octopamine was dissolved in a minimum amount of hot absolute ethanol (3–5 ml.) and added to a solution of *d*-tartaric acid in sufficient hot ethanol to make a total volume of 6 ml. The resulting solution was allowed to stand in a refrigerator for 2 hr. and the salts were collected, washed with a small volume of absolute ethanol, and dried. The yields are based on the amount of octopamine used, with the exception of the single instance in which there was an excess of octopamine; in this case the yield is based upon the *d*-tartaric acid.

Pharmacological Studies with Octapamine Isomers.—The cardiovascular effects of the pure isomers were examined by Korol and Soffer.[8] They found that both isomers produced adrenergic cardiovascular responses in anesthetized dogs and cats as shown in Table II. The D-(−)-form was 3 times more potent

TABLE II[a]

AMOUNTS OF D-(−)- AND L-(+)-OCTOPAMINE AND *l*-NOREPINEPHRINE REQUIRED TO PRODUCE EQUIVALENT RESPONSES

Test	Animal	Octopamine isomer— D-(−)	L-(+)	*l*-Norepinephrine
Coronary flow	Dog	10–30 γ	30 γ	1 γ
Aortic flow (cardiac output)	Dog	100 γ	300 γ	4 γ
Blood pressure	Cat and dog	30 γ/kg.	100 γ/kg.	3 γ/kg.
Nictitating membrane	Cat	30 γ	100 γ	5 γ

[a] B. Korol and L. Soffer, personal communication.

than the L-(+)-form, but both isomers were markedly less potent than *l*-norepinephrine. They concluded that the responses were produced by a direct action of the octopamines on the cardiovascular system and were not dependent upon the release of adrenergic amines from the adrenal medulla or sympathetic nerve endings.

Acknowledgment.—Mrs. Kerin N. Yates carried out the nitrogen analyses reported here.

(8) B. Korol and L. Soffer, *The Pharmacologist*, **5**, 247 (1963).

4,4′-Dihydroxytriphenylacetic Acid

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Our interest in derivatives of hydroxytriphenylmethanes stems from the fact that several such compounds, such as phenolphthalein and *o*-(dihydroxybenzhydryl)benzyl alcohols, are good laxatives.[1]

Homolka[2] claims to have obtained some benzaurin from phenylglyoxylic acid and phenol at 120° in the presence of concentrated sulfuric acid. It was found in this laboratory that phenylglyoxylic acid reacted with phenol only in the presence of a condensing agent such as $ZnCl_2$, $SnCl_4$, or sulfuric acid. Best results were obtained at room temperature and in a solvent such as acetic acid. Without a solvent and at higher temperatures, the reaction was too violent, and only uncrystallizable tars were formed. The compound obtained in 83–96% yield was 4,4′-dihydroxytriphenylacetic acid (I). Its dimethyl ether, on decarboxylation, gave 4,4′-dimethoxytriphenylmethane in 86% yield.

When tested on the Rhesus monkey,[1] I showed no laxative activity. It was not tested for any other pharmacological activity.

(1) M. H. Hubacher, S. Doernberg, and A. Horner, *J. Am. Pharm. Assoc.*, **42**, 28 (1953); M. H. Hubacher, *J. Org. Chem.*, **23**, 1400 (1958).

(2) B. Homolka, *Ber.*, **18**, 988 (1885).

Experimental[3]

4,4′-Dihydroxytriphenylacetic Acid (I).—Concentrated sulfuric acid (2 ml.) was added to a solution, cooled to 20°, of 6.0 g. (0.04 mole) of phenylglyoxylic acid[4] (m.p. 65–66°) and 8.0 g. (0.085 mole) of phenol in 20 ml. of acetic acid. The mixture heated a few degrees and, within 12 hr., crystals formed. After keeping the mixture for 12 to 36 days at room temperature, a slurry with water was made, the crystals were filtered, washed free of SO_4^{-2}, and finally dried at 50° under reduced pressure. The acid (I), a light reddish powder, weighed 10.7–12.2 g. (83–95%) and melted at 251–254° dec.

I contained 0.5 mole of water when recrystallized from 41% ethanol or from 50% acetic acid, or by adding 20 ml. of benzene to a solution of 1 g. in 5 ml. of acetone.

Anal. Calcd. for $C_{20}H_{16}O_4 \cdot 0.5H_2O$: C, 72.95; H, 5.17. Found: C, 73.0 ± 0.6; H, 5.3 ± 0.2.

The acid slowly lost 3% in weight ($C_{20}H_{16}O_4 \cdot 0.5H_2O$, 2.7% H_2O) when dried to constant weight at 90° under high vacuum. It then was analyzed.

Anal. Calcd. for $C_{20}H_{16}O_4$: C, 75.00; H, 5.00; mol. wt., 320. Found: C, 74.76; H, 4.97; neut. equiv., 327.

Anhydrous I melted at 257.8–259.4° decomposing to a red melt. The colorless acid turned orange on exposure to light. On heating I to 260°, water and CO_2 were evolved. After treating the dark residue with acetic anhydride, a small quantity of crystals, melting at 108–109°, was isolated. These were identified as 4,4′-diacetoxytriphenylmethane.

***d*-3-Methoxy-N-methylmorphinan Salt of I.**—A warm solution of 283 mg. of *d*-3-methoxy-N-methylmorphinan (m.p. 107–108°) in 3 ml. of 2-propanol was added to a warm solution of 320 mg. of I in 5 ml. of warm 2-propanol. The crystals which formed were filtered, washed with 2-propanol, and dried at 100° *in vacuo*. They weighed 570 mg., m.p. 258–259° dec.

Anal. Calcd. for $C_{38}H_{41}NO_5$: C, 77.15; H, 6.93; N, 2.36. Found: C, 76.63; H, 7.11; N, 2.01.

Diacetyl Derivative of I.—This compound was prepared from I, acetic anhydride, and sodium acetate and crystallized from 2-propanol. It melted at 250.4–252.3°.

Anal. Calcd. for $C_{24}H_{20}O_6$: C, 71.28; H, 4.95. Found: C, 71.37; H, 5.35.

The methyl ester of I was prepared by adding an ethereal solution of diazomethane to a solution of I in acetone. The compound was obtained as an oil, which slowly solidified. After crystallization from 1,2-dichloroethane or from xylene, the ester melted at 220.9–222.0°.

Anal. Calcd. for $C_{21}H_{18}O_4$: C, 75.45; H, 5.39. Found: C, 75.21; H, 5.27.

Methylation of I.—Dimethyl sulfate (15 ml.) was added slowly to a stirred solution of 10 g. of I in 40 ml. of 5 *N* sodium hydroxide. The compound, which was insoluble in the aqueous sodium hydroxide, weighed 3.5 to 4.9 g. After crystallizations from ethanol, methyl 4,4′-dimethoxytriphenylacetate melted at 135.8–136.4°.

Anal. Calcd. for $C_{23}H_{22}O_4$: C, 76.24; H, 6.08. Found: C, 76.10; H, 6.21.

The precipitate, obtained by acidifying the alkaline filtrate, was recrystallized from 41% ethanol and yielded 5.1 to 7.0 g. of 4,4′-dimethoxytriphenylacetic acid (III), m.p. 194.3–196.7°.

Anal. Calcd. for $C_{22}H_{20}O_4$: C, 75.86; H, 5.75. Found: C, 75.54; H, 5.88.

On heating 3.48 g. of III and 0.05 g. of basic cupric carbonate in 10 ml. of quinoline to 220°,[5] 0.422 g. of CO_2 was evolved, accounting for 96% of the carboxyl group, and 2.63 g. (86%) of 4,4′-dimethoxytriphenylmethane, m.p. 100.3–100.6°, was obtained.

Acknowledgment.—The author is indebted to Mr. Sidney Doernberg for the animal experiments.

(3) All melting points are corrected.

(4) Sold by S. B. Penick & Co. under the name of benzoylformic acid.

(5) M. H. Hubacher, *Ind. Eng. Chem. Anal. Ed.*, **21**, 945 (1949).