Photocyclization of *keto*-D-Fructose Pentaacetate and *keto*-L-Sorbose Pentaacetate[1]

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Ultraviolet irradiation of both 1,3,4,5,6-penta-*o*-acetyl-*keto*-D-fructose (1) and 1,3,4,5,6-penta-*o*-acetyl-*keto*-L-sorbose (2) (epimeric at the γ carbon) has been found to produce crystalline 1(*S*),4(*S*)-diacetoxymethyl-2(*S*),-3(*S*),4-triacetoxycyclobutan-1-ol (3), the former giving a yield of 11.6% and the latter a yield of 26.2%. Reaction is envisioned from 1,4 biradicals in the triplet state, but no other diastereoisomers resulted. The cyclic photoproduct was converted to its hexaacetate and was also deacetylated to a hexose isomer, $C_{16}H_{12}O_6$. The deacetylated material was converted to a tetra-*p*-toluenesulfonylate, in which all but the tertiary hydroxyl functions were derivatized. This derivative was reduced by lithium aluminum hydride to 1(*S*),4(*S*)-dimethyl-3(*S*)-cyclobutanetriol. A minor photoproduct was produced in a 0.9% yield from 1. It presumably resulted from δ-hydrogen abstraction and formation of a 1,5-biradical intermediate, which underwent ring closure to *meso*-(1,2,3/4,5)-2-acetoxymethyl-1,3,4,5-tetraacetoxycyclopentan-2-ol (4).

Examination of the extensive literature[2,3] on alkanone photochemistry reveals that those possessing γ hydrogen atoms react almost exclusively to give smaller ketones and olefins, and cyclobutanols. It is evident that a useful route to cyclic polyols might be through the photoexcitation of appropriate ketoses, provided cyclization is maximized and the fragmentation route minimized. It is gratifying, therefore, to find that photoexcitation of acetylated open-chain ketoses leads to acceptable yields of polyhydroxycyclobutane. In addition, the reaction provides interesting information on the stereochemistry of the ring closure in these compounds.

Irradiation of 1,3,4,5,6-penta-*O*-acetyl-*keto*-D-fructose (1) in benzene requires 60 hr for complete conversion to photoproducts, but, in a mixture of *tert*-butyl alcohol with only sufficient benzene present to allow solubility, the reaction is complete in 18 hr with formation of 11.6% of cyclic product. Polar solvents are known to increase the rate of formation of photoproducts from alkanones.[4] Irradiation of 1,3,4,5,6-penta-*O*-acetyl-*keto*-L-sorbose (2) in benzene causes complete disappearance of starting material in 18 hr with formation of 26.2% of cyclic product. *tert*-Butyl alcohol cannot be used with 2 because of insolubility of the ketose derivative.

It appears that only one and the same polyhydroxy cyclobutane derivative 3 is produced from either 1 or 2. Three diastereomeric cyclobutanols could possibly arise from ring closure of the 1,4 biradical generated from irradiation of 1 or 2. These three are shown in Figure 1 and would be expected to have very similar R_f values on silica gel and be eluted from the column together. Crystallization of the column eluate resulted in the formation of a sharp-melting compound, however, and repeated crystallizations of the mother liquor yielded only additional amounts of 3. This suggests that both 1 and 2 are converted to the same most thermodynamically stable polyhydroxycyclobutane derivative. The other diastereomeric cyclobutane derivatives must have much higher instability factors, since none of these were produced.

The elemental analysis, nmr, and mass spectra of the photoproduct 3 show it to be isomeric with the starting ketoses 1 and 2. This is consistent with hydrogen abstraction followed by closure of a biradical intermediate. Acetylation of the free hydroxyl group attached to C-1 results in derivative 5, which possesses a twofold axis of symmetry, and the nmr spectrum indicates that the substituents on the ring become magnetically equivalent in pairs. The acetate of structure C (Figure 1) has no such axis of symmetry. Proof that the common photoproduct of ketoses 1 and 2 has the structure represented by 3 can be obtained from closer examination of the nmr spectra of the product and its acetylated derivative, 5. In rigid ring systems, the presence of an hydroxyl function cis to an α proton (nearly eclipsed) results in an upfield shift of the α proton of 0.56 ppm in the acenaphthene system[5] and 0.88–1.17 ppm in bicyclo[2.2.1]-heptane[6,7] and bicyclo[2.2.2]octane systems.[8] Such an arrangement exists in structure B (Figure 1) and protons C and D would be expected to differ significantly in chemical shift. However, a difference of only 0.18 ppm is observed for 3. Also the proton bonded to C-2 is observed to undergo a downfield shift of 0.12 ppm following acetylation of 3 to produce 5. Such a small α shift suggests a trans relationship between the C-1 hydroxyl function in 3 and the proton bonded to C-2. An α-cis proton (as in B, Figure 1) would be expected to shift downfield to a greater extent owing to the anisotropic effect of the carbonyl oxygen atom of the acetyl group. The small shift (0.12 ppm) observed is in agreement with the magnitude of α shifts of trans protons observed upon acetylation of an α-hydroxyl group in the rigid bicyclo[2.2.2]-octane[8] system and is further support for the structural assignments as 3. The reaction scheme leading to the cyclobutanol 3 from both ketones 1 and 2 is given in Figure 2.

Cyclobutanol has been shown from spectroscopic[9] and thermodynamic measurements[10] to be puckered and scale models show that there are two types of positions in cyclobutane, somewhat analogous to the axial–equatorial positions in cyclohexane. A group in the equatorial position is of lower enthalpy than

(1) This work was supported in part by a grant from the U. S. Department of Agriculture, 12-14-100-9984 (71). Journal Paper No. 5003 of the Purdue Agricultural Experiment Station, Lafayette, Ind. 47907.

(2) P. J. Wagner and G. S. Hammond, *Advan. Photochem.*, **5**, 21 (1968).

(3) J. C. Dalton and N. J. Turro, *Ann. Rev. Phys. Chem.*, **21**, 499 (1970).

(4) P. J. Wagner, *J. Amer. Chem. Soc.*, **89**, 5898 (1967).

(5) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance to Organic Chemistry," 2nd ed, Pergamon Press, Elmsford, N. Y., 1969.

(6) K. L. Williamson, *J. Amer. Chem. Soc.*, **85**, 516 (1963).

(7) J. C. Davis and T. Van Auken, *J. Amer. Chem. Soc.*, **87**, 3900 (1965).

(8) K. Tori, Y. Takano, and K. Kitahonoki, *Ber.*, **97**, 2798 (1964).

(9) J. D. Dunitz and V. Schomaker, *J. Chem. Phys.*, **20**, 1703 (1952).

(10) G. W. Rathjens, Jr., N. K. Freeman, W. D. Gwinn, and K. S. Pitzer, *J. Amer. Chem. Soc.*, **75**, 5634 (1953).

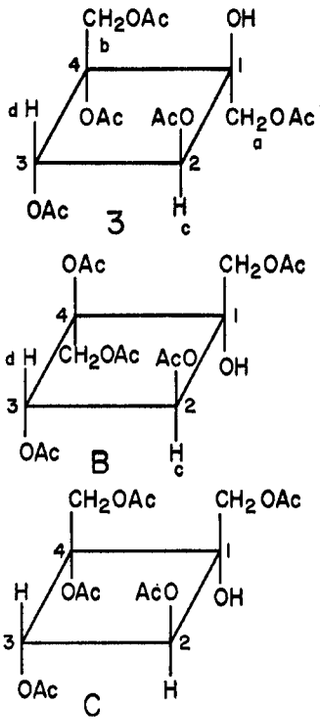

Figure 1.—Structures of the three cyclobutanol isomers that may result from ring closure of the 1,4 biradical generated upon irradiation of 1 and 2.

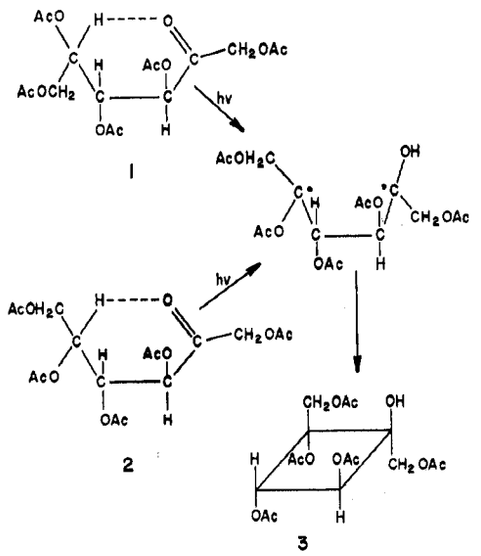

Figure 2.—Reaction sequence leading to the formation of 3 from 1 and 2.

one in the axial position and a 1,2-trans diequatorial relationship of substituents would be favored over an axial relationship.[11,12] If it is safe to assume that the acetoxymethyl substituents in the photoproduct **3** should be diequatorially oriented, this requires that the acetoxy groups on C-2 and C-3 also be diequatorial, while the acetoxy groups on carbon atoms C-2 and C-3 in B (Figure 1) would be axially oriented. Figure 3 shows the two isomeric cyclobutanols in the conformation expected to be the most stable for each, and

(11) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. B. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965, p 200.

(12) N. L. Allinger and L. A. Tushaus, *J. Amer. Chem. Soc.*, **87**, 1945 (1965).

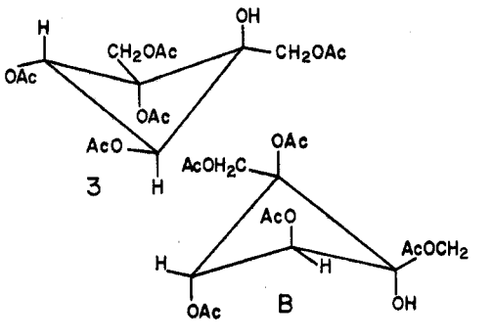

Figure 3.—Conformational representations of the isomeric cyclobutanols 3 and B.

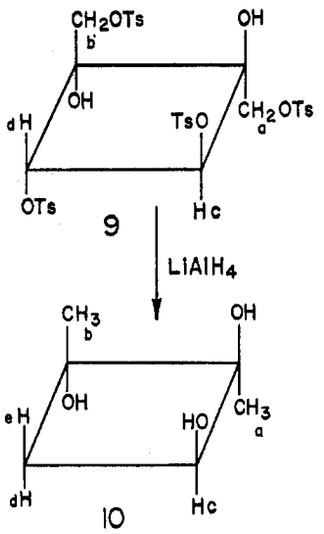

Figure 4.—Reduction of 9 to 10 by lithium aluminum hydride.

it appears that **3** would be more stable than B. Likewise, the 1,4-biradical conformation that led to **3** would be in a conformation more stable than that which might have led to B.

The nmr spectrum of the lithium aluminum hydride reduction product of the *p*-tolysulfonyl-oxylated product **9** further supports structure **3**. That the structure of this product is 1(*S*),4(*S*)-dimethyl-2(*S*)-cyclobutanetriol (**10**) is strongly supported by the observation that the ring methylene protons d and e (Figure 4) in this compound are magnetically very similar and their resonance occurs over a very narrow range (δ 1.50–1.61). If the reduction product were derived from the tetra-*p*-toluenesulfonate ester with the configuration of structure B (Figure 1), the two methylene protons would have very different chemical shifts. One would be shielded by two vicinal cis hydroxyl groups and its resonance would occur at a much higher field than the other, which would be trans to both hydroxyl groups.

A minor photoproduct is produced from **1** in a 0.9% yield. If such a product was formed from ketose **2**, it was not observed. The elemental analysis, nmr, and mass spectra of the product indicated it to be isomeric with **1**. The product's optical inactivity suggests that it may have formed by ring closure of a 1,5-biradical product[13] after δ-hydrogen abstraction by the photoexcited carbonyl group in **1**. The diastereomeric cyclopentanols from such a 1,5 biradical are

(13) L. M. Stephenson and J. L. Parlett, *J. Org. Chem.*, **36**, 1093 (1971).

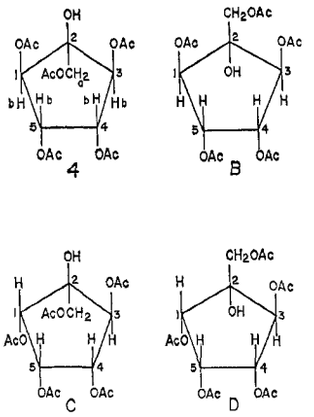

Figure 5.—Structures of the four cyclopentanol isomers that may result from ring closure of the 1,4 biradical generated upon irradiation of 1.

shown in Figure 5. All would be expected to have very similar R_f values on silica gel and be eluted from the column together. Crystallization of the column eluate resulted in the formation of a sharply melting compound, however, and repeated crystallizations of the mother liquor yielded only more of the same compound. Only **4** and B (Figure 5) would be optically inactive and that **4** is the photoproduct (Figure 6) is supported by the similar chemical shifts of the protons designated b (Figure 5). If the hydroxyl function in the cyclopentanol were cis to the α protons (as in B, Figure 5), they should be significantly upfield from the equivalent β protons. However, the four protons are present as a multiplet spread over only 0.3 ppm. Also, the α protons undergo but a small shift upon acetylation of the vicinal hydroxyl group (**4**, **7**), suggesting the trans relationship of the hydroxyl group with the α protons as in **4**.

The 1,4 biradicals produced by irradiation of the ketoses **1** and **2** apparently also decay by fragmenting to smaller molecules. The Norrish II product, 1,3-diacetoxyacetone, is found to be produced in significant amounts.

As benzene was present in the solvent for the irradiations of both ketoses **1** and **2**, it might have been possible that this solvent behaved as a photosensitizer, and product formation was not a result of direct irradiation of the ketones. Irradiations in *p*-dioxane, however, led to rapid conversion of ketoses **1** and **2** to photoproducts, establishing that benzene is not essential. Quenching experiments using *cis*-piperylene establish that the photoproducts from both **1** and **2** arise from the triplet state, as no products are formed when irradiations are conducted with low concentrations of this triplet quencher present.

Experimental Section

Analytical Methods.—Purity of products and the courses of reactions were monitored by thin layer chromatography (tlc) on 5 × 13 cm plates coated with silica gel G.[14] Irrigants employed were A, chloroform–acetone (15:1); B, chloroform–methanol (4:1); C, chloroform–acetone (10:1); and D, chloroform–methanol (7:1). Compounds were located by spraying the dried plates with 5% sulfuric acid in ethanol and heating until permanent char spots were visible. Column chromatography was carried out on silica gel[15] with E, chloroform–acetone (15:1); F, chloroform–acetone (12:1); and G, chloroform–methanol (8:1) as eluents. All solvent ratios are based on volumes. Melting points were measured on a Fisher-Johns apparatus and are corrected. Optical rotations were determined with a Perkin-Elmer 141 polarimeter at 25°. Infrared (ir) spectra were obtained with a Perkin-Elmer Model 337 spectrophotometer and the samples were examined as Nujol mulls. Nuclear magnetic resonance (nmr) spectra were obtained with a Varian Associates A-60 instrument in deuteriochloroform, using tetramethylsilane (TMS) as the internal standard, or in deuterium oxide, using sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) as the internal standard. Evaporations were carried out under diminished pressure with bath temperatures below 40°.

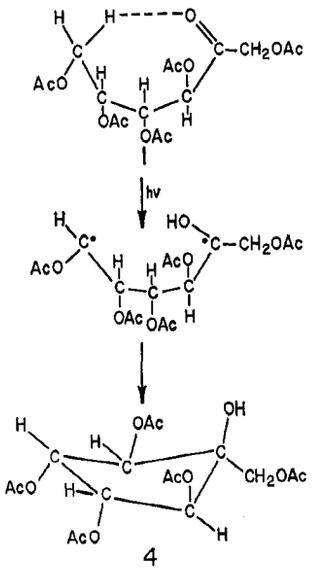

Figure 6.—Reaction sequence leading to the formation of **4** from **1**.

Irradiation Procedures.—Irradiations with unfiltered ultraviolet light were conducted using an Hanovia 450-W mercury lamp (679A36) inserted into a water-cooled quartz immersion well. Solutions were flushed with nitrogen prior to irradiation. Triplet quenching experiments were carried out by irradiating benzene solutions of 1,3,4,5,6-penta-*O*-acetyl-*keto*-D-fructose and 1,3,4,5,6-penta-*O*-acetyl-*keto*-L-sorbose to which *cis*-piperylene had been added in concentrations of 0.067, 0.335, and 1.0 *M*. The *cis*-piperylene was obtained from Chemical Samples Co. and distilled immediately prior to use.

1,3,4,5,6-Penta-*O*-acetyl-*keto*-D-fructose (1).—Finely powdered D-fructose (100 g) was added to a stirred solution of freshly fused zinc chloride (15 g) in acetic anhydride (1 l.) that had been stirred for 1 hr at 0°. Stirring was continued for 12 hr at 0° and 12 hr at 25°, at which time the reaction was complete as revealed by tlc in solvent A. The solution was then poured into 3 l. of ice and water and the mixture was stirred for 24 hr at 0° to hydrolyze the acetic anhydride. A saturated aqueous solution of sodium bicarbonate was then gradually added to neutralize the acetic acid liberated. The solution was then extracted with two 500-ml portions of chloroform and the combined chloroform extracts were washed once with water. The chloroform solution was then dried over anhydrous sodium sulfate and evaporated under reduced pressure to a syrup, which was crystallized from ether (300 ml). The crystals formed overnight at −5° were filtered, as a second crop was found to contain a large amount of an isomer of **1**, 1,2,3,4,5-penta-*O*-acetyl-β-D-fructopyranose. Recrystallization of the first crop of crystals from ether yielded pure **1**: yield 96 g (44%); mp 69–70° (lit.[16,17] mp 69–70°).

1,3,4,5,6-Penta-*O*-acetyl-*keto*-L-sorbose (2).—**2** was prepared by essentially the same procedure as was **1**, except that finely powdered L-sorbose (100 g) was added to the zinc chloride–

(14) Brinkman Instruments, Inc., Westbury, N. Y.

(15) J. T. Baker Chemical Co., Phillipsburg, N. J.

(16) C. S. Hudson and D. H. Brauns, *J. Amer. Chem. Soc.*, **37**, 2736 (1915).

(17) F. B. Cramer and E. Pascu, *J. Amer. Chem. Soc.*, **59**, 1148 (1937).

acetic anhydride solution. Recrystallization from 600 ml of ether–chloroform (2:1, v/v) at 25° yielded pure **2**: yield 135 g (62%); mp 96–97° (lit.[18] mp 96–97°).

Irradiation Products of 1,3,4,5,6-Penta-*O*-acetyl-*keto*-D-fructose (1).—A solution of **1** (100 g) in 1800 ml of *tert*-butyl alcohol–benzene (20:1, v/v) was irradiated for 18 hr, at which time tlc in solvent A (two developments) showed no **1** remaining. Two major products were evident (both with R_f values less than **1**), as were five minor products. The *tert*-butyl alcohol and benzene were removed by concentrating under diminished pressure and a syrup was obtained. This syrup was taken up in 400 ml of ether–hexane (10:1, v/v) under reflux. The solution was stored overnight at −5°, whereupon 13.2 g of a crystalline mixture corresponding on tlc to the two major products was obtained by filtration. This mixture was dissolved in 10 ml of chloroform, applied to a silica gel column (600 g of silica gel), and eluted with solvent E. The column fractions containing the faster moving component were combined and concentrated to a syrup, which was crystallized from 80 ml of ether–chloroform (3:1, v/v) at 0° to give 1(*S*),4(*S*)-diacetoxymethyl-2(*S*),3(*S*)-4-triacetoxycyclobutan-1-ol (**3**): yield 11.6 g (11.6%); mp 114–115°; $[\alpha]^{25}D$ +72° (*c* 1, $CHCl_3$); ir (Nujol) 3420 (m), 1750 cm^{-1} (m); nmr ($CDCl_3$) δ 2–2.12 (15, acetyl), 3.96 (s, 1, hydroxyl, collapses D_2O), 4.19, 4.50 (q, J = 12 Hz, 2, a), 4.69, 5.01 (q, J = 12 Hz, 2, b), 5.16–5.34 (q, J_{cd} = 7 Hz, 2, c, d).

Anal. Calcd for $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68. Found: C, 49.38; H, 5.63.

Further crystallization of the mother liquor yielded only more **3**. The column fraction containing the slower moving component was contaminated with a small amount of **3**, so this was applied to a silica gel column and eluted with solvent F. After an additional small amount of **3** was collected from the column, the lower R_f component came off pure and this fraction was concentrated to a syrup. This syrup was crystallized from 12 ml of chloroform–ether (3:1, v/v) to give *meso*-(1,2,3/4,5)-2-acetoxymethyl-1,3,4,5-tetraacetoxycyclopentan-2-ol (**4**): yield 0.9 g (0.9%); mp 172–173°; $[\alpha]^{25}D$ 0° (*c* 2, $CHCl_3$); ir (Nujol) 3335 (m), 1730 cm^{-1} (m); nmr ($CDCl_3$) δ 2.0–2.13 (15, acetyl), 3.0 (s, 1, hydroxyl, collapses D_2O), 4.02 (s, 2, a), 5.22–5.52 (m, 4, b).

Anal. Calcd for $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68. Found: C, 49.02; H, 5.48.

Further crystallization of the mother liquor yielded only more **4**.

An alternative method for the separation of **3** and **4** reduces the work-up time by several days. The 13.2-g mixture obtained by crystallization of the crude photoreaction mixture from ether–hexane (10:1, v/v) was taken up in 50 ml of ether–chloroform (10:1, v/v). **4** crystallized overnight from this solvent while **3** remained in solution. Filtration afforded pure **4** (0.8 g) while crystallization of the filtrate from 80 ml of ether–chloroform (3:1, v/v) afforded pure **3** (10.7 g). Yields are slightly lower by this procedure.

Irradiation Products of 1,3,4,5,6-Penta-*O*-acetyl-*keto*-L-sorbose (2).—A solution of **2** (50 g) in 1800 ml of benzene was irradiated for 18 hr, at which time tlc in solvent A showed no **2** remaining and the two major products were of similar R_f as the major products (**3** and **4**) produced from **1**. The benzene was removed by concentration under diminished pressure and the syrup obtained was taken up in 160 ml of ether–hexane (10:1, v/v). After storing overnight at −5°, the mixture was filtered and 13.7 g of a mixture corresponding to **3** and a minor product of slightly higher R_f was obtained. This mixture was taken up in acetone (80 ml) and stored overnight at −5°. A flocculent precipitate which was not characterized had formed (360 mg) and this was removed by filtration. The acetone was removed from the filtrate by concentration under diminished pressure and the syrup obtained was taken up in 80 ml of ether–chloroform (3:1, v/v). Storage overnight at −5° yielded 13.1 g (26.2%) of **3**. Only more **3** was obtainable from the mother liquor. The nmr and ir spectra were identical with those of the major photoproduct **3** of **1**, as were the melting point, optical rotation, and elemental analysis. The tlc spot of R_f similar to that of the photoproduct obtained by irradiation of **1**, suggesting a cyclopentanol analogous to **4**, was not obtainable in sufficient purity for subsequent characterization.

1(*S*),4(*S*)-Diacetoxymethyl-1,2(*S*),3(*S*),4-tetraacetoxycyclobutane (5).—To a solution of **3** (1.0 g) in acetic anhydride (15 ml) was added sodium acetate (2.5 g). The solution was refluxed with stirring for 2 hr, at which time no **3** remained as indicated by tlc in solvent A and one product had appeared. The mixture was poured into 25 ml of ice and water and this mixture was stirred for 1 hr to hydrolyze the acetic anhydride. A saturated aqueous solution of sodium bicarbonate was then gradually added until the acetic acid was neutralized. The mixture was transferred to a separatory funnel and extracted with three 25-ml portions of chloroform. The combined chloroform extracts were washed once with water and dried over anhydrous sodium sulfate. This mixture was then filtered and the chloroform solution was concentrated under diminished pressure to a syrup. This syrup was taken up in 8 ml of hexane–ether (1:1, v/v) and put for overnight crystallization at −5°. Pure **5** was obtained: yield 0.78 g (71%); mp 90–91°; $[\alpha]^{25}D$ +2.7° (*c* 1, $CHCl_3$); nmr ($CDCl_3$) δ 2.03–2.11 (18, acetyl), 4.68–4.97 (q, J = 12 Hz, 4, a, b), 5.28 (s, 2, c, d).

Anal. Calcd. for $C_{18}H_{24}O_{12}$: C, 50.00; H, 5.58. Found: C, 50.26; H, 5.57.

1(*S*),4(*S*)-Dihydroxymethyl-2(*S*),3(*S*)-cyclobutanetetrol (6).—To a solution of **3** (10 g) in methanol (50 ml) was added 50 ml of a 0.1 *M* solution of sodium methoxide in methanol. This solution was heated with stirring to 60°, at which time only the deacetylated product was present as indicated by tlc in solvent B. The solution was then neutralized with Amberlite IR-120 (H^+) resin and filtered. The filtrate was concentrated to a syrup which spontaneously crystallized. Recrystallization from 40 ml of methanol–water (19:1, v/v) yielded pure **6**: yield 4.48 g (97%); mp 133–134°; $[\alpha]^{25}D$ +23.8° (*c* 1, H_2O); nmr (D_2O) δ 3.67 (m, 4, a, b), 3.97 (s, 2, c, d).

Anal. Calcd for $C_6H_{12}O_6$: C, 40.00; H, 6.72. Found: C, 40.06; H, 6.81.

***meso*-(1,2,3/4,5)-2-Acetoxymethyl-1,2,3,4,5-pentaacetoxycyclopentane (7).**—To a solution of **4** (1.0 g) in acetic anhydride (25 ml) was added sodium acetate (2.5 g). The solution was refluxed with stirring for 3 hr, at which time no **4** remained as indicated by tlc in solvent A and one product of high R_f had appeared. The mixture was poured into 25 ml of ice and water and this mixture was stirred for 1 hr to hydrolyze the acetic anhydride. A saturated aqueous solution of sodium bicarbonate was then gradually added until the acetic acid was neutralized. This mixture was transferred to a separatory funnel and extracted with three 25-ml portions of chloroform. The combined chloroform extracts were washed once with water and dried over anhydrous sodium sulfate. This mixture was then filtered and the chloroform solution was concentrated under diminished pressure to a syrup. This syrup was taken up in 10 ml of hexane–ether (1:1, v/v) and stored at −5° overnight for crystallization. Pure **7** was obtained: yield 0.65 g (59%); mp 94–95°; $[\alpha]^{25}D$ 0° (*c* 2, $CHCl_3$); nmr ($CDCl_3$) δ 2.09 (s, 18, acetyl), 4.70 (s, 2, a), 6.36–6.58 (m, 4, b).

Anal. Calcd for $C_{18}H_{24}O_{12}$: C, 50.00; H, 5.58. Found: C, 50.15; H, 5.54.

***meso*-(1,2,3/4,5)-2-Hydroxymethylcyclopentanepentol (8).**—To a solution of **4** (1.0 g) in methanol (10 ml) was added 10 ml of a solution of 0.1 *M* sodium methoxide in methanol. This solution was heated with stirring to 60° for 12 hr. at which time only the deacetylated product was present as indicated by tlc in solvent B. The solution was then neutralized with Amberlite IR-120 (H^+) resin and filtered. The filtrate was concentrated to a syrup, which was crystallized from 8 ml of methanol–water (15:1, v/v). Pure **8** was obtained: yield 0.41 g (89%); mp 133–134°; $[\alpha]^{25}D$ 0° (*c* 2, H_2O); nmr (D_2O) δ 3.54 (s, 2, a), 3.78–4.12 (m, 4, b).

Anal. Calcd for $C_6H_{12}O_6$: C, 40.00; H, 6.72. Found: C, 39.74; H, 6.66.

1(*S*),4(*S*)-Di-*p*-tolylsulfonyloxymethyl-2(*S*),3(*S*)-di-*p*-tolylsulfonyloxycyclobutane-1,4-diol (9).—To a solution of **6** (3.0 g, 1 equiv) in pyridine (100 ml) was added *p*-toluenesulfonyl chloride (14.6 g, 10 equiv). This mixture was stirred at 25° for 24 hr, at which time tlc in solvent C indicated that no **6** remained and one major high R_f product was present. With the aid of toluene this solution was concentrated under diminished pressure to a syrup. Then water (25 ml) was added and the mixture was stirred for 1 hr to decompose excess *p*-toluenesulfonyl chloride. A saturated aqueous solution of sodium bicarbonate (10 ml) was then gradually added to neutralize the hydrochloric acid liberated. The residue formed by removal of the water by concentration under diminished pressure was transferred to a separatory funnel with water and chloroform. After extraction

(18) H. H. Schlubach and J. Vorwerk, *Ber.*, **66**, 1251 (1933).

with two 100-ml portions of chloroform, the combined extracts were washed once with water. The chloroform solution was dried over anhydrous sodium sulfate, decolorized with charcoal, and filtered. The filtrate was concentrated to a syrup, which was crystallized from 75 ml of ethanol–chloroform (25:1, v/v) by storage at −5° overnight. Recrystallization from this solvent yielded pure **9**: yield 10.9 g (82%); mp 168–169°; nmr ($CDCl_3$) δ 2.43 (s, 12, CH_3 of tosyl), 3.12 (s, 2, hydroxyls, collapses D_2O), 4.13 (s, 4, a, b), 4.60 (s, 2, c, d), 7.24–7.85 (m, 16, aromatic of tosyl).

Anal. Calcd for $C_{34}H_{36}O_{14}S_4$: C, 51.24; H, 4.55; S, 16.09. Found: C, 51.20; H, 4.33; S, 16.00.

1(*S*),4(*S*)-Dimethyl-2(*S*)-cyclobutanetriol (10).—To a suspension of **9** (5.0 g, 1 equiv) in 150 ml of ether–benzene (2:1, v/v) was added with stirring lithium aluminum hydride (3.8 g, 16 equiv). The mixture was refluxed with stirring for 4 days with an oil bath temperature of 60°. The reaction mixture was shown to contain no **9** but the presence of a major component of lower R_f by tlc in solvent D. Ethyl acetate (50 ml) was then gradually stirred into the cooled reaction mixture to decompose excess lithium aluminum hydride. Then 100 ml of ether–water (10:1, v/v) was added to complete this decomposition. The mixture was then filtered through Celite and the alkaline filtrate was neutralized with Amberlite IR-45 (H^+) resin. The exchange resin was removed by filtration, and the filtrate was concentrated under diminished pressure to a syrup (300 mg). Crystallization of this syrup failed, so it was applied to a silica gel column and eluted with solvent G. A fraction consisting mainly of the major reduction product was obtained (120 mg) and this was further purified by repeated silica gel column chromatography, again using solvent G as eluent. This product was not crystalline: yield 80 mg (11%); nmr ($CDCl_3$) δ 1.13, 1.14 (s, 6, a,b), 1.61–1.5 (m, 2, d,e), 3.60 (s, 3, hydroxyls), 3.76 (m, 1, c).

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A Direct Low Temperature ^1H and ^{19}F Nuclear Magnetic Resonance Study of Boron Trifluoride Complexes with 4-Cholesten-3-one, 1(5β)-Androstene-3,17-dione, 5β-Androstane-3,17-dione, and Obacunone

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A direct low temperature proton and fluorine-19 nmr study of boron trifluoride complexes with steroids **1**–**3** and a limonoid **4** is reported. In these systems ligand exchange is slow enough below −50° for observation of separate pmr signals for bulk ligand and molecules bound to the boron trifluoride. For ligands **1**, **2**, and **4**, the ^1H and ^{19}F nmr data indicate that complexing first occurs solely at the A-ring carbonyl group. In the remaining system **3** and for high BF_3/base ratios of **4**, complexing also occurs at a second site in the base, the carbonyl group in the D ring.

Complexes of boron trihalides with organic bases have been studied using several calorimetric and spectroscopic techniques to ascertain the chemical and structural features of the components which influence these interactions.[1-8] Nmr investigations of boron trihalide complexes include ligands such as trimethylamine, ethers, *N*,*N*-dimethylformamide, ureas and thioureas, and water (^{19}F and proton resonance). Recent publications have demonstrated the usefulness of the direct low temperature nmr method as a supplemental aid for these investigations.[8-12] The success of this low temperature method is based on the ability to slow ligand exchange, thereby allowing the observation of separate pmr signals for the ligand molecules bound to the boron trihalide and the bulk (uncomplexed) ligand. The information obtainable by this means includes chemical shifts induced in the ligand by complex formation, the stoichiometry of the complex, the ligand interaction site or sites, and competition between sites. Previous investigations of this type have been confined largely to ligands of relatively low molecular weight and complexity. To determine whether this low temperature technique could also be applied to larger and more complex ligands, we have now studied complexes of boron trifluoride with three steroids and a limonoid.

Experimental Section

The 2-nitropropane (2NP) used was the highest commercial grade available and was distilled before use. 4-Cholesten-3-one (**1**) and 1(5β)-androstene-3,17-dione (**2**) were generously supplied by Dr. Erich Heftmann, Western Regional Research Laboratory, Albany, Calif. 5β-Androstane-3,17-dione (**3**) was purchased from Mann Laboratories.[13] The purity of these three steroids was verified by their nmr spectra. Obacunone (**4**) was isolated from grapefruit seed meal by methods previously described.[14] Boron trifluoride (J. T. Baker) was purified by fractionation through a −110° petroleum ether (bp 30–60°)–liquid nitrogen cold trap, and its purity verified by ^{19}F nmr in anhydrous CH_2Cl_2. Van Ness Associates No. 105–7PP special purpose nmr sample tubes were employed for all measurements. These are

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