CXCII.—*A New Isomerism of Halogenohydroxybenzoyltoluic Acids. Part II.* 2-(5′-*Chloro*-2′-*hydroxybenzoyl*)-5(4 ?)-*methylbenzoic Acid.*

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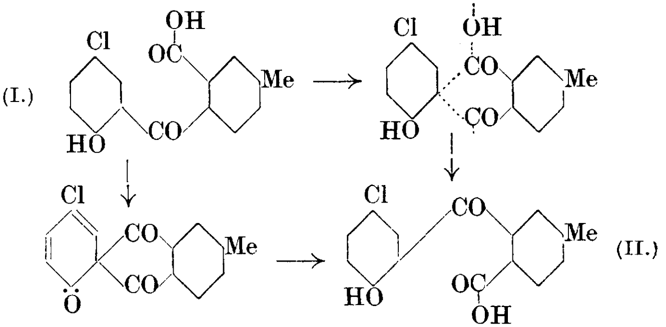
THE author has already reported (J., 1927, 2516) an isomeric change of *m*-chloro-*o*-hydroxybenzoyltoluic and *m*-bromo-*o*-hydroxybenzoyltoluic acids under the influence of concentrated sulphuric acid, and expressed the opinion that this phenomenon could be explained on either a stereoisomeric or a structural basis.

Recent developments in connexion with the stereochemistry of diphenyl derivatives have made the stereochemical hypothesis less probable, and the further work described in this and the following communications affords strong support to the alternative view.

When 4-methylphthalic anhydride was condensed with *p*-chlorophenol in acetylene tetrachloride solution in the presence of aluminium chloride, two chlorohydroxybenzoyltoluic acids, m. p. 239·5—240·5° (A) and m. p. 227·5—228·5° (B), were isolated. These isomerides were readily interconvertible on treatment with concentrated sulphuric acid, and may have the formulæ (I) and (II) in accordance with the rule which was mentioned in the previous paper (*loc. cit.*): their interconversion may be represented by the subjoined scheme.



This explanation is supported by the fact that two isomerides of 2-(5′-chloro-4′-hydroxybenzoyl)benzoic acid (see the next paper) could not be obtained, and by the circumstance that two isomeric benzoyltoluic acids can be obtained from 4-methylphthalic anhydride and benzene, although in this case the isomerides are not interconvertible (see below).

It would therefore appear that the chlorohydroxymethylanthraquinone derived from the chlorohydroxybenzoyltoluic acid (A) should differ from the chlorohydroxymethylanthraquinone derived from the chlorohydroxybenzoyltoluic acid (B). The author, however, could isolate only one chlorohydroxymethylanthraquinone by the dehydration of either acid. This difficulty may be purely experimental, only the chlorohydroxymethylanthraquinone which was produced in larger relative amount being isolated. It is comparatively easy to purify the anthraquinones derived from halogenohydroxybenzoyltoluic acids which form equilibrium mixtures in concentrated sulphuric acid in which the amounts of the isomeric acids are very different, as, for example, 2-(5′-chloro-2′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid or 2-(5′-bromo-2′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid (J., 1927, 2525). On the other hand, it is very difficult to purify the anthraquinones derived from halogenohydroxybenzoyltoluic acids in the equilibrium mixtures of which the proportions of the isomeric acids are comparable, as, for example, in the present case.

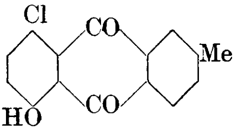
There is no available diagnostic reaction which will enable the constitutional formulæ (I) and (II) to be allocated to the individual chlorohydroxybenzoyltoluic acids (A) and (B), and the constitution of the chlorohydroxymethylanthraquinone derivative, m. p. 214—215° (C), obtained from them is also undetermined. But, taking into account the influence of the methyl group, it seems probable that (A), which was produced in the larger relative amount when 4-methylphthalic anhydride was condensed with *p*-chlorophenol, is 2-(5′-*chloro*-2′-*hydroxybenzoyl*)-5-*methylbenzoic acid* (I), and (B) is 2-(5′-*chloro*-2′-*hydroxybenzoyl*)-4-*methylbenzoic acid* (II). The anthraquinone derivative (C) will be 8-*chloro*-5-*hydroxy*-2-*methylanthraquinone* (III), if the assumption is made that it originated from (A), which is the isomeride present in the larger relative amount in concentrated sulphuric acid solution.

By analogy the author proposes the following corrections of the interpretations given in the previous paper (*loc. cit.*) :

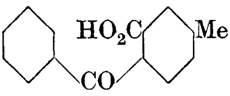
Original.	Corrected.
β-5′-Chloro-2′-hydroxy-2-benzoyl-*m*-toluic acid	2-(5′-Chloro-2′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid
α-5′-Chloro-2′-hydroxy-2-benzoyl-*m*-toluic acid	2-(5′-Chloro-2′-hydroxybenzoyl)-6(or 3)-methylbenzoic acid
Chlorohydroxymethylanthraquinone	8-Chloro-5-hydroxy-1(or 4)-methylanthraquinone
β-5′-Bromo-2′-hydroxy-2-benzoyl-*m*-toluic acid	2-(5′-Bromo-2′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid
α-5′-Bromo-2′-hydroxy-2-benzoyl-*m*-toluic acid	2-(5′-Bromo-2′-hydroxybenzoyl)-6(or 3)-methylbenzoic acid
Bromohydroxymethylanthraquinone	8-Bromo-5-hydroxy-1(or 4)-methylanthraquinone

In Part I (*loc. cit.*), it was pointed out that α-substituted phthalic anhydrides usually condense with phenol and its ethers through the carbonyl group adjacent to the substituent, but as a result of the present and cognate investigations the author is not convinced that this generalisation applies to methylphthalic anhydride and it is proposed to continue the investigation relating to this point.

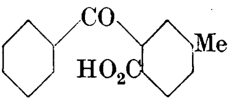
When 4-methylphthalic anhydride was condensed with benzene in the presence of aluminium chloride, two benzoyltoluic acids were obtained, m. p. 150—150·5° (D) and m. p. 145—145·5° (E), and these, which may have the formulæ (IV) and (V), yielded 2-methylanthraquinone on dehydration. Attributing an influence to the methyl group along the usual lines, it seems probable that the benzoyltoluic acid (D) is 2-*benzoyl*-5-*methylbenzoic acid* (IV) and the benzoyltoluic acid (E) is 2-*benzoyl*-4-*methylbenzoic acid* (V). (D) and (E) remained unaltered on being treated with concentrated sulphuric acid at room temperature.



(III.)



(IV.)



(V.)

EXPERIMENTAL.

Preparation of 4-*Methylphthalic Anhydride*.—Methyl 4-nitro-*m*-toluate was obtained (yield, *ca.* 90%) by an application of the method of Jürgens for methyl 2-nitro-*m*-toluate (*Ber.*, 1907, **40**, 4411; also compare Müller, *Ber.*, 1909, **42**, 431, 434).

The ester was dissolved in methyl alcohol (4 vols.), mixed with tin foil, and concentrated hydrochloric acid (*d* 1·19; 3·4 vols.) was gradually added with frequent shaking, the temperature being maintained below 10°. When the reaction had finished, the mixture was treated with an excess of sodium hydroxide and the base isolated by means of ether (yield, 65—92%). This substance after several crystallisations from aqueous alcohol had m. p. 62—62·5° (compare Jürgens, *loc. cit.*) (Found: C, 65·4; H, 6·9; N, 8·8. Calc. for $C_9H_{11}O_2N$: C, 65·4; H, 6·7; N, 8·5%). It is easily soluble in alcohol, acetone, benzene or ether, but is sparingly soluble in light petroleum (compare Panaotovic, *J. pr. Chem.*, 1886, **33**, 69).

A solution of sodium nitrite (14 g.) in water (50 c.c.) was gradually added with frequent shaking to an ice-cooled aqueous solution (water, 150 c.c.) of methyl 4-amino-*m*-toluate (30 g.) and concentrated hydrochloric acid (*d* 1·19; 32·4 c.c.). The filtered, pale yellow solution, cooled with ice, was added to a well-agitated potassium cuprous cyanide solution, maintained at 40—50°; the mixture was then boiled for about 15 minutes. The product was isolated by means of ether and obtained as an orange-coloured substance (19·6 g., 61·5%), m. p. 55·5—59·5°. The *methyl* 4-*cyano*-m-*toluate* crystallised from light petroleum (charcoal) in colourless needles, m. p. 60—60·5° (Found: C, 68·5; H, 5·35; N, 8·3. $C_{10}H_9O_2N$ requires C, 68·5; H, 5·2; N, 8·0%). It is easily soluble in benzene, acetone, chloroform, alcohol, or ether, but sparingly soluble in cold light petroleum.

Methyl 4-cyano-*m*-toluate (m. p. 59—60·5°; 158 g.) was refluxed with 20% hydrochloric acid (1580 c.c.) for about 5 hours; the 4-methylphthalic acid which crystallised was collected, and a further quantity was obtained from the filtrate. The acid was distilled under diminished pressure without further purification and crude 4-methylphthalic anhydride was thus obtained in 91·5% yield (138 g.); this was dissolved in benzene and washed with 1% sodium carbonate solution, and the distillation repeated, b. p. 155—160°/9 mm. Fractional crystallisation from benzene gave methylphthalic anhydride (96 g., 64%), m. p. 91—92° (compare Niementowski, *Monatsh.*, 1891, **12**, 626), and an unidentified substance (7 g.), m. p. 110—195° (Found: C, 66·9; H, 3·85. Calc. for $C_9H_6O_3$: C, 66·7; H, 3·7%).

Condensation of 4-*Methylphthalic Anhydride with* p-*Chlorophenol.*—Powdered aluminium chloride (12·5 g.) was gradually added with frequent shaking to a solution of 4-methylphthalic anhydride (5 g.; m. p. 91·5—92°) and *p*-chlorophenol (5 g.) in acetylene tetrachloride (25 c.c.); when the violent reaction subsided, the mixture was heated at 120—130° until the evolution of hydrogen chloride had almost ceased (3—4½ hours). The product was cooled, mixed with ice-water, and, after the addition of an excess of hydrochloric acid, distilled in steam to remove acetylene tetrachloride. The solid residue was extracted several times with boiling aqueous ammonia; crude 2-(5′-chloro-2′-hydroxybenzoyl)-5(or 4)-methylbenzoic acid (7 g.), m. p. 202—203°, was obtained from the soluble portion, and a substance (0·8 g.), m. p. 193—196°, from the residue. The latter was crystallised from benzene, *iso*butyl alcohol, and glacial acetic acid, and proved to be identical with 8-chloro-5-hydroxy-2(or 3)-methylanthraquinone, which was obtained from 2-(5′-chloro-2′-hydroxybenzoyl)-5(or 4)- or -4(or 5)-methylbenzoic acid, by the mixed melting-point method. The acid fraction, on crystallising several times from alcohol, furnished two substances, the less soluble (2·7 g.) having m. p. 220—232°, and the more soluble (1·8 g.) having m. p. 223—226°.

2-(5′-*Chloro*-2′-*hydroxybenzoyl*)-5(*or* 4)-*methylbenzoic Acid* (A).—The material, m. p. 220—232°, was recrystallised several times from alcohol and obtained in faintly yellow, microscopic crystals, m. p. 239·5—240·5° (Found: C, 62·0; H, 3·8; Cl, 12·1. $C_{15}H_{11}O_4Cl$

requires C, 61·95; H, 3·8; Cl, 12·2%). This acid is easily soluble in acetone or in hot alcohol or hot glacial acetic acid; it dissolves appreciably in benzene and is very sparingly soluble in light petroleum. Its solution in concentrated sulphuric acid is at first yellow, but soon becomes deep red; the alkaline solutions also have a yellow colour. An alcoholic solution of this acid exhibits two absorption bands with heads at λ 3330 and 2790 Å. respectively.

2-(5′-*Chloro*-2′-*hydroxybenzoyl*)-4(*or* 5)-*methylbenzoic Acid* (B).—The further crystallisation of the fraction, m. p. 223—226° (see above), from alcohol gave colourless microscopic cubes, m. p. 227·5—228·5° (Found: C, 62·1; H, 3·8; Cl, 12·0. $C_{15}H_{11}O_4Cl$ requires C, 61·95; H, 3·8; Cl, 12·2%). This acid has properties similar to those of the isomeride (A); its alcoholic solution exhibits two absorption bands with heads at λ 3330 and 2780 Å. respectively.

A solution of 2-(5′-chloro-2′-hydroxybenzoyl)-5(or 4)-methylbenzoic acid (A) (0·5 g.) in sulphuric acid (3 c.c., 100%) was kept at room temperature for about 17 hours. When the product was poured into ice-water, a sticky precipitate separated; after being washed, this was completely soluble in aqueous sodium carbonate. The sticky but almost colourless acid which was recovered on acidification with hydrochloric acid crystallised on being warmed for a few minutes in contact with the solvent; the crude mixture melted at 215—230°. On crystallisation from alcohol, two forms were ultimately separated. The less soluble fractions (0·36 g.) melted at 237—239°, and at 238—240° when mixed with a specimen of 2-(5′-chloro-2′-hydroxybenzoyl)-5(or 4)-methylbenzoic acid (A). The more soluble fractions (0·005 g.) melted at 218—223°, and at 218—225° when mixed with a specimen of 2-(5′-chloro-2′-hydroxybenzoyl)-4(or 5)-methylbenzoic acid (B).

2-(5′-Chloro-2′-hydroxybenzoyl)-4(or 5)-methylbenzoic acid (B) (0·5 g.) was treated with sulphuric acid (100%, 3 c.c.) under the same conditions as the isomeride, and the separation of the products was carried out as before. The less soluble fractions (0·13 g.) melted at 237—239°, and at 238—239° when mixed with a specimen of (A). The more soluble fractions (0·05 g.) melted at 223—225°, and at 224—226° when mixed with a specimen of (B).

8-*Chloro*-5-*hydroxy*-2-(*or* 3)-*methylanthraquinone* (C).—A mixture of chlorohydroxybenzoyltoluic acid (A) or (B) and sulphuric acid (100%, 6 parts by volume) was heated on the steam-bath for ½ hour, cooled, and added to ice-water and the solid was collected and washed with an excess of dilute aqueous sodium carbonate. The yellow crystalline powder (yield, 75%) had m. p. 195—197°, and was many times recrystallised from benzene (charcoal) and ultimately obtained in orange-yellow plates, m. p. 214—215° (Found:

C, 66·1; H, 3·45; Cl, 13·0. $C_{15}H_9O_3Cl$ requires C, 66·05; H, 3·3; Cl, 13·0%). The substance is easily soluble in benzene or acetone and moderately readily soluble in glacial acetic acid, alcohol, or *iso*butyl alcohol when these solvents are hot; it dissolves appreciably in benzene or acetone and is sparingly soluble in glacial acetic acid, alcohol or *iso*butyl alcohol when these solvents are cold. It dissolves to some extent in light petroleum. The crystals become red in contact with dilute aqueous caustic alkali, but very little passes into solution. The solution in concentrated sulphuric acid is deep red. The ultra-violet absorption curve of an alcoholic solution of this substance shows three bands with heads at λ 4100, 3330 and 2610 Å.

Attempts to isolate other substances from the mother-liquor from which 8-*chloro*-5-*hydroxy*-2(*or* 3)-*methylanthraquinone* was separated were unsuccessful.

The author wishes to thank Mr. S. Miyaki, who helped him with a part of this experiment.

Condensation of 4-*Methylphthalic Anhydride with Benzene.*—Anhydrous aluminium chloride (25 g.) was added with frequent shaking to a solution of 4-methylphthalic anhydride (10 g.) in benzene (100 c.c.) and the mixture was heated gradually to the boiling point. After 3 hours, the cooled product was added to ice-water and an excess of hydrochloric acid; the benzene was then removed by distillation in steam. The sticky residue was washed with water and extracted with a hot ammonia solution, leaving a very small brown residue. When the filtrate was acidified with hydrochloric acid, a sticky precipitate separated: this was washed with water, dried at 100°, dissolved in hot benzene and cooled with ice-water; the precipitate produced (6·55 g., m. p. 140—143°) was collected. On concentration and further cooling, the filtrate afforded a second fraction (3·4 g.), m. p. 128—136° (residue in the solution, about 5 g.).

2-*Benzoyl*-5(*or* 4)-*methylbenzoic Acid* (D).—When the material which melted at 140—143° was crystallised several times from glacial acetic acid, fine colourless crystals, m. p. 150—150·5°, were obtained (Found: C, 75·2; H, 5·2. $C_{15}H_{12}O_3$ requires C, 75·0; H, 5·0%).

This *acid* dissolves very easily in alcohol and moderately easily in benzene or glacial acetic acid; it is very sparingly soluble in light petroleum. Its yellow solution in 100% sulphuric acid gradually turns red. It exhibits an absorption band with a head at λ 3335 Å. (solvent, alcohol).

2-*Benzoyl*-4(*or* 5)-*methylbenzoic Acid* (E).—The material, m. p. 128—136°, was recrystallised several times from acetic acid; colourless pillar-like crystals, m. p. 145—145·5°, were obtained (Found:

C, 75·2; H, 5·2%). The solubilities of this *acid* are generally similar to, but greater than, those of the isomeric acid (D). The yellow solution in 100% sulphuric acid is tinged with red more rapidly than that of the (D) acid. It exhibits an absorption band with a head at λ 2450 Å. (solvent, alcohol).

After solutions of the acids (D) and (E) (0·5 g.) in 100% sulphuric acid (3 c.c.) had been separately kept for 48 hours at room temperature, they were poured into ice-water and treated with an excess of sodium carbonate solution. In the first case, very little 2-methylanthraquinone remained undissolved and a colourless precipitate (0·48 g.), m. p. 149—150°, which was proved to be identical with the acid (D) by the mixed melting-point method, was obtained from the yellow filtrate on acidification with hydrochloric acid. In the second case, a smaller amount of 2-methylanthraquinone was obtained, and almost pure acid (E) (0·49 g.), m. p. 144—145°.

2-*Methylanthraquinone*.—The acid (D) (0·5 g.) was heated with 100% sulphuric acid (5 c.c.) in a boiling water-bath for 50 minutes, and the product poured into ice-water. The precipitate obtained was washed with dilute sodium carbonate solution and with water, dried (0·44 g. or 95%), and crystallised from glacial acetic acid, forming very faintly yellow, feathery crystals, m. p. 176—176·5° (Found: C, 81·1; H, 4·7. Calc. for $C_{15}H_{10}O_2$: C, 81·05; H, 4·5%).

The ultra-violet absorption curve of an alcoholic solution of this substance shows two bands with heads at λ 3250 and 2550 Å. (Limpricht and Wiegand, *Annalen*, 1900, **311**, 180; Beilstein, “ Handbuch der Organischen Chemie,” III, 450 and Erg. III, 323).

A solution of the acid (E) (0·58 g.) in 100% sulphuric acid (4·5 c.c.) was heated in a boiling water-bath for 50 minutes and subsequently treated as in the case of the acid (D). A substance (0·51 g., 95%), m. p. 173—176°, was obtained which was recrystallised from glacial acetic acid and proved to be identical with 2-methylanthraquinone.

Appendix.—The author has examined the ultra-violet absorption curves of alcoholic solutions of the substances which were described in the previous paper (*loc. cit.*):

Substance.	Head of absorption bands, Å.
8-Chloro-5-hydroxy-1(or 4)-methylanthraquinone ...	λ 4050
8-Bromo-5-hydroxy-1(or 4)-methylanthraquinone ...	λ 4070
2-(5′-Chloro-2′-hydroxybenzoyl)benzoic acid	λ 3370
4-Chloro-1-hydroxyanthraquinone	λ 4100, 3350, and 2460

In conclusion, the author wishes to express his gratitude to Professor R. Robinson, F.R.S., for his kind advice.

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