Bridged Polycyclic Compounds. XXI. The Ionic Chlorination of 9,10-Dihydro-9,10-ethenoanthracene[1]

STANLEY J. CRISTOL, ROBERT P. ARGANBRIGHT, AND DENNIS D. TANNER

Department of Chemistry, University of Colorado, Boulder, Colorado

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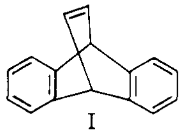
The ionic chlorination of 9,10-dihydro-9,10-ethenoanthracene was shown to yield *exo*- and *endo*-4-*syn*-8-dichlorodibenzobicyclo[3.2.1]octadiene as the sole reaction products. The less stable of these isomers was the preponderant product. The structure proofs of these addition–rearrangement reaction products and some of their chemistry are discussed.

Ionic chlorination of 9,10-dihydro-9,10-ethenoanthracene (I) in carbon tetrachloride gave two isomeric dichlorides, A and B, neither of which were *cis*- or *trans*-11,12-dichlorodibenzobicyclo[2.2.2]octadiene (IV) and (V), which had been previously prepared in this laboratory.[2] Both isomers gave an immediate precipitate of silver chloride when treated with silver nitrate in acetone. Compounds IV and V were unreactive to this reagent under these conditions.

Addition rearrangements during the halogenation of bicyclic olefins have been previously reported,[3–5] and this type of reaction seemed to be the best explanation for the formation of compounds A and B during the chlorination reaction. The formation of four isomeric dichlorinated hydrocarbons, II, III, VI, and VII, from the addition–rearrangement to I is possible.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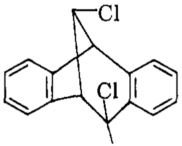

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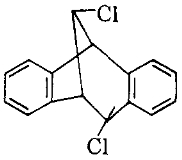

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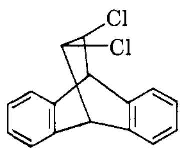

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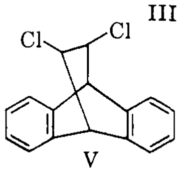

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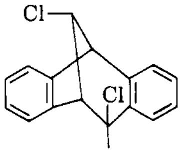

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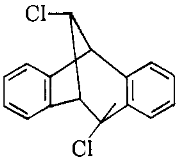
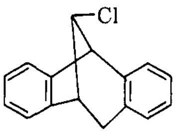
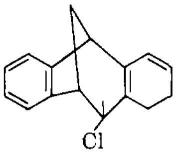


VII

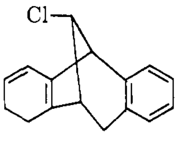
Catalytic hydrogenation of each of the dichlorinated isomers with palladium on barium sulfate yielded the same monochlorinated product (C), which might have any of the structures VIII to XI.



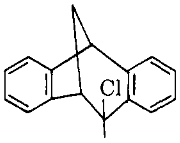
VIII



IX



X



XI

Since the steric arrangement of one of the chlorine atoms in each isomer was thus shown to be identical with that in the other, it then follows that the isomeric pair (A and B) could have only the following combination of structures: II, III; III, VII; VI, VII; or II, VI.

At first, it appeared obvious that hydrogenolysis of the benzyl chloride of the rearranged dichlorides A and B had taken place to produce a monochlorinated hydrocarbon with a chlorine atom substituted at the 8-position. However, it was reported that the specific rate constant for the solvolysis of *anti*-7-chloronorbornene[6] in 80% ethanol at 50° is 8.7×10^{-5} sec.$^{-1}$, and the corresponding constant for α-phenylethyl chloride[7] is 16.4 $\times 10^{-5}$ sec.$^{-1}$. It, therefore, seemed possible that the *syn*-c8-hloride under the influence of the unsaturation from the benzene ring might undergo hydrogenolysis at a faster rate than the benzyl chloride. This involves the perhaps unjustifiable assumption that hydrogenolysis and solvolysis are comparable, and that assistance from the π-electron system is comparable to that from a carbon–carbon double bond.[8]

It, therefore, seemed necessary to establish the position of the chlorine atom which was removed upon hydrogenolysis of the chlorinated products. Addition of *t*-butyl hypochlorite to I in acetic acid gave the same chloroacetate as was obtained from the acetolysis of either A or B.[9] *t*-Butyl hypochlorite, when used as an ionic chlorinating agent, donates a chloronium ion to an olefinic double bond.[10] A positive charge when placed on the 11-position of I induces a Wagner–Meerwein rearrangement and transforms the [2.2.2] ring system into the [3.2.1] ring system[9,11] which then reacts with acetic acid at the benzyl position to give a chloroacetate (XII).

Reduction of XII with lithium aluminum hydride gave the chlorohydrin XIII. Permanganate oxidation of XIII gave a chloro ketone, XIV, which when subjected to Clemmensen reduction gave the same monochlorinated hydrocarbon which was obtained upon hy-

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(1) Previous paper in series: S. J. Cristol, L. K. Gaston, and D. W. Johnson, *Tetrahedron Letters*, in press.

(2) S. J. Cristol and N. L. Hause, *J. Am. Chem. Soc.*, **74**, 2193 (1952).

(3) H. Kwart, *ibid.*, **75**, 5942 (1953).

(4) J. D. Roberts, F. O. Johnson, and R. A. Carboni, *ibid.*, **76**, 5692 (1954).

(5) H. Kwart and L. Kaplan, *ibid.*, **76**, 4072 (1954).

(6) W. G. Woods, R. A. Carboni, and J. D. Roberts, *ibid.*, **78**, 5653 (1956).

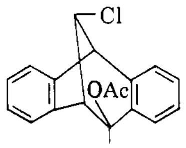
(7) E. Grunwald and S. Winstein, *ibid.*, **70**, 846 (1948).

(8) It has subsequently been shown by P. D. Bartlett and W. P. Giddings that this type of rate enhancement in solvolysis is not so great with a benzene ring as with a double bond. P. D. Bartlett and W. P. Giddings, *ibid.*, **82**, 1240 (1960).

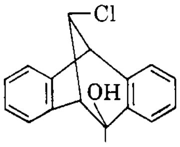
(9) D. D. Tanner, Ph.D. thesis, University of Colorado, 1961.

(10) M. Anbar and D. Ginsberg, *Chem. Rev.*, **54**, 925 (1954).

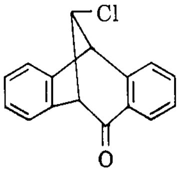
(11) S. J. Cristol and R. K. Bly, *J. Am. Chem. Soc.*, **82**, 6155 (1960).



XII



XIII



XIV

drogenolysis of either A or B. (Numbers XII through XIV refer to the correct structure assignments.)

The method of preparation of XII establishes the position of the chlorine atom which is replaced during hydrogenolysis. The position of the reactive chlorine atom was further investigated by taking an ultraviolet spectrum of XIV. The usual absorption band at 2400–2450 Å. often associated with an aromatic conjugated ketone was not seen in the ultraviolet spectrum of XIV, taken in absolute ethanol. This absence of a strong absorption maximum is not unique since the ketonic band at this wave length fails to appear in the spectra of 1-indanone,[12] 1-tetralone,[13] 2,3-benz-1-suberone,[13] 2-keto-*anti*-8-methyl-3,4,6,7-dibenzo[3.2.1]bicycloöctadiene-1-*syn*-8-dicarboxylic acid,[14] and *syn*-8-hydroxydibenzobicyclo[3.2.1]octadien-2-one.[15]

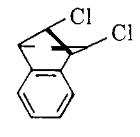
When the spectrum of XIV was taken in concentrated sulfuric acid, a strong absorption band appeared at 3030 Å. (ϵ 13,000). This observation was in good agreement with the fact that conjugated aromatic ketones show a bathochromic shift of 300–600 Å. in concentrated sulfuric acid, and the extinction coefficient of this shifted maximum is very much exalted over the weak, indistinguishable band at 2400 Å.[16,17] Similar halochromic behavior has been observed in the case of all of the above mentioned aryl ketones.

With the establishment of the hydrogenolysis product of A and B as a hydrocarbon substituted in the 8-position by a chlorine atom, the structure of compound C must be either VIII or X.

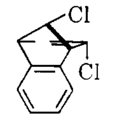
Dipole moments were utilized for the final structure assignments.[18] From the chemical evidence, the isomeric pair of dichlorinated products must either be II and III or VI and VII. Calculated dipole moments for the first pair were 4.0 and 1.9 D., respectively, and for the second pair, 2.2 and 2.7 D., respectively. The observed values for A and B were 3.40 and 1.94 D. The dipole moments of the two isomers thus unequivocally demonstrated that the chlorination products were *exo*-4- and *endo*-4-*syn*-8-dichlordibenzobicyclo[3.2.1]octadiene, II and III, respectively.

Differential infrared analysis[19] established that II and III were found in the reaction mixture at 88% and 12%, respectively

Examination of models of the rearranged dichlorides suggested that the major isomer, II, should be the less stable of the two isomers. The models clearly indicate



II



III

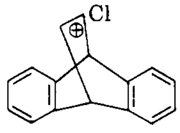
a large steric interaction between the diaxial chlorine atoms in II, which is relieved in III.

When II was dissolved in liquid sulfur dioxide and cresol at room temperature, all of the dichlorinated product that was recovered after column chromatography (55%) was shown to be isomer III.

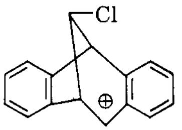
These results made us suspect that the *endo* product III found in the chlorination was the result of an epimerization of the *exo* isomer. We found, however, that the *exo* isomer did not appear to rearrange under simulated reaction conditions or work-up conditions, even for extended time periods so it would appear that III is an initial reaction product. In addition, neither IV nor V is isomerized to II or III under reaction conditions.

The addition–rearrangement reaction is an heterolytic process, as indicated by the fact that the reaction proceeds in the dark and has no apparent induction period. Free-radical reactions in bridged bicyclic systems of this type have not led to rearrangement, although evidence for such rearrangements has been sought.[20–22]

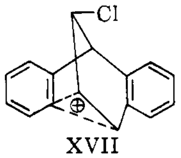
The simplest mechanism which might be proposed involves addition of a chlorine cation to I to yield the classical carbonium ion XV which then rearranges to the more stable benzylic cation XVI. Coördination of XVI with chloride ion would give products II and III. The structure of the principal product (*syn–exo*) II is consistent with that observed in the addition of other ionic species to I[9,23] and also with the concept that XV and XVI represent resonance structures of the mesomeric cation XVII, but the formation of substantial amounts of III appears inconsistent with the latter assumption.[24] As indicated in the models described above for II and III, the *exo* isomer II has interference between the two diaxial chlorine atoms and its formation from XVI would obviously not be favored over that of III on steric grounds.



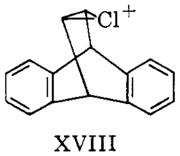
XV



XVI



XVII



XVIII

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(12) R. P. Lucas and J. Jock, *Bull. soc. chim.*, [5] **2**, 327 (1935); **5**, 848 (1938).

(13) R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1951.

(14) W. R. Vaughan, M. V. Andersen, Jr., and R. Q. Little, Jr., *J. Am. Chem. Soc.*, **76**, 1748, 4130 (1954).

(15) C. Bouboulis, Ph.D. thesis, University of Colorado, 1961.

(16) L. C. Anderson, *J. Am. Chem. Soc.*, **55**, 2096 (1933).

(17) L. C. Anderson and C. M. Gooding, *ibid.*, **57**, 999 (1935).

(18) D. D. Tanner and T. S. Gilman, unpublished work.

(19) I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," 3rd ed., The Macmillan Co., New York, N. Y., 1952, p. 632.

(20) S. J. Cristol and G. D. Brindell, *J. Am. Chem. Soc.*, **76**, 5699 (1954).

(21) J. A. Berson and W. M. Jones, *ibid.*, **78**, 6045 (1956).

(22) N. A. LeBel, *ibid.*, **82**, 623 (1960).

(23) F. Pwu, Ph.D. dissertation, University of Colorado, 1961.

(24) The *syn–exo*- configuration of the addenda in this bicycloöctane ring system is similar to the corresponding additions in bicycloheptane systems,[3–5] and to oxide-ring openings in bicycloheptane[25–27] and bicycloöctane systems.[11,28]

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

(26) H. Kwart and W. E. Vosburgh, *ibid.*, **76**, 5400 (1954).

(27) S. B. Soloway and S. J. Cristol, *J. Org. Chem.*, **25**, 327 (1960).

(28) H. Kwart and G. C. Gatos, *J. Am. Chem. Soc.*, **80**, 881 (1958).

On the other hand, stereoelectronic considerations may be invoked to rationalize the preferred formation of II from XVI. p–π-Overlap of the benzylic carbon atom with the benzene ring will be lost less rapidly if chloride ion coördinates from the axial (*exo*) position than from the equatorial (*endo*) position, so that the transition state for the former situation may be expected to be more stable than that for the latter. This argument is also consistent with the greater reactivity observed[9] for solvolysis reactions of *exo* (axial) substituents in these systems. Rearrangement of II to III may also proceed through XVI and is consistent with the solvolysis reactivities.

This mechanism does not rationalize the fact that only *syn*-8-chloro isomers are found—that is that only the bond *anti* to the entering chlorine cation migrates. This result could be accommodated by the assumption that XV is in fact not involved, but that donation of a chlorine cation by chlorine or by *t*-butyl hypochlorite gives the chloronium ion XVIII which opens with rearrangement directly to XVI. This latter explanation does not appear consistent with observations that the [3.2.1] ring system analogous to XVI may undergo rearrangements to the [2.2.2] systems analogous to XV under appropriate conditions, and again with stereochemical purity.[9,23] For the present, this problem remains unsettled.

Experimental

The Chlorination of 9,10-Dihydro-9,10-ethenoanthracene (I).—The chlorination reactions of I are summarized as follows.

Experiment 1.—In a glass-stoppered flask, wrapped with aluminum foil to exclude light, was placed 2.002 g. (9.80 mmoles) of compound I,[2] m.p. 119.5–122°, dissolved in 30 ml. of dry carbon tetrachloride. The flask was cooled in an ice bath to 0°. To this mixture was added a chilled solution of 1.04 g. (0.014 mole) of chlorine in 20 ml. of dry carbon tetrachloride. The reaction mixture was stoppered and allowed to stand at room temperature for 41 hr. The solvent was removed by rotary evaporation, and 2.739 g. (101%) of a gummy, white crystalline product was obtained, m.p. 91–124°. The product was dissolved in benzene, and the benzene was removed by rotary evaporation. The product was dried under vacuum over phosphorus pentoxide and paraffin. An analysis for chlorine was obtained on this mixture.

Anal. Calcd. for $C_{16}H_{12}Cl_2$: Cl, 25.77. Found: Cl, 25.85.

The reaction mixture was subjected to infrared analysis and found to contain 12% of the *endo* dichloride III and 88% of the *exo* dichloride II.

Experiment 2.—To a continuously stirred solution of 1.361 g. (6.66 mmoles) of I in 25 ml. of dry carbon tetrachloride was added dropwise 18 ml. of dry carbon tetrachloride containing 630 mg. (8.88 mmoles) of chlorine. The solution was added in the dark over a period of 1 hr. at room temperature, and the solvent was removed by rotary evaporation. The dried reaction mixture was subjected to infrared analysis and found to contain 12% *endo* dichloride III and 88% of the *exo* dichloride II.

Experiment 3.—To a solution of 20 ml. of dry carbon tetrachloride containing 700 mg. (9.87 mmoles) of chlorine was added dropwise a solution of 1.352 g. (6.61 mmoles) of I dissolved in 45 ml. of dry carbon tetrachloride. The solution was added in the dark over a period of 1 hr. at room temperature, and the solvent was removed by rotary evaporation. The dried reaction mixture was subjected to infrared analysis and found to contain 12% *endo* dichloride III and 88% of the *exo* dichloride II.

Experiment 4.—To a solution of 344 mg. (1.68 mmoles) of I in 30 ml. of dry carbon tetrachloride was added 20 ml. of carbon tetrachloride containing 240 mg. (3.38 mmoles) of chlorine. The mixture was stoppered and allowed to stand in the dark for 13 days. The dried reaction products were subjected to infrared analysis, which showed the product composition to be 18% III and 82% II.

Experiment 5.—Experiment 4 was repeated, only the solvent was removed by rotary evaporation immediately after addition of the chlorine solution. The yellow color of chlorine had disappeared 13 min. after the addition of the chlorine solution, and all the solvent had been removed by the time 28 min. more had elapsed. Infrared analysis showed a product composition of 18% of III and 82% of II.

The discrepancy in the analytically determined product composition between experiments 1, 2, and 3 and experiments 4 and 5 may possibly be within experimental error. However, it must be noted that the reactions which yielded 12% *endo* dichloride (experiments 1, 2, and 3) were done under conditions where the temperature of the solution remained relatively constant, while the reactions yielding 18% *endo* product (experiments 4 and 5) were subjected to local heating due to the exothermic nature of the reaction.

Isolation of II and III.—A solution of 1.63 g. (8.0 mmoles) of I in 30 ml. of carbon tetrachloride was placed in a foil-wrapped flask. Then, 604 mg. (8.5 mmoles) of chlorine dissolved in 10 ml. of carbon tetrachloride was added. Evaporation of the solvent left 2.21 g. of material. Crystallization from 27 ml. of ethanol gave 1.77 g. (81%) of II, m.p. 122–128°. Purification by sublimation gave II, m.p. 128–129°.

Anal. Calcd. for $C_{16}H_{12}Cl_2$: C, 69.83; H, 4.40. Found: C, 69.77; H, 4.57.

The mother liquors were evaporated to dryness and absorbed on 20 ml. of activated alumina (Fisher). Elution with chloroform gave 120 mg. (5.5%) of III, m.p. 98–98.5°.

Anal. Calcd. for $C_{16}H_{12}Cl_2$: C, 69.83; H, 4.40. Found: C, 69.66; H, 4.65.

Both II and III gave precipitates of silver chloride within 5 min., when treated with silver nitrate in acetone.

Infrared Analysis of the Products of Chlorination of I.—The ratio of II and III in the chlorination of I was determined by differential quantitative infrared analysis, using a double-beam Perkin-Elmer Model 137 Infracord spectrophotometer. Potassium bromide optics were used to obtain the desired frequency range, 13–25 μ. The *exo* isomer II had absorption peaks at 14.4, 15.7, 16.3, 16.6, 17.7, 18.3, 18.9, 20.7, and 22.8 μ, and the *endo* isomer III had peaks at 14.6, 15.3, 16.3, 17.3, 17.7, 18.1, 19.2, 21.2, 22.3, and 23.3 μ. Analytical results seem to be correct to ±3%.

Hydrogenolysis of II and III.—A mixture of 50 mg. of 10% palladium on barium sulfate catalyst in 18 ml. of ethanol and 2 ml. of 1.2 *N* sodium hydroxide was pre-reduced with hydrogen at room temperature and atmospheric pressure. Then 100 mg. (0.363 mmole) of II was added and the flask shaken under an atmosphere of hydrogen for 24 hr. The catalyst was removed by filtration and water was added to precipitate the product. Recrystallization from aqueous ethanol gave 70 mg. (80%) of *syn*-8-chlorodibenzobicyclo[3.2.1]octadiene (VIII), m.p. 143.5–144.5°.

Anal. Calcd. for $C_{16}H_{13}Cl$: C, 79.53; H, 5.44. Found: C, 79.83; H, 5.61.

Similarly, 64 mg. of III was hydrogenated. The product was identical with the sample of VIII produced from II.

Attempts to remove the second chlorine atom by further hydrogenolysis over platinum led to saturation of one of the benzene rings without removal of the chlorine atom. Which ring was hydrogenated was not determined. Fifty milligrams of III was shaken under hydrogen with 30 mg. of Adam's platinum oxide catalyst in 14 ml. of ethanol containing 5 ml. of 5 *N* hydrochloric acid for 24 hr. The product was precipitated with water and recrystallized from ethanol, m.p. 60–61°. A Beilstein test indicated the presence of chlorine in the product.

Anal. Calcd. for $C_{16}H_{19}Cl$: C, 77.87; H, 7.76. Found: C, 78.00; H, 7.49.

***syn*-8-Chlorodibenzobicyclo[3.2.1]octadien-*exo*-2-yl Acetate (XII).**—To a stirred and cooled solution of 1.100 g. (5.39 mmoles) of ethenoanthracene, I, in 70 ml. of glacial acetic acid was added 1.00 g. of *t*-butyl hypochlorite (9.80 mmoles)[29] over the course of 30 min. After the addition of the hypochlorite, the reaction mixture was poured into an excess of water, and the precipitate which formed was filtered and dried over phosphorus pentoxide. The crude yield was 1.441 g. (89.5%) of an oily white gum. The product was dissolved in hot petroleum ether (b.p. 60–70°) and chromatographed on an alumina column. Three oily fractions were obtained by elution with 5% chloroform in carbon tetrachloride, 10% chloroform in carbon

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[29] C. F. Irwin and G. F. Hennion, *J. Am. Chem. Soc.*, **63**, 858 (1941).

tetrachloride, and 100% chloroform, and weighed 500 mg., 675 mg. and 129 mg., respectively.

When fraction 1 was crystallized from absolute ethanol, it gave 193 mg. of a white crystalline compound, m.p. 135–148.5°; recrystallization gave 105 mg., m.p. 146.5–154.5°.

When fraction 2 was crystallized from absolute ethanol, there sesulted 390 mg. of white crystals, m.p. 150–153°. An analytical rample was taken from this product, and the recrystallized product melted at 157–158°.

Anal. Calcd. for $C_{18}H_{15}ClO_2$: C, 72.36; H, 5.06. Found: C, 72.31; H, 4.89.

When fraction 3 was recrystallized from absolute ethanol, it yielded 22 mg. of white crystals, m.p. 145–155°. Mixture melting points with fractions 1 and 2 were not depressed. Mixture melting points and solution infrared spectra of this compound showed it to be identical with the chloroacetate obtained from the acetolysis of II or III.[8]

***syn*-8-Chlorodibenzobicyclo[3.2.1]octadien-*exo*-2-ol. (XIII).**—A slurry of 40 mg. of crushed lithium aluminum hydride in approximately 20 ml. of ether, which had been dried over sodium ribbon, was stirred while an ethereal solution of 134 mg. (0.448 mmole) of the combined fractions 1 and 2 above (compound XII) was slowly added. The reaction mixture was stirred at room temperature for 2.5 hr., and the excess lithium aluminum hydried was destroyed by the addition of water. The solution was decanted, the residual aluminum hydroxide was washed several times with ether, and the decantates were combined. The solvent was evaporated in an air stream and the residue was dride under vacuum over phosphorus pentoxide, leaving 112 mg. (97%) of white crystals, m.p. 111–122°. An infrared spectrum taken in carbon disulfide solution showed a strong hydroxyl peak at 2.80 μ and no acetate carbonyl absorption.

The product was recrystallized from absolute ethanol, yielding 35 mg. of white crystals, m.p. 130–134.5°. A second crop of crystals was taken, yield 13 mg., m.p. 127.5–136.5°. The crude yield was 42%. Crop 1 was recrystallized twice from absolute ethanol to give pure XIII, m.p. 137.5–138.5°.

Anal. Calcd. for $C_{16}H_{13}ClO$: C, 74.78; H, 5.10. Found: C, 74.91; H, 5.03.

***syn*-8-Chlorodibenzobicyclo[3.2.1]octadien-2-one (XIV).**—A mixture of 312 mg. (1.21 mmoles) of crude XIII (m.p. 120–135°), 40 ml. of benzene, 2 g. of potassium permanganate (12.7 mmoles), 20 ml. of *t*-butyl alcohol and 6 ml. of water was heated at 60° for 75 hr. with constant stirring. The excess potassium permanganate was destroyed by the addition of aqueous sodium bisulfite. The solution was dried under vacuum, 40 ml. of water was added, and the manganese dioxide precipitate was filtered and washed with water. The filter cake was extracted with hot chloroform, and the extract dried over sodium sulfate. The organic solvent was removed under vacuum, leaving 190 mg. of a white crystalline material, m.p. 106–112°. The product was dried over phosphorus pentoxide under vacuum, and the infrared spectrum showed no hydroxyl absorption and a strong carbonyl absorption at 5.88 μ.

Of the 190 mg. obtained, 72 mg. of the product was chromatographed on an alumina column. By dissolving in hot petroleum ether (b.p. 60–70°) and eluting with chloroform, a fraction weighing 66 mg. (60%), m.p. 114.7–116°, was obtained. Recrystallization from absolute ethanol gave *syn*-8-chlorodibenzobicyclo[3.2.1]octadien-2-one (XIV), m.p. 115.5–116.5°.

Anal. Calcd. for $C_{16}H_{11}ClO$: C, 75.44; H, 4.35. Found: C, 75.47; H, 4.38.

The Reduction of *syn*-8-Chlorodibenzobicyclo[3.2.1]octadien-2-one (XIV).—A mixture of 110 mg. (0.432 mmole) of XIV, 5 g. of amalgamated zinc, 6 ml. of concentrated hydrochloric acid, 5 ml. of acetic acid, and 5 ml. of toluene was heated at reflux for 22 hr. During this time, three 5-ml. portions of concentrated hydrochloric acid were added. The reaction mixture was extracted three times with 30-ml. portions of benzene. The benzene extracts were washed with sodium carbonate solution, followed by several washings with water, and dried over anhydrous sodium sulfate. The solvent was removed under vacuum, leaving a thick, yellow oil. The product was chromatographed on an alumina column (25 g. of Merck Co., acid-washed alumina packed in petroleum ether, b.p. 60–70°) and was eluted with carbon tetrachloride. The crude yield was 73 mg., m.p. 110–143°. Recrystallization from absolute ethanol yielded a product weighing 32 mg., m.p. 142–144.5° (36%).

Mixture melting point showed no depression with the hydrogenolysis product of compound II, and the infrared spectrum was identical with that of product VIII.

Isomerization of Dichloride II to III in Liquid Sulfur Dioxide.—In a sealed Pyrex tube was placed 1 ml. of *o*-cresol, 398 mg. of II, and approximately 50 ml. of liquid sulfur dioxide. The mixture was allowed to stand for 4 hr. at 0° and then at room temperature for 10 hr. The sulfur dioxide was allowed to evaporate, and the solution was chromatographed on alumina by dissolving in petroleum ether (b.p. 60–70°) and eluting with carbon tetrachloride. Two fractions were obtained. The first was 220 mg. (55%) of a white crystalline product, m.p. 95–99°. After recrystallization from absolute ethanol, a melting point of 100–100.5° was obtained. The product had an infrared spectrum identical with that of III, and a mixture melting point with that compound showed no depression. A mixture melting point with II was depressed. The second fraction was an oil, 23 mg. (6%), which was not investigated.

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The Synthesis of 2-Acetamido-2-deoxy-3-*O*-(β-D-galactopyranosyl)-α-D-glucose[1]

Harold M. Flowers[2] and Roger W. Jeanloz

Laboratory for Carbohydrate Research, Departments of Biological Chemistry and Medicine, Harvard Medical School and the Massachusetts General Hospital, Boston, Massachusetts

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The synthesis of 2-acetamido-2-deoxy-3-*O*-(β-D-galactopyranosyl)-α-D-glucose, a product of degradation of a tetrasaccharide isolated from human milk and of various glycoproteins, is described, starting from D-galactose and D-glucosamine.

The structure of 2-acetamido-2-deoxy-3-*O*-(β-D-galactopyranosyl)-D-glucose (VI) has been assigned to a disaccharide of D-galactose and D-glucosamine, which has been isolated from the products resulting from the degradation of oligosaccharides obtained from human milk.[3,4] This compound has also been found, together with 2-acetamido-2-deoxy-4-*O*-(β-D-galactopyranosyl)-D-glucose, in the controlled acid-hydrolyzate of blood group A substance,[5–7] in which it forms an essential

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[2] On leave of absence from the Weizmann Institute, Rehovoth, Israel

[3] R. Kuhn, A. Gauhe, and H. H. Baer, *Chem. Ber.*, **87**, 289 (1954).

[4] R. Kuhn, H. H. Baer, and A. Gauhe, *ibid.*, **87**, 1553 (1954).

[5] R. H. Côté and W. T. J. Morgan, *Nature*, **178**, 1171 (1956).

[6] I. A. F. L. Cheese and W. T. J. Morgan, *ibid.*, **191**, 149 (1961).

[7] G. Schiffman, E. A. Kabat, and S. Leskowitz, *J. Am. Chem. Soc.*, **84**, 73 (1962).