453. *Action of Aluminium Chloride on Derivatives of* o-*Benzoylbenzoic Acid.*

By G. Baddeley, G. Holt, and S. M. Makar.

At least one derivative of anthraquinone is obtained when each of a series of substituted *o*-benzoylbenzoic acids is treated with aluminium chloride. Some of the acids are susceptible to isomerisation and afford anthraquinones after migration of substituents. *o*-(2 : 4 : 6-Trimethylbenzoyl)- and *o*-(2 : 3 : 5 : 6-tetramethylbenzoyl)-benzoic acid readily provide isomeric acids which are amenable to ring closure. *o*-(6-Hydroxy-2 : 4-dimethylbenzoyl)- and *o*-(2 : 4-diethyl-6-hydroxybenzoyl)-benzoic acid rearrange to the corresponding *o*-(3 : 4-dialkyl-6-hydroxybenzoyl)-benzoic acids which can be cyclised to the corresponding 1 : 2-dialkyl-4-hydroxyanthraquinones. The factors which determine the products of reaction are discussed.

o-Aroylbenzoic acids are readily obtained by saturating a solution of phthalic anhydride in methylene or ethylene chloride with aluminium chloride (2 mols.) and adding the solution of the complex to an aromatic hydrocarbon (see Experimental); they afford anthraquinone derivatives by fusion with excess of aluminium chloride (Kränzlein, "Aluminium Chlorid in der Organischen Chemie," Verlag Chemie, Berlin, 1932, p. 53; cf. Gleason and Dougherty, *J. Amer. Chem. Soc.*, 1929, **51**, 310). The latter application of the chloride is especially important when, owing to ready sulphonation, ring closure cannot be produced by sulphuric acid; the chloride is, however, a well-known agent of isomerisation and, therefore, may not convert derivatives of *o*-benzoylbenzoic acid into the corresponding derivatives of anthraquinone. In particular, as *o*-alkylaryl ketones, including 2-alkylbenzophenones, can be irreversibly isomerised by fusion with excess of aluminium chloride (*J.*, 1944, 232), *o*-*o*′-alkylaroylbenzoic acids may not provide the corresponding 1-alkylanthraquinones. Further, as 2 : 6-dialkylaryl ketones are readily isomerised, for example, acetylmesitylene (I) provides first acetyl*pseudo*cumene (II) and then 5-acetylhemimellitene (III), *o*-2 : 6-dialkylaroylbenzoic acids may change into the 2 : 5- and 3 : 5-isomers which may then provide anthraquinone derivatives. All these possibilities have now been realised; the data are assembled in the table and the reactions are illustrated in the scheme on p. 2417.

Ring closures effected through sulphuric acid were not accompanied by isomerisation and provided anthraquinones which were used for identifications. Sulphonation occurs only when *o*-(2 : 4 : 6-trimethylbenzoyl)- and *o*-(2 : 3 : 5 : 6-tetramethylbenzoyl)-benzoic acids

Products of interaction of o-*aroylbenzoic acids* (*o*-Ar·CO·C_6H_4·CO_2H) *and aluminium chloride.*

Initial acid Ar·CO- in *o*-Ar·CO·C_6H_4·CO_2H	Temp.	Time (hrs.)	Products: Ar·CO- in *o*-Ar·CO·C_6H_4·CO_2H	Products: Anthraquinone derivative
2 : 5-$Me_2C_6H_3$·CO-	165°	1·5	—	1 : 3- and 1 : 4-Me_2-
,, ...	220	1·5	—	1 : 3- and 1 : 4-Me_2-
2 : 4-$Me_2C_6H_3$·CO-	175	1	—	1 : 3-Me_2- (88%)
2 : 5-$Et_2C_6H_3$·CO-	160	2	—	1 : 3-Et_2- (90%)
2 : 4 : 6-$Me_3C_6H_2$·CO- ...	160	1	3 : 4 : 5-$Me_3C_6H_2$·CO- (16%)	1 : 2 : 3-Me_3- (80%)
,, ...	105	1	2 : 4 : 5-$Me_3C_6H_2$·CO- (96%)	1 : 2 : 4-Me_3- (4%)
2 : 4 : 5-$Me_3C_6H_2$·CO- ...	135	1	3 : 4 : 5-$Me_3C_6H_2$·CO- (20%) ...	1 : 2 : 3-Me_3- (55%)
2 : 3 : 5 : 6-Me_4C_6H·CO-	165	2	—	1 : 2 : 3 : 4-Me_4- (95%)
,,	105	3	2 : 3 : 4 : 5-Me_4C_6H·CO- (70%)	1 : 2 : 3 : 4-Me_4- (28%)
6-OH-2 : 4-$Me_2C_6H_2$·CO-	100	1	6-OH-2 : 4-$Me_2C_6H_2$·CO- (99%)	—
,,	155	3	6-OH-3 : 4-$Me_2C_6H_2$·CO- (17%)	4-OH-1 : 2-Me_2- (80%)
,,	175	3	—	,, (96%)
6-OH-3 : 4-$Me_2C_6H_2$·CO-	165	1	6-OH-3 : 4-$Me_2C_6H_2$·CO- (22%)	,, (78%)
6-OH-2 : 4-$Et_2C_6H_2$·CO-	105	4	6-OH-3 : 4-$Et_2C_6H_2$·CO- (90%)	4-OH-1 : 2-Et_2- (10%)
,,	170	3	—	,, (80%)

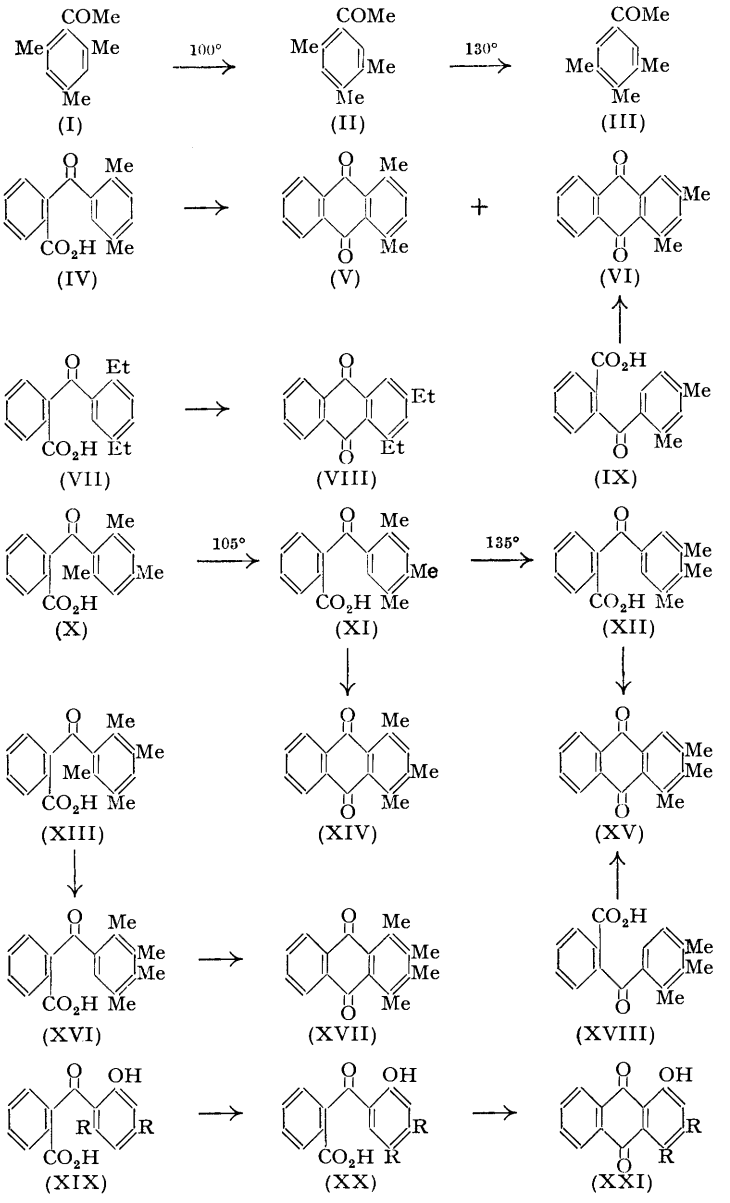
The yields are only approximate, and differences of less than 5% are not significant.

(X and XIII) are warmed with sulphuric acid; these reactions are further illustrations of the anomalous susceptibility of aromatic ketones to electrophilic substitution when the mesomeric effect of the carbonyl group is sterically inhibited by bulky groups in the *o*- and the *o'*-position (*Nature*, 1939, **144**, 444). Sulphonic acids are also obtained by the action of sulphuric acid on the *o*-(6-hydroxy-2 : 4-dialkylbenzoyl)benzoic acids (XIX).

None of the anthraquinones is affected by fusion with aluminium chloride; the isomerisations are consequent upon attack by a proton, provided by hydrogen chloride in the presence of aluminium chloride (*J.*, 1950, 994), and are a feature of the *o*-aroylbenzoic acids. These are affected by the electrophilic attack largely as a consequence of steric inhibition of mesomerism (*loc. cit.*); for example, *o*-(2 : 4 : 6-trimethylbenzoyl)benzoic acid (X) provides first the 2 : 4 : 5- (XI) and then the 3 : 4 : 5-isomer whereas the anthraquinones are protected by the mesomeric effect of carbonyl groups which are coplanar with the benzenoid rings. The products of fusion with aluminium chloride are determined, therefore, by the relative rates of isomerisation and of ring closure of the *o*-aroylbenzoic acids.

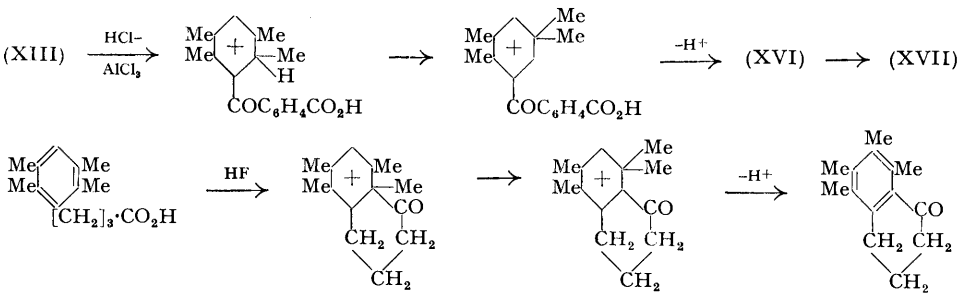
Earlier work (*loc. cit.*) showed the ethyl group to be more mobile than the methyl group; for example, 2-ethylacetophenone provides the 3-isomer by intramolecular migration of the ethyl group while 2-methylacetophenone affords the 4-isomer by displacement of the acetyl group; this difference in mobility is now illustrated by the formation of only 1 : 3-diethylanthraquinone from *o*-(2 : 5-diethylbenzoyl)benzoic acid (VII ⟶ VIII), *i.e.*, isomerisation is complete, whereas *o*-(2 : 5-dimethylbenzoyl)benzoic acid is only partially isomerised and affords a mixture of 1 : 4- and 1 : 3-dimethylanthraquinone (IV ⟶ V + VI). [Quayle and Reid (*J. Amer. Chem. Soc.*, 1925, **47**, 2357), using a mixture of diethylbenzenes, obtained a diethylanthraquinone which they considered might be the 1 : 3-isomer; it melted at 83—85° whereas our sample melts at 123—124° and affords anthraquinone-1 : 3-dicarboxylic acid by oxidation with nitric acid.] The 2-methyl group of 2 : 5-dimethylaryl ketones is more mobile than that of the corresponding 2 : 4-isomers as electrophilic attack by a proton at the 2-position of the benzene ring is aided more by a 5- than by a 4-methyl group; this difference is now illustrated by the partial isomerisation of *o*-(2 : 5-dimethylbenzoyl)benzoic acid while, under comparable conditions, the 2 : 4-isomer does not isomerise (IX ⟶ VI). Isomerisation becomes more conspicuous with increase in temperature: at 105° *o*-(2 : 4 : 6-trimethylbenzoyl)benzoic acid afforded the 2 : 4 : 5-isomer and 1 : 2 : 4-trimethylanthraquinone (X ⟶ XI ⟶ XIV), whereas, at 135° and again at 160°, *o*-(3 : 4 : 5-trimethylbenzoyl)benzoic acid and 1 : 2 : 3-trimethylanthraquinone

were obtained (X ⟶ XII ⟶ XV). [Unambiguous synthesis of *o*-(3 : 4 : 5-trimethylbenzoyl)benzoic acid is not readily effected and, as this acid has not been described previously, its structure was established by showing that, although it depresses the melting point of the 2 : 3 : 4-isomer on admixture, it provides 1 : 2 : 3-trimethylanthraquinone when warmed with sulphuric acid.]



o-(2 : 3 : 4 : 5-Tetramethylbenzoyl)benzoic acid was isolated as intermediate in the transformation of the 2 : 3 : 5 : 6-isomer into 1 : 2 : 3 : 4-tetramethylanthraquinone (XIII ⟶ XVI ⟶ XVII). The reaction is, therefore, not comparable with the cyclisation of γ-durenylbutyric acid, *in one step* and through the agency of anhydrous hydrofluoric acid, to 5 : 6 : 7 : 8-tetramethyl-1-tetralone (Aitken, Badger, and Cook,

J., 1950, 331): a methyl group is displaced by a proton in the former reaction and by an acyl cation in the latter:



Acetyldurene, when fused with aluminium chloride at 100°, provides not only acetylprehnitene (80%), but also diacetyldurene (10%) and aromatic hydrocarbon (10%); 5-acetylhemimellitene and hexamethylbenzene are obtained at higher temperatures (*J.*, 1952, 807). These intermolecular migrations of acyl and methyl groups respectively are not a feature of the action of aluminium chloride on *o*-(2 : 3 : 5 : 6-tetramethylbenzoyl)benzoic acid.

The isomerisations of 2-hydroxyaryl ketones by aluminium chloride are strictly analogous to those of the corresponding aryl ketones (*loc. cit.*; *J.*, 1943, 273); in particular, 6-hydroxy-2 : 4-dimethyl- and 2 : 5-diethyl-6-hydroxybenzophenone rearrange to the corresponding 6-hydroxy-3 : 4-dialkyl derivatives. It is not surprising, therefore, that *o*-(6-hydroxy-2 : 4-dimethylbenzoyl)- and *o*-(2 : 4-diethyl-6-hydroxybenzoyl)-benzoic acid (XIX; R = Me and Et respectively) afford the corresponding *o*-(3 : 4-dialkyl-6-hydroxybenzoyl)benzoic acids (XX) which can be cyclised to the corresponding 1 : 2-dialkyl-4-hydroxyanthraquinones (XXI). The isomerisation occurs readily at 105° when R is ethyl, but requires higher temperatures (< 120°) when R is methyl.

Experimental

o-*Aroylbenzoic Acids.*—Powdered phthalic anhydride was added to a suspension of finely powdered aluminium chloride (2·5 mols.) in methylene or ethylene chloride, and the mixture agitated for 0·5 hour at room temperature. The solution was decanted from undissolved aluminium halide into a solution of aromatic hydrocarbon (1 mol.) in methylene or ethylene chloride. After a further 0·5 hour, the mixture was decomposed with dilute hydrochloric acid, solvent was removed by distillation, and the solid product was isolated and recrystallised from acetic acid. The following derivatives of benzoic acid were prepared in this way; the yields are given in parentheses:

o-(2 : 5-Dimethylbenzoyl)- (95%), m. p. 149—150° (Barnett and Low, *Ber.*, 1931, **64**, 49); *o*-(2 : 4-dimethylbenzoyl)- (89%), m. p. 142—143° (Dougherty and Gleason, *J. Amer. Chem. Soc.*, 1930, **52**, 1026); *o*-(2 : 4 : 6-trimethylbenzoyl)- (73%), m. p. 211—212° (Underwood and Walsh, *ibid.*, 1935, **57**, 940); *o*-(2 : 4 : 5-trimethylbenzoyl)- (69%), m. p. 146—147° (Found: C, 76·1; H, 6·1. Calc. for $C_{17}H_{16}O_3$: C, 76·1; H, 6·0%) (Meyer, *Ber.*, 1882, **15**, 638); *o*-(2 : 3 : 4-*trimethylbenzoyl*)- (69%), m. p. 160—161° (Found: C, 75·7; H, 6·0. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%); *o*-(2 : 3 : 5 : 6-tetramethylbenzoyl)- (89%), m. p. 263—264° (Underwood and Walsh, *loc. cit.*); *o*-(2 : 3 : 4 : 5-*tetramethylbenzoyl*)- (85%), m. p. 162—163° (Found: C, 76·6; H, 7·1. $C_{18}H_{18}O_3$ requires C, 76·6; H, 6·4%).

o-(2 : 5-Diethylbenzoyl)benzoic acid was not obtained crystalline.

o-(6-*Hydroxy*-2 : 4-*dimethylbenzoyl*)*benzoic Acid.*—A mixture of *m*-5-xylenol (12·2 g.), phthalic anhydride (14·8 g.), and aluminium chloride (15 g.) in tetrachloroethane (100 c.c.) was refluxed for 1 hour. Evolution of hydrogen chloride was now complete and the mixture was cooled and poured into dilute hydrochloric acid. The organic layer was separated, washed with dilute hydrochloric acid, then with water, and extracted with sodium carbonate solution. The extract was clarified with activated charcoal and acidified; the required *acid* (18·1 g.) crystallised from acetic acid in yellow needles, m. p. 210—211° (Found: C, 71·2; H, 5·2%; equiv., 270. $C_{16}H_{14}O_4$ requires C, 71·7; H, 5·2%; equiv., 270).

o-(6-*Hydroxy*-3 : 4-*dimethylbenzoyl*)*benzoic Acid.*—A mixture of powdered phthalic anhydride and aluminium chloride (2 mols.) in tetrachloroethane was warmed on the steam-bath for 10 minutes, cooled, and added to a solution of *o*-4-xylenol (1 mol.) and aluminium chloride (1 mol.) in tetrachloroethane. The reaction was completed on the steam-bath, and the required acid was isolated in 76% yield as described for the previous experiment; it crystallised from ethanol in colourless needles, m. p. 172—174° (Fairbourne and Gauntlett, *J.*, 1923, 1137).

o-(2 : 4-Diethyl-6-hydroxybenzoyl)benzoic acid was prepared similarly but could not be obtained crystalline. It was dried under reduced pressure over phosphoric oxide.

Interactions with Aluminium Chloride.—For each g. of organic acid, aluminium chloride (10 g.) and sodium chloride (1·5 g.) were powdered together and heated by an oil-bath to 140°. The homogeneous melt was continuously stirred and brought to a selected temperature, and the organic acid was gradually added. After a selected time the mixture was cooled and decomposed by addition to ice and dilute hydrochloric acid, and the organic material was separated.

o-(2 : 5-*Dimethylbenzoyl*)*benzoic acid.* This acid (4 g.) after 1 hour at 175° or at 220° provided an alkali-insoluble product (3·8 g.), m. p. 112—131°. Recrystallisation from acetic acid afforded a mixture of needles and plates, and these were separated by hand and recrystallised from acetic acid. The former were 1 : 4-dimethylanthraquinone, m. p. and mixed m. p. 140—141°, and the latter the 1 : 3-isomer, m. p. and mixed m. p. 161—162°. Authentic specimens were obtained by the action of concentrated sulphuric acid at 100° for 2 hours on *o*-(2 : 5-dimethylbenzoyl)- and *o*-(2 : 4-dimethylbenzoyl)-benzoic acid respectively (Helber, *Ber.*, 1910, **43**, 2890; Elbs and Günther, *Ber.*, 1887, **20**, 1364). These anthraquinones were also separated chromatographically by benzene on an alumina column; the 1 : 4-isomer is the more mobile.

o-(2 : 4-*Dimethylbenzoyl*)*benzoic acid.* After an hour at 175°, this provided 1 : 3-dimethylanthraquinone (88%), m. p. and mixed m. p. 161—162°; the presence of the 2 : 3-isomer was not detected.

o-(2 : 5-*Diethylbenzoyl*)*benzoic acid.* The acid (5 g.), after 2 hours at 160°, provided alkali-insoluble material (4·5 g.); attempted separation on an alumina column gave only 1 : 3-*diethylanthraquinone* which crystallised from acetic acid in yellow needles, m. p. 123—124° (Found : C, 81·8; H, 5·8. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%). Oxidation with nitric acid at 220° afforded anthraquinone-1 : 3-dicarboxylic acid, m. p. and mixed m. p. 322—325° (decomp.) (Fieser and Martin, *J. Amer. Chem. Soc.*, 1936, **58**, 1443).

o-(2 : 4 : 6-*Trimethylbenzoyl*)*benzoic acid.* After 1 hour at 160° this (5 g.) afforded *o*-(3 : 4 : 5-trimethylbenzoyl)benzoic acid (0·8 g.), m. p. 201—202° after recrystallisation from acetic acid, and 1 : 2 : 3-*trimethylanthaquinone* (4·1 g.) which, after treatment with charcoal, crystallised from acetic acid in long golden-yellow needles, m. p. 187—188° (Found : C, 81·1; H, 5·6. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%). The latter is identical (m. p. and mixed m. p.) with the product of interaction of *o*-(2 : 3 : 4-trimethylbenzoyl)benzoic acid and sulphuric acid, and is oxidised by nitric acid to anthraquinone-1 : 2 : 3-tricarboxylic acid (trimethyl ester, m. p. 183—184°; Cook, *J.*, 1933, 1592, gives m. p. 184—185°).

After 1 hour at 105° the acid afforded *o*-(2 : 4 : 5-trimethylbenzoyl)benzoic acid (4·8 g.), m. p. and mixed m. p. 146—147° after crystallisation from acetic acid, and an alkali-insoluble product (0·2 g.) which provided 1 : 2 : 4-trimethylanthraquinone, m. p. and mixed m. p. 162—163°, when recrystallised from acetic acid (Elbs, *J. prakt. Chem.*, 1890, **41**, 121).

o-(2 : 4 : 5-*Trimethylbenzoyl*)*benzoic acid.* This (3 g.), after 1 hour at 133°, afforded 1 : 2 : 3-trimethylanthraquinone (1·6 g.), m. p. and mixed m. p. 187—188°, and an alkali-soluble fraction (1·3 g.) from which the initial acid (0·08 g.) and o-(3 : 4 : 5-*trimethylbenzoyl*)*benzoic acid* (0·6 g.), m. p. 202—203° (Found : C, 75·7; H, 6·0. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%), were isolated. The latter is identical with the acid obtained from *o*-(2 : 4 : 6-trimethylbenzoyl)benzoic acid at 160°; like the 2 : 3 : 4-isomer, it affords 1 : 2 : 3-trimethylanthraquinone when heated with sulphuric acid.

o-(2 : 3 : 5 : 6-*Tetramethylbenzoyl*)*benzoic acid.* After 2 hours at 165°, this acid (4 g.) afforded 1 : 2 : 3 : 4-tetramethylanthraquinone (3·7 g.), m. p. and mixed m. p. 234—235° (Hewett, *J.*, 1940, 293, gives m. p. 232—233°) (crystallised from acetic acid). An authentic specimen was obtained by interaction of *o*-(2 : 3 : 4 : 5-tetramethylbenzoyl)benzoic acid and sulphuric acid.

Heating for 3 hours at 105° provided 1 : 2 : 3 : 4-tetramethylanthraquinone (1·1 g.) and *o*-(2 : 3 : 4 : 5-tetramethylbenzoyl)benzoic acid (2·8 g.).

o-(6-*Hydroxy*-2 : 4-*dimethylbenzoyl*)*benzoic acid.* The acid (3 g.) was recovered unchanged after 1 hour at 100° and after 4 hours at 120°. After 2 hours at 143°, half of the product (*i.e.*, 1·5 g.) was insoluble in sodium carbonate solution and afforded 4-hydroxy-1 : 2-dimethyl-

anthraquinone in orange-yellow needles, m. p. and mixed m. p. 168—169° (from acetic acid); Fairbourne and Gauntlett (*loc. cit.*) give m. p. 169°. This formed an acetate, m. p. 158—159° after crystallisation from aqueous acetone; Fairbourne and Foster (*J.*, 1930, 1275) give m. p. 158°. This anthraquinone was obtained in yields of 80 and 96% after 3 hours at 155° and 175° respectively. The carbonate-soluble material (1·5 g.) crystallised from ethanol and afforded *o*-(6-hydroxy-3 : 4-dimethylbenzoyl)benzoic acid, m. p. and mixed m. p. 172—174°.

o-(6-*Hydroxy*-3 : 4-*dimethylbenzoyl*)*benzoic acid.* This acid afforded the above anthraquinone in 78% yield after 1 hour at 165°, and in 40% yield by the action of concentrated sulphuric acid for 1 hour at 100°.

o-(2 : 4-*Diethyl*-6-*hydroxybenzoyl*)*benzoic acid.* The acid (4 g.), after 4 hours at 105°, afforded 1 : 2-*diethyl*-4-*hydroxyanthraquinone* (0·3 g.) which crystallised from acetic acid in yellow needles, m. p. 121—122° (Found : C, 77·0; H, 5·1. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·7%), and o-(3 : 4-*diethyl*-6-*hydroxybenzoyl*)*benzoic acid* (3·6 g.), m. p. 195—196° (from acetic acid) (Found : C, 72·6; H, 6·0. $C_{18}H_{18}O_4$ requires C, 72·5; H, 6·0%). The latter acid, like 3 : 4-dialkyl-6-hydroxyaryl ketones (*loc. cit.*), afforded a *monobromo*-derivative, m. p. 190—191° (Found : C, 56·7; H, 4·5; Br, 21·2. $C_{18}H_{17}O_4Br$ requires C, 57·3; H, 4·5; Br, 21·2%), by the action of excess of bromine in aqueous acetic acid, and 1 : 2-diethyl-4-hydroxyanthraquinone when heated with phosphoric oxide in benzene or with excess of aluminium chloride at 170° for 3 hours.

FACULTY OF TECHNOLOGY, UNIVERSITY OF MANCHESTER. [*Received, March 25th*, 1952.]