

tion of the brown residue from ligroin (b.p. 88–98°). The hydrazine separated in the form of small yellow-orange needles, m.p. 145–150° dec. (darkening from about 130°).

Anal. Calcd. for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.45. Found: C, 81.08; H, 5.95; N, 13.14.

Acknowledgment.—We acknowledge with thanks the excellent technical assistance of Joe Mayo and Siegfried Herliczek in the preparation of some of the intermediates and in determination of the ultraviolet spectra.

Rearrangements of Norbornene Oxide

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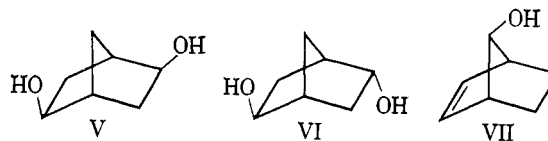
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The acid-catalyzed hydration of norbornene oxide has been reinvestigated. Isomerization of the oxide under acidic conditions produces 3-cyclohexene-1-carboxaldehyde, norcamphor, and nortricyclanol. Rearrangement under strongly basic conditions gives nortricyclanol exclusively.

During the course of an investigation on the bicyclo-[2.2.1]heptane-2,5-diols,² a brief examination of the related 2,7-diols was undertaken. The present report is an account of the resulting studies.

The product obtained either by acid-catalyzed hydration of *exo*-2,3-epoxybicyclo[2.2.1]heptane (I, norbornene oxide) or by peracid hydroxylation of norbornene has been the subject of several publications. The structure II was suggested³ for this material at an early data on the expectation of a normal *trans* addition of water to the epoxide ring. Independent studies by two groups^{4,5} resulted in the revision of this assignment to bicyclo[2.2.1]heptane-*exo*-2-*syn*-7-diol (III). The diol gave a negative vicinal diol test, had a strong intramolecular hydrogen

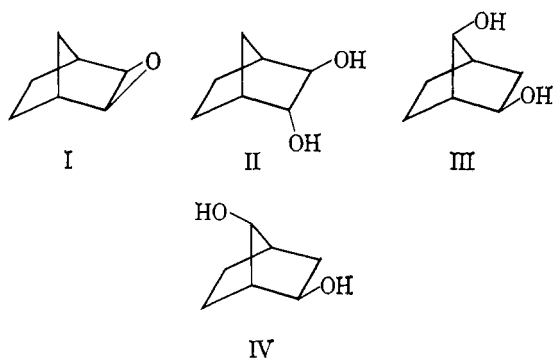
the 200° material was found to be a mixture which consisted of *ca.* 80% of a major component plus *ca.* 20% of three other diols. The minor components were identified as III, V,² and VI² on the basis of g.l.c. retention times. Column chromatography provided a homogeneous sample of the major component, m.p. 204.5–206°. This diol was shown to possess structure IV by comparison with an authentic sample.



The authentic sample was prepared by subjecting the tetrahydropyranyl ether of *anti*-7-hydroxybicyclo[2.2.1]hept-2-ene⁷ (VII) to the hydroboration-oxidation procedure⁸ of Brown. Utilization of bicyclo[2.2.1]heptenes in this reaction has been shown to give *exo* alcohols without the occurrence of skeletal rearrangements.⁹ This determines IV as the structure of the synthetic product and this material is identical in every respect with the diol obtained above.

A more quantitative estimate of the diol mixture was obtained by treating I with aqueous perchloric acid⁵ and examining the total crude product by g.l.c. In this manner the mixture was found to consist of 74% III, 22% IV, and 4% total of V and VI. The observed major and minor products formed by the hydration of norbornene oxide can now be rationally interpreted as resulting from various combinations of the usual Wagner-Meerwein rearrangements and 1,3-hydride shifts.¹⁰ Chart I shows a scheme.

During the course of the above work an attempt was made to purify a sample of I by preparative g.l.c. However, when I was passed through a column of Carbowax 20M on Chromosorb P at 120°, three new compounds were eluted from the column while the epoxide was completely consumed.¹¹ This unexpected



bond in its infrared spectrum, and formed a cyclic acetal with *p*-nitrobenzaldehyde in good yield. Later work by Krieger,⁶ however, resulted in the separation of this material into a low melting diol (181°) and a higher melting product (200°). The properties of the former were uniquely accommodated by III, while the higher melting product was assigned formula IV, mainly on the basis of mechanistic considerations.

In the present work the two products were examined by gas-liquid chromatography (g.l.c.) of the derived acetates. Although the 181° diol was homogeneous,

(1) (a) National Institutes of Health Predoctoral Fellow, 1960–1963. (b) Correspondence should be addressed to the Department of Chemistry, Indiana University, Bloomington, Ind. 47405.

(2) J. Meinwald, J. K. Crandall, and P. G. Gassman, *Tetrahedron*, **18**, 815 (1962).

(3) S. F. Birch, W. S. Oldham, and E. A. Johnson, *J. Chem. Soc.*, 818 (1947).

(4) H. M. Walborsky and D. F. Loncrini, *J. Am. Chem. Soc.*, **76**, 5396 (1954).

(5) H. Kwart and W. G. Vosburgh, *ibid.*, **76**, 5400 (1954).

(6) H. Krieger, *Suomen Kemi.*, **B31**, 340 (1958).

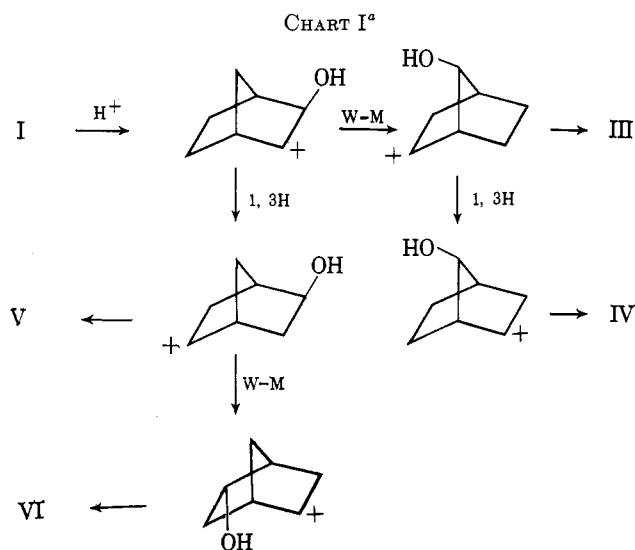
(7) P. R. Story, *J. Org. Chem.*, **26**, 287 (1961).

(8) For a detailed discussion of this synthetic method and related ones, see H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.

(9) See ref. 8, p. 126.

(10) J. A. Berson, "Molecular Rearrangements," Vol. 1, P. de Mayo, Ed., Interscience Publishers, New York, N. Y., 1963, p. 111. This reference provides an excellent review of these interesting topics.

(11) K. Watanabe, C. N. Pillar, and H. Pines, *J. Am. Chem. Soc.*, **84**, 3934 (1962). These workers have also observed that I gives three peaks upon g.l.c. on a Carbowax column. However, they tentatively suggested that the standard epoxidation procedure had produced a mixture of isomeric oxides.



^a The intermediates are drawn here as ordinary cations for the sake of clarity, although bridged ions may be important in these processes.

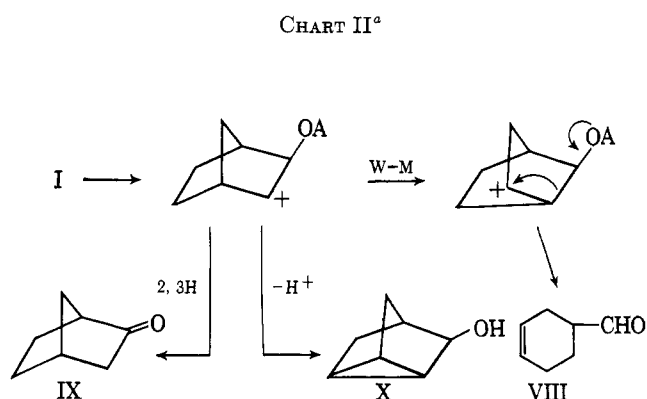
result prompted further studies on the behavior of I under various isomerizing conditions.

The new compounds produced during g.l.c. were collected and identified. They were found to be 3-cyclohexene-1-carboxaldehyde (VIII), norcamphor (IX), and nortricyclanol (X); the relative proportions were 47:43:10. It was demonstrated that the observed transformation is not simply a thermal rearrangement on the injector block, since I was recovered unchanged when a 1,2,3-tris(2-cyanoethoxy)propane column was used under the identical thermal conditions. The nature of these products suggests that an acid-catalyzed process is occurring with the liquid phase, and contained impurities, or perhaps the solid support was functioning as a Lewis acid. Chart II formulates the reaction in these terms. The intermediate cation can lose a proton from C-5 to give X¹⁰; it can undergo a 2,3 hydride shift to give IX; or it can experience a Wagner–Meerwein shift, followed by electron migration to the new cationic site, thus effecting ring cleavage to the monocyclic aldehyde VIII. Although IX and X were expected acid isomerization products of norbornene epoxide, the formation of aldehyde VIII was somewhat surprising since examples involving the conversion of bicyclo[2.2.1]heptane derivatives to monocyclic products are reported to be relatively rare.¹² A direct analogy, however, is provided by the zinc bromide catalyzed¹³ conversion of α -pinene oxide (XI) to campholenic aldehyde (XII). A related example, involving participation of a π -bond rather than a σ -bond, is found in the isomerization¹⁴ of XIII to XIV. A similar sequence of oxide ring heterolysis, rearrangement, and electron migration to the deficient site again best accounts for these results.

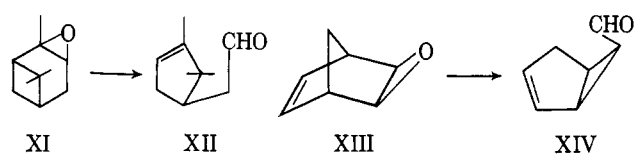
(12) See ref. 10, p. 161. However, several further examples of this type of cleavage are known: for example, see L. G. Donaruma and W. Z. Heldt, *Org. Reactions*, **11**, 136 (1960); D. Scharf and F. Korte, *Tetrahedron Letters*, 821 (1963).

(13) B. Arbusow, *Ber.*, **68**, 1430 (1935).

(14) J. Meinwald, S. S. Labana, and M. S. Chadha, *J. Am. Chem. Soc.*, **85**, 582 (1963). Further work has established that XIII is an isolable intermediate in the formation of XIV by the epoxidation of norbornadiene (S. S. Labana, Ph.D. Thesis, Cornell University, 1963).



^a The intermediates are drawn here as ordinary cations for the sake of clarity, although bridged ions may be important in these processes.



In order to substantiate the proposed course of the decomposition on the g.l.c. column, a number of reactions were carried out in an attempt to effect the acid isomerization under more definable conditions. Treatment of an ether solution of I with either boron trifluoride etherate or magnesium bromide¹⁵ gave small quantities of VIII, IX, and X as shown by g.l.c., but in each case the major product was a pair of less volatile alcohols. The product from the magnesium bromide reaction crystallized on standing; recrystallization gave a crystalline alcohol, m.p. 72–74°, which produced an immediate, copious precipitate with alcoholic silver nitrate solution. Further characterization of this material was not carried out, but it is likely that the magnesium bromide reaction of I has produced a mixture of bromohydrins similar in composition to that obtained¹⁶ from the addition of hydrobromic acid to I. The alcohols from the boron trifluoride rearrangement were not investigated; however, the analogous formation of fluorohydrins appears reasonable.¹⁷ The epoxide was also treated with *p*-toluenesulfonic acid in refluxing benzene and with both acidic and neutral alumina in pentane. None of these conditions promoted the reaction of I.

In view of these failures to promote isomerization, recourse was made to more severe reaction conditions not involving an external nucleophile. Cope and Hecht¹⁸ have studied the pyrolysis of cyclooctene oxides over activated alumina and have rationalized the products as being formed by acid-catalyzed rearrangement on the surface of the alumina. When I was pyrolyzed over Woelm neutral alumina at 270°, and

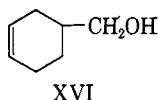
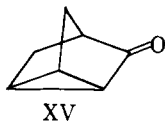
(15) H. Kwart and T. Takeshita, *J. Org. Chem.*, **28**, 670 (1963). These workers report, without experimental details, that the coordination of I with magnesium halide gave norcamphor as the principle product.

(16) H. M. Walborsky and D. F. Loncrini, *J. Org. Chem.*, **22**, 1117 (1957). A crystalline bromohydrin, m.p. 75.5–76°, was isolated from the crude product; this was converted to 7-bicyclo[2.2.1]heptanol by hydrogenolysis.

(17) For a discussion of fluorohydrin formation in the reaction of boron trifluoride etherate with epoxides, see D. J. Goldsmith, *J. Am. Chem. Soc.*, **84**, 3913 (1962).

(18) A. C. Cope and J. K. Hecht, *ibid.*, **84**, 4872 (1962).

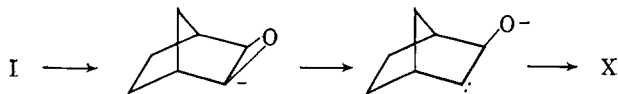
the crude pyrolysate examined by g.l.c., seven major components were observed. Fortunately, all but one of these were readily identified by their characteristic g.l.c. retention times and by infrared spectral comparisons of the pure components (separated by preparative g.l.c.). These were found to be (in order of elution with relative per cents in parentheses): unreacted epoxide (24%), aldehyde VIII (25%), an unidentified, unsaturated alcohol, m.p. 87–89° (7%), norcamphor (IX) (18%), nortricyclanone (XV) (7%), nortricyclanol (X) (8%), and 3-cyclohexene-1-methanol (XVI) (11%). Despite the larger number of products, it seems likely that the initial products of the pyrolysis are the same as those found in the original g.l.c. rearrangement.



The other products are then formed in secondary oxidation–reduction processes presumably of the Oppenauer–Meerwein, Ponndorf, Verley type. Thus, both reduction of aldehydes to primary alcohols¹⁸ and oxidation of bicyclic alcohols to the corresponding ketones¹² have been observed previously under comparable experimental conditions. Pyrolyses were carried out on the presumed primary products to substantiate this point. Norcamphor was unaffected under the pyrolysis conditions; aldehyde VIII was partially reduced to XVI as expected. Nortricyclanol was partially converted to nortricyclanone and norcamphor in a 1:5 ratio. The formation of the latter product was unexpected but several mechanisms can be visualized for its formation on the alumina surface. The sole unidentified product observed in the pyrolysis of I is apparently also a primary product, but further studies were not carried out since it accounts for only a small fraction of the product. The melting point and g.l.c. retention time of this unknown alcohol are not consistent with those of any of the known norbornenols.

These pyrolyses, on the whole, do lend support to the postulated cationic mechanism for the rearrangement of I under milder conditions and, at the very least, they define the reaction conditions under which the isomerization takes place.

Finally, the reaction of I under strongly basic conditions was studied. Treatment of I with lithium diethylamide resulted in a very clean conversion of the epoxide to nortricyclanol. This transformation probably proceeds by base abstraction of an oxide ring proton, opening of the ring to a "carbenoid anion" intermediate and insertion of the carbene carbon into an opposing C–H bond.¹⁹ Norbornyl carbenes are known to react in exactly this way.²⁰ This mech-



(19) The formation of the carbene and its insertion may actually be compressed into one concerted process.²¹

(20) For example: U. Heubaum and W. A. Noyes, *J. Am. Chem. Soc.*, **52**, 5070 (1930); J. W. Powell and M. C. Whiting, *Tetrahedron*, **7**, 305 (1959); W. G. Dauben and F. G. Willey, *J. Am. Chem. Soc.*, **84**, 977 (1962).

anism is favored over other possibilities, since Cope and co-workers have shown by deuterium labeling that a similar process is operative in the medium-ring epoxides.²¹

This base-promoted rearrangement may provide a synthetically useful route to substituted nortricyclanes from readily available norbornene oxides.

Experimental

Melting points were taken in sealed capillaries and are uncorrected. Analyses were performed by Scandinavian Microanalytical Laboratory.

Performic Acid Oxidation of Norbornene.—The oxidation procedure described by Kwart and Vosburgh⁵ was run on 23.5 g. (0.26 mole) of norbornene yielding 17.8 g. (65%) of crude diol. This material was fractionated according to Krieger's procedure.⁶ Extraction with warm carbon disulfide separated the crude product into a soluble and an insoluble fraction. The soluble portion was recrystallized from cyclohexane and sublimed under vacuum to give a sample of III, m.p. 179.5–181°. The infrared spectrum was identical with the published one⁶ and g.l.c. of the derived diacetate as previously described² for the 2,5-diols demonstrated the homogeneity of this sample.

The carbon disulfide insoluble material was repeatedly recrystallized from nitromethane to give a product with m.p. 200–201° in less than 10% recovery from the crude product. G.l.c. analysis of this product revealed that it was only about 80% IV. The remaining 20% was composed of three additional compounds having retention times identical with the acetates of III, V, and VI. Chromatography on grade III Woelm neutral alumina with ether as eluent gave a pure sample of IV, m.p. 204.5–206° after recrystallization from nitromethane and sublimation. This product was homogeneous by g.l.c. A small sample of V, m.p. 181.5–182.5°, was also obtained from the chromatography. This identity was established by infrared and mixture melting point comparisons.

Bicyclo[2.2.1]heptane-*exo*-2-*anti*-7-diol (IV).—A mixture of 0.9 g. of dihydropyran, 0.71 g. of *anti*-7-hydroxybicyclo[2.2.1]-hept-2-ene, and 1 drop of concentrated hydrochloric acid was allowed to stand for 3 hr. at room temperature. The resulting mixture was taken up in ether, washed with dilute sodium hydroxide solution, and dried (MgSO₄). Removal of the solvent and distillation of the residual oil gave 0.95 g. (76%) of the tetrahydropyranyl ether, b.p. 82–83° (3 mm.), *n*_D²⁰ 1.4840.

To a stirred solution of 0.80 g. (4.1 mmoles) of the tetrahydropyranyl ether and 0.20 g. of sodium borohydride in 20 ml. of dry tetrahydrofuran under a nitrogen atmosphere was added 1.0 g. of boron trifluoride etherate during the space of 1 hr. After an additional 3 hr. of stirring, the reaction vessel was cooled in an ice bath and 0.3 g. of sodium hydroxide in 20 ml. of water was added. Hydrogen peroxide (2.2 ml., 30%) was added dropwise and the reaction stirred for several hours. The reaction mixture was extracted four times with 25-ml. portions of ether and the combined extracts were dried (MgSO₄). The solvent was removed to give 1.03 g. of a clear oil. This was dissolved in 50 ml. of methanol containing 1 drop of hydrochloric acid and the resulting solution was heated to reflux for 3.5 hr. Evaporation of the methanol gave a white solid which was sublimed and recrystallized from ether–petroleum ether to give 0.30 g. (57%) of IV, m.p. 203.5–205.0°. Recrystallization from the nitromethane and vacuum sublimation gave an analytical sample, m.p. 204.5–205.5°.

Anal. Calcd. for C₇H₁₂O₂: C, 65.59; H, 9.44. Found: C, 65.64; H, 9.41.

Hydration of I.—A sample of *exo*-2,3-epoxybicyclo[2.2.1]-heptane was hydrated with dilute perchloric acid according to the published procedure. A sample of the crude product was analyzed by g.l.c.² There was found 74% III, 22% IV, and 4% total of V and VI. (A short retention time peak was also observed. This probably corresponds to a small amount of nortricyclanol in the product.)

G.l.c. of I.—A concentrated solution of I in ether was injected into a Beckman GC-2 gas chromatograph with the injector at 300° and the column at 120°. When the column was 10 ft. of

(21) A. C. Cope, G. A. Berchtold, P. E. Peterson, and S. H. Sharman, *ibid.*, **82**, 6370 (1960).

a 10% Carbowax 20M on firebrick preparative column, three products were obtained; the proportions were 47:43:10 in order of elution. The total recovery was 50%.

The first material was a volatile aldehyde with an infrared spectrum (neat) at 3.31, 3.70, 5.80, and 6.06 μ . This was shown to be 3-cyclohexene-1-carboxaldehyde by comparison of the infrared spectrum and g.l.c. retention time with those of an authentic sample.

The second component was a solid waxy ketone, m.p. 90–91°. The infrared spectrum and g.l.c. behavior were identical with those of norcamphor and a mixture melting point was undepressed.

The third product was a solid alcohol, m.p. 107–108°. Infrared and g.l.c. comparisons demonstrated that this material was nortricyclanol (lit.²² m.p. 108–109°).

When the column was 5 ft. of 20% 1,2,3-tris(2-cyanoethoxy)propane on firebrick, the epoxide was recovered unchanged under the identical thermal conditions. (The products were all stable to the chromatographic conditions on either column.)

Treatment of I with Magnesium Bromide.—Bromine (800 mg.) was added to a stirred mixture of 120 mg. of magnesium turnings in 15 ml. of dry ether. After the exothermic reaction had subsided, a solution of 0.50 g. of I in 10 ml. of ether was added to the two phase mixture and stirred for 3 hr. The reaction mixture was poured into ice-water and extracted with ether. The extracts were washed with sodium bicarbonate solution and dried ($MgSO_4$). The solvent was removed by distillation to give a viscous oil. Examination of the total crude product by g.l.c. under conditions where I was stable showed traces of VIII, IX, and X, but the bulk of the product was eluted as a pair of peaks with considerably longer retention times. Upon standing the crude product crystallized. Recrystallization from petroleum ether (b.p. 60–70°) gave a white solid, m.p. 72–74°. An immediate heavy precipitate was observed with ethanolic silver nitrate.

Treatment of I with Boron Trifluoride.—To 0.5 g. of I in 40 ml. of dry ether at 0° was added 0.2 ml. of boron trifluoride etherate. After standing overnight the reaction mixture was washed with dilute aqueous ammonia and water. After drying ($MgSO_4$) the crude product was examined by g.l.c. Trace quantities of VIII and IX were observed, but the main product was again a pair of unidentified, crystalline, hygroscopic alcohols. (These are apparently isomeric fluorohydrins.)

Treatment of I with *p*-Toluenesulfonic Acid.—To 35 ml. of benzene was added 250 mg. of *p*-toluenesulfonic acid monohydrate. Ten milliliters of benzene was distilled off. One gram of I was added, and the mixture was refluxed overnight. Examination of the reaction mixture by g.l.c. showed only starting material.

Treatment of I with Alumina.—Stirring a solution of I in pentane overnight with either neutral or acidic alumina gave only recovered starting material.

Pyrolysis of I over Alumina.—Two grams of Woelm neutral alumina was preconditioned by heating for 1 hr. at 270° and 20-mm. pressure. A solution of 1.00 g. of I in 20 ml. of pentane was dropped slowly onto the alumina in a flask at 270°. A stream of nitrogen was passed through the reaction vessel to carry the volatile products into a Dry Ice-acetone trap. After the addition was complete the pyrolysis products were chased with 5 ml. of pentane. The pentane was removed from the mixture in the trap by distillation through a short column to yield ca. 1 g. of crude product. Preparative g.l.c. gave seven major components. In order of elution, these were unreacted I (24%), aldehyde VIII (25%), an unidentified, unsaturated alcohol, m.p. 87–89° (7%), norcamphor (18%), nortricyclanolone (7%), nortricyclanol (8%), and alcohol XVI (11%). In each case the identity of the component was determined by g.l.c. retention time and infrared spectral comparisons with authentic samples. 3-Cyclohexene-1-methanol was prepared by lithium aluminum hydride reduction of VIII; VIII and IX were commercial products; the preparation of X and XV will be described in a later publication.

Pyrolysis of VIII.—The pyrolysis of 2.00 g. of VIII over 4.0 g. of alumina was carried out as described above. The pyrolysate was mainly unreacted starting material along with a small amount of XVI.

Pyrolysis of X.—Nortricyclanol (233 mg.) was pyrolyzed over 1.0 g. of alumina. The crude product was separated by g.l.c. into norcamphor (49%), nortricyclanolone (11%), and unreacted starting material (40%).

Pyrolysis of IX.—One gram of norcamphor was pyrolyzed over 2.0 g. of alumina. Only starting material was observed.

Treatment of I with Lithium Diethylamide.—Ten milliliters of a 15% solution of commercial butyllithium was added to a cooled solution of 1.5 g. of diethylamine in 10 ml. of dry benzene under a nitrogen atmosphere. After several minutes a solution of 1.0 g. (9.1 mmoles) of I in 10 ml. of benzene was added and the solution was heated to reflux for 48 hr. The reaction mixture was cooled and poured into 100 ml. of ice-water. The resulting mixture was extracted with ether and the extract was washed with ammonium chloride solution and water. After drying ($MgSO_4$) of the solution, the solvent was removed and the residue sublimed to give 0.55 g. (55%) of nortricyclanol, m.p. 105–109°. A second sublimation gave a pure sample, m.p. 108–109.5°. Melting point and infrared comparisons with an authentic sample established the identity of the product. (Examination of the crude product by g.l.c. showed only one peak with the correct retention time for X.)

Acknowledgment.—The author wishes to thank Dr. Jerrold Meinwald for providing the facilities for this work and for his advice and encouragement during its progress.

(22) J. D. Roberts, E. R. Trumbull, W. Bennett and R. Armstrong, *J. Am. Chem. Soc.*, **72**, 3116 (1950).