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Ionic Reactions in Bicyclic Systems. IV. Stereochemistry of the Acetolysis of (+)-*endo*-Bicyclo[2.2.2]oct-5-en-2-yl *p*-Toluenesulfonate[1]

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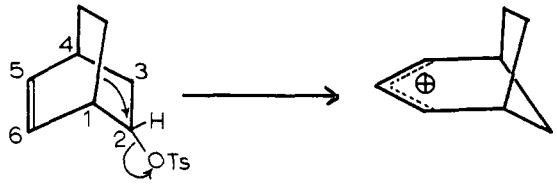
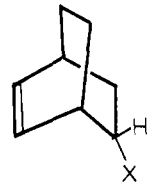
Acetolysis of (+)-*endo*-bicyclo[2.2.2]oct-5-en-2-yl *p*-toluenesulfonate (I) results in equal first-order rates of loss of optical activity and solvolysis. The major component in the product (98.6%) is *exo*(*axial*)-bicyclo-[3.2.1]oct-3-en-2-yl acetate (IVb) and this appears to be completely racemic. These results, together with the observation that acetolysis is anchimerically accelerated, are consistent with the view that ionization results in the direct formation of the symmetrical bicyclo[3.2.1]oct-3-en-2-yl carbonium ion (II) which is stereoselectively converted to the *exo*-acetate IVb.

Introduction

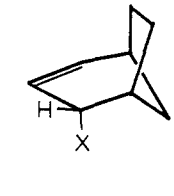
In work reported in earlier papers in this series it was found that acetolysis of *endo*-bicyclo[2.2.2]oct-5-en-2-yl *p*-toluenesulfonate (I) is anchimerically accelerated[3] and gives *exo*(*axial*)-bicyclo[3.2.1]oct-3-en-2-yl acetate (IVb).[4] This combination of kinetic and stereochemical behavior was of interest for the following reason. The rate enhancement indicates that ionization results in the direct formation of the stable bicyclic allylic carbonium ion II and thus the combined results suggest that II is stereoselectively converted to *endo*(*axial*)-acetate IVb.



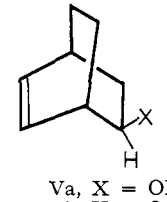
In connection with our interest in stereoelectronic factors involved in formation and reactions of allylic cyclohexenyl intermediates[5] it was desirable to: (a) re-examine the stereo-selectivity using a more precise analytical method (capillary gas chromatography) than was available for the earlier work and (b) obtain independent evidence that II is an intermediate. This paper describes an investigation of the stereochemistry of the acetolysis of optically active I. It can be seen that if II is an intermediate, C_1 and C_5 in the substrate become equivalent and the allylic acetate IVb derived from optically active I will be racemic.



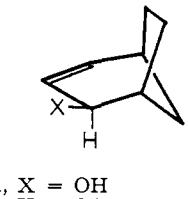
IIIa, X = OH
b, X = OAc
c, X = $O_2CC_6H_4NO_2$
d, X = $O_2CC_6H_4CO_2H$



IVa, X = OH
b, X = OAc
c, X = $O_2CC_6H_4NO_2$
d, X = $O_2CC_6H_4CO_2H$



Va, X = OH
b, X = OAc



VIa, X = OH
b, X = OAc

Results and Discussion

endo-Bicyclo[2.2.2]oct-5-en-2-ol (IIIa) was obtained from a binary mixture of the isomeric bicyclo[2.2.2]oct-5-en-2-ols (73% IIIa, 27% Va)[6] prepared by the Diels–Alder reaction of cyclohexadiene and vinyl acetate.[4] The *endo* isomer was separated and purified as the *p*-nitrobenzoate derivative IIIc.[4] Hydrolysis gave *endo*-alcohol IIIa containing less than 1.5% of the *exo* isomer. For comparison purposes a sample of *exo*-bicyclo[2.2.2]-oct-5-en-2-ol (Va) was separated from a mixture of the epimeric alcohols by preparative gas chromatography. The structure of Va was established by oxidation (manganese dioxide) to bicyclo[2.2.2]oct-5-en-2-one.

The *endo*-bicyclo[2.2.2]oct-5-en-2-yl system (III) was resolved by recrystallization of the cinchonidine salt of the acid phthalate derivative IIId. The specific rotation of optically pure *endo*-acid phthalate (IIId) was determined by an isotope dilution method[7] and in this way it was shown that the (+)-IIId obtained from the resolution was 66% optically pure.[8] This was converted to (+)-*endo*-alcohol (+IIIa) which contained 0.6% of the *exo* isomer. Specific rotations of optically pure (+)-IIIa, (+)-IIId and the corresponding ketone, (+)-bicyclo[2.2.2]oct-5-en-2-one, are given in the second column of Table I. The (+)-*endo*-bicyclo [2.2.2]oct-5-en-2-yl *p*-toluenesulfonate (I) used in the kinetic and product studies was prepared from 66% optically pure (+)-IIIa. Presumably, after purification the (+)-I was configurationally homogeneous and >66% optically pure—recrystallization of (+)-I results in enrichment of optical purity.

The polarimetric (k_α) and titrimetric (k_t) rate constants for acetolysis of (+)-I at 30.4° ([ROTs] = 0.03 *M*, [NaOAc] = 0.04 *M*) were found to be indistinguishable ($k_\alpha = 3.24 \pm 0.02 \times 10^{-5}$ sec.$^{-1}$, $k_t = 3.27 \pm 0.10 \times 10^{-5}$ sec.$^{-1}$) and in good agreement with the value reported earlier[3] for 30.07° (3.10×10^{-5} sec.$^{-1}$). In each case the reaction was followed to about 90% completion and the rate constants were steady from the outset. This also indicates that the substrate was diastereoisomerically homogeneous because contamination by the more reactive *exo* isomer results in a downward drift in the first-order rate during early stages of the reaction.[3,9] Infinity titers after ten half-periods were within 1% of the calculated values; however, there was a small residual optical rotation.

(1) This work was supported in part by the National Institutes of Health (Grant RG-8619) and in part by the Air Force Office of Scientific Research (AF49(638)-721).

(2) du Pont Summer Research Fellow, 1959, 1960.

(3) H. L. Goering and M. F. Sloan, *J. Am. Chem. Soc.*, **83**, 1992 (1961).

(4) H. L. Goering, R. W. Greiner and M. F. Sloan, *ibid.*, **83**, 1391 (1961).

(5) H. L. Goering and R. R. Josephson, *ibid.*, **84**, 2779 (1962).

(6) Isomeric compositions were determined by capillary gas chromatography (g.c.) using a 300-ft. column coated with Ucon polyglycol LB-550-X and an operating temperature of 135°.

(7) (a) J. A. Berson and D. Willner, *J. Am. Chem. Soc.*, **84**, 675 (1962); (b) H. L. Goering and J. T. Doi, *ibid.*, **82**, 5850 (1960).

(8) All optically active compounds had infrared spectra indistinguishable from those of authentic racemic samples.

(9) R. R. Fraser and S. O'Farrel, *Tetrahedron Letters*, 1143 (1962), have recently reported that the rate of acetolysis of *exo*-bicyclo[2.2.2]oct-5-en-2-yl *p*-toluenesulfonate is 33 times faster than that of the *endo* isomer. The *exo*-*p*-toluenesulfonate was prepared from Va, which, as in the present work, was separated from a mixture of Va and IIIa by gas chromatography.

The same conditions and concentrations were used for the product studies as for the kinetic experiments. In a control experiment it was found that (+)-*exo*-(*axial*)-bicyclo[3.2.1]oct-3-en-2-yl acetate (+IVb) does not racemize under these conditions. However, if excess sodium acetate is not present, *p*-toluenesulfonic acid produced by acetolysis causes rapid acid-catalyzed racemization of active IVb. Optically active axial acetate (+IVb) was prepared as follows. The *exo*-(*axial*)-bicyclo[3.2.1]oct-3-en-2-yl system (prepared by acetolysis of I)[4] was resolved *via* the cinchonidine salt of the acid phthalate derivative IVd. The resulting (+)-IVd was found to be 99$^+$% optically pure (isotope dilution)[7] and configurationally homogeneous.[6] This derivative was converted to (+)-*exo*(*axial*)-bicyclo-[3.2.1]oct-3-en-2-ol (+IVa), which in turn was converted to the acetate (+)-IVb, *p*-nitrobenzoate (+)-IVc and ketone, (+)-bicyclo[3.2.1]oct-3-en-2-one.[8] Since these transformations do not result in change in the optical purity, the specific rotations of these compounds correspond to those of optically pure substances. These values are given in the third column of Table I.

TABLE I

OPTICAL ROTATIONS OF *endo*-BICYCLO[2.2.2]OCT-5-EN-2-YL DERIVATIVES (III), *exo*(*axial*)-BICYCLO[3.2.1]OCT-3-EN-2-YL DERIVATIVES (IV) AND PRODUCT (AND DERIVATIVES) RESULTING FROM ACETOLYSIS OF (+)-*endo*-BICYCLO[2.2.2]OCT-5-EN-2-YL *p*-TOLUENESULFONATE (I)

Derivative	III[a] $[\alpha]^{25}D$	System IV[a] $[\alpha]^{25}D$	Acetolysis product[b] $[\alpha]^{25}D$
Alcohol	74 ($CHCl_3$)	219 ($CHCl_3$)	1.8 ($CHCl_3$)
Acetate		640 (neat)	3.28 (neat)
p-Nitrobenzoate		254 ($CHCl_3$)	3.2 ($CHCl_3$)
Acid phthalate	56 ($CHCl_3$)	233 ($CHCl_3$)	0.7 ($CHCl_3$)
Ketone	497 ($CHCl_3$)[c]	348 (pentane)	4.4 (pentane)

[a] Rotations for optically pure derivatives. [b] Acetolysis product of (+)-I, $[\alpha]^{25}D$ 35.2° ($CHCl_3$), at 30° ([ROTs] = 0.03 *M*; [NaOAc] = 0.04 *M*). [c] Calculated from relative rotations for acid phthalate and ketone reported by Mislow and Berger (ref. 10).

The acetolysis product derived from 66 + % optically pure (+)-I, $[\alpha]^{25}D$ 35.2° ($CHCl_3$), was isolated after ten half-periods in such a way as to avoid fractionation or racemization. The product was slightly active, $[\alpha]^{25}D$ 3.28° (neat), and consisted of 98.6% *axial*-[3.2.1]acetate IVb, 0.5% *equatorial*-[3.2.1]acetate VIb, 0.4% *endo*-[2.2.2]acetate IIIb and 0.5% of an unidentified compound (assumed to be an isomeric acetate).[6] *exo*-Bicyclo[2.2.2]oct-5-en-2-yl acetate (Vb), the inverted unrearranged substitution product, was not formed in detectable amounts.

That the three minor components in the product were derived from *endo*-[2.2.2]*p*-toluenesulfonate (I) rather than from a contaminant in the substrate (*e.g.*, the *exo* isomer) was established as follows. The optically active substrate used in the above experiment was partially solvolyzed in ethanol and then recrystallized several times. It has been shown[3,4] that this treatment removes the more reactive *exo*-*p*-toluenesulfonate. The resulting (+)-I had a rotation of $[\alpha]^{25}D$ 42.4° ($CHCl_3$). This material gave an acetolysis product having the same composition as described above and a rotation of $[\alpha]^{25}D$ 3.66° (neat). Together, these experiments indicate that the minor components and the optically active species in the product are derived from (+)-I.

The observed rotation of the acetolysis product corresponds to that of *ca.* 0.5% optically pure *axial*-acetate IVb—the observed rotation would have been >420° in the first experiment and >500° in the second if the product IVb had the same optical purity as the reactant. Thus, if the activity were entirely due to active IVb the transformation of active I to IVb would result in >99% loss of optical activity. However, there is evidence that the trace of activity is due to some component other than IVb and that in fact the conversion of active I to IVb probably results in complete loss of optical activity.

The specific rotations of the acetolysis product and various derivatives prepared from it are shown in the last column of Table I. These compounds were isolated in a manner so as to minimize fractionation of structural, geometric and optical isomers (solid products were isolated by column chromatography). Although in all cases the infrared spectra were indistinguishable from those of the corresponding *exo*(*axial*)-bicyclo-[3.2.1]oct-3-en-2-yl derivatives IV, the relative rotations are not those that would be expected for IV (*cf.* last two columns in Table I). Thus presumably the trace of optical activity results from the presence of an optically active minor component. The small amount of *endo*-[2.2.2] isomer III in the product cannot account for the optical activity because even if this were formed with complete preservation of optical configuration, ten times more than is present in the product would be required to give the observed rotation.

The present results establish beyond reasonable doubt that II is an intermediate in the acetolysis of I (C_1 and C_5 become equivalent) and confirm the earlier observation that the reaction is highly stereoselective; the ratio of *exo*(*axial*)-acetate IVb to *endo*(*equatorial*)-acetate VIb is *ca.* 200. Judging from the magnitude of the anchimeric acceleration[3] it seems likely that ionization results in direct formation of II. The stereoselective conversion of II to VIb is consistent with the idea, outlined elsewhere,[5] that in allylic cyclohexenyl systems formation and cleavage of *quasi-axial* bonds is stereoelectronically favored over formation and cleavage of *quasi-equatorial* bonds.

Experimental[8]

Materials.—*dl-endo*-**Bicyclo[2.2.2]oct-5-en-2-yl *p*-nitrobenzoate (IIIc)** was derived from the cyclohexadiene vinyl acetate adduct as described earlier.[4] After ten recrystallizations from ethanol (39% recovery) it melted at 111–112.5° (lit.[4] m.p. 109.8–110.8°) and contained <1.6% of the *exo* isomer. The progress of the separation of isomers—the mixture obtained from the Diels–Alder product consisted of 73% *endo* isomer and 27% *exo* isomer[6]—was followed by reduction of *ca.* 20-mg. samples of the *p*-nitrobenzoate with lithium aluminum hydride and determining the isomeric composition of the resulting alcohol by g.c.[6]

Saponification[4] of the *p*-nitrobenzoate derivative IIIc gave ***dl-endo*-bicyclo[2.2.2]oct-5-en-2-ol (IIIa)**, m.p. 166.1–166.4° (sublimation) (lit.[4] m.p. 167.0–169°), which contained <1.4% *exo*-alcohol Va. The *endo*-alcohol IIIa was converted to ***dl-endo*-bicyclo-[2.2.2]oct-5-en-2-yl acid phthalate (IIId)**, m.p. 168.0–168.6° (lit. 167.6–168°,[4] 168–168.5°[10]), in 90% yield.

The *endo*-alcohol IIIa was also converted[11] to ***dl-endo*-bicyclo-[2.2.2]oct-5-en-2-yl acetate (IIIb)**. Hydrolysis of 1.2 g. of IIIb by refluxing with 30 ml. of methanol containing 1.2 g. of potassium hydroxide gave pure IIIa, m.p. 167.4–168.4°. The g.c. retention time and infrared spectrum of the latter were indistinguishable from those of the original alcohol IIIa.

Oxidation of 10 g. of a mixture of 90% *endo*-IIIa and 10% *exo*-alcohol Va according to the general procedure of Brown and Garg[12] gave **bicyclo[2.2.2]oct-5-en-2-one** which was purified by sublimation. This material, obtained in 40% yield (after sublimation), melted at 89.7–90.6° (lit.[10] m.p. 91.5–93.0°). Reduction of the unsaturated ketone with sodium borohydride in isopropyl alcohol gave a binary mixture of IIIa (70%) and Va (30%).

***exo*-Bicyclo[2.2.2]oct-5-en-2-ol (Va)** was obtained from the mixture of IIIa and Va resulting from reduction of the ketone.

(10) K. Mislow and J. G. Berger, *J. Am. Chem. Soc.*, **84**, 1956 (1962).

(11) R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 212.

(12) H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, **83**, 2952 (1961).

The *exo* isomer was separated with a 3-m. preparative g.c. column packed with Ucon polyglycol LB-550-X (20%) on Celite (140°). After two sublimations the product was over 98% pure and melted at 168.4–170.8° (lit.[9] m.p. 175–176°). It was contaminated with 0.9% *endo* isomer IIIa and 0.7% ketone.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.25; H, 9.79.

The structure of the *exo*-alcohol Va was established by oxidation (manganese dioxide)[4,10] to bicyclo[2.2.2]oct-5-en-2-one. A small amount of Va was converted[11] to ***exo*-bicyclo[2.2.2]oct-5-en-2-yl acetate (Vb)**.

***dl-endo(axial)*-Bicyclo[3.2.1]oct-3-en-2-ol (IVa)**, m.p. 82.7–83.7° (lit.[4] m.p. 85.5–87.0°), was prepared from the acetolysis product of I as described earlier.[4] This material contained <2% of the *equatorial* isomer VIa and was converted to ***dl-endo(axial)*-bicyclo[3.2.1]oct-3-en-2-yl acid phthalate (IVd)** in 89% yield. After recrystallization from benzene and petroleum ether, IVd melted at 96.8–97.9°; neutral equivalent 270 (theory 272).

Anal. Calcd. for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.51; H, 5.95.

Resolution of the Bicyclo[2.2.2]oct-5-en-2-yl System (III).[8]—To 54 g. (0.20 mole) of *dl-endo*-bicyclo[2.2.2]oct-5-en-2-yl acid phthalate (IIId) in 113 ml. of acetone was added 58.8 g. of cinchonidine. The solution was filtered and 113 ml. of isopropyl alcohol was added. After 2 days at 0° the first crop of crystals (38 g.) was collected. A second crop (39 g.) was obtained by removing the solvent under reduced pressure and replacing it with 80 ml. each of isopropyl alcohol and acetone. The two crops were combined and recrystallized three times from a 50:50 mixture of acetone and isopropyl alcohol. The resulting 22 g. of cinchonidine salt had $[\alpha]^{25}D$ −34.6° (*c* 0.8, $CHCl_3$).

Hydrolysis[13] of the salt gave **(+)-*endo*-bicyclo[2.2.2]oct-5-en-2-yl acid phthalate (+IIId)**, m.p. 161.2–162.3°, $[\alpha]^{25}D$ 36.6° (*c* 1, $CHCl_3$). The specific rotation of optically pure (+)-IIId was found to be 55.8 ± 0.8° ($CHCl_3$) by the isotope dilution experiment outlined below. Thus the (+)-IIId described above was 66 ± 2% optically pure.

Anal. Calcd. for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.79; H, 6.03.

Optically active (+)-IIId, $[\alpha]^{25}D$ 50.5° ($CHCl_3$), has recently been reported by Mislow and Berger.[10]

The (+)-IIId, $[\alpha]^{25}D$ 36.6° ($CHCl_3$), was saponified as follows. A solution of 16 g. (0.059 mole) of (+)-IIId and 20 g. (0.36 mole) of potassium hydroxide in 150 ml. of methanol was refluxed for 1 hr. The mixture was then diluted with 300 ml. of H_2O and continuously extracted with pentane for 24 hr. After removal of the pentane the residual 5.6 g. (78%) of **(+)-*endo*-bicyclo[2.2.2]-oct-5-en-2-ol (+IIIa)** was purified by sublimation and had m.p. 166.2–166.8°, $[\alpha]^{25}D$ +48.3° (*c* 1, $CHCl_3$). This material contained 0.6% of the *exo* epimer Va. Presumably this material, like the acid phthalate from which it was derived, was 66 ± 2% optically pure and thus $[\alpha]^{25}D$ for optically pure (+)-IIIa is 74 ± 2°.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.64; H, 9.86.

The (+)-IIIa was converted[4] to **(+)-*endo*-bicyclo[2.2.2]oct-5-en-2-yl *p*-toluenesulfonate (+I)** in 97% yield. The crude derivative had $[\alpha]^{25}D$ 34.7° (*c* 1.2, $CHCl_3$) and was presumably 66 ± 2% optically pure. Thus $[\alpha]^{25}D$ for optically pure I is 53 ± 2.0°. After recrystallization from an ether–pentane mixture the (+)-I had m.p. 71.6–72.8°, $[\alpha]^{25}D$ 35.2° (*c* 0.7, $CHCl_3$). This material was used in the kinetic and product studies.

Anal. Calcd. for $C_{15}H_{18}O_3S$: C, 64.74; H, 6.52. Found: C, 64.62; H, 6.64.

Resolution of the *exo(axial)*-Bicyclo[3.2.1]oct-3-en-2-yl System IV.—To a solution of 9 g. (33 mmoles) of *dl-exo(axial)*-bicyclo[3.2.1]oct-3-en-2-yl acid phthalate (IVd) dissolved in 120 ml. of acetone was added 9.7 g. (33 mmoles) of cinchonidine. The resulting solution was filtered and 24 ml. of methanol was added. After standing, the white fibrous crystals were collected and recrystallized twice from 5:1 acetone–methanol. The resulting cinchonidine salt (5 g.) was converted[13] to **(+)-*exo(axial)*-bicyclo[3.2.1]oct-3-en-2-yl acid phthalate (+IVd)**, m.p. 79.7–81.2°, $[\alpha]^{25}D$ 195° (*c* 1, $CHCl_3$). This material was found to be 84% optically pure (isotope dilution). Additional recrystallizations of the cinchonidine salt resulted in complete resolution.

Anal. Calcd. for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.63; H, 5.91.

Saponification of a sample of optically pure (+)-IVd, $[\alpha]^{25}D$ 233°, by the method described above for hydrolysis of (+)-IIId, gave optically pure **(+)-*exo(axial)*-bicyclo[3.2.1]oct-3-en-2-ol (+IVa)** in 90% yield. After sublimation the (+)-IVa had $[\alpha]^{25}D$ 219° (*c* 0.6, $CHCl_3$), m.p. 81.8–82.6°.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.49; H, 9.68.

(13) H. L. Goering and J. P. Blanchard, *J. Am. Chem. Soc.*, **76**, 5405 (1954).

Optically pure (+)-IVa was converted[11] to **(+)-*exo(axial)*-bicyclo[3.2.1]oct-3-en-2-yl acetate (+IVb)** which was isolated by continuous extraction with pentane. This material was 99.5% pure (g.c.): $[\alpha]^{25}D$ 640° (neat), $\alpha^{25}D$ 320° (*l* 0.5, neat), $[\alpha]^{25}D$ 270° (*c* 0.2, HOAc). An analytical sample was purified by preparative gas chromatography (Ucon polyglycol column and conditions described above).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.94; H, 8.49.

Saponification of optically pure (+)-IVb gave (+)-IVa, m.p. 81.2–82.0°, $[\alpha]^{25}D$ 216° (*c* 0.6, $CHCl_3$). This shows that esterification and saponification results in very little if any racemization.

(+)-*exo(axial)*-Bicyclo[3.2.1]oct-3-en-2-yl *p*-nitrobenzoate (+IVc), $[\alpha]^{25}D$ 243° (*c* 0.8, $CHCl_3$), was obtained from 96% optically pure (+)-IVa. This derivative was isolated and purified in such a way as to avoid fractionation of optical isomers (column chromatography on silicic acid using chloroform as eluent). Thus presumably the (+)-IVc was of the same optical purity as the alcohol, in which case optically pure (+)-IVc has $[\alpha]^{25}D$ 254° ($CHCl_3$).

Oxidation of (+)-IVa, $[\alpha]^{25}D$ +199°, with manganese dioxide according to the procedure used for the racemic alcohol[4] gave **(+)-bicyclo[3.2.1]oct-3-en-2-one** in 40% yield. The ketone was homogeneous (g.c.); b.p. 105–110° (30 mm.), $n^{24}D$ 1.5133, λ_{max}^{EtOH} 228 mμ (log ε 3.94), $[\alpha]^{23}D$ 716° (neat), $[\alpha]^{23}D$ 316° (*c* 1.5, pentane). Since these are the same conditions under which (+)-*cis*-5-methyl-2-cyclohexenol is oxidized to (+)-5-methyl-2-cyclohexenone with complete preservation of optical purity[14] it is apparent that in the present case the ketone has the same optical purity as the alcohol from which it is derived, 91%. Thus optically pure (+)-bicyclo[3.2.1]oct-3-en-2-one has $[\alpha]^{23}D$ 348° (*c* 1.5, pentane), $[\alpha]^{23}D$ 787° (neat).

Anal. Calcd. for $C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.32; H, 8.50.

Acetolysis of (+)-*endo*-Bicyclo[2.2.2]oct-5-en-2-yl *p*-Toluenesulfonate (+I).—Three grams (11 mmoles) of (+)-I, $[\alpha]^{25}D$ 35.2° (67% optically pure), and 1.20 g. (15 mmoles) of sodium acetate were dissolved in 365 ml. of anhydrous acetic acid.[3] These are the same concentrations as were used in the kinetic experiments. The reaction mixture was heated at 30.4° for 72 hr. (10 solvolytic half-lives) and then diluted with water to 1000 ml. and extracted continuously for 48 hr. with pentane. After washing with aqueous sodium bicarbonate and water and then drying (Na_2SO_4) the pentane was removed under reduced pressure. The residual acetate, 1.52 g. (83%), had $[\alpha]^{25}D$ 3.28° (neat). The composition of the solvolysis product was determined by g.c.[6] and found to be 98.6% IVb, 0.5% VIb, 0.4% IIIb and 0.5% of an unidentified acetate (not Vb). The infrared spectrum of the acetolysis product was indistinguishable from that of authentic IVb.[4]

The residual acetate was saponified and continuously extracted with pentane as described earlier.[4] The resulting alcohol, 1 g. (88%), was purified by sublimation (90° water aspirator); m.p. 85.4–87.0°, $[\alpha]^{25}D$ 1.85° (*c* 1, $CHCl_3$). The infrared spectrum of this material was indistinguishable from that of authentic IVa. Gas chromatography showed this material to be mainly IVa (95%) with minor amounts of isomeric alcohols.

A portion of the alcohol fraction was converted to an acid phthalate derivative which was isolated and purified by chromatography on silicic acid using chloroform as eluent. This derivative was obtained in 48% yield, m.p. 92.1–94.8°, $[\alpha]^{25}D$ 0.70° (*c* 1.6, $CHCl_3$). The infrared spectrum was indistinguishable from that of authentic IVd.

Another portion of the alcohol fraction was converted to the *p*-nitrobenzoate derivative which was isolated and purified by chromatography (silicic acid). This derivative was obtained in 91% yield, m.p. 85.9–97.2° (lit.[4] m.p. 86.2–86.6°), $[\alpha]^{25}D$ 3.2° (*c* 1.6, $CHCl_3$). The infrared spectrum was indistinguishable from that of authentic IVc.

The alcohol fraction was also oxidized to the ketone (manganese dioxide).[4] This product was isolated by preparative g.c. (isomers were not separated) and obtained in 50% yield, $[\alpha]^{25}D$ 3.9° (*c* 1.5, pentane), λ_{max}^{EtOH} 228 mμ (log ε 3.95), $n^{25}D$ 1.5126 (lit.[4] λ_{max}^{EtOH} 227 mμ (log ε 3.98), $n^{25}D$ 1.5123). The infrared spectrum was indistinguishable from that of authentic bicyclo[3.2.1]oct-3-en-2-one.

In another product-study experiment (+)-I was purified by partial solvolysis in ethanol (5 min. at 70°), a method that has been demonstrated to remove the more reactive *exo*-*p*-toluenesulfonate.[4] The remaining (+)-I was isolated[4] and recrystallized three times from ether–pentane. The purified (+)-I was recovered in 50% yield, m.p. 73.2–74.6°, $[\alpha]^{25}D$ 42.4° ($CHCl_3$). This corresponds to 80 ± 3% optical purity. The acetolysis product derived from this sample of (±)-I had the same isomeric composition as the product obtained in the experiment described above and the rotation was $[\alpha]^{25}D$ 3.66°. This duplicate experi-

(14) H. L. Goering and E. F. Silversmith, *ibid.*, **77**, 5173 (1955).

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 ($\alpha^{25}D$) of this solution was 2.347°. After 8 days at 30.4° (27 half-lives for acetolysis of I) $\alpha^{25}D$ 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* $HClO_4$ in acetic acid (final $HClO_4$ 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 IVb[6]; 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 ($k\alpha$)[15] and titrimetric (k_t)[3] first-order rate constants for acetolysis of (+)-I at 30.4° were determined using methods described earlier. The same reaction mixture ([ROTs] = 0.03 *M*, [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 $3.27 \pm 0.10 \times 10^{-5}$ sec.$^{-1}$. The average (and average deviation) of 14 values of $k\alpha$ was $3.24 \pm 0.02 \times 10^{-5}$ sec.$^{-1}$.

Determination of Optical Purity of (+)-IIId and (+)-IVd. A. (+)-IIId.—*dl-endo*-Bicyclo[2.2.2]oct-5-en-2-yl acid phthalate-7-^{14}C was prepared[7b] from pure IIIa and phthalic anhydride-7-^{14}C (Tracerlab Inc., 0.35 μc./g. after dilution). After several recrystallizations from benzene the *dl*-IIId-^{14}C 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 (+)-IIId, $[\alpha]^{25}D$ 31.4° (*c* 1, $CHCl_3$), and 0.4059 g. of the *dl*-IIId-^{14}C 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 (+)-IIId 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 (+)-IIId is 55.8 ± 0.8° ($CHCl_3$).[7]

B. (+)-IVd.—In this experiment a mixture of 0.6978 g. of (+)-IVd, $[\alpha]^{25}D$ 231.0° (*c* 1, $CHCl_3$), and 0.4133 g. of *dl*-IVd-^{14}C, 5844 c./min./mmole, was resolved as described above. The resulting (+)-IIId had $[\alpha]^{25}D$ 230.3° (*c* 1, $CHCl_3$), 1350 ± 8 c./min./mole. From these data it can be shown[7] that $[\alpha]^{25}D$ for optically pure (+)-IIId is 232 ± 2° ($CHCl_3$).

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

(16) The ^{14}C 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-Cycloöctatriene by 1,4-Radical Addition to Cycloöctatetraene and its Intramolecular Isomerization to a Bicyclo[4.2.0]octa-2,4-diene[1a]

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The reaction of cycloöctatetraene 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-cycloöctatriene (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-cycloöctatriene, 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 cycloöctatetraene. Strictly speaking, cycloöctatetraene 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–cycloöctatetraene 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-cycloöctatrienes.

Results and Discussion

Reaction of Cycloöctatetraene with α-Cyanoisopropyl Radicals.—Cycloöctatetraene 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]

Cycloöctatetraene–AIBN reaction products could be obtained, however, albeit in low yield, if the azo compound (1 *M*) was decomposed in bulk cycloöctatetraene. 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.

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