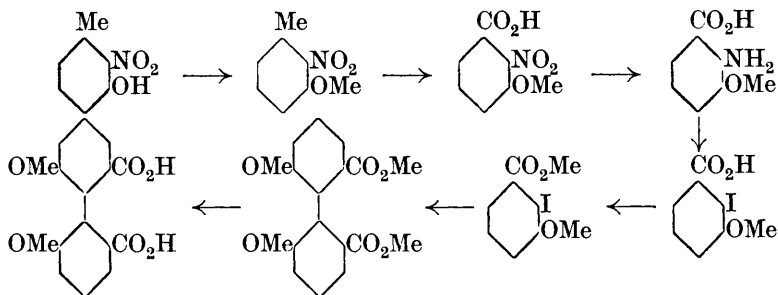


CCCIX.—*The Molecular Configurations of Polynuclear Aromatic Compounds. Part VIII. 6:6'-Dimethoxydiphenic Acid.*

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THE relatively simple method of preparing 2-nitro-*m*-cresol devised by Gibson (J., 1923, **123**, 1273; compare Hodgson and Beard, J., 1925, **127**, 498) has rendered it easily accessible and thus provided a convenient starting point for the synthesis of 6:6'-*dimethoxy-*

diphenic acid. This has been achieved by the following series of reactions :



The acid was found to be asymmetric, and was conveniently resolved into optically active forms by means of its *quinine* salts, a partial resolution being also achieved by means of *quinidine*.

EXPERIMENTAL.

2-Nitro-m-cresol.—The conditions of sulphonation and nitration of *m-cresol* prescribed by Gibson (*loc. cit.*) were followed, but it was found advisable to employ only 50 c.c. of water in place of 100 c.c. for dilution prior to steam distillation, and to conduct this operation at first so that the temperature of the vapour issuing from the distillation flask was 110°. After about 200 c.c. of distillate had been collected, the temperature of distillation was rapidly raised to 130—160°. The buttery mass of 2-nitro-*m-cresol* then obtained was suitable for immediate treatment with methyl sulphate and alkali, but could, if desired, be further purified by freezing. It was unnecessary to distil the crude methyl ether, since it crystallised when stirred or inoculated with the pure material, and could then be purified by crystallisation from dilute alcohol. For its oxidation, the ether (5 g.) was boiled with a solution of potassium permanganate (13 g.) in water (550 c.c.).

2-Amino-3-methoxybenzoic acid (Pschorr, *Annalen*, 1912, **391**, 27) was converted by the ordinary procedure into *2-iodo-3-methoxybenzoic acid*, which crystallised from dilute alcohol in yellowish needles, m. p. 150—151° (Found: *M*, 281. $C_8H_7O_3I$ requires *M*, 279). Its *methyl* ester crystallised from benzene-light petroleum in prisms, m. p. 57°, and was converted by treatment with an equal weight of copper powder at 205—210° into *methyl 6:6'-dimethoxydiphenate*, which crystallised from benzene in small prisms, m. p. 137—138° (Found: C, 65.01; H, 5.78. $C_{18}H_{18}O_6$ requires C, 65.45; H, 5.45%). *6:6'-Dimethoxydiphenic acid* was precipitated as a gummy mass from a cold solution of its sodium salt, but in the

crystalline condition from hot solutions; by crystallisation from alcohol, it was obtained in stout prisms, m. p. 288—290° (decomp.) (Found: C, 63·25; H, 4·7; *M*, 153. $C_{16}H_{14}O_6$ requires C, 63·57; H, 4·6%; *M*, 151).

Brucine hydrogen dimethoxydiphenate was obtained as a uniform salt, m. p. 268° (Found: N, 4·4. $C_{39}H_{40}O_{10}N_2$ requires N, 4·0%), and acid to phenolphthalein, when the acid was treated with two molecular proportions of brucine hydrate. Its sparing solubility in acetone rendered it easily separable from the unneutralised brucine, and the salt separated in prisms from a mixture of chloroform and acetone.

Resolution of the Acid into Optically Active Components.—A solution of the acid (3 g.) in methyl alcohol (70 c.c.) was neutralised by a solution of quinine hydrate (7·54 g.) in methyl alcohol (30 c.c.), and the solvent then evaporated. When the residue was triturated with successive amounts of cold acetone (200 c.c. in all), 4·5 g. remained undissolved, whilst a resinous mass (5·3 g.) was recovered from the acetone. In other experiments a similar separation was achieved by means of ethyl acetate.

Quinine l-dimethoxydiphenate (Found: N, 5·91. $C_{56}H_{60}O_{10}N_4$ requires N, 5·89%), the less soluble of the two salts thus obtained, melted at 172—173° after crystallisation from acetone, and this m. p. was unaffected by two further crystallisations from the same solvent. It had $[\alpha]_D + 126^\circ$ ($c = 0\cdot95$ in chloroform; $l = 1$), and the corresponding ammonium salt, prepared by shaking the quinine salt with chloroform and a slight excess of dilute ammonia, and repeatedly extracting the aqueous solution with chloroform, had $[\alpha]_D - 291^\circ$ ($c = 0\cdot59$ in water; $l = 1$): the strength of the solution was determined by evaporating an aliquot portion. The free *l-acid* was precipitated from a solution of the sodium salt similarly prepared, and, after being dried in a vacuum at the ordinary temperature to constant weight, had $[\alpha]_D - 115^\circ$ ($c = 0\cdot56$ in acetone; $l = 2$); it was only sparingly soluble in chloroform or ether, and melted at 294—295°.

When the resin mentioned above was rubbed with successive small quantities of cold ether, it was obtained in the form of a powder which gradually shrank and decomposed about 60°. It was easily soluble in benzene, but was precipitated as an oil by ligroin, and could not be crystallised; when dried to constant weight it had $[\alpha]_D - 68^\circ$ ($c = 1\cdot27$ in chloroform; $l = 1$) and an aqueous solution of the ammonium salt prepared from it had $[\alpha]_D + 254^\circ$. Clearly, therefore, the resin was a fairly pure sample of *quinine d-dimethoxydiphenate*.

A mixture of salts was also obtained when the acid (4·5 g.) was

neutralised by anhydrous quinidine (9.75 g.) in methyl-alcoholic solution. The product was easily soluble in methyl alcohol, acetone, and ethyl acetate, but an incomplete separation was achieved by allowing the solution of the mixed salts in benzene (50 c.c.) and ligroin (300 c.c.; b. p. 90—110°) spontaneously to evaporate. The weights, melting points, and specific rotatory powers in 2% alcoholic solution of the five successive fractions of prismatic crystals obtained were 1.8 g., m. p. 171—174°, $[\alpha]_D +88^\circ$ (Found: N, 5.5%); 3.3 g., 170—176°, -23° ; 1.0 g., 169—175°, -20° ; 1.5 g., 170—175°, $+50^\circ$; 1.7 g., 173—179°, $+76^\circ$ (Found: N, 5.8. $C_{56}H_{60}O_8N_4$ requires N, 5.9%). For a 0.4% solution of the sodium salt prepared from the first fraction, $[\alpha]_D -216^\circ$, whilst the second fraction yielded a totally inactive solution.

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