preparations: C, 51.82, 52.70, 52.08, 52.28; H, 4.73, 5.80, 5.25, 5.53; OCH_3, nil; neut. equiv., 127.

Although three of the four C–H values are appreciably above the theoretical, the $C_{11}H_{12}O_7$ formula is supported by analyses of the dimethyl ester and ester–acetate of compound III (see below).

Compound III Dimethyl Ester.—To 100 mg. of compound III dissolved in *ca.* 1 ml. of methanol was added 10 ml. of ether, followed by ethereal diazomethane until a faint yellow color persisted. The solution was evaporated under reduced pressure, the residue extracted with *ca.* 10 ml. of boiling benzene and the extract cooled slowly. After several hours at 4° the product was removed by filtration and recrystallized from benzene. White needles were obtained, m.p. 115°, in a yield of 80 mg. The product was dried for analysis for 4 hours at 1 mm. and 65°. Since it still gave a positive test with *p*-diazobenzenesulfonic acid, the phenol group was not methylated.

Anal. Calcd. for $C_{13}H_{16}O_7$: C, 54.93; H, 5.67; OCH_3, 21.83. Found: C, 54.94; H, 5.69; OCH_3, 21.35, 21.91.

Compound III Dimethyl Ester–Triacetate.—To 80 mg. of the dimethyl ester of compound III suspended in 0.5 ml. of acetic anhydride was added *ca.* 0.02 ml. of concentrated sulfuric acid. After standing for 15 minutes at room temperature, the mixture was chilled in an ice-bath and 1 ml. of water added slowly with shaking. Small white needles separated, which were filtered off and washed twice with water. The reaction mixture was diluted with an additional 1.5 ml. of water, and a further batch of crystals formed after 12 hours storage at 4°. The combined crystalline product was recrystallized once from water, and yielded 55 mg. of long needles, m.p. 84–85° after drying 10 hours at 1 mm. and 67°. The product was very soluble in benzene and in ether but very slightly soluble in water. It gave no test for phenols with *p*-diazobenzenesulfonic acid.

Anal. Calcd. for $C_{19}H_{22}O_{10}$: C, 55.61; H, 5.40; OCH_3, 15.12; acetyl, 31.46; mol. wt., 410.4. Found: C, 55.52; H, 5.59; OCH_3, 15.00, 15.90; acetyl[19], 31.30, 31.42; mol. wt. (Rast), 438.

Paper Chromatography.—Ascending paper chromatograms were run using Whatman No. 1 paper in 14 × 45 cm. sealed, glass jars. The developing solvent was *n*-butyl alcohol 50 ml., benzyl alcohol 50 ml., water 10 ml., 90% formic acid 1.1 ml.[20] Samples of 10–50 μg. were used. The solvent front was allowed to move about 30 cm. (16 hours) after a 16-hour equilibration period. The acids were detected by spraying the paper with *p*-diazobenzenesulfonic acid prepared by the method of Hanke and Koessler[5] and made alkaline immediately before use by mixing 2 ml. of the diazo reagent with 8 ml. of 1.1% sodium carbonate. Stable pink spots were obtained. The R_f values found were: compound I, 0.40; compound II, 0.85; compound III, 0.43.

Infrared Spectra.—The infrared spectra of compounds I, II and III are given in full in the Ph.D. thesis of R. R. Smeby.[21]

Acknowledgments.—The authors are indebted to Dr. R. M. Bock, Mr. Rex Smith and Mr. Nan-Sing Ling for assistance with some of the electrometric titrations and to Mr. Don Johnson and Dr. E. E. van Tamelen for the infrared spectra.

(19) The authors are indebted to Mr. George Drummond for the acetyl analyses.

(20) J. B. Stark, A. E. Goodban and H. S. Owens, *Anal. Chem.*, **23**, 413 (1951).

(21) R. R. Smeby, Ph.D. Thesis, University of Wisconsin, 1954.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF WISCONSIN]

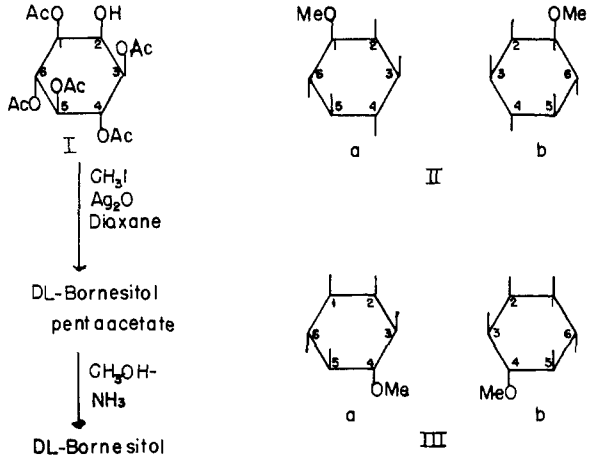
The Synthesis of DL-Bornesitol[1]

BY LAURENS ANDERSON AND AURORA M. LANDEL

RECEIVED JUNE 24, 1954

An acyl migration occurs during the methylation of 1,3,4,5,6-penta-*O*-acetyl-*myo*-inositol. The methylated product has been identified as penta-*O*-acetyl-DL-bornesitol. Crystalline DL-bornesitol was prepared from the acetate.

Bornesitol is a *myo*-inositol[2] methyl ether which was first isolated from "Borneo rubber" by Girard[3] in 1871. The supply of material which Flint and Tollens used in 1892 for their analytical work[4] likewise came from a rubber then being used in commerce, but the currently practical source of this cyclitol is opepe wood,[5] (*Sarcocephalus diderrichii*, West Africa). Bornesitol has also been found in opepe bark.[6] Since it is optically active, it must have one of the formulas IIa, IIb, IIIa or IIIb. Foster and Stacey[7] support formula IIa or IIb on the basis of the ionophoretic mobility of the borate complex, but no further evidence on the position of the methyl group in bornesitol was available when this paper was being written.



The purpose of the communication is to describe the synthesis of DL-bornesitol. Unfortunately, no deductions as to the position of the methyl group can be based on this synthesis. But since we are not planning direct work on bornesitol, it seemed desirable to report the results we have obtained.

Our original aim was to methylate the free hy-

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(2) The system recently proposed by H. G. Fletcher, Jr., L. Anderson and H. A. Lardy, *J. Org. Chem.*, **16**, 1238 (1951), is used for naming and numbering the compounds described in this paper.

(3) A. Girard, *Compt. rend.*, **73**, 426 (1871).

(4) E. R. Flint and B. Tollens, *Ann.*, **272**, 288 (1892).

(5) F. E. King and L. Jurd, *J. Chem. Soc.*, 1192 (1953).

(6) Unpublished data obtained by V. Prelog, Zurich.

(7) A. B. Foster and M. Stacey, *Chemistry & Industry*, 273 (1953).

droxyl in 1,3,4,5,6-penta-*O*-acetyl-*myo*-inositol (I) and compare the resulting 2-*O*-methyl-*myo*-inositol with sequoyitol, an optically inactive, naturally occurring *myo*-inositol methyl ether.[8] However, an acyl migration, apparently effected by the silver oxide catalyst, took place prior to the methylation,[9] and the formation of DL-bornesitol pentaacetate instead of the desired 2-ether resulted. DL-Bornesitol was apparently obtained in 1915, by Griffin and Nelson[10] from the mixture formed when *myo*-inositol was methylated with dimethyl sulfate and alkali. These authors did not identify their product, but Professor S. J. Angyal has informed us that on repeating their procedure he obtained a product identical with ours and, except for its racemic nature, with natural bornesitol.

The nature of our synthetic product was first suggested by the fact that the melting points of both the free ether and the pentaacetate are nearly the same as those of natural bornesitol and its pentaacetate. A comparison of the solubilities, crystal form and chromatographic behavior of natural bornesitol and the synthetic ether confirmed the similarity of the two substances. The characterization was completed by comparing the infrared spectra of the acetates. These are completely superimposable, and in view of Angyal's[11] finding that a change in the position of the methyl group produces a considerable change in the spectrum, this superimposability is the strongest argument for the identity of the samples. Slight depressions are naturally observed in mixed melting point experiments, but the evidence would seem to leave little doubt that the synthetic product differs from natural bornesitol only in being racemic. The synthesized compound must therefore have either the formula IIa + IIb, or IIIa + IIIb.

It is stated above that the acyl migration takes place during the methylation step. This statement assumes that no migration took place during the preparation of the starting material from the corresponding keto compound, and that the starting material thus really has the formula I. No positive evidence on this point has heretofore been offered, but such was obtained during the present investigation. I was reoxidized by chromic anhydride to penta-*O*-acetyl-*myo*-inosose-2, its precursor, in 58% yield. The accepted formula,[12] as shown, would thus seem to be the correct one.

Acknowledgments.—The authors thank Miss Emily Swan for running the paper chromatograms; Prof. F. E. King (Nottingham) for a sample of natural bornesitol; Prof. S. J. Angyal (Sydney) for communicating the results of his investigations; and Dr. A. B. Foster for testing the synthetic bornesitol by ionophoresis.

(8) E. C. Sherrard and E. F. Kurth, THIS JOURNAL, **51**, 3139 (1929).

(9) Many instances of acyl migration during methylation with silver oxide and methyl iodide have been recorded; *cf.* W. N. Haworth, E. L. Hirst and Ethel Teece, *J. Chem. Soc.*, 1405 (1930); 2858 (1931). S. J. Angyal (private communication) was unable to methylate I using silver carbonate as the catalyst. He suggests that the axial hydroxyl at position 2 is very resistant to methylation and that silver carbonate is not sufficiently alkaline to bring about an acyl migration which would unmask one of the more reactive equatorial hydroxyls.

(10) E. G. Griffin and J. M. Nelson, THIS JOURNAL, **37**, 1566 (1915).

(11) S. J. Angyal, private communication.

(12) B. M. Iselin, THIS JOURNAL, **71**, 3822 (1949).

Experimental

Starting Materials.—*myo*-**Inosose-2**[13] was acetylated as directed by Carter, *et al.*,[14] to give **penta-*O*-acetyl-*myo*-inosose-2**, which may be obtained in either of two forms. The low melting form has been used by Iselin[12] and the high-melting form used by May[15] for hydrogenation. In our hands the low-melting form (146–148°) gave better yields; otherwise, May's directions were followed in preparing **1,3,4,5,6-penta-*O*-acetyl-*myo*-inositol (I)**. As reported by May, compound I also may be obtained in two crystal modifications. Crystals of our material melted at 166–168° in soft glass tubes, and at 177–179° in Pyrex tubes. If the sample was first ground, it showed the higher melting point even in a soft glass capillary. Ethanol was used as the recrystallizing solvent.

Chromic Acid Oxidation.—Compound I (200 mg.) was added to 0.7 ml. of a 5% glacial acetic solution of chromium trioxide at ice-bath temperature. The mixture was allowed to stand in ice for six hours, then filtered through a sintered glass funnel. On washing the solid with glacial acetic acid, white crystals were obtained. After recrystallization from hot glacial acetic acid, the melting point was 146–148°, undepressed by admixture with an authentic sample of the low melting form of penta-*O*-acetyl-*myo*-inosose-2. The yield was 110 mg. (58%).

Penta-*O*-acetyl-DL-bornesitol.—To one part of I, about 6 parts dry dioxane, 4 parts methyl iodide and 0.8 part of silver oxide were added. The silver oxide was prepared according to Purdie and Young.[16] The mixture was stirred in an oil-bath at 70–75°, and at hourly intervals, dioxane, methyl iodide and silver oxide were added in the proportions mentioned until five additions had been made. The stirring and heating were continued for a total of 24 hours. The silver salts were then filtered off and washed with dioxane. Evaporation of the combined filtrate and washings *in vacuo* gave a sirup which was dissolved in hot ethanol and filtered while hot. The filtrate, on standing at 0° overnight, deposited a white crystalline solid which, after two recrystallizations from ethanol, melted at 154–154.5°. The pentaacetate of natural bornesitol is dimorphic, and the two forms melt at 138–139° and 157°, respectively.[5] The yields ranged from 48 to 67%. The infrared spectra were determined[17] on 0.37 *M* solutions in chloroform.

Anal.[18] Calcd. for $C_{17}H_{24}O_{11}$ (404.36): C, 50.49; H, 5.98; OCH_3, 7.67. Found: C, 50.83; H, 6.26; OCH_3, 7.55, 7.71.

DL-Bornesitol.—To 100 mg. of the pentaacetate in a glass stoppered 10-ml. flask, methanolic ammonia (saturated at 0°) was added drop by drop till the solid dissolved. The solution was allowed to stand at room temperature for 12 hours, then at 0° for another 12 hours. It was then concentrated *in vacuo* to a sirup. Two ml. of hot absolute ethanol was added to the sirup and the resulting solution was filtered. The filtrate was kept at 0°, whereupon 45 mg. (89%) of white prisms formed.

The compound is quite soluble in water, and melted at 200–201°. Natural bornesitol is likewise soluble in water and slightly soluble in ethanol, and it likewise crystallizes in prisms. It melts[5] at 201–202°.

Anal. Calcd. for $C_7H_{14}O_6$ (194.18): C, 43.29; H, 7.27; OCH_3, 15.98. Found: C, 43.50; H, 7.50; OCH_3, 15.91.

Paper Chromatography and Ionophoresis.—The synthetic ether and natural bornesitol were chromatographed on Whatman no. 1 paper in acetone–water 95:5 v./v.[19] In

(13) Kindly provided by the Corn Products Refining Co., New York.

(14) H. E. Carter, *et al.*, *J. Biol. Chem.*, **174**, 415 (1948).

(15) E. L. May, *J. Org. Chem.*, **17**, 286 (1952).

(16) Cited by F. J. Bates, *et al.*, "Polarimetry, Saccharimetry and the Sugars," National Bureau of Standards, Circular C440, Washington, D. C., 1942, p. 507.

(17) By the Instrumental Laboratory of the Analytical Division of the Chemistry Department, Prof. V. W. Meloche, Director.

(18) Carbon–hydrogen analyses by the Micro-Tech Laboratories, Skokie, Ill.

(19) C. E. Ballou and A. B. Anderson, THIS JOURNAL, **75**, 648 (1953).

this system they traveled equal distances. Angyal[11] further found identical R_f values in four other solvent systems. Dr. A. B. Foster tested a sample of the synthetic ether in his borate ionophoresis system,[7] and found that the compound paralleled natural bornesitol in its behavior.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

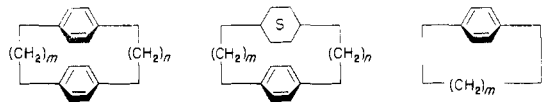
Macro Rings. VII. The Spectral Consequences of Bringing Two Benzene Rings Face to Face[1]

BY DONALD J. CRAM, NORMAN L. ALLINGER[2] AND H. STEINBERG

RECEIVED MAY 12, 1954

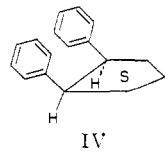
The preparation of the paracyclophane with $n = m = 3$, of II with $n = 3$, $m = 4$ and with $n = m = 4$, and of III with $n = 12$ are reported. The variations in spectral properties of these classes of compounds with their molecular geometries are discussed. The ultraviolet absorption spectra of *cis*- and *trans*-1,2-diphenylcyclopentane are compared.

The previous papers in this series[3] have reported the preparation of the series of eight paracyclophanes I in which $n = m$ and in which $n = m - 1$ for all values of n and m from $n = m = 2$ to $n = m = 6$, with exception of the compound in which $n = m = 3$. The less symmetrical cycles (I) with $n = 2$, $m = 4$, with $n = 3$ and $m = 6$, and with $n = 4$, $m = 6$ have also been reported,[3] as well as compounds of class III with $m = 9$[4a] and 10.[3e,4b]



I II III

These two groups of compounds (I and III) offer unique opportunities for the study of certain kinds of transannular electronic and steric effects on physical and chemical properties. Spectral abnormalities, particularly in the ultraviolet region, have been observed to characterize the smaller paracyclophanes I,[3a] and have been attributed to one or both of the following causes: (1) π-electron interactions between the two benzene rings, (2) distortion of the benzene rings from their normal planar configurations. The present investigation reports an attempt to separate and identify these effects through a comparison of the spectral properties of three types of compounds: the paracyclophanes (I) themselves; compounds belonging to classes II and III; compounds possessing the geometry of IV.



IV

In compounds of class I, although the smallest obtainable member ($n = m = 2$)[5a] contains nonplanar benzene rings,[5] the possibility is evident that as the steric constraints are released by increasing the length of the methylene bridges the aromatic nuclei might become planar before the π-electrons of each ring cease to affect each other's spectral characteristics. In compounds of class II and III the possibility exists that bent benzene rings might be produced without the complicating feature of a second aromatic nucleus being in the vicinity of the first. Finally, in compounds of class IV, it was hoped that two benzene rings could be brought face to face without any accompanying complications due to distortion of the aromatic rings from planar configurations.

Results

The synthesis of the paracyclophane with $m = n = 3$ was carried out by the sequence formulated. The mixture of the four *cis–trans* isomers of diester IX obtained by the reduction of the aromatic diester VIII was not separated into its components, but was used directly in the acyloin condensation. The impure acyloin (probably a mixture of position isomers) was submitted directly to a modified Clemmensen reduction, the saturated hydrocarbon XI being obtained in a 1% over-all yield from diester IX. This yield is indicative of the unfavorable steric situation found for the ring-closing step and compares with the yields for analogous sequences in the preparation of the two next larger cycles as follows: compound I with $m = 3$, $n = 4$, yield 6%; I with $m = n = 4$, yield 22%. Dehydrogenation of the saturated hydrocarbon furnished the aromatic cycle, XII.

Several other potential syntheses of XII were also investigated. Reduction of unsymmetrical diester VIII with lithium aluminum hydride followed by treatment of the resulting diol with hydrogen bromide furnished the dibromide XIII. This substance failed to cyclize when subjected to the conditions of the Wurtz reaction, as had the dibromide XIV previously.[3d] Similarly, an attempt to obtain XII by an intermolecular Wurtz reaction of dibromide XV and *p*-dibromobenzene failed to give the desired cycle. It would appear that the successful application of the Wurtz reaction to preparation of the paracyclophanes is limited to those com-

(1) This work was supported in part by the Office of Naval Research.

(2) Dow Predoctoral Fellow at U.C.L.A., 1953–1954.

(3) (a) D. J. Cram and H. Steinberg, THIS JOURNAL, **73**, 5691 (1951); (b) H. Steinberg and D. J. Cram, *ibid.*, **74**, 5388 (1952); (c) D. J. Cram and N. L. Allinger, *ibid.*, **76**, 726 (1954); (d) N. L. Allinger and D. J. Cram, *ibid.*, **76**, 2362 (1954); (e) D. J. Cram and H. U. Daeniker, *ibid.*, **76**, 2743 (1954); (f) J. Abell and D. J. Cram, *ibid.*, **76**, 4406 (1954).

(4) (a) M. F. Bartlett, S. K. Figdor and K. Wiesner, *Canadian J. Chem.*, **30**, 291 (1952); (b) K. Wiesner, D. M. MacDonald, R. B. Ingraham and R. B. Kelly, *Canadian J. Research*, **B28**, 561 (1950).

(5) (a) C. J. Brown, *J. Chem. Soc.*, 3265 (1953); (b) 3279 (1953).