CXCIV.—*A New Isomerism of Halogenohydroxybenzoyltoluic Acids. Part IV. 2-(4′-Chloro-2′-hydroxybenzoyl)-3(or 6)-methylbenzoic Acid and 2-(2′-Chloro-4′-hydroxybenzoyl)-3(or 6)-methylbenzoic Acid.*

By MOSUKE HAYASHI.

IN succession to the previous papers, the author now reports the results of an investigation of isomeric changes of certain halogenohydroxybenzoyltoluic acids in which the halogen is situated in the *m*-position to the hydroxyl group.

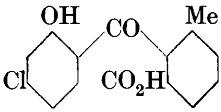
When 3-methylphthalic anhydride was condensed with *m*-chlorophenol or with *m*-chloroanisole in the presence of anhydrous aluminium chloride, two chlorohydroxybenzoyltoluic acids were obtained in both cases; one melted at 219·5—220·5° (A) and the other at 218—218·5° (B). When these two acids were separately treated with concentrated sulphuric acid at room temperature, an isomeric change occurred, and chlorohydroxybenzoyltoluic acid, m. p. 177·5—178° (A′) from the former (A), and chlorohydroxybenzoyltoluic acid, m. p. 201—202° (B′) from the latter (B), were produced. Acids (A) and (A′) exhibit two absorption bands with heads at λ 3210, 2630 Å. and λ 3230, 2660 Å., respectively. The acids (B) and (B′) show an absorption band with a head at λ 2830 and λ 2840 Å., respectively.

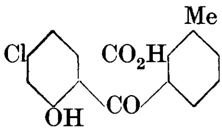
2-(5′-Chloro-2′-hydroxybenzoyl)-3- and -6-methylbenzoic acid (J., 1927, 2521), 2-(5′-chloro-2′-hydroxybenzoyl)-5- and -4-methylbenzoic acid (see Part II; this vol., p. 1513), and 2-(5′-chloro-2′-hydroxybenzoyl)benzoic acid (see Part II) show absorption bands with heads at λ 3350, 2860, λ 3390, 2860, λ 3330, 2790, λ 3330, 2780, and λ 3370 Å., respectively. 2-(3′-Chloro-4′-hydroxybenzoyl)benzoic acid (see Part III; preceding paper) and 2-(3′-chloro-4′-hydroxybenzoyl)-3- and -6-methylbenzoic acid (see Part III) have an absorption band with a head at λ 2840, λ 2840, and λ 2850 Å., respectively. Reasoning from the great similarity of these absorption bands, (A) or (A′) should have the formula which has the hydroxyl group in the *o*-position to the carbonyl group, and (B) or (B′) should have the formula which has the hydroxyl group in the *p*-position to the carbonyl group.

This view is in agreement with the following observations. When 2-(5′-chloro-2′-hydroxybenzoyl)-3- or -6-methylbenzoic acid, 2-(5′-chloro-2′-hydroxybenzoyl)-5- or -4-methylbenzoic acid, 2-(5′-chloro-2′-hydroxybenzoyl)benzoic acid, or the acid (A) or (A′) was heated with concentrated sulphuric acid, an anthraquinone derivative was produced comparatively easily. But an anthraquinone derivative was not produced by mere heating of 2-(3′-chloro-4′-hydroxybenzoyl)-benzoic acid, 2-(3′-chloro-4′-hydroxybenzoyl)-3- or -6-methylbenzoic acid, or the acid (B) or (B′) with concentrated sulphuric acid.

As in previous cases, the allotment of precise formulæ is only possible by taking into account the known influence of the methyl group; it is highly probable that (A), (A′), (B) and (B′) are 2-(4′-*chloro-2′-hydroxybenzoyl*)-3- and -6-*methylbenzoic acids* (I, II), and 2-(2′-*chloro-4′-hydroxybenzoyl*)-3- and -6-*methylbenzoic acids* (III, IV), respectively, as in the case of the *o*-chlorophenol derivatives (see Part III).

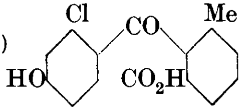
(I.) (A)

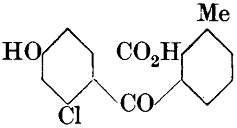




(II.) (A′)

(III.) (B)





(IV.) (B′)

These results are far more readily accommodated by the structural theory of the isomeric change than by any purely stereochemical explanation of the phenomena.

EXPERIMENTAL.

Condensation of 3-*Methylphthalic Anhydride with* m-*Chlorophenol.*—3-Methylphthalic anhydride (11 g.) was condensed with *m*-chlorophenol (10 g.) in acetylene tetrachloride solution (50 c.c.) in the presence of anhydrous aluminium chloride (27·5 g.) under conditions similar to those employed in the case of *o*-chlorophenol (see Part III). From the portion insoluble in ammonia, an anthraquinone derivative, m. p. 172—176°, was obtained in 5·4% yield. Recrystallised from glacial acetic acid or from *iso*butyl alcohol, it melted at 196·5—197° and was proved to be identical with 6-chloro-8-hydroxy-1(or 4)-methylanthraquinone by the method of mixed melting points. The ammoniacal solution was freed from ammonia and diluted; the precipitate (4 g.) that separated was removed and, from the acidified filtrate (charcoal), a grey substance, m. p. 175—186°, was obtained in 71% yield. Fractional crystallisation from aqueous alcohol or from acetic acid afforded two forms. The less soluble fraction (4·7 g.; 23·8%) melted at 218—220°, and the more soluble fraction (3·5 g.; 17·8%) at 217—218°.

2-(4′-*Chloro-2′-hydroxybenzoyl*)-3(*or* 6)-*methylbenzoic Acid* (A).—After crystallising several times from acetic acid, the less soluble fraction had m. p. 219·5—220·5° (Found : C, 61·7; H, 4·05; Cl, 12·1. $C_{15}H_{11}O_4Cl$ requires C, 61·95; H, 3·8; Cl, 12·2%). The *acid* separated in colourless microscopic pillars and dissolved somewhat easily in alcohol, but it was scarcely soluble in benzene or light petroleum. Its alkaline solutions are faintly yellow; in concentrated sulphuric acid, it gives a yellow solution that gradually becomes red. The acid exhibits two absorption bands with heads at λ 3210 and 2630 Å. (solvent, alcohol).

2-(2′-*Chloro-4′-hydroxybenzoyl*)-3(*or* 6)-*methylbenzoic Acid* (B).—The more soluble fraction crystallised from acetic acid in colourless microscopic pillars, m. p. 218—218·5° (Found : C, 61·9; H, 4·0; Cl, 12·1%), with properties generally similar to those of the isomeride. This acid has an absorption band with a head at λ 2830 Å. (solvent, alcohol).

2-(4′-*Chloro-2′-hydroxybenzoyl*)-6(*or* 3)-*methylbenzoic Acid* (A′).—After a solution of 2-(4′-chloro-2′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid (A) (1 g.) in 98% sulphuric acid (6 c.c.) had been kept for 1 day at room temperature, the product was treated with an excess of sodium carbonate, leaving no solid residue. The pale yellow precipitate (1 g.) obtained on acidification had m. p. 168—170°, and crystallised from acetic acid in pale yellow, flat, parallelogram-shaped crystals, m. p. 177·5—178° (Found : C, 61·8; H, 4·1; Cl, 12·1%).

The properties of this *acid* are similar to those of isomerides previously described. It exhibits two absorption bands with heads at λ 3230 and 2660 Å. (solvent, alcohol).

2-(2′-*Chloro-4′-hydroxybenzoyl*)-6(*or* 3)-*methylbenzoic Acid* (B′).—The precipitate which was obtained when 2-(2′-chloro-4′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid (B) was treated with 98% sulphuric acid under the same conditions as the (A) acid melted at 179—182°. It crystallised from acetic acid in microscopic, colourless, rectangular plates, m. p. 201—202° (anhydrous) (Found in air-dried material: loss at 105° in a vacuum, 6·1. $C_{15}H_{11}O_4Cl,H_2O$ requires H_2O, 5·84%. Found in anhydrous material: C, 61·7; H, 3·9; Cl, 12·2. $C_{15}H_{11}O_4Cl$ requires C, 61·95; H, 3·8; Cl, 12·2%).

This *acid* resembles its isomerides and exhibits an absorption band with a head at λ 2840 Å. (solvent, alcohol).

When the acid (B) or (B′) was heated with 98% sulphuric acid in the steam-bath or at 120—130° for 1 hour, the acid (B′) separated in a crude condition, but no anthraquinone derivative was obtained. When the acid (B) (0·5 g.) was heated with concentrated sulphuric acid (3 c.c.) at 200—210° for 3—4 minutes, a substance which did not dissolve in sodium carbonate solution was obtained. It melted at about 115° (0·14 g.). After recrystallising from light petroleum in colourless needles, it melted at about 118°. This unidentified substance sublimed even at room temperature.

6-*Chloro*-8-*hydroxy*-1(*or* 4)-*methylanthraquinone*.—A mixture of 2-(4′-chloro-2′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid (A) (0·27 g.) and 98% sulphuric acid (1·7 c.c.) was heated at 200° for 3 minutes, cooled, and poured into ice-water; the green precipitate that separated was collected and treated with an excess of sodium carbonate solution. A yellow substance (0·05 g.), m. p. 170—180°, remained undissolved; it crystallised from acetic acid in yellow, microscopic, feathery needles, m. p. 196·5—197° (Found: C, 66·2; H, 3·6; Cl, 13·0. $C_{15}H_9O_3Cl$ requires C, 66·05; H, 3·3; Cl, 13·0%). This anthraquinone derivative dissolves with difficulty in alcohol or in light petroleum; it is sparingly soluble in cold benzene or in cold glacial acetic acid, but somewhat easily soluble in the hot solvents. It is scarcely soluble in aqueous caustic alkali solutions, but the yellow colour becomes red. Two absorption bands with heads at λ 3950 and 2450 Å. were observed (solvent, alcohol). A very small amount of the anthraquinone was obtained when the acid (A) was heated in the steam-bath or at 120—130° with concentrated sulphuric acid.

Condensation of 3-*Methylphthalic Anhydride with* m-*Chloroanisole*.—When 3-methylphthalic anhydride (5 g.) was condensed with *m*-chloroanisole (5 g.) under the same conditions as *o*-chlorophenol (*loc. cit.*), crude 6-chloro-8-hydroxy-1(or 4)-methylanthraquinone, m. p. 173—178°, was obtained in 8·3% yield from the part insoluble in ammonia, and a substance, m. p. 200—213°, was obtained in 67% yield from the part soluble in ammonia, as in the case of *m*-chlorophenol. The substance, m. p. 200—213°, was fractionally crystallised from aqueous alcohol or from acetic acid; crude 2-(2′-chloro-4′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid (B), m. p. 216—218°, and crude 2-(4′-chloro-2′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid (A), m. p. 217—220°, were obtained in 26·8% and 7·8% yield, respectively.

2-(2′ : 5′-*Dihydroxybenzoyl*)-3(*or* 6)-*methylbenzoic Acid*.—The synthesis of dihydroxybenzoyltoluic acid has been studied by Majima (*Acta Phytochim.*, 1922, **1**, 47) and by Sakurai, but details of these experiments have not yet been published. The author has prepared the substance in order to study its behaviour under the influence of sulphuric acid. No isomeric change was observed in this case, but, under the usual conditions, much methylquinizarin was produced.

3-Methylphthalic anhydride (5 g.) was dissolved in acetylene tetrachloride (25 c.c.) mixed with quinol (3·8 g.), and powdered anhydrous aluminium chloride (12·5 g.) gradually added. The mixture was heated at 120—130° for 2 hours, and the product isolated in the usual manner. The portion insoluble in ammonia, crystallised from *iso*butyl alcohol, had m. p. 234—235° (0·15 g.) and was proved by the mixed melting point method to be identical with the 5 : 8-dihydroxy-1-methylanthraquinone which was derived from the benzoylbenzoic acid derivative obtained by condensing 3-methylphthalic anhydride with *p*-chlorophenol (J., 1927, 2524).

The portion soluble in ammonia was treated as in the case of the product from *o*-chlorophenol (see Part III), and crystallised from acetic acid in very pale yellow, lustrous, pillar-like crystals, m. p. 232·5—233° (Found : C, 66·0; H, 4·5. $C_{15}H_{12}O_5$ requires C, 66·15; H, 4·45%). The solubilities of this *acid* are similar to those of the chlorohydroxybenzoyltoluic acids. Its alkaline solutions are orange, and its solution in concentrated sulphuric acid is at first red, but soon becomes deep red. It exhibits an absorption band with a head at λ 3630 Å. (solvent, alcohol).

When a solution of 2-(2′ : 5′-dihydroxybenzoyl)-3(or 6)-methylbenzoic acid (0·1 g.) in 98% sulphuric acid (1 c.c.) was kept overnight at room temperature, only 5 : 8-dihydroxy-1-methylanthraquinone was obtained, a small quantity of the original substance being recovered.

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