made possible purchase of the NMR spectrometer used in this study. Two of us (Thomas H. Crawford and Cody E. Staples) are grateful for National Science Foundation Cooperative Graduate Fellowships held during 1958–1959, 1959–1960, and 1960–1961.

The Rearrangement of a Keto Epoxide to a Lactone. A Novel Transformation in the Bicyclo[2.2.1]heptane Series[1]

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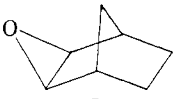
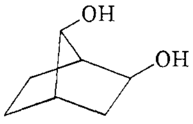
Received December 26, 1961

In a study concerned with the ability of a carbonyl function to serve as a participating and migrating group in molecular rearrangements, *exo*-2,3-epoxybicyclo[2.2.1]heptan-5-one (IV) was synthesized and subjected to acid hydrolysis. The resultant product was found to be the lactone VI, previously characterized as the chief peracetic acid oxidation product of dehydronorcamphor (V), rather than either of the expected ketodiols (IX or X). This novel rearrangement may be rationalized in terms of a 1,3-diol cleavage of the hydrate of IV, and finds analogy in the facile cleavage of *exo*-bicyclo[2.2.1]heptan-2-ol-6-one (XIV) to the ketoaldehyde XV. The possibility that the peracetic acid oxidation of V to give VI may have involved IV as an intermediate is considered and rejected, since peracetic acid was found to oxidize IV to the epoxy lactone XVII.

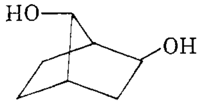
The acid-catalyzed opening of the epoxide ring of *exo*-2,3-epoxybicyclo[2.2.1]heptane (I) has been shown to yield *exo*-2-*syn*-7-bicyclo[2.2.1]heptanediol (II),[3] accompanied by *exo*-2-*anti*-7-bicyclo-[2.2.1]-heptanediol (III).[4] In an attempt to make use of this type of rearrangement to evaluate the possible role of the carbonyl function as a participating and migrating group,[5] we have studied the acid-catalyzed rearrangement of the keto epoxide IV.



I



II



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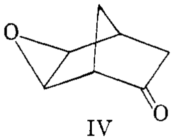
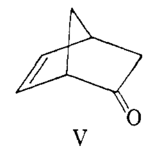
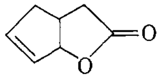


IV

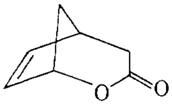
In an initial attempt to prepare IV, the peracetic acid oxidation of dehydronorcamphor (V) was found to yield a lactonic product (VI accompanied by a small amount of VII) rather than the desired epoxide.[6] We have now found that Sarett oxidation of the corresponding epoxy alcohol VIII provides a satisfactory route to IV.[7,8]



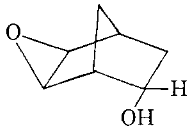
V



VI



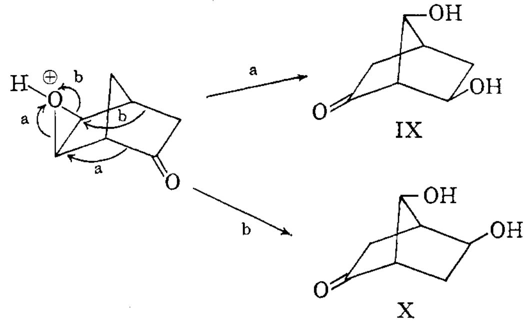
VII



VIII

It was anticipated that acid hydrolysis of IV would yield IX in the event that the carbonyl function migrated (*a*) or X in the event that the methylene group migrated (*b*) (Chart I).

CHART I



In fact, this hydrolysis yielded neither IX nor X; the product showed no hydroxylic absorption in the

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[1] The support of this work by a research grant from the National Science Foundation is gratefully acknowledged.

[2] Fellow of the Alfred P. Sloan Foundation.

[3] H. M. Walborsky and D. F. Loncrini, *J. Am. Chem. Soc.*, **76**, 5396 (1954); H. Kwart and W. G. Vorsburgh, *ibid.*, **76**, 5400 (1954); K. Alder and H. Wirtz, *Ann.*, **601**, 138 (1956).

[4] H. Krieger, *Suomen Kemistilehti*, **B31**, 340 (1958) has shown that this reaction is more complex than was realized.

[5] For some examples of carbonyl migrations, see A. Eschenmoser, H. Schintz, R. Fischer, and J. Colonge, *Helv. Chim. Acta*, **34**, 2329 (1951); H. O. House, *J. Am. Chem. Soc.*, **76**, 1235 (1954); H. O. House and R. L. Wasson, *ibid.*, **79**, 1488 (1955).

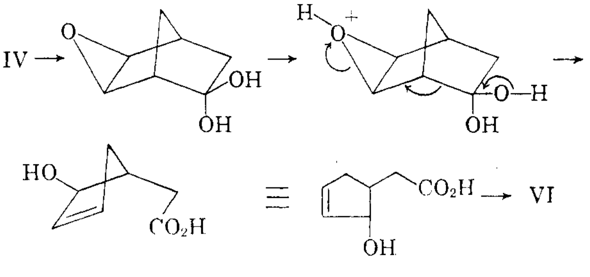
[6] J. Meinwald, M. C. Seidel, and B. C. Cadoff, *ibid.*, **80**, 6303 (1958).

[7] Several other approaches to IV are described in the Experimental. We have omitted any discussion of the synthesis or proof of configuration of VIII, since recent work of Henbest and Nicholls,[8] published after our own studies in this area were completed, have already covered these points adequately.

[8] H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 221 (1959).

infrared, and failed to give carbonyl derivatives. Elementary analysis revealed that this substance was isomeric with the starting material (IV), and its infrared spectrum was superimposable upon that of an authentic sample of the lactone VI. Although we are aware of no precedents for this β,γ-epoxy ketone to lactone rearrangement, a probable mechanism is easily discerned (Chart II).

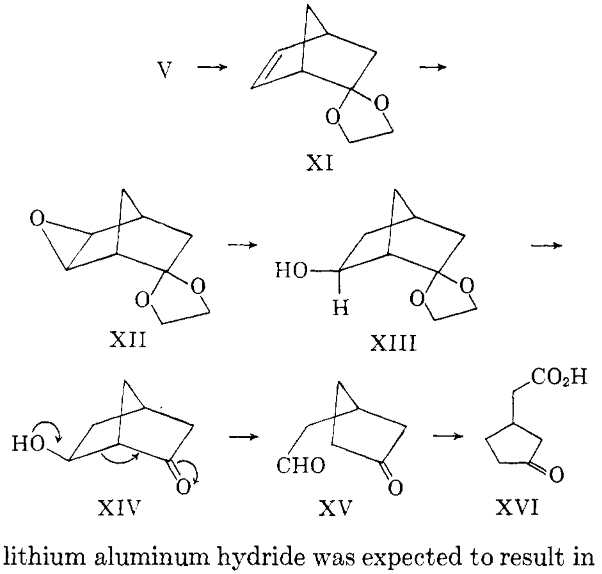
CHART II



In this scheme, the ready hydration of the strained, unhindered carbonyl group is quite reasonable.[9] The cleavage itself is related to the well known "1,3-diol" cleavage.[10] The final lactonization of the resultant allylic alcohol might be expected to proceed particularly easily.

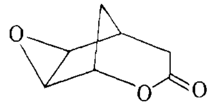
We have observed another case of cleavage of the bicycloheptane skeleton which is closely related to that described above. *exo*-Bicyclo[2.2.1]heptan-2-ol-6-one (XIV) was synthesized as shown in Chart III. The reduction of the epoxy ketal XII by

CHART III



lithium aluminum hydride was expected to result in attack at C-5 to give XIII. This course was confirmed by the fact that the ketol XIV underwent a facile reverse aldol reaction giving the ketoaldehyde XV, whose structure was established by oxidation to the known keto acid XVI.

The discovery that IV rearranges to VI opens up the possibility that our originally postulated mechanism for the peracetic acid oxidation of dehydronorcamphor (V), involving a Baeyer-Villiger type of reaction,[6] may have been incorrect, and that VI actually arises *via* rearrangement of an initially formed epoxide IV. To test this possibility, IV was treated with peracetic acid under mild conditions. This treatment resulted in the formation of a new epoxylactone, to which we assign structure XVII on



XVII

the basis of its elementary analysis, infrared spectrum, and analogous Baeyer-Villiger oxidations.[11] It follows that IV cannot have been the precursor of VI in the dehydronorcamphor oxidation, and our original explanation does not appear to require revision.

Experimental

***exo*-2,3-Epoxy-5-cyano-5-acetoxybicyclo[2.2.1]heptane.**—To 14.0 (0.079 mole) of 2-acetoxy-2-cyanobicyclo[2.2.1]hept-5-ene[12] was added an ether solution containing 12.0 g. (0.087 mole) of perbenzoic acid. The reaction mixture was kept at 5° for 3 days, extracted with 10% sodium hydroxide, and washed with water. After drying and evaporating the ether, the residue was crystallized from ether–petroleum ether to give 8.1 g. (53%) of the expected epoxide. Its infrared spectrum (Nujol mull) showed characteristic cyano and epoxide peaks at 4.48 and 11.72 μ. Two recrystallizations from ether–petroleum ether afforded an analytical sample, m.p. 86°.

Anal. Calcd. for $C_{10}H_{11}O_3N$: C, 62.16; H, 5.74; N, 7.25. Found: C, 62.45; H, 5.76; N, 7.34.

A variety of attempts to bring about a base cleavage of the acetate group, to give IV, resulted only in the formation of intractable products.

***exo*-2,3-Epoxy-5-acetoxybicyclo[2.2.1]hexane.**—The epoxidation of dehydronorbornyl acetate[13] with ethereal perbenzoic acid was carried out at 5° for 4 days. Work-up in the usual way gave 80% of product, b.p. 102–104° (8 mm.), m.p. 53–54°. Its infrared spectrum showed the characteristic 11.70-μ epoxide band. An analytical sample, b.p. 64° (0.25 mm.), n^{25}_{D} 1.4770 [lit.,[8] b.p. 114–115° (14 mm.), m.p. 53–54°], was obtained by distillation.

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.43; H, 7.07.

***exo*-2,3-Epoxybicyclo[2.2.1]heptan-2-ol (VIII).**—To 5.6 g. of the epoxy acetate was added 300 ml. of 5% aqueous sodium hydroxide. The resultant mixture was stirred at room temperature for 20 min., saturated with potassium carbonate, and extracted thoroughly with ether. From this extract, 3.3 g. (80%) of crude VIII, m.p. 165–169°, was obtained. Two recrystallizations from chloroform–cyclohexane, followed by two sublimations, gave an analytical sample, m.p. 185–187° (sealed capillary) [lit,[8] m.p. 155–161° (sublimes) on Kofler block]. It shows a characteristic 11.72-μ epoxide absorption band in the infrared. An identical

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[9] C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, pp. 143–149.

[10] J. English, Jr., and F. V. Brutcher, Jr., *J. Am. Chem. Soc.*, **74**, 4279 (1952).

[11] R. Sauers, *ibid.*, **81**, 925 (1958); A. Rassatt and G. Ourisson, *Bull. soc. chim. France*, 1133 (1959); J. Meinwald and E. Frauenglass, *J. Am. Chem. Soc.*, **82**, 5235 (1960).

[12] P. D. Bartlett and B. E. Tate, *ibid.*, **78**, 2473 (1956).

[13] J. D. Roberts, E. R. Trumbull, Jr., W. Bennett, and R. Armstrong, *ibid.*, **72**, 3116 (1950).

product was obtained in somewhat lower yield by direct epoxidation of dehydronorborneol.

Anal. Calcd. for $C_7H_{10}O_2$: C, 66.64; H, 7.99. Found: C, 66.17; H, 7.94.

A 3,5-dinitrobenzoate, m.p. 138–139°, was formed in the usual way, and recrystallized from ethanol.

Anal. Calcd. for $C_{14}H_{12}O_7N_2$: C, 52.50; H, 3.78; N, 8.75. Found: C, 52.69; H, 3.79; N, 8.66.

***exo*-2,3-Epoxybicyclo[2.2.1]heptan-5-one (IV).**—To a mixture of 20 g. of chromium trioxide and 200 ml. of pyridine[14] was added a solution of 8.7 g. of epoxy alcohol VIII in 80 ml. of pyridine. The reaction mixture was left at room temperature overnight, poured into 500 ml. of water and ice, and filtered through a glass wool mat. The filtrate was extracted thoroughly with ether, and the extract washed with cold, dilute hydrochloric acid, followed by water. After drying and evaporating the ether extract there remained a solid residue which was sublimed to give 2.7 g. (31%) of product. Three recrystallizations from cyclohexane gave an analytical sample, m.p. 139–140° (sealed capillary) showing (Nujol mull) characteristic carbonyl and epoxide bands at 5.72 and 11.75 μ.

Anal. Calcd. for $C_7H_8O_2$: C, 67.73; H, 6.50. Found: C, 67.24; H, 6.38.

A semicarbazone was prepared in the usual manner.

Anal. Calcd. for $C_8H_{11}O_2N_3$: C, 53.03; H, 6.12; N, 23.19. Found: C, 52.85; H, 6.02; N, 22.98.

Rearrangement of IV to VI.—A solution containing 1.8 g. of IV in 60 ml. of water was heated to boiling. A total of 15 drops of concd. hydrochloric acid was then added; after 1 min. the solution became opalescent and yellow. The reaction was allowed to come to room temperature, and on the following day was saturated with ammonium chloride and extracted with ether. The usual work-up gave 1.2 g. (67%) of product. Redistillation at 39° (0.07 mm.) gave a pure sample of VI, identified by direct comparison of its infrared spectrum with that of an authentic sample.[6]

Dehydronorcamphor Ethyleneketal (XI).—To 20 g. of dehydronorcamphor (V) was added 150 ml. of redistilled ethylene glycol, 300 ml. of dry benzene, and 1 g. of *p*-toluenesulfonic acid. The mixture was refluxed for 24 hr., using a water separator to collect the water. After cooling the reaction mixture and diluting with water, the benzene solution was washed with 10% aqueous sodium bicarbonate and with water. Evaporation of the benzene and distillation of the residue gave 27 g. (96%) of product, b.p. 90–91° (22 mm.), whose infrared spectrum revealed no carbonyl absorption. Redistillation afforded an analytical sample, b.p. 100° (33 mm.), $n^{20}D$ 1.4878.

Anal. Calcd. for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.26; H, 8.16.

***exo*-2,3-Epoxy-5-ethylenedioxybicyclo[2.2.1]heptane (XII).**—A benzene solution of 23 g. of perbenzoic acid was treated with 17.0 g. of XI. The reaction mixture was kept at 5° for 4 days, during which time aliquots were removed for titration. The reaction was worked up in the usual way, to give 15.8 g. (84%) of epoxy ketal, b.p. 106–107° (8 mm.). This product showed characteristic epoxide absorption at 11.7 μ. Redistillation yielded an analytical sample, b.p. 53° (0.25 mm.), $n^{25}D$ 1.4922.

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.48; H, 7.14.

***exo*-6-Ethylenedioxybicyclo[2.2.1]heptan-2-ol (XIII).**—Treatment of the epoxyketol XII with lithium aluminum hydride in *N*-ethylmorpholine for 15 hr. at 95° (*cf.* ref. 3) gave essentially unchanged starting material, and only a 6% yield of the desired product, b.p. 66–71° (0.10 mm.). At reflux temperatures (138–139°), the hydride appeared to decompose, giving a black deposit. Under these conditions, a 25% yield of the desired product, b.p. 79–82° (0.15 mm.) was obtained. Finally, reduction in *N*-ethylmorpholine carried out at 110–115° for 5 days gave a mixture of starting material (10%), and XIII, b.p. 70–72° (0.10 mm.), in 68% yield. This product, which showed strong hydroxylic absorption at 2.90 μ, and showed no epoxide absorption, was redistilled to give an analytical sample, b.p. 68° (0.10 mm.), $n^{25}D$ 1.4972.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.40; H, 8.26.

A 3,5-dinitrobenzoate, prepared in the usual manner, melted at 142–143° after three recrystallizations from ethanol.

Anal. Calcd. for $C_{16}H_{16}O_8N_2$: C, 52.75; H, 4.43; N, 7.69. Found: C, 52.74; H, 4.71; N, 7.78.

***exo*-Bicyclo[2.2.1]heptan-2-ol-6-one (XIV).**—To 3.0 g. of the hydroxy ketal XIII in 100 ml. of water was added 20 drops of concd. hydrochloric acid. After 30 min. at room temperature, the solution was saturated with ammonium chloride and extracted thoroughly with ether. After drying the solution over anhydrous magnesium sulfate, the ether was evaporated to give 1.3 g. (59%) of semisolid residue. Recrystallization from ether–petroleum ether followed by sublimation gave a sticky but crystalline solid, m.p. 112–113° (Kofler block), showing characteristic infrared maxima (Nujol mull) at 2.90 and 5.75 μ, but no aldehydic absorption.

Anal. Calcd. for $C_7H_{10}O_2$: C, 66.64; H, 7.99. Found: C, 67.06; H, 8.00.

A 3,5-dinitrobenzoate melted at 151–152° after two recrystallizations from ethanol–acetone.

Anal. Calcd. for $C_{14}H_{12}O_7N_2$: C, 52.50; H, 3.78; N, 8.75. Found: C, 52.74; H, 3.90; N, 8.86.

A *p*-toluenesulfonate ester, recrystallized from ether–petroleum ether, showed m.p. 68–69°.

Anal. Calcd. for $C_{14}H_{16}O_4S$: C, 59.98; H, 5.75; S, 11.44. Found: C, 59.91; H, 5.88; S, 11.67.

An analytical sample of a *p*-bromobenzenesulfonate, m.p. 93–94°, was obtained by crystallization from cyclohexane.

Anal. Calcd. for $C_{13}H_{13}O_4SBr$: C, 45.53; H, 3.80; Br, 23.15; S, 9.29. Found: C, 45.30; H, 3.75; Br, 23.25; S, 9.53.

Rearrangement of XIV to XV.—To 10 ml. of a 10% solution of potassium carbonate was added 200 mg. of the hydroxy ketone, XIV. The solution was allowed to stand for 10 min., and was then extracted with ether. This solution yielded a mixture of starting material and 3-ketocyclopentylacetaldehyde (XV) showing infrared absorption at 2.90, 3.70, 5.75, and 5.80 μ. A dimedone derivative of XV, m.p. 165–167°, was obtained as an analytical sample by recrystallization from methanol–water.

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.33; 8.35.

Oxidation of a sample of crude XV by silver nitrate and sodium hydroxide at room temperature gave 3-ketocyclopentylacetic acid (XVI), identified by comparison of its infrared spectrum with that of an authentic sample, and by preparation of its semicarbazone, m.p. 199–200°, mixture m.p. 200–205°.[15]

Peracetic Acid Oxidation of IV.—A solution of 0.50 g. of sodium acetate in 2.7 ml. of 40% peracetic acid (Becco) was added slowly to a stirred solution of 0.70 g. of epoxy ketone IV in 10 ml. of chloroform. During the addition the temperature of the reaction mixture was not allowed to rise above 0°, and this temperature was maintained for 1 hr. after the addition had been completed. The reaction mixture was neutralized with 20% sodium carbonate, again maintaining a 0° temperature. The product was extracted into ether, and the resultant solution dried and evaporated to give 0.55 g. (70%) of a crystalline product, which showed infrared maxima at 5.80 and 11.80 μ, corresponding to a δ-lactone and epoxide, respectively.

An analytical sample, m.p. 107–108° (sealed capillary), was obtained by crystallization from ether.

Anal. Calcd. for $C_7H_8O_3$: C, 59.99; H, 5.75. Found: C, 59.87; H, 5.88.

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[14] G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *ibid.*, **75**, 422 (1953).

[15] An authentic sample of this derivative was kindly supplied by Dr. E. Frauenglass (for its preparation, see ref. 11).