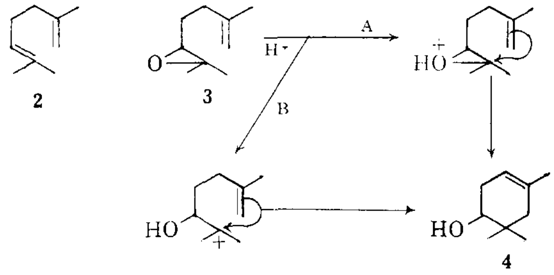


Fig. 1.

It has been shown by House[8a,b] that treatment of the epoxyketone **5**, among others, with a limited amount of boron fluoride etherate in diethyl ether led to the formation of a fluorohydrin, **6**. Further treatment of **6** with boron fluoride etherate in ether produced the same dicarbonyl compound **7** obtained directly from the reaction of the original oxide with boron fluoride etherate in benzene solution. No conclusive evidence was adduced, however, to indicate whether fluorohydrins were intermediates in the formation of carbonyl compounds or merely the products of a competitive side reaction. Some indication that the boron fluoride etherate-catalyzed reactions in benzene and in ether follow different mechanistic pathways was found by Henbest and Wrigley.[9] These

---

[1] For a recent review see T. T. Tchen in D. M. Greenberg, "Metallic Pathways," Vol. 1, Second Edition, Academic Press, Inc., New York, N. Y., 1960, p. 389.

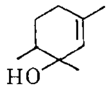
[2] (a) A. Eschenmoser, L. Ruzicka, O. Jeger and D. Arigoni, *Helv. Chim. Acta*, **38**, 1890 (1955); (b) J. Hendrickson, *Tetrahedron*, **7**, 82 (1959).

[3] For leading references see P. A. Stadler, A. Eschenmoser, H. Schinz and G. Stork, *Helv. Chim. Acta*, **40**, 2191 (1950).

[4] An interesting example of this type of cyclization in terpene chemistry has been found by D. H. R. Barton, O. C. Bockman and P. deMayo, *J. Chem. Soc.*, 2263 (1960). Interestingly, it has been reported by M. Mousseron-Canet and C. Levallois, *Bull. soc. chim. France*, 443 (1961), that geranyl acetate monoepoxide does not cyclize with either boron fluoride etherate or *p*-toluenesulfonic acid.

[5] F. Tiemann and F. W. Semmler, *Ber.*, **26**, 2724 (1893).

[6] The cyclohexanol represented by **4** is a mixture of double bond isomers excepting, from the infrared spectrum, the exocyclic olefin. The n.m.r. spectrum shows resonance lines at 4.83 (multiplet) and 5.0 μ (quartet) in the approximate ratio of 2:1 indicating $66^2/_3\%$ **4** and $33^1/_3\%$ **4a**.

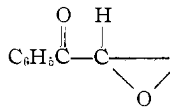


4a

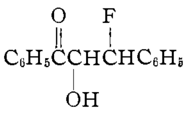
[7] A discussion of the variety of mechanisms operative in the opening of epoxides may be found in, R. E. Parker and N. S. Issacs, *Chem. Revs.*, **59**, 737 (1959).

[8] (a) H. O. House, *J. Am. Chem. Soc.*, **78**, 2298 (1956); (b) H. O. House and G. D. Ryerson, *ibid.*, **83**, 979 (1961).

[9] H. B. Henbest and T. I. Wrigley, *J. Chem. Soc.*, 4596, 4765 (1957).

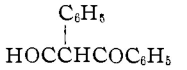


5



$C_6H_5\overset{\overset{O}{\|}}{C}CH\overset{\overset{F}{|}}{C}HC_6H_5$ with $\underset{|}{}OH$ below: $C_6H_5\overset{\overset{O}{\|}}{C}C\underset{\underset{OH}{|}}{H}\overset{\overset{F}{|}}{C}HC_6H_5$

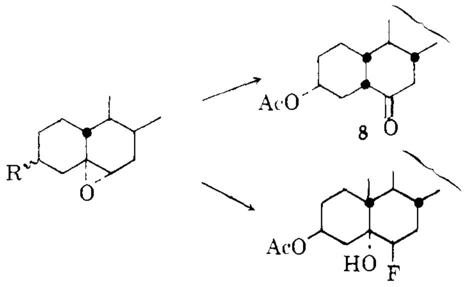
6



$HOC\overset{\overset{C_6H_5}{|}}{C}HCOC_6H_5$

7

workers studied the rearrangement of steroidal epoxides. Although they used only benzene as a solvent they were able to produce either fluorohydrins or ketones depending on the nature of the substituents in ring A. The most pertinent feature of this work in terms of the present discussion is the fact that these products are derived from opposite modes of cleavage of the epoxide carbon–oxygen bonds, as can be seen from the products obtained, **8** and **9**. The carbonyl compound cannot be obtained from the fluorohydrin by either rearrangement or elimination of hydrogen fluoride. It seems highly improbable, therefore, that **9** serves as a precursor of the ketone **8**. Additional evidence for the formation of ketones and fluorohydrins by different mechanisms was found by Henbest who demonstrated that **9** was the result of the usual *trans*-diaxial opening of the epoxide ring. The results of these workers suggest, therefore, that the reaction of an epoxide with boron fluoride etherate to yield a fluorohydrin is a concerted process. Moreover the use of ether as a solvent would appear to give only this type of product.[8a]

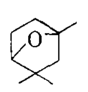


8

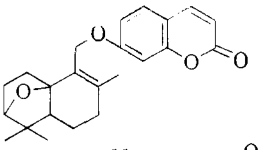
9

Consideration of this apparent difference in mechanism suggests that the path of cyclization of geraniolene monoepoxide might be controlled. If the mechanism of the boron fluoride-catalyzed opening of an epoxide ring in ether is as suggested, the reaction of **3** under these conditions should lead, at least in part, to **4** by a concerted process, the double bond acting in the same nucleophilic sense as external fluoride ion. It will be demonstrated in the sequel that the reactions of geraniolene monoepoxide with boron fluoride etherate in ether and benzene do in part follow different courses.

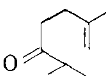
When geraniolene monoepoxide was treated with approximately one-third of an equivalent of boron fluoride etherate in benzene a mixture of products was obtained. The infrared spectrum of the crude mixture contained bands attributable to both alcoholic and carbonyl components. Analysis by gas chromatography showed the presence of three compounds, none of which corresponded to the original epoxide. The relative ratios of the three in order at increasing volatility were 1:1.2:1.3. All three compounds gave analytical values in accord with the empirical formula $C_9H_{16}O$, isomeric with **3**. The first compound was of greater volatility than **3** and showed no bands in the infrared attributable to carbonyl, alcoholic, unsaturated or epoxide functions. Instead, the spectrum contained a complex fingerprint region including a strong band at 1000 cm.$^{-1}$ characteristic of the 1,4-endoxocyclohexane system.[10] Consideration of the infrared spectrum and the reaction conditions suggested for this material the bicyclic ether structure **10**. Full confirmation of this structure was given by the n.m.r. spectrum of **10**. It displays resonance peaks at 8.99 τ (doublet, $-\overset{|}{C}(CH_3)_2$), 8.75 τ (doublet, $H-\underset{|}{\overset{\overset{H}{|}}{C}}-\overset{|}{C}-O$), 8.64 τ (singlet, $O-\underset{|}{\overset{|}{C}}-CH_3$), 8.25 τ (multiplet) and 6.28 τ (doublet, $H-\underset{|}{\overset{|}{C}}-O-$). The identical line positions and splittings have been found in the spectrum of farnisiferol-C, **11**.[11] The structure of the second isomer was easily demonstrated to be that of the ketone **12**. Its infrared spectrum showed the presence of a saturated carbonyl function (1709 cm.$^{-1}$), *gem*-dimethyl group (doublet at 1379 and 1361 cm.$^{-1}$) and a terminal double bond (890 cm.$^{-1}$). The third and least volatile component proved to be the desired cyclohexenol **4**. The hydroxyl group, double bond and *gem*-dimethyl group were clearly indicated by the infrared spectrum. Only one mole of hydrogen was absorbed when **4** was reduced over palladium and the resulting saturated alcohol **13** was oxidized to the known 2,2,4-trimethylcyclohexanone, **14**. The identity of the



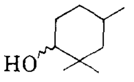
10



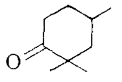
11



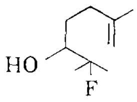
12



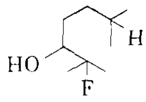
13



14



15



16

---

(10) J. C. Martin and P. D. Bartlett, *J. Am. Chem. Soc.*, **79**, 2533 (1957).

(11) L. Caglioti, H. Naef, D. Arigoni and O. Jeger, *Helv. Chim. Acta*, **42**, 2557 (1959). It is interesting to speculate on the reasons why **10** is formed only in benzene solution. In order to form the cyclohexanol **4**, a base must be present to remove a proton from the intermediate cation shown in Fig. 2. In ether solution, that base is obviously present in high concentration. In benzene, however, there must be a competition between the small amount of ether present and the potential hydroxyl oxygen. The latter may neutralize the positive charge by formation of the ether bridge of **10**. It would be expected that use of boron fluoride itself rather than the ether complex would increase the yield of this type of product. That **10** is not simply derived from **4** under the reaction conditions is demonstrated by the fact that only 12% of **4** could be transformed to **10** under vigorous conditions. These ideas are being applied to a total synthesis of farnisiferol-C.

TABLE I

RELATIVE RATIOS OF PRODUCTS IN ETHER[a]

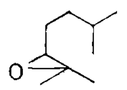
Geraniolene monoepoxide	$BF_3 \cdot Et_2O$	Time, min.	Epoxide	Product ketone	Fluorohydrin	Cyclic alcohol
100 mg. (0.7 mmole)	0.02 ml. (0.2 mmole)	15	4.9	1	20	3.2
100 mg. (0.7 mmole)	.02 ml. (0.2 mmole)	60	1.2	1	22	2.7
560 mg. (4 mmole)	.6 ml. (6 mmole)	60	1	1	2.3	0.7

[a] Ratios determined by integration of the vapor phase chromatogram by means of a disk chart integrator.

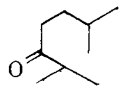
ketone obtained in this manner was shown by comparison of its semicarbazone with that derived from an authentic sample.

When geraniolene monoepoxide was treated with boron fluoride etherate in ether solution at room temperature a different product mixture was obtained. Four materials could be detected by gas chromatography. They were identified as **3**, **4**, **12** and the fluorohydrin **15**. The latter gave analytical values in agreement with the formulation $C_9H_{17}FO$. One mole of hydrogen was absorbed on catalytic reduction, and comparison of the infrared spectra of **15** and the dihydrofluorohydrin **16** demonstrated the presence of a terminal olefin in **15**. Moreover, treatment of **15** with potassium *tert*-butoxide reconverted it to **3**. Equivalent treatment of the dihydrofluorohydrin gave **17**. The relative ratios of these components varied with time and with the amount of catalyst. Some of these results are shown in Table I.

It can be seen that the rate of fluorohydrin formation is considerably faster than that of ketone formation when roughly equivalent amounts of epoxide and catalyst are used. The over-all reaction rate here is also slower than that of the equivalent reaction in benzene.[12] After fifteen minutes some 17% of the starting material remained unchanged in ether. In benzene total conversion to products has occurred in fifteen minutes. The following secondary transformations have also been found. In agreement with the work of House,[8] the fluorohydrin **15** when treated with boron fluoride etherate in ether is converted to **12**. The former compound does not, however, serve as an intermediate in the formation of **12** in benzene. When **15** is allowed to react under the same conditions in benzene a complex mixture of materials more volatile than any of the C_9-compounds of this series is formed. The ketone comprises only an extremely small percentage of this mixture. Compound **12** itself is stable to boron fluoride etherate in benzene. It cannot be concluded, however, that fluorohydrins are not convertible to ketones with boron fluoride in benzene in the absence of competing reactions. For example, treatment of **17**, obtained from **3** by hydrogenation, with boron fluoride etherate in ether yields a mixture of starting material, fluorohydrin and a small amount of ketone. The fluorohydrin was shown to be **16** since its infrared spectrum was identical with that of the saturated fluorohydrin obtained from **15** by catalytic reduction. Further treatment of **16** with boron fluoride in ether gave a ketone. The same ketone, **18**, was obtained from the saturated epoxide using benzene as the reaction medium.



17



18

The reaction of **16** with boron fluoride etherate in benzene also yielded the same ketone. In this case the fluorohydrin, being saturated, has no low energy reaction path to products other than the sample carbonyl compound. There appears to be no way of knowing here if the fluorohydrin is an intermediate in the formation of **18** in benzene other than by determining relative rates. With the unsaturated fluorohydrin, however, the rate of its conversion to **12** in benzene is clearly slower than its rate of fragmentation and its intermediacy in the production of **12** is therefore not possible.

A number of suggestions about the mechanisms of these reactions may be made from the above results. The opening of the epoxide ring of **3** in benzene seems to involve, at least in part, a transition state of greater carbonium ion character than the equivalent reaction in ether. If a carbonium ion were formed in both solvents one would expect the ketone **12** to be a primary product in each case. In point of fact, it is found as a primary product in benzene alone, its formation in ether apparently resulting only at the expense of the fluorohydrin. The products found in ether solution most likely arise through a cationic intermediate in which the integrity of the carbon–oxygen bond is for the most part maintained (Fig. 2, path a).[13] It seems reasonable, therefore, that formation of the cyclo-

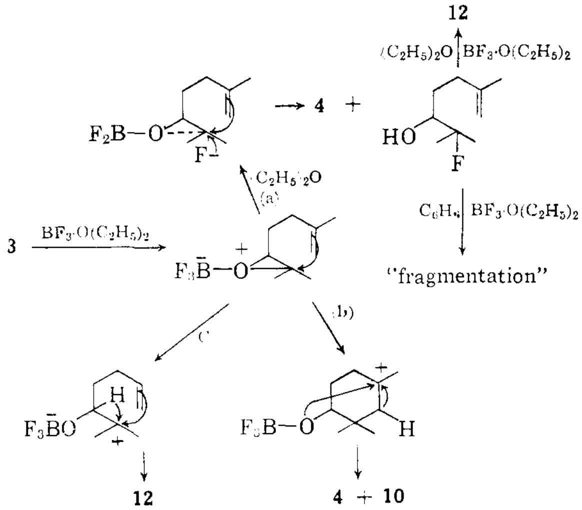


Fig. 2.

---

[12] An explanation of this rate difference is given by H. O. House and D. J. Reif, *J. Am. Chem. Soc.*, **77**, 6525 (1955).

[13] The actual source of fluoride ion in this reaction is not known. It may result from dissociation of either the boron fluoride epoxide complex (Fig. 2, path b) or the ether complex.

hexenol **4** also follows a "concerted" pathway in ether.

The formation of products in benzene solution appears to be the result of both concerted and nonconcerted epoxide opening. As indicated above, the production of the ketone **12** in benzene suggests the intermediacy of a carbonium ion (path b, Fig. 2). Both **4** and **10** are also derivable from this ion. That the latter two compounds are also formed by ring opening with participation of the double bond (path c, Fig. 2) is suggested by the fact that the rate of disappearance, in benzene, of **3** is faster than that of the saturated epoxide. When an equimolar mixture of **3** and **17** was treated with boron fluoride etherate in benzene for 15 minutes, only 79% of **17** was converted to ketone. As noted above the unsaturated oxinane **3** is completely transformed into products under these conditions.

A similar comparative experiment in ether solution showed a much less striking difference in the rates of disappearance of the two epoxides. After one hour, 37% of the saturated epoxide remained unreacted, in contrast to 26% of the epoxyolefin **3**. This small difference in rate is consistent with the fact that **3** is consumed by the formation of more than one product.

A detailed kinetic study is being undertaken to establish the validity of these mechanistic suggestions.

Acknowledgment.—This investigation was supported by a research grant, No. RG-8679, from the Division of General Medical Sciences of the National Institutes of Health.

Experimental

Melting points and boiling points are uncorrected. Microanalyses by Midwest Microlab, Inc., Indianapolis, Ind. Nuclear magnetic resonance spectra were measured with a Varian model A-60 spectrometer. Infrared spectra were measured on a Perkin-Elmer model 137-B Infracord spectrophotometer. Neat liquids were used except as otherwise noted. Gas chromatographic (g.c.) analyses and product separations were carried out using all glass columns of 2.2 m. length and 6 mm. inner diameter. The column packing was 40-60 mesh Tide, dried 24 hr. at 110° before use. Helium was used as the carrier gas. The stability of all materials to the g.c. conditions was checked by infrared analysis before and after passage through the column.

Geraniolene (**2**).—Geranic acid, prepared from citral by the method of Bernhauer and Forster,[14] was distilled at atmospheric pressure.[5] The fraction boiling from 100° to 140° was collected, dried and redistilled through a 0.8 × 50 cm. spinning band column. From 150 g. of citral there was obtained 82.4 g. (67% yield) of geraniolene, b.p. 139-141° (760 mm.) (lit.[5] 142-143°, 760 mm.). The infrared spectrum showed a strong band at 890 cm.$^{-1}$.

Geraniolene Monoepoxide (**3**).—Geraniolene (64.8 g., 0.52 mole) was dissolved in 1 l. of chloroform and the solution stirred and cooled in ice during the addition over 1 hour of 1 l. of 0.52 *N* monoperphthalic acid[15] solution in ether. Stirring was continued for an additional 3 hours at room temperature. Phthalic acid was removed by filtration and the filtrate was washed with saturated aqueous sodium bicarbonate and saturated salt solution. The solution was dried over sodium sulfate and distilled under reduced pressure on a water-bath at 60°. The residue was then distilled on a 0.8 × 50 cm. spinning band column and the fraction boiling at 93-94° (72 mm.) collected. There was obtained 42 g., 57% of epoxide (pure by g.c. at 100°, 6 p.s.i.), n^{24}D 1.4307. The infrared spectrum showed bands at 1124 and 890 cm.$^{-1}$.

Anal. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.18; H, 11.54.

Rearrangement of Geraniolene Monoepoxide (3). (I) Boron Fluoride Etherate in Benzene.—A solution of 5 g. of geraniolene monoepoxide (**3**) in 100 ml. of dry benzene was cooled in ice. The solution was stirred by means of a magnetic bar and 1 ml. of boron fluoride etherate (freshly distilled at reduced pressure) was added by means of a syringe. The ice-bath was removed and stirring was continued for 15 minutes during which time the solution became cloudy and reddish in color. The reaction mixture was poured into ice and water and, after shaking, the layers were separated. The benzene layer was shaken three times with saturated sodium bicarbonate solution and dried over anhydrous potassium carbonate. The benzene was removed by distillation through a 60-cm. Podbielniak column. As separation of the products could not be effected by fractional distillation, the residue was distilled through a short path apparatus to yield 6.2 g. of material, boiling range 40-80° (25 mm.), containing 27% benzene by gas chromatography.

Analysis of the product mixture by g.c. at 110° (7 p.s.i.) revealed three components with retention times relative to air of 4 min., 7 min. and 14 min. Their separation and purification was effected by collection from the g.c. column through use of an 18 cm. no. 18 hypodermic needle attached to the exit vent of the detector cell.

(a) **2,2,4-Trimethyl-1,4-endoxycyclohexane** (**10**).—The material of retention time 4 minutes was collected and then repassed through the column to effect final purification. Gas chromatographic analysis of this purified material showed a single component, n^{25}D 1.4383. Its infrared spectrum showed representative bands at 2899(s), 2857(m), 1449(s), 1377(s), 1361(m), 1325(m), 1258(m), 1190(m), 1130(m), 1000(s), 980(m), 877(s), 870(m) and 833(m) cm.$^{-1}$. When the cyclic alcohol **4** (0.2 g.) was treated with 0.05 ml. of boron fluoride etherate in 3 ml. of dry benzene for 2 hr. at 65°, **10** could be detected to the extent of 12% by g.c. analysis of the benzene solution after the usual work-up. The rest of the reaction mixture (88%) consisted of unchanged **4**. At room temperature for 2 hr. only a trace of **10** could be detected by g.c.

Anal. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.25; H, 11.32.

(b) **2,6-Dimethylhept-6-en-3-one** (**12**).—Collection of the component of intermediate volatility followed by repassage and recollection yielded purified **12**, n^{25}D 1.4507. It gave a yellow dinitrophenylhydrazone and showed bands in the infrared at 1709(s), 1669(m), 1379(s), 1361(m) and 890(s) cm.$^{-1}$.

Anal. Calcd. for $C_9H_{16}O$: C. 77.09; H. 11.50. Found: C, 76.93; H, 11.52.

(c) **2,2,4-Trimethylcyclohex-3-enol** (**4**).[6]—The least volatile component was collected and purified as above to give a colorless liquid, n^{24}D 1.4696. In the infrared it absorbed at 3333(s), 1667(w), 1379(m), 1361(m) and 1035(s) cm.$^{-1}$.

Anal. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.83; H, 11.48.

Conversion of 4 to 2,2,4-Trimethylcyclohexanone (4).—The cyclic alcohol was stirred under an atmosphere of hydrogen in the presence of 0.15 g. of 10% palladium-on-charcoal. The material absorbed 45.8 ml. of hydrogen (calcd. at 25°, 42.9 ml.). The catalyst was filtered and the solvent evaporated to yield 0.12 g. of material. The saturated alcohol (0.1 g.) was then dissolved in a mixture of 6 g. of chromium trioxide in 6 ml. of pyridine[16] and stirred for 24 hours at room temperature.

It was then poured into ether and water and the product extracted into ether. Removal of the solvent gave 0.064 g. of a pale yellow oil. The semicarbazone was prepared directly without further purification and recrystallized from alcohol to give needles, m.p. 196.5-199°. No depression of melting point occurred on admixture with an

---

[14] K. Bernhauer and R. Forster, *J. prakt. Chem.*, **147**, 199 (1936).

[15] Prepared either by the method of L. F. Fieser, "Experiments in Organic Chemistry," third edition, revised, D. C. Heath and Co., Boston, Mass., p. 329; or H. Bohme, "Organic Syntheses," Coll. Vol. III, J. Wiley and Sons, Inc., New York, N. Y., 1955, p. 619.

[16] G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

authentic sample (see below) and the infrared spectra of the two semicarbazones in chloroform were identical.

2,2,4-Trimethylcyclohexanone (14).—To a stirred solution of 7.8 g. (0.2 mole) of potassium in 200 ml. of dry *tert*-butyl alcohol was added 22.4 g. (0.2 mole) of 4-methylcyclohexanone (Eastman Kodak Co.). After 5 minutes 30 g. (0.21 mole) of methyl iodide was added dropwise over 1 hour. The mixture was stirred for 3 hours at room temperature. Most of the alcohol was removed by distillation, water added and the product extracted with ether. After removal of the solvent the residue was distilled to give 11.6 g. of 2,4-dimethylcyclohexanone, b.p. 50–52° (2 mm.). The semicarbazone melted at 183–188°. Mixture melting point with the semicarbazone of 4-methylcyclohexanone gave m.p. 179–189°.

Repetition of the above conditions on 2,4-dimethylcyclohexanone gave 3 g. of a colorless liquid, b.p. 106–108° (70 mm.), $n^{25}\text{D}$ 1.4449 (lit.[17] b.p. 80° (23 mm.), $n^{24}\text{D}$ 1.4426). The semicarbazone was crystallized from alcohol; m.p. 196.5–199° (lit.[17] 212°).

(II) **Boron Fluoride Etherate in Ether.**—(a) Analytical scale reactions were run on 0.1-g. samples of **3** dissolved in 3 ml. of anhydrous ether. To the stirred chilled solution was added by means of a dry syringe 0.02 ml. of boron fluoride etherate complex. The results of reaction times of 15 and 60 minutes, respectively, at room temperature are given in Table I. The third reaction reported in Table I was done using 0.56 g. of **3** in 10 ml. of dry ether solution with 0.6 ml. of catalyst. The reactions were worked up as described below.

(b) On a preparative scale 5 g. of geraniolene monoepoxide was dissolved in 100 ml. of dry ether. To the chilled, stirred solution was added by means of a dry syringe 1 ml. of freshly distilled boron fluoride etherate complex. The ice-bath was removed and the reaction was allowed to proceed for 1 hour at room temperature. It was then poured into ice and water and the layers separated after thorough shaking. The ethereal solution was washed three times with saturated aqueous sodium bicarbonate and dried over anhydrous potassium carbonate. The ether was removed by distillation at atmospheric pressure through a 60-cm. Podbielniak column. Fractional distillation could not be effected as the material decomposed at 100°. The residue was distilled at a pressure of 1 mm. and a bath temperature of 90° through a short path apparatus to yield 5.4 g. of material containing approximately 10% ether by g.c. Gas chromatographic analysis of this preparative scale product gave the same relative ratios as described for the second experiment in Table I. At 106° (7 p.s.i.) compounds **3**, **12**, **15** and **4**, showed retention times of 6, 7.5, 13 and 19 minutes. The identities of **3**, **12** and **4** were demonstrated by collection of these materials and the comparison of their infrared spectra and g.c. retention times with known samples.

(c) **2-Fluoro-2,6-dimethylhept-6-en-3-ol** (15).—Collection of the material of retention time 13 min. gave a colorless liquid which after a second purification by g.c. was homogeneous, $n^{24}\text{D}$ 1.4344. Its infrared spectrum showed strong bands for a hydroxyl group (3344 cm.$^{-1}$) a *gem*-dimethyl grouping (1383 and 1370 cm.$^{-1}$) and a terminal double bond (890 cm.$^{-1}$). Qualitative analysis for fluorine[18] was positive. Treatment of 0.1 g. of the fluorohydrin with 0.4 mg. of potassium in 100 ml. of *tert*-butyl alcohol under reflux for 2 hours yielded geraniolene monoepoxide as shown by the identity of their infrared spectra and gas chromatographs.

Anal. Calcd. for $C_9H_{17}FO$: C, 67.46; H, 10.69. Found: C, 67.73; H, 10.70.

(d) **2-Fluoro-2,6-dimethylheptan-3-ol** (16).—Hydrogenation of **15** (0.44 g.) was carried out in ethanol solution at atmospheric pressure in the presence of a palladium-on-barium sulfate catalyst. Absorption of hydrogen ceased after the uptake of one mole (65 ml., calcd. 69 ml. at 27°). Filtration from the catalyst was followed by distillation of the alcohol at reduced pressure. The residue was taken up in ether and thoroughly washed with water. Removal of the ether after drying afforded 0.35 g. of material. Purification by g.c. (120°, 7 p.s.i.) gave a colorless liquid, $n^{25}\text{D}$ 1.4152, the infrared spectrum of which showed no band at 890 cm.$^{-1}$.

Anal. Calcd. for $C_9H_{19}FO$: C, 66.62; H, 11.80; F, 11.71. Found: C, 66.80; H, 11.92; F, 11.58.

The unsaturated fluorohydrin (0.15 g.) was also reduced in *tert*-butyl alcohol solution and after completion of the hydrogenation the mixture was filtered directly into a solution of potassium in *tert*-butyl alcohol. After 0.5 hr. under reflux the alcohol was removed at reduced pressure, the residue diluted with ether and the excess alcohol removed by washing with ice-water.

Gas chromatographic analysis of the residue showed the presence of material the retention time of which was identical with that of authentic **17** separately and on admixture. This fraction was collected and its infrared spectrum was also identical with that of **17**.

(III) **Transformations of the Primary Products with Boron Fluoride Etherate.**—(a) To a chilled and stirred solution of 0.1 g. of the fluorohydrin **15** in 2 ml. of dry ether was added 0.02 ml. of boron fluoride etherate. After 3 hours the reaction was worked up in the usual manner. The retention time of the major product (65%) on Tide was identical with that of the ketone **12**. The infrared spectrum of a purified sample of this component was superimposable with that of authentic **12**. The rest of the reaction mixture consisted of a complex mixture of materials of greater volatility than the ketone.

(b) Repetition of the above in benzene solution gave a mixture of volatile substances consisting of approximately 15% ketone **12**.

(c) The ketone **12** (0.213 g.) in 3 ml. of dry benzene was let stand for 3 hours at room temperature in the presence of 0.05 ml. of boron fluoride etherate. Workup and analysis in the usual manner showed unchanged starting material.

Dihydrogeraniolene Monoepoxide (17).—Geraniolene monoepoxide (8.3 g.) was hydrogenated in alcohol at atmospheric pressure in the presence of 1 g. of palladium-on-calcium carbonate. After approximately one mole of hydrogen had been absorbed the catalyst was filtered. The crude product obtained after removal of the solvent was distilled using a 0.8 × 50 cm. spinning band column. The fraction boiling at 96–97° (1.0 g.), $n^{24}\text{D}$ 1.4121, displayed a band at 1124 cm.$^{-1}$ in the infrared. The terminal olefin band at 890 cm.$^{-1}$ was absent.

Anal. Calcd. for $C_9H_{18}O$: C, 75.94; H, 12.76. Found: C, 75.88; H, 13.00.

Reaction of 17 with Boron Fluoride Etherate. (a) **Ether Solution.**—Treatment of 0.069 g. of **17** in 2 ml. of dry ether with 0.015 ml. of boron fluoride etherate gave a mixture of a fluorohydrin, a ketone and unreacted epoxide. The infrared spectrum of the fluorohydrin was identical with that of **16** obtained by hydrogenation of **15**. Qualitative analysis for fluorine was positive.[18]

Three drops of the saturated fluorohydrin **16** was dissolved in 3 ml. of dry ether and stirred 0.5 hour in the presence of 0.05 ml. of BF_3. Gas chromatographic analysis of the crude reaction mixture in ether (after base washing) showed the presence of unreacted fluorohydrin and as the major fraction the ketone **18** described below.

(b) **Benzene Solution.**—Treatment of 0.042 g. of **17** in 2 ml. of dry benzene for 15 min. with 0.015 ml. of boron fluoride etherate gave a mixture of **17** and a single transformation product, **18**, which absorbed at 1720, 1379 and 1361 cm.$^{-1}$ in the infrared. The saturated fluorohydrin **16** under the same conditions gave the same compound.

Anal. Calcd. for $C_9H_{18}O$: C, 75.99; H, 12.76. Found: C, 76.05; H, 12.60.

(c) **Relative Rates of Reaction of 3 and 17 in Benzene Solution.**—A mixture of 0.205 g. (1.46 mmoles) of epoxyolefin **3** and 0.202 g. (1.42 mmoles) of saturated epoxide **17** in 10 ml. of dry benzene was treated with 0.08 ml. of boron fluoride etherate, in the usual manner, for 15 min. The reaction was quenched with water and ice, and the benzene solution was washed with sodium bicarbonate solution and dried over anhydrous potassium carbonate. Gas chromatographic analysis of this solution at 120°, 6.5 p.s.i., showed the presence of five components. Comparison with synthetic mixtures revealed these to be, in order of volatility, **10**, **17**, **18**, **12** and **4**. No unsaturated epoxide **3** could be detected. All six possible compounds were sharply resolved in the chromatogram of the appropriate synthetic mixture.

Integration of the peak areas of the reaction mixture

---

[17] R. Calas, *Compt. rend.*, **208**, 1413 (1939).

[18] R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 2nd ed., J. Wiley and Sons, Inc., New York, N. Y., 1956, p. 62.

chromatogram indicated 21% unreacted **17**. In addition, the ratio of the sum of the peak areas of **10**, **12** and **14** to that of **17** and **18** was 1.03:1. The molar ratio of **3** to **17** in the original reaction mixture was 1.02:1.

(d) **Relative Rates of Reaction of 3 and 17 in Ether Solution.**—A mixture of 0.192 g. (1.37 mmoles) of **3** and 0.192 g. (1.35 mmoles) of **17** was treated with 0.08 ml. of boron fluoride etherate in 10 ml. of dry ether for 1 hour at room temperature. The reaction mixture was worked up in the usual manner, and the dried ethereal solution analyzed at 112°, 8 p.s.i. Measurement of peak areas indicated 37% unreacted **17** and 26% unreacted **3**.

[Contribution from the Department of Chemistry, University of Colorado, Boulder, Colo.]

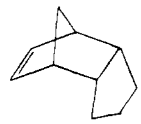
Bridged Polycyclic Compounds. XIX. Some Addition and Solvolysis Reactions in Norbornane Systems[1]

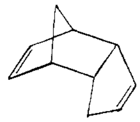
By Stanley J. Cristol, Wolfgang K. Seifert, Donald W. Johnson and J. Byrne Jurale

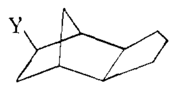
Received June 14, 1962

Acid-catalyzed additions of acetic acid, formic acid and water to *endo*-dihydrodicyclopentadiene (I) lead to products in which almost complete ring isomerizations (to III, or its analogs) has occurred. On the other hand, addition of methanol (or of water in methanol solvent) to I or to dicyclopentadiene (II), followed by hydrogenation, gives a mixture containing about 1 part of *endo* skeleton unrearranged product (VI, Y = OMe, OH) to 6 parts of *exo* skeleton product III. Solvolysis of the toluenesulfonates of III and VI in methanol both give a large preponderance of *exo* product (*ca.* 30:1 = III:VI). Addition of methanol or of acetic acid to norbornadiene (X) gives substantially more dehydronorbornyl methyl ether (XI, Y = OMe) or dehydronorbornyl acetate (XI, Y = OAc) in the mixture with nortricyclyl products XII (Y = OCH_3, $OCOCH_3$) than solvolysis of the *p*-bromobenzenesulfonate of either XI or XII. Possible explanations of these results are discussed.

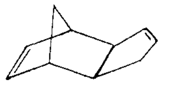
Ionic additions to *endo*-1,2-dihydrodicyclopentadiene (I) and to *endo*-dicyclopentadiene (II) have been reported to give products III (or the dehydro analogs) with *exo* configuration of addenda and also with rearranged, *i.e.*, *exo* ring skeletons.[2] *exo*-Dicyclopentadiene (IV) is reported,[2f] in contrast, to add HY reagents without rearrangement and thus to give products identical with those from II. In general, then, isomers with *endo* ring skeletons were not observed from addition to olefins with either *endo* or *exo* ring systems. In addition, it has been reported[3] that the *exo-exo* product III (Y = OAc) resulted from the acetolysis of the *p*-toluenesulfonate related to either *exo*-III or its epimer, or of the *p*-toluenesulfonate of *endo*-VI or its epimer. At the time most of the work listed in references 2 and 3 was done, techniques for analysis of very minor constituents were not available, so that products with *endo* ring systems might understandably be missed. We decided, therefore, to reinvestigate selected portions of this problem, and our initial results in this and analogous systems are reported herein.

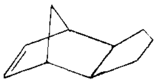

I

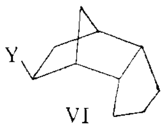

II



III


IV


V



VI

Addition of formic acid to *endo*-dihydrodicyclopentadiene (I) or to *endo*-dicyclopentadiene (II) and of acetic acid (catalyzed by 1.5% of sulfuric acid) to II led (after hydrogenation, where applicable) preponderantly, as suggested by earlier work,[2] to products with *exo* ring skeletons and *exo* substituents (III, Y = OCHO, $OCOCH_3$). The products were investigated by saponification or lithium aluminum hydride reduction to the alcohols; it was observed that the alcohol mixtures, which were largely III (Y = OH), were contaminated with small amounts of *endo* skeleton isomers VI (Y = OH). When we first began work on this problem, infrared analytical procedures were the best available to us, and our results indicated that the *endo* ring system was being converted to *exo* in substantially over 90% of the product. Work was not conducted with *exo*-olefin V, as it was felt that analytical methods were not precise enough to analyze mixtures using infrared techniques. Hydration of *endo*-olefin I with 22% sulfuric acid in water gave a product which was principally *exo* skeleton III (Y = OH), as reported earlier.[2a,d] This product was now analyzed by vapor-phase chromatography and contained about 2% *endo* skeleton; the reaction conversion was about 45%, and the remaining olefin was not isomerized. Again there appeared to be no reason to study the *exo*-olefin V, in view of the almost complete rearrangement observed with I.

The results described above appeared consistent with the idea that the products were derived largely, if not entirely, from a single *product-determining* intermediate, presumably a non-classical carbonium ion such as VII, for which the resonance structures VIII and IX can be written. This intermediate presumably could be the immediate precursor of both *endo* and *exo* products. Reaction

---

[1] Previous paper in series: S. J. Cristol, J. R. Douglass, W. C. Firth, Jr., and R. E. Krall, *J. Org. Chem.*, **27**, 2711 (1962).

[2] See, *inter alia:* (a) H. A. Bruson and T. W. Riener, *J. Am. Chem. Soc.*, **67**, 723 (1945); (b) **67**, 1178 (1945); (c) **68**, 8 (1946); (d) P. D. Bartlett and A. Schneider, *ibid.*, **68**, 6 (1946); (e) F. Bergmann and H. Japhe, *ibid.*, **69**, 1826 (1947); (f) P. D. Bartlett and I. S. Goldstein, *ibid.*, **69**, 2553 (1947); (g) M. Gates and P. S. Malchick, *ibid.*, **76**, 1378 (1954); (h) K. Alder, F. H. Flock and H. Wirtz, *Chem. Ber.*, **91**, 609 (1958); (i) P. Wilder, Jr., C. F. Culbertson and G. T. Youngblood, *J. Am. Chem. Soc.*, **81**, 655 (1959); (j) S. J. Cristol, W. K. Seifert and S. B. Soloway, *ibid.*, **82**, 2351 (1960).

[3] (a) R. S. Barnes, Ph.D. thesis, Harvard University, 1951; (b) P. D. Bartlett, Abstracts of Papers, 12th National Organic Chemistry Symposium, June, 1951, p. 1.