Acknowledgment. The authors gratefully acknowledge support of this and related research by the National Science Foundation.

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Synthesis of *p*-Biphenylyl β-D-Glucopyranosiduronic Acid and Its Optical and Crystallographic Properties

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Received October 8, 1956

A compound believed to be *p*-biphenylyl β-D-glucopyranosiduronic acid has been isolated as a urinary metabolite of *p*-phenylphenol in rabbits[1] and of biphenyl in rats.[2] In order to establish the structure, authentic *p*-biphenylyl β-D-glucopyranosiduronic acid was synthesized by chemical means and shown to be the same as the metabolite obtained by workers at this laboratory from the urine of rats on a diet containing biphenyl.[3] This work was conducted in connection with chronic-toxicity studies on biphenyl.

EXPERIMENTAL

p-Biphenylyl β-D-glucopyranosiduronic acid. A modification of the method used by Marsh[4] to oxidize a glucopyranoside to a glucopyranosiduronic acid was employed. Platinum on charcoal was used as a catalyst instead of platinum black. A suspension of 1.85 g. of *p*-biphenylyl β-D-glucopyranoside[5] and 0.400 g. of platinum on charcoal in 300 ml. of water was heated with stirring to 65°C., while oxygen was bubbled through the mixture over a period of 4 hr. A solution of sodium bicarbonate was added when necessary to keep the reaction neutral to litmus. After 4 hr. reaction the mixture was filtered and the insoluble cake of unreacted crystalline glucoside and catalyst was resuspended in water, heated to 65°C., and allowed to react as before. The isolation was repeated and a fresh portion of platinum on charcoal catalyst (0.200 g.) was added for the third oxidation treatment. The filtrates were combined and concentrated under reduced pressure. The *p*H was adjusted to 3 with dilute hydrochloric acid. The precipitated material was filtered and a yield of 0.330 g. (23% based on reacted starting material) of needle-like crystals was obtained from hot water. In addition 0.54 g. of starting material was recovered. The analyses of the product remained unchanged upon repeated crystallization.

Two dimensional paper chromatography was conducted on the synthetic material and the metabolite from ra urine. These materials chromatographed alike and both showed the same degree and kind of fluorescence. Upon acid hydrolysis the synthetic glucuronide showed the presence of only *p*-phenylphenol and glucuronic acid by paper chromatography. The analyses of the synthetic material are as follows:

Anal. Calcd. for $C_{18}H_{18}O_7$: C, 62.4; H, 5.2. Found: C, 62.0; H, 5.31 $[\alpha]_D^{25}$ (*c* 1, 95% ethanol) −80.2;[6] melted with decomposition, 185–187°C. $[\alpha]_D^{28}$ (*c* 1, ethanol) −85.2;[2] m.p., 185°.[2] The rotation given by Dodgson,[1] $[\alpha]_D^{20}$ −90.6, was measured from a 0.1*N* sodium hydroxide solution.

Optical and crystallographic properties of synthetic p-biphenylyl β-D-glucopyranosiduronic acid. Form and habit. Crystals grown by slowly cooling a hot aqueous solution are colorless in splintery clusters of nearly parallel needles or blades tapering to slender points. Longitudinal striations are common. Transverse cleavage is likely to occur when crystals are handled or when the cover glass is moved on crystals immersed in oil. Common views of the crystals all show parallel extinction with the slow ray crosswise, α lengthwise. The crystal system is probably orthorhombic.

Refractive indices. (Sodium light, 27°C.) α = 1.558, β = 1.602, γ = 1.73.

Optic axial angle. (+) $2V = 64°40'$ calculated from α, β, γ. $2E = 118°$ calculated from α, β, γ.

Dispersion. ($r > v$) slight.

Optic orientation. The axial plane is lengthwise, α is lengthwise. Centered Bx_a interference figures are obtainable from some blades, although the angle $2E$ is too large to measure accurately (melatopes at edge of field). Some crystals appear to be twisted so that the transverse index changes from β to γ along the length of the crystal. β and γ were determined on crystals whose orientation was checked by means of interference figures.

The optical and crystallographic properties of the metabolite from rat urine were the same as those of the synthetic *p*-biphenylyl β-D-glucopyranosiduronic acid.

X-ray powder diffraction. The *d* values for the major lines and their relative intensities are reported in Table I.

TABLE I

X-RAY POWDER DIFFRACTION DATA[a]

d, A	I/I_1	*d*, A	I/I_1	*d*, A	I/I_1
9.46	41.7	4.13	46.7	3.18	16.7
8.65	25.0	4.01	83.3	3.08	20.8
6.68	37.5	3.85	40.0	2.93	14.6
6.12	16.7	3.75	8.3	2.84	4.2
4.84	100.0	3.67	15.0	2.76	7.3
4.58	53.3	3.49	37.5	2.66	16.7
4.40	16.7	3.37	29.2	2.42	12.5
4.21	83.3	3.28	10.4	1.878	8.3

[a] The camera radius was 7.181 cm. λ for CuKα = 1.5418 A. and a nickel filter was used. The relative intensities were visually determined with a calibrated intensity scale.

Acknowledgment. The authors are indebted to Dr. Kenneth J. Palmer for assistance in obtaining the x-ray powder diffraction data and to Mr. L. M. White and Miss G. E. Secor for the microanalyses.

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