**2-(*cis*-2-Hydroxycycloheptyl)propenol (22).**—The procedure described for the cyclohexyl analog **9** was employed except 1,2-dimethoxyethane was used as the solvent throughout, and the mineral oil was not washed from the sodium hydride. An equal volume of ether was added to aid granulation of the salts after the addition of aqueous sodium hydroxide. From 2.87 g. of lactone ester **21** and 2.0 g. of 50% sodium hydride in mineral oil was obtained 3.3 g. of crude product.

This material was chromatographed on 60 g. of silica gel. Elution with 50% ether in benzene gave 0.31 g. (14%) of crystalline lactol **28**. The analytical sample, m.p. 95.5–97°, was obtained after two recrystallizations from hexane followed by sublimation at 30° (0.05 mm.): $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.95 (OH), 8.15, 9.00, 9.17, 9.25, 10.15, 10.64 $\mu$; $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ 5.25 [CHC*H*(OH)O–; doublet, $J$ = 4 c.p.s.], 5.0–3.8 (C*H*O–, OH), 0.97 p.p.m. (CHC$\mathit{H}_3$; doublet, $J$ = 6 c.p.s.).

*Anal.* Calcd. for $C_{10}H_{18}O_2$: C, 70.53; H, 10.68. Found: C, 70.6; H, 10.7.

Elution with ether gave 0.73 g. (32%) of oily diol **22**: $\lambda_{\max}^{\mathrm{CHCl_3}}$ 3.0 (OH), 6.08 ($\mathrm{C{=}CH_2}$), 10.9 $\mu$; $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ 5.02 ($\mathrm{C{=}CH_2}$; doublet, $J$ = 1.5 c.p.s.), 4.88 ($\mathrm{C{=}CH_2}$; doublet, $J$ = 1.5 c.p.s.), 5.4–4.7 (OH), 4.0 p.p.m. (C$\mathit{H}_2$OH). A sample of the oil was distilled, b.p. 80–90° (bath temperature) (0.2 mm.).

The carbomethoxylation experiment described for lactone ester **21** was repeated using 1.54 g. of lactone **20**. The dimethyl carbonate was removed under reduced pressure after carbomethoxylation was complete and the residual enolate was reduced using 1.7 g. of lithium aluminum hydride according to the procedure described for lactone ester **9**. Chromatography on silica gel gave 0.25 g. of lactol **28** and 0.81 g. of diol **22**.

**2-(*cis*-2-Hydroxycycloheptyl)propenoic Acid Lactone (4).**—The procedure described for diol **19** was followed using 0.26 g. of chromatographed diol **22**. The resulting lactone (0.15 g., 58% yield) was distilled and the distillate, b.p. 60–70° (bath temperature) (0.05 mm.), was chromatographed on 6 g. of silica gel. Elution with 5% ether in benzene afforded 0.1 g. of material which was distilled for analysis: $\lambda_{\max}^{\mathrm{film}}$ 5.68 (lactone CO), 6.00 ($\mathrm{C{=}CH_2}$), 7.87, 8.62, 8.87, 9.99, 12.26 $\mu$; $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ 6.27 ($\mathrm{C{=}CH_2}$; doublet, $J$ = 3 c.p.s.), 5.56 ($\mathrm{C{=}CH_2}$; doublet, $J$ = 3 c.p.s.), 4.72 p.p.m. [C*H*O–; triplet of doublets, $J$ (triplet) = 9 c.p.s., $J$ (doublet) = 4 c.p.s.].

*Anal.* Calcd. for $C_{10}H_{14}O_2$: C, 72.24; H, 8.51. Found: C, 72.8; H, 8.7.

**2-(*trans*-2-Hydroxycyclohexyl)propanoic Acid Lactone (25).**—A stirred solution containing 341 mg. of crude lactol **23** in 5 ml. of acetone at 0° was treated dropwise with 8 *M* chromic acid reagent until the red color was no longer dissipated (0.55 ml. required). The mixture was diluted with aqueous sodium bicarbonate and the product was isolated with ether.[17b] The crude material was treated with 10 ml. of 10% ethanolic potassium hydroxide, and the solution was warmed briefly on a steam bath and allowed to stand at room temperature for 3 hr. Water was added, and the mixture was washed with ether. The alkaline solution was acidified with concentrated hydrochloric acid and saturated with salt, and the product was isolated with ether. The crude hydroxy acid was dissolved in 40 ml. of benzene, 10 mg. of *p*-toluenesulfonic acid was added, and the solution was stirred under reflux with continuous removal of water *via* a Dean–Stark trap. The cooled solution was washed with saturated sodium bicarbonate solution and dried over anhydrous sodium sulfate, and the product was distilled giving 195 mg. (58%), b.p. 55–70° (bath temperature) (0.05 mm.).

This compound was identical with the lactone **25** previously prepared by Herz and Glick[14] as evidenced by infrared and n.m.r. spectral comparison.[24]

**2-(*cis*-2-Hydroxycyclohexyl)propanoic Acid Lactone (29).**—A solution containing 103 mg. of crude lactol **27** in 2 ml. of acetone was oxidized using 0.16 ml. of standard chromic acid reagent. The material was processed according to the procedure described for the *trans* isomer **25** except the benzene azeotrope procedure was unnecessary. Distillation afforded 57 mg. (56%) of lactone **29**,[14] b.p. 70–80° (bath temperature) (0.2 mm.). The identity of this material was ascertained by comparison of the infrared and n.m.r. spectra with those of authentic lactone **29**.[24]

**2-(*trans*-2-Hydroxycycloheptyl)propanoic Acid Lactone (26).**—A solution containing 205 mg. of crude lactol **24** in 3 ml. of acetone was oxidized with 0.3 ml. of standard chromic acid reagent. The material was processed according to the procedure described above for lactone **29**, and the crude lactone was chromatographed on 10 g. of silica gel. Elution with 10% ether in benzene gave 100 mg. (50%) of lactone **26**[14] identified by comparison of the infrared and n.m.r. spectra with those of authentic material.[24]

**2-(*cis*-2-Hydroxycycloheptyl)propanoic Acid Lactone (30).**—The procedure described above for the *trans* isomer **26** was followed using 33 mg. of crystalline lactol **28** and 0.05 ml. of standard chromic acid solution. The product was isolated with ether and distilled giving 33 mg. (100%) of lactone **30**,[14] b.p. 70–80° (bath temperature) (0.15 mm.).

**Acknowledgment.**—We thank the Public Health Service for support of this work through a research grant (AI-04965) from the National Institute of Allergy and Infectious Diseases and a fellowship (5-F1-GM-19,839) from the National Institute of General Medical Sciences.

---

[24] The infrared and n.m.r. spectra of this material were kindly provided by Professor Herz.

---

# Acid-Catalyzed Reactions of 4,5-Epoxy-2,2,4-trimethylpentyl Isobutyrate[1]

WAYNE V. McCONNELL AND WILLIAM H. MOORE

*Research Laboratories, Tennessee Eastman Company, Division of Eastman Kodak Company, Kingsport, Tennessee*

*Received April 1, 1965*

4,5-Epoxy-2,2,4-trimethylpentyl isobutyrate was found to rearrange to tetrahydro-2,4,4-trimethylfurfuryl isobutyrate and 2,2,4-trimethyl-5-oxopentyl isobutyrate in the presence of boron fluoride. In reactions catalyzed by other acids, this epoxy ester isomerized to the aldehydic ester, 2,2,4-trimethyl-5-oxopentyl isobutyrate, but did not give the tetrahydrofurfuryl ester. The greatest emphasis was placed on the boron fluoride catalyzed rearrangement of the 4,5-epoxyalkyl ester to the tetrahydrofurfuryl ester, since this reaction has not been previously reported. The reactions could be directed to give either the tetrahydrofurfuryl ester or the aldehydic ester as the major product by varying the medium and temperature used for the reaction.

A 4,5-epoxypentyl ester, 4,5-epoxy-2,2,4-trimethylpentyl isobutyrate (**1**), has been found to undergo an unexpected rearrangement in the presence of boron fluoride. The authors previously disclosed an acid-catalyzed rearrangement of 3,4-epoxyalkyl esters to substituted tetrahydro-3-furyl esters and briefly mentioned the above 4,5-epoxyalkyl ester in the earlier publication.[2]

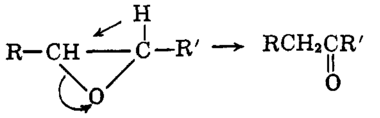
In considering the chemistry of epoxides, reactions of the epoxy group generally involve an attack by an external nucleophilic group. However, it has been recognized that an attack on an epoxy group can be initiated by a nucleophilic site on the epoxide molecule

---

[1] Presented at the 147th National Meeting of the American Chemical Society, Philadelphia, Pa., April 1964.

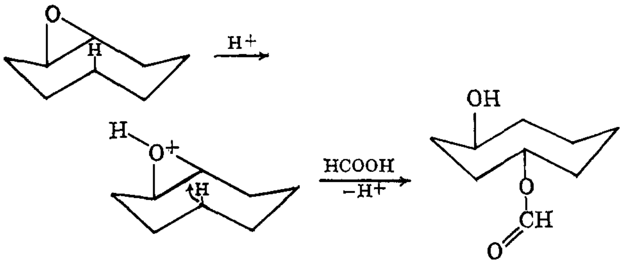
[2] W. V. McConnell and W. H. Moore, *J. Org. Chem.*, **28**, 822 (1963).

itself. The isomerization of an epoxide to an aldehyde or ketone is the best known example of such a reaction. This isomerization has been considered to involve the attack of a hydride ion.[3] Cope and coworkers observed that formolysis of epoxycyclooctane

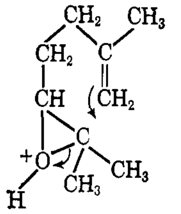


$$R{-}CH{-}C(H){-}R' \longrightarrow RCH_2\overset{\displaystyle O}{\overset{\|}{C}}R'$$

resulted in the formation of 1,4-cyclooctanediol monoformate rather than the 1,2-diol monoformate.[4] Although this reaction involves an external anion, the attack on the epoxy group is attributed to a transannular attack by a hydride ion as shown below. A

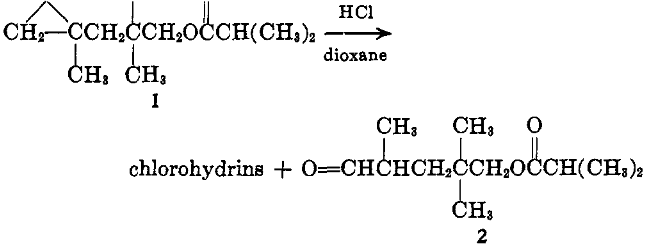


rearrangement arising from epoxide ring opening which resulted from an intramolecular attack was recently disclosed by Goldsmith in a study of geraniolene monoepoxide.[5] In this compound the olefinic group was considered to serve as the nucleophile according to the following scheme. The rearrangements of the epoxy



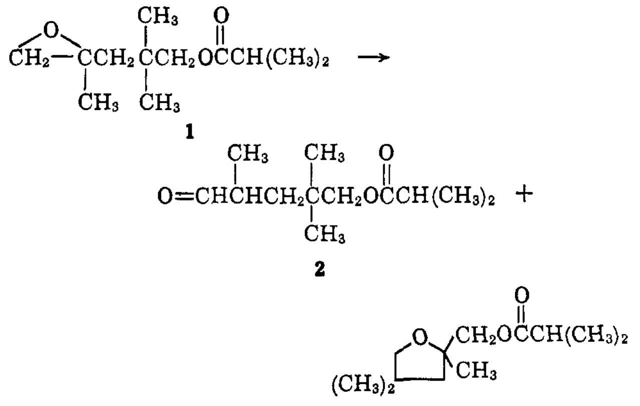
esters appeared to be related to such internal interactions, with the ester groups functioning as the nucleophilic sites.

In our previous disclosure, it was reported that the 4,5-epoxyalkyl ester 1 underwent hydrogen chloride addition under the conditions of functional group analysis.[2] The other significant product from this reaction was the aldehydic ester, 2,2,4-trimethyl-5-oxopentyl isobutyrate (2). A further study has demonstrated that isomerization of this 4,5-epoxyalkyl ester 1 to the aldehydic ester 2 is generally encountered in the presence of acid catalysts.



$$\underset{\mathbf{1}}{\overset{O}{CH_2{-}}\underset{CH_3}{C}CH_2\overset{CH_3}{\underset{CH_3}{C}}CH_2O\overset{O}{\overset{\|}{C}}CH(CH_3)_2} \xrightarrow[\text{dioxane}]{HCl} \text{chlorohydrins} + \underset{\mathbf{2}}{O{=}CH\overset{CH_3}{C}HCH_2\overset{CH_3}{\underset{CH_3}{C}}CH_2O\overset{O}{\overset{\|}{C}}CH(CH_3)_2}$$

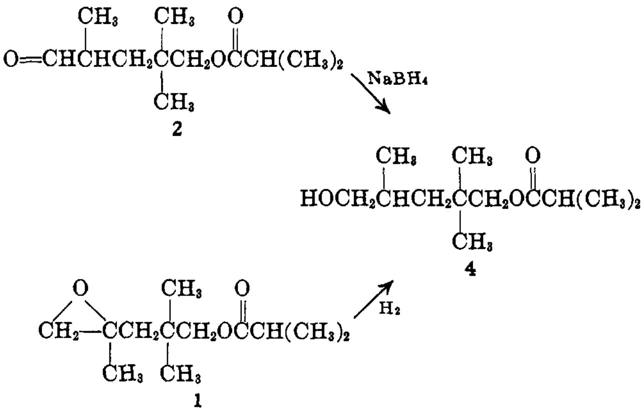
When boron fluoride was used as the catalyst, however, a rearrangement of the 4,5-epoxyalkyl ester 1 to tetrahydro-2,4,4-trimethylfurfuryl isobutyrate (3) was observed. This reaction was first observed when boron fluoride etherate was added to a solution of the epoxy ester 1 in cyclohexane. An exothermic reaction resulted and the epoxy ester 1 was immediately converted to other products. A gas chromatogram of the reaction mixture, obtained by using a column heated at 165° and containing Carbowax 20M as the liquid phase, showed two peaks having retention times of 1.6 and 3.1 min. The retention time for the starting epoxy ester 1 under these conditions was 2.8 min. The product responsible for the peak with the shorter retention time was the tetrahydrofurfuryl isobutyrate 3 and the product which was eluted last was the aldehydic ester 2.



$$\underset{\mathbf{1}}{\overset{O}{CH_2{-}}\underset{CH_3}{C}CH_2\overset{CH_3}{\underset{CH_3}{C}}CH_2O\overset{O}{\overset{\|}{C}}CH(CH_3)_2} \longrightarrow \underset{\mathbf{2}}{O{=}CH\overset{CH_3}{C}HCH_2\overset{CH_3}{\underset{CH_3}{C}}CH_2O\overset{O}{\overset{\|}{C}}CH(CH_3)_2} + \mathbf{3}$$

3

The following evidence enabled the identification of products 2 and 3. The presence of an aldehyde group in 2 was indicated from its n.m.r. spectrum (doublet at 9.47 p.p.m.). The 2,4-dinitrophenylhydrazone of the compound melted at 77°. Reduction of the aldehydic ester 2 gave the corresponding hydroxy ester, 2,2,4-trimethyl-1,5-pentanediol 1-isobutyrate (4), identified by comparison with the authentic compound obtained by hydrogenolysis of the 4,5-epoxyalkyl ester 1.



$$\underset{\mathbf{2}}{O{=}CH\overset{CH_3}{C}HCH_2\overset{CH_3}{\underset{CH_3}{C}}CH_2O\overset{O}{\overset{\|}{C}}CH(CH_3)_2} \xrightarrow{NaBH_4} \underset{\mathbf{4}}{HOCH_2\overset{CH_3}{C}HCH_2\overset{CH_3}{\underset{CH_3}{C}}CH_2O\overset{O}{\overset{\|}{C}}CH(CH_3)_2} \xleftarrow{H_2} \underset{\mathbf{1}}{\overset{O}{CH_2{-}}\underset{CH_3}{C}CH_2\overset{CH_3}{\underset{CH_3}{C}}CH_2O\overset{O}{\overset{\|}{C}}CH(CH_3)_2}$$

Elemental analysis and the saponification equivalent of 3 indicated that it is isomeric with the starting epoxy ester 1. Its infrared spectrum contained a strong band for a carbonyl group, but there was no band for a hydroxy group. Since 3 had a lower boiling point than the epoxy ester 1, cyclization to a five- or six-membered ring was suspected. The direction of ring opening of the epoxide determined whether the

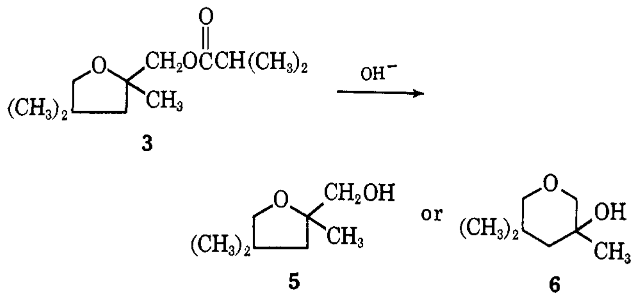
---

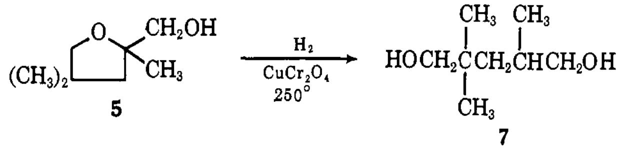
[3] R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 737 (1959).

[4] A. C. Cope, A. Fournier, Jr., and H. E. Simmons, Jr., *J. Am. Chem. Soc.*, **37**, 3905 (1957).

[5] D. J. Goldsmith, *ibid.*, **84**, 3913 (1962).

tetrahydropyran or the tetrahydrofuran derivative was formed. The n.m.r. spectrum of the alcohol obtained by saponification of **3** was consistent with structure **5** or **6** but it did not distinguish between these structures. The identification was completed by chemical means. The alcohol (**5** or **6**) was stable in the presence of strong acids under conditions which would be expected to lead to dehydration of **6**. The conversion of the alcohol by hydrogenolysis to 2,2,4-trimethyl-1,5-pentanediol (**7**) confirmed the identity as tetrahydro-2,4,4-trimethylfurfuryl alcohol (**5**). The identity of **3** was established as tetrahydro-2,4,4-trimethylfurfuryl isobutyrate.





The tetrahydrofurfuryl isobutyrate **3** was obtained as the major product only in reactions catalyzed with boron fluoride. However, the temperature and the solvent used for the reaction exerted a pronounced effect on the ratio of products **2** and **3**. In some solvents the effect was sufficient to favor the formation of the aldehydic ester **2**. In the experiments that supplied the data shown in Table I, a 25% solution of the epoxy ester **1** in the solvent used for the reaction was added dropwise to a solution comprising boron fluoride etherate and the solvent. In most instances, the epoxy ester **1** was converted to **2** and **3** immediately upon contact with the catalyst. In ethyl ether or benzene medium, the combined yield of **2** and **3** was approximately 90%. A small quantity of boron fluoride was sufficient to catalyze the reaction, and the catalyst concentration over the range studied did not greatly alter the ratio of the tetrahydrofurfuryl ester **3** to the aldehydic ester **2**. It can be seen from Table I that, at a concentration of 0.03 mole of boron fluoride/mole of epoxy ester **1**, the rearrangement is much slower in ethyl ether than in benzene. Low reaction temperatures favored the formation of the tetrahydrofurfuryl ester **3**. The effect of solvents on the ratio of the reaction products was shown to be even more dramatic. Rearrangement to the tetrahydrofurfuryl ester **3** predominated in benzene and in ethyl ether, whereas isomerization to the aldehydic ester **2** was favored in solvents which greatly suppress the electrophilic character of boron fluoride. In dimethyl sulfoxide, the most basic solvent used, only a trace of the tetrahydrofurfuryl ester **3** was formed, whereas the aldehydic ester **2** was obtained in 60% yield.

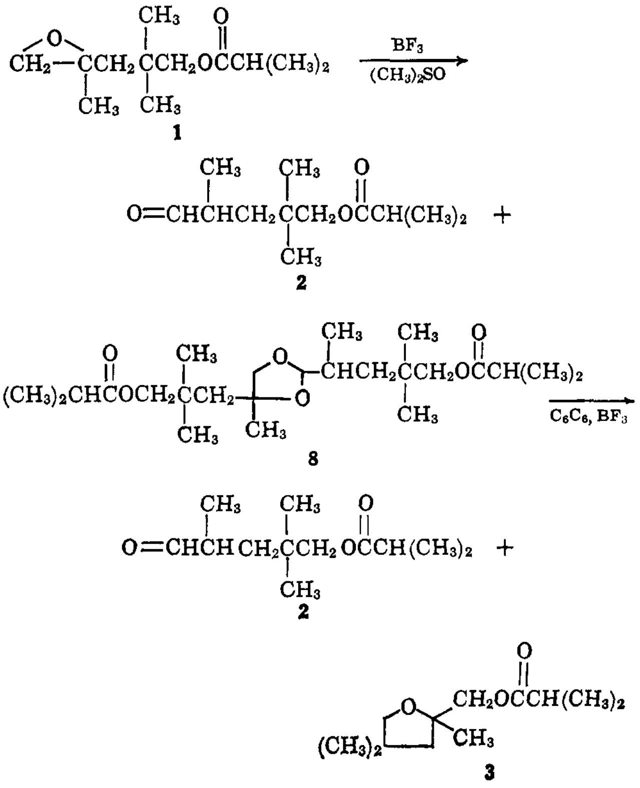
Table I

Effects of Temperature and Solvent on the Rearrangement of 4,5-Epoxy-2,2,4-trimethylpentyl Isobutyrate

| Solvent | Boron fluoride/ epoxide, mole ratio | Reaction time, hr. | Reaction temp., °C. | Wt. ratio of products, 3/2 |
|---|---|---|---|---|
| Ethyl ether | 0.16 | <0.1 | 10 | 3.2 |
| Ethyl ether | 0.03 | 1.5 | 35 | 2.3 |
| Ethyl ether | 0.16 | <0.1 | 35 | 2.6 |
| Ethyl ether | 1.0 | <0.1 | 35 | 2.0 |
| Benzene | 0.16 | <0.1 | 10 | 3.0 |
| Benzene | 0.03 | <0.1 | 35 | 1.4 |
| Benzene | 0.16 | <0.1 | 35 | 1.6 |
| Benzene | 1.0 | <0.1 | 35 | 1.6 |
| Benzene | 0.16 | <0.1 | 75 | 1.2 |
| Toluene | 0.16 | <0.1 | 100 | 0.9 |
| Acetonitrile | 0.16 | 2.0 | 35 | 1.0 |
| Ethyl acetate | 0.16 | <0.1 | 25 | 0.7 |
| Dimethyl sulfoxide | 0.16 | 6.0 | 25 | 0.0 |

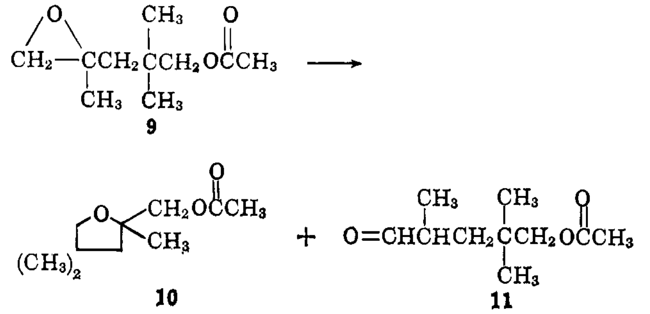
Although the boron fluoride catalyzed reactions generally led to the formation of the tetrahydrofurfuryl and the aldehydic esters as the major products, one other product deserves consideration. In the preparations in which boron fluoride and dimethyl sulfoxide were employed as the catalyst and solvent, respectively, a new compound **8** was formed along with the aldehydic ester **2**. **8** was purified by molecular distillation. Molecular weight determination and carbon and hydrogen analyses indicated that it was a dimer of the starting epoxy ester **1**. Assignment of the cyclic acetal structure to **8** was made when acid cleavage was effected by refluxing a solution of **8** in benzene in the presence of boron fluoride. The aldehydic ester **2** and the tetrahydrofurfuryl ester **3** were the products of the reaction. The dimeric acetal **8** was also ob-

Chart I



tained as a prominent product from the epoxy ester **1** in reactions catalyzed by other acids such as sulfuric, phosphoric, and *p*-toluenesulfonic acids. With these catalysts, the tetrahydrofurfuryl ester **3** was generally detected in only trace amounts if at all. (See Chart I.)

The behavior of 4,5-epoxy-2,2,4-trimethylpentyl acetate (**9**) was found to be analogous to that of the corresponding isobutyrate. In the presence of boron fluoride etherate (0.16 mole of boron fluoride/mole of **9**) in ethyl ether, **9** rearranged immediately to tetrahydro-2,4,4-trimethylfurfuryl acetate (**10**) and to 2,2,4-trimethyl-5-oxopentyl acetate (**11**).

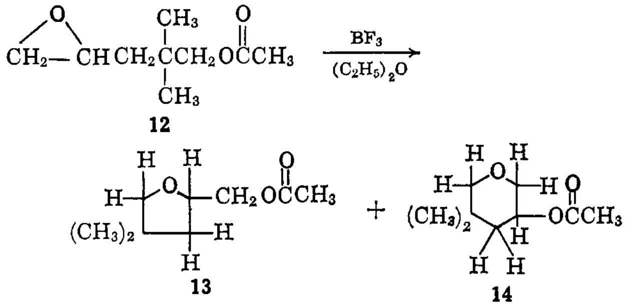


**9**

**10**

**11**

Rearrangement to a tetrahydrofurfuryl ester was also observed with 4,5-epoxy-2,2-dimethylpentyl acetate (**12**), which does not have a methyl substituent on C-4. In a boron fluoride catalyzed reaction, this epoxy ester **12** was converted to tetrahydro-4,4-dimethylfurfuryl acetate (**13**) and a small amount of an isomeric ester, tetrahydro-5,5-dimethyl-3-pyranyl acetate (**14**). The significantly slower reaction of **12** required about 10 to 30 min. to go to completion under conditions which led to the immediate rearrangement of the 4,5-epoxy-2,2,4-trimethylpentyl esters.

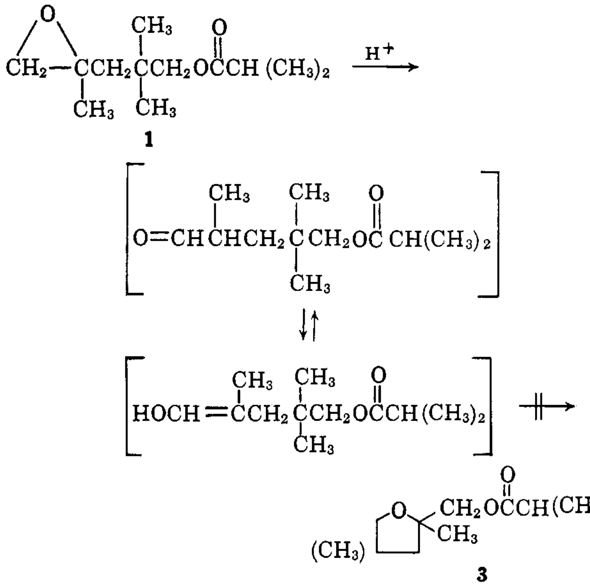


**12**

**13**

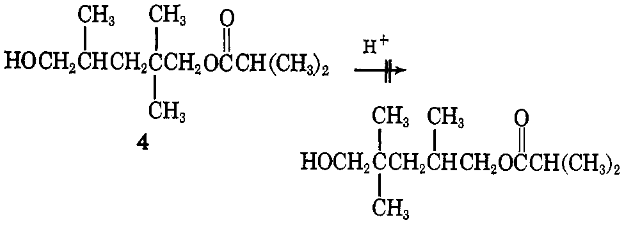
**14**

Since the rearrangement leading to the formation of the tetrahydrofurfuryl esters has not been previously disclosed, this reaction was of particular interest. It required the rupture of the epoxide linkage accompanied by ring closure to the tetrahydrofuran structure and acyl group migration from C-1 to C-5. In a search for an intermediate for the rearrangement, the aldehydic ester **2** was considered. However, an investigation of this possibility showed that none of the tetrahydrofurfuryl ester **3** was formed from the aldehydic ester **2** when conditions that were the most conducive to the preparation of the furan derivative **3** from the epoxy ester **1** were used. Also, the possibility of the cyclic acetal dimer **8** as an intermediate was discounted since its cleavage to **2** and **3** required much more vigorous conditions than were necessary for the rearrangement of the epoxy ester **1** to these products. In addition, under conditions that led to the conversion of the epoxy ester **1** mostly to the tetrahydrofurfuryl ester **3**, the aldehydic ester **2** was the major product derived from the cyclic acetal **8**. Another pertinent study involved unsuccessful attempts to effect an acid-catalyzed isomerization of 2,2,4-trimethyl-1,5-pentanediol 1-isobutyrate (**4**) to its isomer, the 5-isobutyrate.



**1**

**3**

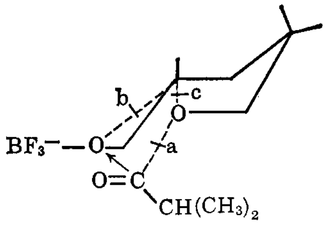


$$HOCH_2CH(CH_3)CH_2C(CH_3)_2CH_2OC(=O)CH(CH_3)_2 \;\not\xrightarrow{H^+}\; HOCH_2C(CH_3)_2CH_2CH(CH_3)CH_2OC(=O)CH(CH_3)_2$$

**4**

It appeared likely that the rearrangement of **1** involved interaction of the ester and the epoxide functions. A separate experiment indicated that an intramolecular process was involved. A mixture of 4,5-epoxy-2,2,4-trimethylpentyl isobutyrate (**1**) and 4,5-epoxy-2,2-dimethylpentyl acetate (**12**) in a 1:1 mole ratio was treated with boron fluoride in ethyl ether at 35°. The products derived from this mixture were only those obtained from **1** and **12** when these epoxides were rearranged separately under similar conditions. The presence of other esters such as tetrahydro-2,4,4-trimethylfurfuryl acetate (**10**) or tetrahydro-4,4-dimethylfurfuryl isobutyrate, for example, would be expected if the rearrangement were intermolecular in character. None of the esters which would result from an interaction of **1** and **12** were detected.

From the evidence at hand, it appeared that the formation of the tetrahydrofurfuryl esters required the orientation of the 4,5-epoxy-2,2,4-trimethylpentyl esters into a structure which would promote ring closure to the tetrahydrofuran nucleus and acyl group migration. Boron fluoride was the only catalyst which led to the formation of tetrahydrofurfuryl compounds in significant yields. The following transition state of the



epoxy ester would permit the required transformations. This conformation would enable the ether oxygen of the ester group to attack the carbon atom of the epoxide function. The resultant formation of bond c is accompanied by bond rupture at a and b and by migration of the acyl group as shown. If the required orientation does not take place, the formation of bond c is not effected and the epoxide is converted to the aldehydic ester by a hydride shift. The observation (Table I) that the tetrahydrofurfuryl ester is favored by low reaction temperatures suggests that the decreased thermal motion of the ester molecules under these conditions provides a better opportunity for orientation to the cyclic transition state.

In the 4,5-epoxy-2,2,4-trimethylpentyl esters, the methyl substituent on C-4 assisted in the rupture of bond b. In the absence of this methyl group, however, as in the case of 4,5-epoxy-2,2-dimethylpentyl acetate (**12**), there was evidence of attack by the ether oxygen of the ester group on both of the carbon atoms of the epoxy group; the attack on C-4 predominated.

This investigation provides an extension of our previous disclosure concerning the rearrangement of 3,4-epoxyalkyl esters. It further demonstrates that intramolecular rearrangements of epoxyalkyl esters may occur when steric and electronic factors are suitable for the interaction of epoxy and ester groups.

## Experimental Section

**Preparation of Unsaturated Alcohols. A. 2,2,4-Trimethyl-4-penten-1-ol.**—This alcohol was prepared by the sodium borohydride reduction of 2,2,4-trimethyl-4-pentenal as was previously described.[2]

**B. 2,2-Dimethyl-4-penten-1-ol.**—The reduction of 2,2-dimethyl-4-pentenal by sodium borohydride gave a 65% yield of 2,2-dimethyl-4-penten-1-ol, b.p. 77–79° (43 mm.). The unsaturated aldehyde was prepared according to the procedure described by Brannock.[6]

**Preparation of Unsaturated Esters. A. 2,2,4-Trimethyl-4-penten-1-yl Isobutyrate.**—2,2,4-Trimethyl-4-penten-1-ol was acylated with isobutyric anhydride in the presence of potassium carbonate to give the desired unsaturated ester, b.p. 77–79° (5 mm.).[2]

**B. 2,2,4-Trimethyl-4-penten-1-yl Acetate.**—By employing a procedure similar to that just described for the corresponding isobutyrate, 2,2,4-trimethyl-4-penten-1-yl acetate was obtained in 80% yield from 2,2,4-trimethyl-4-penten-1-ol and acetic anhydride in the presence of potassium carbonate. The product distilled at 71.5–73.0° (10 mm.).

**C. 2,2-Dimethyl-4-penten-1-yl Acetate.**—A mixture of 2,2-dimethyl-4-penten-1-ol and acetic anhydride was heated on a steam bath in the presence of potassium carbonate to give an 88% yield of 2,2-dimethyl-4-penten-1-yl acetate, b.p. 81–83° (35 mm.).

**Epoxidation of Unsaturated Esters. General Procedure.**—The epoxidations of the unsaturated esters were carried out by a general procedure in which preformed peroxyacetic acid was used.[7] The reactions were followed by means of gas chromatography. Reaction conditions and physical constants of the epoxy esters are shown in Table II.

TABLE II

EPOXIDATION CONDITIONS AND PHYSICAL CONSTANTS OF THE 4,5-EPOXYALKYL ESTERS

| Epoxy ester | Reaction temp., °C. | Reaction time, hr. | Yield, % | B.p., °C. (mm.) | $n^{20}_{D}$ |
|---|---|---|---|---|---|
| 4,5-Epoxy-2,2,4-trimethylpentyl isobutyrate | 25 | 6 | 73 | 84–86 (1.8) | 1.4369 |
| 4,5-Epoxy-2,2,4-trimethylpentyl acetate | 35 | 6 | 65 | 85–86 (4.0) | 1.4371 |
| 4,5-Epoxy-2,2-dimethylpentyl acetate | 45 | 11 | 67 | 81–82 (4.0) | 1.4351 |

**Tetrahydro-2,4,4-trimethylfurfuryl Isobutyrate (3).**—A solution of boron fluoride etherate (5.3 g.) in benzene (50 ml.) was stirred and warmed to 35°. A solution of 4,5-epoxy-2,2,4-trimethylpentyl isobutyrate (50 g.) in benzene (150 ml.) was then added over a 20-min. period while the temperature was maintained at 35 ± 3°. The reaction mixture was washed immediately with sodium acetate solution and then with water. The benzene layer, after drying over magnesium sulfate, was distilled through a 16-in. packed column. The tetrahydrotrimethylfurfuryl isobutyrate **3** (26 g.) was obtained in 95% purity in the fraction distilling at 97–100° (6 mm.). A higher boiling fraction [20 g., b.p. 76–80° (0.6 mm.)] was composed of 89% of 2,2,4-trimethyl-5-oxopentyl isobutyrate (**2**) and 10% of **3**. A portion of the tetrahydrofurfuryl ester **3** was purified by means of a preparative gas chromatographic column, $n^{20}_{D}$ 1.4329.

*Anal.* Calcd. for $C_{12}H_{22}O_3$: C, 67.3; H, 10.3. Found: C, 67.6; H, 10.1.

**2,2,4-Trimethyl-5-oxopentyl Isobutyrate (2). A. Isomerization of 4,5-Epoxy-2,2,4-trimethylpentyl Isobutyrate (1) in the Presence of Boron Fluoride.**—A solution of epoxy ester **1** (50 g.) in dimethyl sulfoxide (50 ml.) was added to a stirred solution of boron fluoride etherate (10.5 g.) in dimethyl sulfoxide over a period of 15 min. At a temperature of 25–30°, the reaction required 6 hr. to be brought to completion. The course of the reaction was followed by means of gas chromatography. The reaction mixture was poured into an aqueous solution (450 ml.) of sodium acetate (5 g.) and sodium chloride (25 g.). The oil layer was separated, dried over magnesium sulfate, and distilled. The fraction (32 g.) boiling at 82–84° (0.8 mm.) was the aldehydic ester **2**. The residue was composed mainly of the dimeric cyclic acetal **8**.

The 2,4-dinitrophenylhydrazone of **2** melted at 77°.

*Anal.* Calcd. for $C_{18}H_{26}N_4O_6$: N, 14.2. Found: N, 14.5.

**B. Isomerization of Epoxy Ester 1 in the Presence of Sulfuric Acid.**—A procedure for the isomerization of 4,5-epoxy-2,2,4-trimethylpentyl isobutyrate (1) in the presence of sulfuric acid is included in the subsequent description of the preparation of the dimeric cyclic acetal **8**.

**4-(3-Hydroxy-2,2-dimethylpropyl)-β,β,δ,4-tetramethyl-1,3-dioxolane-2-butanol Diisobutyrate (8).**—Two solutions, one consisting of 4,5-epoxy-2,2,4-trimethylpentyl isobutyrate (150 g.) in cyclohexane (150 ml.) and the other of a 50% aqueous sulfuric acid solution (15 g.), were added concurrently to 150 ml. of cyclohexane contained in a three-necked 1-l. flask. The temperature of the stirred mixture was kept at 25–30°. The addition required 15 min., after which time gas chromatographic analysis showed that the reaction of the epoxy ester **1** was complete. The organic layer was separated and washed with sodium bicarbonate solution and then with water. After the solvent was flashed off, the product was distilled. The fraction (51 g.) distilling at 70–85° (0.7 mm.) was 2,2,4-trimethyl-5-oxopentyl isobutyrate (**2**) of 90% purity. The residue (85 g.) was subjected to molecular distillation and gave 62 g. of the cyclic acetal **8**.

*Anal.* Calcd. for $C_{24}H_{44}O_6$: C, 67.3; H, 10.3; mol. wt., 429. Found: C, 67.5; H, 10.5; mol. wt., 433.

**Boron Fluoride Catalyzed Rearrangement of 4,5-Epoxy-2,2,4-trimethylpentyl Isobutyrate (1). General Procedure Showing Effects of Solvent and Temperature.**—Solutions of boron fluoride etherate in the solvents listed in Table I were prepared in concentrations of 2.1, 10.5, and 66.0% (wt./vol.). For each experiment 5 ml. of one of these catalyst solutions was adjusted to the temperature specified in Table I. To this solution was added 5 g. of 4,5-epoxy-2,2,4-trimethylpentyl isobutyrate (1) in 15 ml. of the particular solvent used for the boron fluoride catalyst solution. This addition was made dropwise over a 5-min. period while the temperature was maintained within 3° of that recorded in Table I. The reaction was followed by means

---

[6] K. C. Brannock, *J. Am. Chem. Soc.*, **81**, 3379 (1959).

[7] T. W. Findley, D. Swern, J. T. Scanlan, *ibid.*, **67**, 412 (1945).

of gas chromatography with Carbowax 20M as the liquid phase. Generally, the rearrangements were completed immediately after contacting the epoxy ester 1 with the catalyst. Under some of the conditions, however, the reactions were slower; the approximate reaction times are included in the table. The combined yields of the aldehydic ester 2 and the tetrahydrofurfuryl ester 3 were greater than 90% when benzene or ethyl ether was employed as the solvent.

**Rearrangement of 4,5-Epoxy-2,2-dimethylpentyl Acetate (12).**—A solution of 12 (34.4 g.) in ethyl ether (100 ml.) was added dropwise over a period of 20 min. to 44 ml. of a 10.5% (wt./vol.) solution of boron fluoride etherate in ethyl ether. The temperature was controlled to maintain a gentle reflux during the addition of the epoxy ester and until the reaction was completed (10 min.). The mixture was washed with sodium acetate solution and then with water. Distillation of the mixture gave a fraction (16 g.) distilling at 72–76° (4.2 mm.) which consisted of a binary mixture of 75% of tetrahydro-4,4-dimethylfurfuryl acetate (**13**) and 25% of tetrahydro-5,5-dimethyl-3-pyranyl acetate (**14**). An unidentified viscous oil remained after the distillation of **13** and **14**. Products **13** and **14** were isolated by means of a preparative gas chromatographic column. Infrared spectra showed the presence of a carbonyl group (5.8 $\mu$) and the absence of a hydroxy group in each of the two compounds. The boiling point range of the binary mixture and elemental analyses of the isolated components indicated that both products were isomeric with the starting epoxy ester **12**. Their identifications were completed by n.m.r. analyses. The n.m.r. spectrum for **13** showed multiplet peaks with an area equivalent to three protons $(\text{—O—}\overset{|}{\text{C}}\text{H—CH}_2\text{—O—}\overset{|}{\text{C}}\text{=O})$ at 4.15, single peak with an area equivalent to two protons ($\text{-OCH}_2\text{-}$) at 3.47, multiple peaks accounting for two protons ($\text{-CH}_2\text{-}$) centered at 1.60, single peak for the three protons of the acetyl group at 2.01, and single peak for six protons $\left(>\text{C}<\begin{smallmatrix}\text{CH}_3\\ \text{CH}_3\end{smallmatrix}\right)$ at 1.12 p.p.m. (*Anal.* Calcd. for $C_9H_{16}O_3$: C, 62.8; H, 9.4. Found: C, 62.4; H, 9.3.) The n.m.r. spectrum of **14** showed multiple peaks $(\text{—}\overset{|}{\text{C}}\text{H—O}\underset{|}{\text{C}}\text{=O})$ at 4.90 (the peak for this proton would be expected to be downfield from the $\text{-O-}\overset{|}{\underset{|}{\text{C}}}\text{-H}$ proton in **13**), multiple peaks ($\text{-CH}_2\text{-O-CH}_2\text{-}$) at 3.0 to 4.0, singlet $(\text{CH}_3\overset{|}{\text{C}}\text{=O})$ at 1.97, multiple peaks ($\text{-CH}_2\text{-}$) centered at 1.50, and two singlets $\left(>\text{C}<\begin{smallmatrix}\text{CH}_3\\ \text{CH}_3\end{smallmatrix}\right)$ at 1.04 and 0.95. The areas for the various peaks of this spectrum were also consistent with the number of protons involved in the above assignments. (*Anal.* Calcd. for $C_9H_{16}O_3$: C, 62.8; H, 9.4. Found: C, 62.8; H, 9.3.)

**Hydrogenolysis of Tetrahydro-2,4,4-trimethylfurfuryl Alcohol (5).**—A mixture of 19 g. of tetrahydro-2,4,4-trimethylfurfuryl alcohol (**5**), 225 ml. of cyclohexane, and 5 g. of copper chromite (Harshaw Cu-1106P) was heated in a stirred autoclave for 18 hr. at 250° and 5000-p.s.i. hydrogen pressure. After the catalyst was filtered, the product was distilled to give 8.5 g. of 2,2,4-trimethyl-1,5-pentanediol (**7**), b.p. 93–97° (1.2 mm.), $n^{20}\text{D}$ 1.4565. Gas chromatographic analysis of the lower boiling fractions (9.8 g.) indicated the presence of unreacted tetrahydro-2,4,4-trimethylfurfuryl alcohol (5.1 g.), tetrahydro-2,2,4,4-tetramethylfuran (2.1 g.), and an unknown component (1.2 g.) tentatively identified as tetrahydro-3,3,5-trimethylpyran from its n.m.r. spectrum.

**Analysis for Oxirane Oxygen.**—The epoxy compounds were analyzed for oxirane oxygen by a modification of the King[8] procedure as described by Jungnickel, *et al.*[9] Phenolphthalein was used as the indicator for the titration of the hydrogen chloride solution.

**Gas Chromatographic Columns.**—Columns 6 ft. in length were constructed from 0.25-in. aluminum tubing coiled in a cylindrical spiral. The columns were packed with 40–50-mesh Chromosorb W containing 10% either of Carbowax 20M or of silicone GE-SF 96-40 as the liquid phase. Hydrogen was employed as the carrier gas at a flow rate of 90 cc./min. The detector was a thermal conductivity cell, the output of which was measured by a recording potentiometer.

**N.m.r. Spectra.**—The n.m.r. spectra were recorded by using a Varian Associates A-60 (60 Mc./sec.) spectrometer. The chemical shift positions were determined relative to tetramethylsilane as an internal standard.[10]

---

[8] G. King, *Nature*, **164**, 706 (1949).

[9] J. L. Jungnickel, E. D. Peters, A. Polgar, and F. T. Weiss, "Organic Analysis," Vol. I, J. Mitchell, Jr., I. M. Kolthoff, E. J. Proskauer, and A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1953, p. 135.

[10] The n.m.r. spectra were recorded and interpreted by Dr. V. W. Goodlett.

---

# Liquid Crystals as Solvents. II. Further Studies of Liquid Crystals as Stationary Phases in Gas–Liquid Chromatography[1]

Michael J. S. Dewar and J. P. Schroeder

*Department of Chemistry, The University of Texas, Austin, Texas*

*Received May 3, 1965*

Six nematic and/or smectic compounds have been evaluated as liquid phases for the separation of benzene position isomers by gas–liquid chromatography. All of these gave better separations of *meta* and *para* isomers than a conventional silicone liquid phase, and the *para* isomer was invariably eluted last. Two of the compounds, 4,4′-bis(4-methoxybenzylideneamino)-3,3′-dichlorobiphenyl and *p*-phenylene bis-4-*n*-heptyloxybenzoate, were particularly effective. Two cholesteric compounds were also examined.

Liquid crystals[2] are unusual states of matter, intermediate between crystalline solids and normal isotropic liquids. Mechanically they behave as liquids, but the molecules in them possess some order in that they cannot rotate freely. The molecules of a typical liquid crystal are rod-shaped and are constrained to lie parallel, rotation being permitted only about the long axis; materials of this kind behave therefore as anisotropic liquids and are normally birefringent. Two main types of liquid crystals are known; nematic liquid crystals, in which the only restraint on the molecules is the restriction of their rotation indicated above, and smectic liquid crystals, in which the molecules are further constrained to move in layers. Smectic liquid crystals indeed have a layer structure, somewhat analogous to that of graphite.

Liquid crystals should show unusual solvent properties, due to the ordered arrangement of their molecules. One obvious consequence of this is that foreign substances should dissolve more easily in liquid crystals, the more easily their molecules fit into the liquid crystal "lattice"; different position isomers in particular should show different solubilities in liquid crystals, owing to the differences in shape between their molecules.

---

[1] This research was supported by grants from the National Science Foundation and The Robert A. Welch Foundation.

[2] G. W. Gray, "Molecular Structure and the Properties of Liquid Crystals," Academic Press Inc., New York, N. Y., 1962.