

ment shows that the reported (a) isomeric composition of the acetolysis product and (b) relative optical rotations of substrate and product are reproducible.

In a control experiment 0.107 g. (0.7 mmole) of (+)-*exo*(*axial*)-bicyclo[3.2.1]oct-3-en-2-yl acetate (+IVb), $[\alpha]^{25}_D$ 640° (neat), was dissolved in 50 ml. of anhydrous acetic acid containing 0.164 g. (2 mmoles) of anhydrous sodium acetate. The rotation (α^{25}_D) of this solution was 2.347°. After 8 days at 30.4° (27 half-lives for acetolysis of I) α^{25}_D was 2.218°. This shows that under the conditions of the product studies optically active IVb racemizes to only a very small extent.

Acidification of the above solution with an equal volume of 0.0418 *N* HClO₄ in acetic acid (final HClO₄ concentration = 0.001 *N*) resulted in immediate loss of optical activity.

In another experiment 1.7 g. of *dl*-*axial*-acetate IVb was dissolved in 5 ml. of 0.042 *N* perchloric acid in acetic acid. After 0.5 hr. at room temperature a 2-ml. aliquot was treated with excess sodium acetate (0.2 g.) and the resulting solution was diluted with water and the acetate isolated by continuous extraction as described above. The composition of the acetate was 19% equatorial-acetate VIb and 81% axial-acetate IVb⁵; other compounds were present in small amounts. After 24 hr. another 2-ml. aliquot was worked up in the same way. The equatorial-VIb:axial-IVb ratio was the same as above, but the amounts of the other components were larger.

These experiments show that (+)-IVb is quite stable in acetic acid containing sodium acetate, but that if mineral acid is present the acetate racemizes and isomerizes rapidly.

Kinetic Experiments.—Polarimetric ($k\alpha$)¹⁶ and titrimetric (k_t)⁸ first-order rate constants for acetolysis of (+)-I at 30.4° were determined using methods described earlier. The same

(15) H. L. Goering, T. D. Nevitt and E. F. Silversmith, *J. Am. Chem. Soc.*, **77**, 5026 (1955).

reaction mixture ($[\text{ROT}] = 0.03 M$, $[\text{NaOAc}] = 0.04 M$) was used for both experiments. The reaction was followed both polarimetrically and titrimetrically to about 90% completion and no drifts were detected in either $k\alpha$ or k_t . The average value of 8 properly spaced determinations of k_t (and average deviation) was $3.27 \pm 0.10 \times 10^{-5} \text{ sec.}^{-1}$. The average (and average deviation) of 14 values of $k\alpha$ was $3.24 \pm 0.02 \times 10^{-5} \text{ sec.}^{-1}$.

Determination of Optical Purity of (+)-IIIId and (+)-IVd. A. (+)-IIIId.—*dl*-endo-Bicyclo[2.2.2]oct-5-en-2-yl acid phthalate-7-¹⁴C was prepared^{7b} from pure IIIa and phthalic anhydride-7-¹⁴C (Tracerlab Inc., 0.35 $\mu\text{c./g.}$ after dilution). After several recrystallizations from benzene the *dl*-IIIId-¹⁴C had: m.p. 166.4–167.4°, 5442 ± 8 counts per minute per millimole (c./min./mmole).¹⁶

A mixture of 0.9587 g. of (+)-IIIId, $[\alpha]^{25}_D$ 31.4° (*c* 1, CHCl₃), and 0.4059 g. of the *dl*-IIIId-¹⁴C described above was dissolved in 3 ml. of acetone containing 1.48 g. of cinchonidine. The resulting cinchonidine salt was recrystallized four times from a 1:1 isopropyl alcohol-acetone mixture and hydrolyzed. The (+)-IIIId after recrystallization from benzene had m.p. 158–159.1°, $[\alpha]^{25}_D$ 43.8°, 1328 ± 12 c./min./mmole. From these data it can be calculated that $[\alpha]^{25}_D$ for optically pure (+)-IIIId is $55.8 \pm 0.8^\circ$ (CHCl₃).⁷

B. (+)-IVd.—In this experiment a mixture of 0.6978 g. of (+)-IVd, $[\alpha]^{25}_D$ 231.0° (*c* 1, CHCl₃), and 0.4133 g. of *dl*-IVd-¹⁴C, 5844 c./min./mmole, was resolved as described above. The resulting (+)-IIIId had $[\alpha]^{25}_D$ 230.3° (*c* 1, CHCl₃), 1350 ± 8 c./min./mole. From these data it can be shown⁷ that $[\alpha]^{25}_D$ for optically pure (+)-IIIId is $232 \pm 2^\circ$ (CHCl₃).

(16) The ¹⁴C contents were determined with a Packard Tri-Carb liquid scintillation spectrometer model 314-DC (toluene-2,5-diphenyloxazole solution). We are indebted to Professor C. Heidelberger for making these facilities available.

CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF THE UNIVERSITY OF SOUTH CAROLINA, COLUMBIA, S. C., OREGON STATE UNIVERSITY, CORVALLIS, ORE., AND OHIO STATE UNIVERSITY, COLUMBUS, OHIO

The Formation of a 1,3,6-Cyclooctatriene by 1,4-Radical Addition to Cyclooctatetraene and its Intramolecular Isomerization to a Bicyclo[4.2.0]octa-2,4-diene^{1a}

BY JOHN L. KICE^{1b} AND THOMAS S. CANTRELL^{1c}

RECEIVED MARCH 9, 1963

The reaction of cyclooctatetraene with the α -cyanoisopropyl radicals produced by decomposition of azobisisobutyronitrile occurs by 1,4-addition to the tetraene, giving 5,8-bis-(α -cyanoisopropyl)-1,3,6-cyclooctatriene (I). This compound, on being heated in solution, isomerizes readily to 3,8-bis-(α -cyanoisopropyl)-bicyclo[4.2.0]octa-2,4-diene (III). The mechanism of this interesting isomerization is believed to involve an initial intramolecular 1,5-transannular migration of hydrogen. This gives 3,8-bis-(α -cyanoisopropyl)-1,3,5-cyclooctatriene, which then undergoes valence tautomerization to the bicyclo[4.2.0]octa-2,4-diene.

As part of a program concerned with the reaction of non-benzenoid aromatic hydrocarbons with free radicals, we undertook a study of the products formed when a typical radical source, azobisisobutyronitrile (AIBN), was decomposed in solutions of cyclooctatetraene. Strictly speaking, cyclooctatetraene should not be considered an aromatic hydrocarbon at all. However, in most general discussions of non-benzenoid aromatics it is usually included.² In the present study we were particularly interested in determining if any of the interesting ring contractions and rearrangements which are so manifest in previously reported cyclooctatetraene chemistry^{3,4} would also be observed in its reactions with the α -cyanoisopropyl radicals from AIBN.

As it turns out, our most interesting observation was the discovery of a remarkably facile intramolecular isomerization of the principal radical-cyclooctatetraene reaction product. Elucidation of the structures of the compounds involved indicates that this isomerization involves an initial 1,5-transannular hydrogen migration. It is thought that the occurrence of this reaction may have significant implications for the chemistry of 1,3,6-cyclooctatrienes.

Results and Discussion

Reaction of Cyclooctatetraene with α -Cyanoisopropyl Radicals.—Cyclooctatetraene is not particularly reactive toward radicals. This was evident from the fact that decomposition of AIBN in dilute benzene solutions of the tetraene (0.05 *M*) gave no radical-tetraene reaction products. Under these same conditions high yields of reaction products had earlier been obtained from diphenylfulvene^{5a} and dimethylfulvene.^{5b}

Cyclooctatetraene-AIBN reaction products could be obtained, however, albeit in low yield, if the azo compound (1 *M*) was decomposed in bulk cyclooctatetraene. Careful chromatography allowed their separation from the considerable amount of tetramethylsuccinonitrile also formed.

(1) (a) Supported by National Science Foundation Grant NSF-G4205; (b) to whom requests for reprints should be directed at the Department of Chemistry, Oregon State University.

(2) Cf. W. Baker and J. F. W. McOmie, Chap. 2 in "Progress in Organic Chemistry," Vol. 3, Academic Press, Inc., New York, N. Y., 1955; R. A. Raphael in "Non-benzenoid Aromatic Compounds," D. Ginsburg, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, p. 465 ff.

(3) (a) W. Reppe, O. Schlichtling, K. Klager and T. Toepel, *Ann.*, **560**, 1 (1948); (b) A. C. Cope and M. Burg, *J. Am. Chem. Soc.*, **74**, 168 (1952); (c) A. C. Cope, N. A. Nelson and D. S. Smith, *ibid.*, **76**, 1100 (1954); (d) C. G. Overberger, M. A. Klotz and H. Mark, *ibid.*, **75**, 3186 (1953); (e) A. C. Cope, D. A. Liss and D. S. Smith, *ibid.*, **79**, 240 (1957).

(4) C. R. Ganellin and R. Petit, *ibid.*, **79**, 1767 (1957); *J. Chem. Soc.*, 55, 576 (1958).

(5) (a) J. L. Kice and F. M. Parham, *J. Am. Chem. Soc.*, **80**, 3792 (1958);

(b) J. L. Kice and F. Taymoorian, *J. Org. Chem.*, **25**, 1786 (1960).

The principal cyclooctatetraene-AIBN reaction product I, m.p. 154–155°, was a substance of molecular formula $C_{16}H_{20}N_2$. This compound exhibited no ultraviolet absorption maximum above 210 $m\mu$ although it did show strong end absorption (ϵ_{220} 5700, ϵ_{240} 1070). Its n.m.r. spectrum⁶ consisted of a doublet (rel. area 1) at 3.62 τ (J 9.3 c.p.s.), a singlet (rel. area 1) at 4.25 τ , a pair of partially overlapping doublets (rel. area 1) centered at 4.71 τ (J 9.3 c.p.s., J' 7.1 c.p.s.), a doublet (rel. area 1) at 7.11 τ (J 7.1 c.p.s.) and a singlet (rel. area 6) at 8.62 τ . The first three groups of lines are ascribed to olefinic protons of various types; the doublet at 7.11 τ is presumably due to tertiary hydrogens on

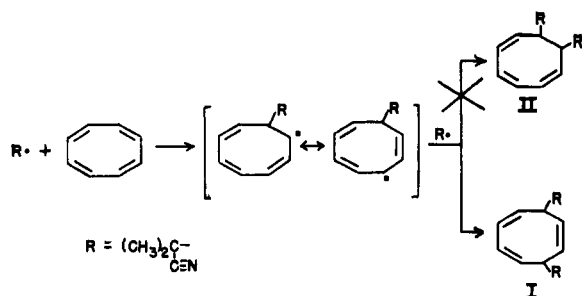
a saturated carbon ($-C-H$), and the peak at 8.62 τ is

undoubtedly due to the methyl hydrogens of the α -cyanoisopropyl groups. Since the molecular formula indicates that each molecule of I contains two such α -cyanoisopropyl groups, compound I has a total of 12 methyl hydrogens, 6 olefinic hydrogens and two methine hydrogens.

Compound I did not react with maleic anhydride at room temperature. On hydrogenation over 10% palladium-on-charcoal in ethyl acetate solution it readily absorbed two moles of hydrogen to give tetrahydro-I, $C_{16}H_{24}N_2$, m.p. 47–48°. That tetrahydro-I still contained an unreduced double bond was apparent from its n.m.r. spectrum, which exhibited olefinic proton absorption (rel. area 1) as a pair of doublets between 4.3 and 4.5 τ (J 4.3 c.p.s., J' 1.5 c.p.s.). The other peaks were a diffuse hump at 7.1 τ (rel. area 1), a broad line at 8.26 τ (rel. area 4) and the methyl singlet (rel. area 6) at 8.62 τ . Evidently compound I contains three carbon-carbon double bonds, but two of these are much more easily reduced than the third.

Structure of I.—Its molecular formula indicates compound I is composed of one cyclooctatetraene residue and two α -cyanoisopropyl groups. Since the molecule also contains three carbon-carbon double bonds and six olefinic hydrogens, we performe are dealing with a simple adduct formed by combination of an α -cyanoisopropyl radical with the radical which results from initial addition of the same species to the tetraene (see Chart I). The absence of an ultraviolet absorption maximum in I rules out the 1,2-adduct II for consideration; 1,3,5-cyclooctatriene, for example, has a λ_{max} at 265 $m\mu$.⁷ On the other hand, as the ensuing

CHART I

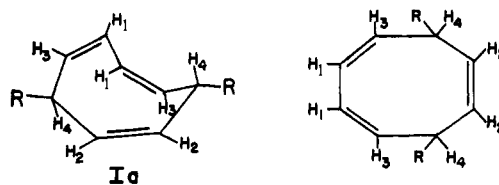


discussion will show, the properties of I are entirely consistent with those expected for the 1,4-adduct. Compound I is accordingly formulated as 5,8-bis(α -cyanoisopropyl)-1,3,6-cyclooctatriene.

It is already known that the parent compound 1,3,6-cyclooctatriene, does not exhibit an ultraviolet absorption maximum.⁷ Inspection of molecular models of

(6) N.m.r. spectra were determined using a Varian A-60 instrument and $CDCl_3$ solutions containing tetramethylsilane and chloroform as internal standards.

(7) A. C. Cope and F. A. Hochstein, *J. Am. Chem. Soc.*, **72**, 2515 (1950).



$$\tau_1 = 3.62, \tau_2 = 4.25, \tau_3 = 4.71, \tau_4 = 7.11.$$

$$J_{13} = 9.3 \text{ cps}; J_{34} = 7.1 \text{ cps}; J_{24} < 0.3 \text{ cps}.$$

Fig. 1.—Stereochemistry and n.m.r. assignments for I.

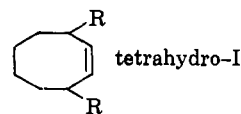
this compound or of I reveals that this is because the conjugated diene system in such a triene is very badly skewed. Examples of similar behavior by skewed diene chromophores are by now sufficiently numerous^{8–10} to require no further comment.

The 1,3,6-cyclooctatriene structure for I is also consistent with the n.m.r. spectrum. Figure 1 shows a projection drawing of the molecule. We believe that formation of the *trans* stereoisomer, in which both bulky R groups can simultaneously be quasiequatorial, will be strongly favored over the alternative *cis* isomer in which one of the R groups must take the quasixial position occupied by an H_4 in Fig. 1. In the latter stereoisomer there is serious steric interference between the *t*-butyl-like α -cyanoisopropyl group and the carbons of the ring.

For the *trans* stereoisomer Ia one would expect, as found, sizable values for J_{13} and J_{34} . On the other hand, since Dreiding models indicate the dihedral angle between H_2 and H_4 is around 100°, J_{24} would be predicted to be very much smaller.¹¹ Apparently the actual angle is close to 90°, since J_{24} was too small to be experimentally measurable.

The n.m.r. and ultraviolet spectra of the compound are thus in good accord with the proposed structure Ia. The failure of I to react readily with maleic anhydride is also expected.

The course of the hydrogenation of I to tetrahydro-I is not definitely established. Since only two of the double bonds in I are catalytically reduced under the reaction conditions employed, these most probably are the double bonds of the conjugated diene system in I. This would give tetrahydro-I the structure shown below.



The n.m.r. spectrum of tetrahydro-I is not inconsistent with this structure if one assumes that each of the olefinic protons is coupled both to the methine proton immediately adjacent (J 4.3 c.p.s.) and more weakly to the methine proton located in an allylic position (J' 1.5 c.p.s.).

An effort was made to verify this structure for tetrahydro-I by attempting to prepare the compound by another route—the addition of α -cyanoisopropyl radicals to 1,3-cyclooctadiene. Unfortunately, along with 1,4-addition having the required *trans* stereochemistry, there apparently is enough either 1,2-addition or *cis*-1,4-addition so that, although a viscous oil having infrared and n.m.r. spectra with all the essential features of tetrahydro-I was obtained, crystalline tetrahydro-I could not be isolated from it.

(8) A. T. Blomquist and A. Goldstein, *ibid.*, **77**, 998 (1955).

(9) E. E. van Tamelen, S. Levin, G. Brenner, J. Wolinsky and P. Aldrich, *ibid.*, **81**, 1666 (1959).

(10) A. T. Blomquist and D. T. Longone, *ibid.*, **79**, 3916 (1957).

(11) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

Isomerization of I to III.—By far the most interesting facet of the chemistry of I is the ease with which it undergoes an unusual isomerization. Much to our initial surprise, we found that when a solution of I in xylene was merely refluxed the compound isomerized quantitatively to another substance of molecular formula $C_{16}H_{20}N_2$ (III), m.p. 87–88°. The isomerization also occurred, albeit more slowly, even in refluxing benzene; after 75 hr. an 87% yield of III could be isolated. Although the isomerization could be accelerated slightly by addition of acid, the rate in the presence of 0.05 *M* added acetic or 0.03 *M* added *p*-toluenesulfonic acids was only about 20% larger than the rate in the absence of acid. The same was true of the effect of added organic bases such as triethylamine. Thus acidic or basic catalysts are not necessary for the isomerization to occur.

Structure of III.—The ultraviolet absorption spectrum of III showed a maximum at 271 $m\mu$ (ϵ 5900) and a minimum at 228 $m\mu$ (ϵ 570). Compound III reacted readily with maleic anhydride at room temperature in ether to give an adduct $C_{20}H_{22}N_2O_3$ (V). Hydrogenation of III in ethanol over palladium-on-charcoal led to the uptake of two moles of hydrogen.

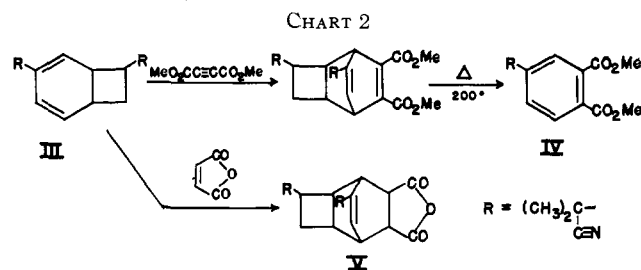
The ultraviolet spectrum of compound III and its facile reaction with maleic anhydride suggested, as a good working hypothesis, that the molecule was a bis-(α -cyanoisopropyl)-substituted bicyclo[4.2.0]octa-2,4-diene. 1,3-Cyclohexadienes are usually quite reactive in Diels–Alder reactions.¹² The ultraviolet spectrum of the parent compound, bicyclo[4.2.0]octa-2,4-diene, exhibits its maximum at 274 $m\mu$,¹³ and the 7,8-dichloro derivative shows a maximum at 270 $m\mu$.^{3b}

If III is a bicyclo[4.2.0]octa-2,4-diene, Diels–Alder reaction of the compound with dimethyl acetylenedicarboxylate, followed by pyrolysis of the adduct, should lead to a phthalate ester. Compound III was accordingly subjected to a Diels–Alder reaction with dimethyl acetylenedicarboxylate. The resulting adduct was then pyrolyzed for 4 hr. at 200°, and the reaction product was purified by chromatography and molecular distillation. A 57% yield of a compound identified as dimethyl 4-(α -cyanoisopropyl)-phthalate (IV) was obtained. The evidence that the compound is the 4-substituted phthalate rather than the 3-substituted isomer is: first, except for the –CN band, the infrared spectrum is essentially identical with that of the model compound, dimethyl 4-*t*-butylphthalate,^{18a} particularly in the key 10–15 μ region. On the other hand, it is very different from the 10–15 μ region in the infrared spectrum of dimethyl 3-ethylphthalate.^{18b} Second, and probably more definitive, the integrated n.m.r. spectrum of the maleic anhydride adduct of III (V) shows the presence of only *one* olefinic proton. If the α -cyanoisopropyl group of the phthalate were originally located on a terminal carbon of the diene system in III the maleic anhydride adduct V would have two olefinic protons rather than one.

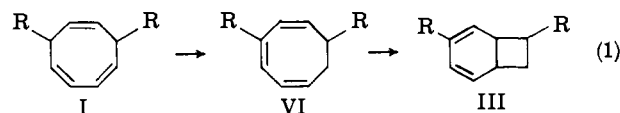
The results of this degradative sequence are thus not only in accord with the hypothesis that III is a bis-(α -cyanoisopropyl)-substituted bicyclo[4.2.0]octa-2,4-diene, but they also tell us that one of the α -cyanoisopropyl groups is attached to the 3-carbon of the bicyclic system. This, incidentally, is consistent with the integrated n.m.r. spectrum of III, which shows 12 methyl protons, 5-methylene or methine protons and only 3 olefinic protons.

In view of the structure of I, finding an α -cyanoisopropyl group attached to one of the diene carbons in

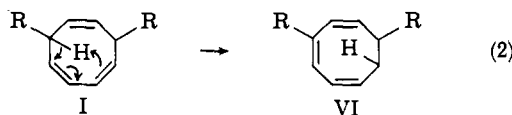
III requires that the isomerization of I to III involve, if nothing else, migration of one of the H_4 -hydrogens in Fig. 1. As it turns out (*vide infra*), such a migration, leading to rearrangement of the 1,3,6-cyclooctatriene to a 3,8-disubstituted 1,3,5-cyclooctatriene, followed by valence isomerization of the latter to a bicyclo[4.2.0]octa-2,4-diene, appears sufficient to describe the entire course of the isomerization. Consequently, although the location of the second α -cyanoisopropyl group in III is not unequivocally established, the 8-position seems strongly favored. We accordingly formulate III as 3,8-bis-(α -cyanoisopropyl)-bicyclo[4.2.0]octa-2,4-diene. The several transformations involving III are shown in Chart 2.



Mechanism of the Isomerization of I to III.—The over-all course of the isomerization of I to III is shown in eq. 1. Since there is ample precedent for the valence tautomerization of a 1,3,5-cyclooctatriene to a bicyclo[4.2.0]octa-2,4-diene,^{3b,7,13} it seems almost certain the last step in the reaction is a process of this sort. The real mechanistic question in the isomerization, then, is how does the 1,3,6-cyclooctatriene I isomerize to the 1,3,5-cyclooctatriene VI? Although isomerization of a 1,3,6-cyclooctatriene to a 1,3,5-cyclooctatriene has been



observed in the presence of strong base,⁷ the small effect of acid or base on the present reaction shows that in our case such catalysis is not necessary for the isomerization to occur. This necessitates the required hydrogen migration takes place intramolecularly, as shown in eq. 2. Two questions arise concerning this mechanism. (1) Can reasons be given why such a transannular 1,5-migration of hydrogen should occur particularly readily in the present system? (2) Is there any evidence in the chemistry of related com-



pounds for such a 1,5-migration of hydrogen? Happily, as the ensuing discussion will show, both these questions can be answered in the affirmative.

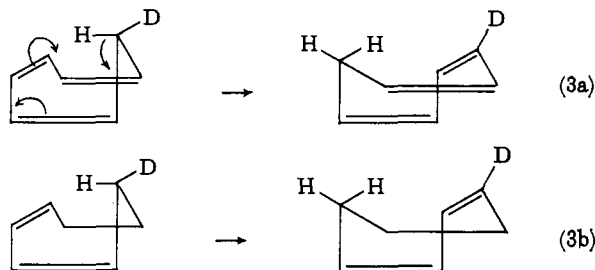
Examination of molecular models reveals that in Ia the hydrogen which migrates is located almost directly over one of the double bonds of the diene system. This can be seen fairly well by reference to Fig. 1. The distance of H_4 from the π -cloud of the double bond between C_{H_1} and C_{H_2} is only a little over 1.5 Å. and the relative geometry of the double bond and the hydrogen is certainly ideal for a transannular process of the type shown in eq. 2. We conclude, therefore, that the stereochemistry of Ia is very favorable for a 1,5-hydrogen migration of this sort.

Furthermore, there is precedent for such a reaction in a closely related system. ter Borg, Kloosterziel and van Meurs¹⁴ have recently reported that at 100–

(12) M. Kloetzel, Vol. IV, "Organic Reactions," John Wiley and Sons, New York, N. Y., 1948, p. 22.

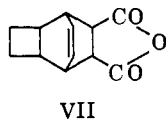
(13) A. C. Cope, A. C. Haven, Jr., F. L. Ramp and E. R. Trumbull, *J. Am. Chem. Soc.*, **74**, 4867 (1952).

140° 7-deuterio-1,3,5-cycloheptatriene undergoes a 1,5-transannular migration of hydrogen (eq. 3a); in the same communication they note that 7-deuterio-1,3-cycloheptadiene appears to give a similar reaction (eq. 3b). Since models show the relative stereo-



chemistry of the hydrogen and the double bond is actually less favorable in both these cases than in that of I, the occurrence of the 1,5-migration in the cycloheptatriene and diene systems provides strong evidence that a similar transannular shift of hydrogen could occur readily in the 1,3,6-cycloöctatriene system.

Finally, one might note some indirect evidence for a transannular 1,5-hydrogen migration in 1,3,6-cycloöctatriene itself. Sanne¹⁵ reported that 1,3,6-cycloöctatriene, 1,3,5-cycloöctatriene and bicyclo[4.2.0]octa-2,4-diene all gave the same Diels-Alder adduct (VII) with maleic anhydride. It was already known that both the 1,3,5-triene and the bicyclic diene give VII on reaction with



maleic anhydride.¹³ Consequently, to us, the simplest explanation for the behavior of the 1,3,6-triene is that it isomerizes to the 1,3,5-triene under the reaction conditions. The exact reaction conditions employed are not stated by Sanne,¹⁵ but one assumes they involved heating the compounds with maleic anhydride in an inert solvent. If so, isomerization of 1,3,6-cycloöctatriene must also be able to occur intramolecularly under relatively mild conditions, a result consistent with our hypothesis that it is the particular stereochemistry of the 1,3,6-cycloöctatriene system which allows the 1,5-transannular migration of hydrogen to take place so easily. In fact we would expect that all 1,3,6-cycloöctatrienes should undergo relatively facile intramolecular isomerization to the corresponding 1,3,5-triene. It will be interesting to see if experiments on other members of this class bear out this prediction.^{16a}

Experimental

Materials. Cycloöctatetraene.—The commercial product of the General Aniline and Film Co.¹⁶ was fractionally distilled immediately before use, b.p. 42–43° (17 mm.). **Azobisisobutyronitrile** (Westville Chemical Co.) was recrystallized from methanol; m.p. 101° dec. All solvents were reagent grade and were fractionally distilled before use.

(14) A. P. ter Borg, H. Kloosterziel and N. van Meurs, *Proc. Chem. Soc.*, 359 (1962).

(15) W. Sanne, *Festschrift Carl Wurster zum 60 Geburtstag*, 79 (1960); *Chem. Abstr.*, **56**, 9995b (1962).

(15a) NOTE ADDED IN PROOF.—Since the submission of this manuscript the thermal isomerization of 1,3,6-cycloöctatriene to 1,3,5-cycloöctatriene has been reported by two groups of investigators (W. von E. Doering and W. R. Roth, *Tetrahedron*, **19**, 715 (1963); W. Sanne and O. Schlichting, *Angew. Chem.*, **74**, 156 (1963)). In addition, a number of other examples of thermal transannular 1,5-migrations of hydrogen have been described by Doering and Roth (*Angew. Chem., Intern. Ed.*, **2**, 115 (1963)). It seems apparent that such reactions are of much more frequent occurrence in medium-ring systems than has previously been realized.

(16) Because of difficulty in obtaining sufficient cycloöctatetraene through commercial sources, we are particularly grateful to Prof. A. C. Cope for a generous gift of the tetraene at a critical juncture of this work.

Reaction of AIBN with Cycloöctatetraene. Formation of I.—The reactions were carried out in a round-bottom flask equipped with a sealed-on reflux condenser and nitrogen inlet tube. A mineral oil trap connected to the exit of the condenser prevented back-diffusion of air into the system. In a typical reaction 4.1 g. (0.025 mole) of AIBN and 25 ml. of freshly distilled cycloöctatetraene were placed in the reaction flask, and a rapid stream of dry nitrogen was bubbled through the mixture for 1 hr. The flask was then placed in an oil-bath maintained at 80° for 8–10 hr., a very slow stream of nitrogen being passed through the solution during this time. The bulk of the cycloöctatetraene was then recovered by distillation through a semi-micro Vigreux column at 15–18 mm. pressure, and the residue was chromatographed on a 35 × 350 mm. column of acid-washed alumina. Elution with hexane and hexane-benzene gave a small amount of unchanged cycloöctatetraene. The column was then eluted with 250 ml. each of benzene, 1:1 ether-benzene, 1:9 ether-benzene, 1:4 ether-benzene, 1:2 ether-benzene and pure ether. Forty fractions of approximately 30 ml. each were collected and evaporated under reduced pressure. Fractions 8–17 contained a total of 2.12 g. (72%) of tetramethylsuccinonitrile, identified by comparison with a known sample.

Fractions 18–22 contained a solid, which was recrystallized from methanol to give 0.330 g. (5.5% based on azonitrile decomposed) of I, 5,8-bis-(α -cyanoisopropyl)-1,3,6-cycloöctatriene, colorless plates, m.p. 151–152°. Two additional recrystallizations from methanol gave analytically pure material, m.p. 154–155°.

Anal. Calcd. for C₁₆H₂₀N₂: C, 79.95; H, 8.39; N, 11.66; mol. wt., 240. Found: C, 79.73; H, 8.13; N, 11.60; mol. wt., 234 (osmometric in CHCl₃).

The compound absorbs in the infrared at 3.35(s), 3.50(w), 4.48(m), 6.19(w), 6.81(s), 7.19(m), 7.29(m), 7.78(w), 8.1–8.4(w, broad), 8.57(w), 10.11(w), 10.26(w) and 10.41(w) μ . The important features of its ultraviolet and n.m.r. spectra have already been described.

Fractions 23–36 also contained material whose infrared spectrum indicated it consisted of cycloöctatetraene-AIBN reaction products. Some crystalline material melting over a broad range (94–112°) could be isolated from fractions 23–27. This melting point was not changed by repeated recrystallization. No definitive evidence as to the structure or the composition of the 94–112° melting material was obtained. Fractions 28–36 could not be made to yield any crystalline material and were not further investigated.

Hydrogenation of I.—A solution of 0.126 g. of I in 10 ml. of ethyl acetate was shaken over 58 mg. of 10% palladium-on-charcoal under 1 atm. of hydrogen. After 1.5 hr., uptake of hydrogen ceased with 26.4 ml. (103% of two double bonds) of hydrogen being consumed. Filtration of the catalyst and evaporation of the solvent gave a colorless oil. Cooling a methanol-water solution overnight at 5° gave 0.096 g. of tetrahydro-I, white needles, m.p. 47–48°. The n.m.r. spectrum of tetrahydro-I has already been described. The compound is tentatively assigned the structure 3,8-bis-(α -cyanoisopropyl)-cycloöctene.

Anal. Calcd. for C₁₆H₂₄N₂: N, 11.50. Found: N, 11.37.

Isomerization of I to III.—A solution of 0.300 g. of I in 10 ml. of dry xylene was deaerated with nitrogen for 1 hr. and was then refluxed for 20 hr. under nitrogen. The solvent was evaporated under reduced pressure, and the residue was chromatographed on a 20 × 250 mm. column of acid-washed alumina. Elution with 1:10 ether-benzene followed by evaporation gave a colorless oil which crystallized on standing. Recrystallization from methanol-water gave 0.245 g. (82%) of III, 3,8-bis-(α -cyanoisopropyl)-bicyclo[4.2.0]octa-2,4-diene, white prisms, m.p. 87–88°.

Anal. Calcd. for C₁₆H₂₀N₂: C, 79.95; H, 8.39; N, 11.66; mol. wt., 240. Found: C, 80.15; H, 8.15; N, 11.77; mol. wt., 231 (osmometric in CHCl₃), 213 (cryoscopic in benzene).

Compound I also isomerized to III in refluxing benzene; after 20 hr. a 42% yield of III could be isolated. After 75 hr. the yield of III was increased to 87%. Compound III exhibits infrared bands at 3.35(s), 3.40(s), 4.47(m), 6.03(w), 6.81(s), 7.20(m), 7.31(m), 8.0–8.4(m, broad), 9.40(m), 10.05(w), 10.51(w), 11.12(w) and 12.04(m) μ . The ultraviolet spectrum has already been described. The n.m.r. spectrum showed the lines: a somewhat broadened line centered at 4.2 τ (rel. area 2), broad line centered about 4.42 τ (rel. area 1), a diffuse set of lines at 7.2–8.2 τ (total rel. area 5), a singlet at 8.57 τ (rel. area 6) and two sharp singlets at 8.72 and 8.79 τ (total rel. area 6). The different methyl proton signals in III show the two α -cyanoisopropyl groups are no longer structurally equivalent, the methyl protons in one of them now appearing as a pair of lines at slightly higher τ . The fact that a pair of lines is observed is probably due to molecular asymmetry and its effect on the instantaneous environment of the methyls of the α -cyanoisopropyl group attached to the four-membered ring.¹⁷

Reaction of III with Maleic Anhydride.—Compound III (0.24 g., 1.0 mmole) and 0.11 g. (1.1 mmoles) of resublimed maleic anhydride were dissolved in 10 ml. of dry ether. The solution was deaerated with nitrogen and allowed to stand at room temperature for 20 hr. Evaporation of the ether left a tan semi-solid residue. Recrystallization from benzene-hexane gave the adduct V as white needles, m.p. 148–150°. Two additional recrystallizations gave 0.185 g. (54%) of pure V, m.p. 150–151°. The n.m.r. spectrum of V showed a single olefinic proton resonance centered at 3.65 τ . Comparison of its relative area with that of the combined signals of the methyl protons of the α -cyanoisopropyl groups showed these were in the ratio of 1:12.

Anal. Calcd. for $C_{20}H_{22}N_2O_3$: C, 70.98; H, 6.55; N, 8.28. Found: C, 71.16; H, 6.44; N, 8.33.

Hydrogenation of III.—Compound III (0.118 g.) was hydrogenated in 9 ml. of 95% ethanol at atmospheric pressure. Initially 39 mg. of 10% palladium-on-charcoal was added. Two 20-mg. portions of fresh catalyst were added during the course of the hydrogenation. Hydrogen uptake ceased after 25.6 ml. (102% of two double bonds) of hydrogen was taken up. A fourth portion of catalyst led to no further consumption of hydrogen. Filtration of the catalyst and evaporation of the solvent gave a colorless oil which could not be induced to crystallize.

Reaction of III with Dimethyl Acetylenedicarboxylate and Pyrolysis of the Resulting Adduct.—A solution of 0.24 g. of III and 0.42 g. of dimethyl acetylenedicarboxylate in 5 ml. of dry xylene was refluxed for 6 hr. under nitrogen. The xylene and excess dimethyl acetylenedicarboxylate were evaporated at 1 mm. pressure on the steam-bath. The residue, a viscous, almost colorless oil, amounted to 0.36 g. (94%). Its infrared spectrum showed strong bands at 5.82, 6.96, 7.90 and 8.8–8.9 μ , as in the spectrum of the adduct of dimethyl acetylenedicarboxylate and 7,8-dichlorobicyclo[4.2.0]octa-2,4-diene.^{3b}

The adduct was pyrolyzed by heating it for 4 hr. at 200–210° in a flask equipped with an air condenser. The cooled, dark brown reaction mixture was chromatographed directly on a 20 \times 300 mm. alumina column. Elution with benzene gave a colorless oil whose infrared spectrum indicated it was mainly an α -cyano-

isopropyl-substituted phthalate ester. This material was evaporatively distilled in a Hickman still at 0.2 mm., bath temp. 170–180°, to give 0.14 g. (57%) of dimethyl 4-(α -cyanoisopropyl)-phthalate (IV) as a colorless oil which set to a glass at -40°.

Anal. Calcd. for $C_{14}H_{15}NO_4$: C, 64.37; H, 5.79; N, 5.36; mol. wt., 261. Found: C, 63.98; H, 5.93; N, 5.28; mol. wt., 244 (osmometric in $CHCl_3$).

The infrared spectrum of IV in the 4–15 μ region showed bands at 4.49(w), 5.83(vs), 7.19(w), 7.28(w), 7.7–8.2(vs), 8.91(s), 9.41(s), 11.42(m), 11.80(m), 12.20(m), 12.33(sh), 12.69(m), 12.99(m), 13.76(w), 14.21(m), and 14.75(m) μ . The n.m.r. spectrum consisted of a closely spaced multiplet at 2.36 τ (rel. area, 1), a singlet at 6.18 τ (rel. area 2) and a singlet at 8.29 τ (rel. area 2). The infrared spectrum of IV, except for the -CN band at 4.49 μ , was very similar to that of dimethyl 4-*t*-butylphthalate.^{18a} In the key 10–15 μ region the 4-*t*-butyl ester showed bands at 10.32(m), 11.41(m), 11.80(m), 12.23(m), 12.65(m), 12.97(m), 13.78(w) and 14.20(w) μ . In contrast, dimethyl 3-ethylphthalate^{18b} had bands at 10.04(m), 10.50(m), 11.53(m), 12.11(m) and 14.39(m) μ .

Reaction of AIBN with 1,3-Cyclooctadiene.—A solution of 4.1 g. of AIBN in 25 ml. each of 1,3-cyclooctadiene and benzene was deaerated with nitrogen and then heated at reflux under nitrogen for 8 hr. The benzene and excess cyclooctadiene were evaporated under reduced pressure, and the residue was chromatographed on a 35 \times 350 mm. column of acid-washed alumina. Elution with benzene and ether-benzene mixtures gave, first, 0.95 g. of tetramethylsuccinonitrile, and then in later fractions, 3.84 g. of colorless viscous oil. All attempts to isolate a crystalline isomer from this oil failed. Its infrared spectrum was almost identical with that of tetrahydro-I. The n.m.r. spectrum was also very similar to that of tetrahydro-I, the principal difference being that the olefinic proton lines at 4.4 τ were a complex multiplet instead of a pair of doublets. Models suggest that the *cis*- and *trans*-1,4-adducts should be of comparable stability. It therefore seems quite reasonable that radical addition to cyclooctadiene should give substantial amounts of both stereoisomers. Separation of tetrahydro-I, which is thought to be the *trans* isomer, from the *cis* isomer could well be difficult, particularly since both may be contaminated with some 1,2-addition product.

(17) G. Fraenkel, private communication. We wish to thank Dr. Fraenkel for this and other valuable discussions of the interpretation of the various n.m.r. spectra.

(18) (a) B. W. Larner and A. T. Peters, *J. Chem. Soc.*, 680 (1952); (b) prepared from the anhydride [K. Alder and W. Vogt, *Ann.*, **571**, 137 (1951)] by the same procedure as used in ref. 18a.

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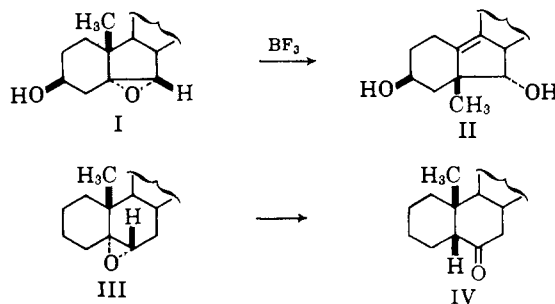
The Preparation of 8 α -B-Norsteroid Derivatives^{1,2}

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The effect of changes in bond hybridization at C-3 in a B-norsteroid on the thermodynamic stability of a remote center has been investigated in the B-norcoprostane-3,6-dione (V) series. In dione V an *anti*-B/C-ring juncture was found to be the stable form whereas a *syn*-B/C-ring juncture was favored in the 3-ol-6-one series. The chemistry of the various compounds was investigated.

In the course of a study directed toward the establishment of the stereochemistry of various B-norsteroid derivatives,⁴ the boron trifluoride etherate-catalyzed rearrangement of 5 α ,6 α -oxido-B-norcholestane-3 β -ol (I) was studied. It was found that migration of the C-10 methyl group took place to form a Westphalen type of diol II. This result is in contrast to the usual rearrangement of 5 α ,6 α -oxidocholestane (III) to 6-oxocoprostanone (IV).⁵ This marked change in the reaction course of a B-nor oxide must be due to indefinite long range conformational effects⁶ which, in turn, may affect the steric strain introduced into the B-nor molecule by the presence of the methyl group at C-10. Since bond angle changes tend to bring about these



long range conformational effects, it was of interest to see if modifying the bond angles in ring A by changing the hybridization at C-3 from tetrahedral to trigonal could also introduce a similar effect.

Earlier it had been found that the diketone V, possessing the *cis-anti-trans* orientation, was the most thermodynamically stable configuration of the molecule.^{7,8} If conversion of C-3 to a tetrahedral state

(1) For a preliminary publication of a portion of these results see W. G. Dauben, *Bull. soc. chim. France*, 1338 (1960).

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(3) General Electric Co. Fellow in Chemistry, 1958–1959.

(4) W. G. Dauben, G. A. Boswell, Jr., W. Templeton, J. W. McFarland and G. H. Berezin, *J. Am. Chem. Soc.*, **85**, 1672 (1963).

(5) H. B. Henbest and T. I. Wrigley, *J. Chem. Soc.*, 4596 (1957).

(6) D. H. R. Barton, F. McCapra, P. J. May and T. Thudium, *ibid.*, 1297 (1960), and earlier papers.

(7) L. F. Fieser, *J. Am. Chem. Soc.*, **75**, 4386 (1953).

(8) W. G. Dauben and G. J. Fonken, *ibid.*, **78**, 4736 (1956).