CCCLXXVII.—*Substituted Diaryl Ethers. Part II. The Friedel–Crafts Reaction applied to Di-*p*-tolyl Ether.*

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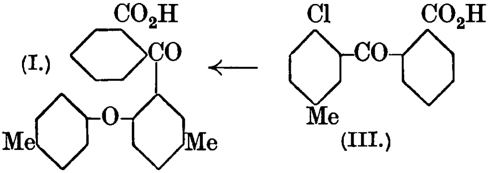
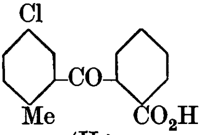
ALTHOUGH there are two similar benzene nuclei in di-*p*-tolyl ether in both of which substitution may occur, the authors find that this ether yields only monoketonic derivatives in the Friedel–Crafts reaction. The condensation of di-*p*-tolyl ether proceeds more readily with phthalic anhydride than with benzoyl chloride, substitution occurring in one position only; from benzoyl chloride more than one substance appears to be formed.

Condensation of 2-hydroxy-5-methylbenzophenone-2′-carboxylic acid with *p*-bromotoluene gives 2-o-*carboxybenzoyldi*-p-*tolyl ether* (I), identical with the product of interaction between phthalic anhydride and di-*p*-tolyl ether. The formation of a 2-ketone in the latter reaction is what would be expected and is in line with the authors' recent work on the nitration of di-*p*-tolyl ether (this vol., p. 68) showing that the oxygen atom exerts the main orienting influence.



(I.) (III.)



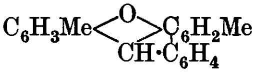
(II.)

The substance (I) has also been obtained by condensing *p*-cresol with the chloromethylbenzophenone-*o*-carboxylic acid which Heller and Schulke (*Ber.*, 1908, **41**, 3627) prepared from *p*-chlorotoluene and phthalic anhydride. Their ketone therefore has formula (III), not (II), the chlorine atom exerting a greater directive influence than the methyl group.

The product obtained by heating (I) with concentrated sulphuric acid is, not an anthraquinone derivative, but 2 : 7-dimethylfluoran, identical with that obtained by Drewsen (*Annalen*, 1882, **212**, 341) from phthalic anhydride, *p*-cresol, and sulphuric acid; it gives 2 : 2′-dihydroxy-5 : 5′-dimethylbenzophenone and benzoic acid on fusion with potassium hydroxide.

Although *2-benzoyldi-*p*-tolyl ether* (formula as I) has not been directly synthesised, its constitution as an ortho-substituted diaryl ether is indicated by the following facts. Its solutions in acetic and sulphuric acids are yellow and fluorescent, indicating xanthhydrol formation through ring closure. From these solutions, 9-phenyl-2 : 7-dimethylxanthen was isolated identical with that obtained by Feuerstein and Lipp (*Ber.*, 1902, **35**, 3255) by the dry distillation of 6 : 6′-dihydroxy-3 : 3′-dimethyltriphenylmethane.

The conditions employed by Feuerstein and Lipp in preparing the phenyldimethylxanthen were so drastic that its constitution is not beyond doubt. Moreover, its formation from benzoyldi-*p*-tolyl ether in acetic acid—the change is more readily effected by boiling alcoholic hydrochloric acid—is difficult to understand. It seems to the authors that the substance may be a fluorene,



$$C_6H_3Me\left<\begin{matrix}O\\ CH\cdot C_6H_4\end{matrix}\right>C_6H_2Me$$

but to this view there is the objection that the molecule of such a substance would be in a state of considerable strain; the formula also shows linkage at a position (1 in the xanthen ring) which is not only sterically hindered but is also meta with respect to the oxygen atom. In support of the fluorene formula, however, may be quoted the following facts: (1) Phenyldi-α-naphthylcarbinol, on boiling with acetic acid, changes into phenyldi-α-naphthafluorene (Schoepfle, *J. Amer. Chem. Soc.*, 1922, **44**, 190); (2) Ullmann and Mourawiew-Winigradoff (*Ber.*, 1905, **38**, 2213), on heating diphenyl-α-naphthylcarbinol with an acetic acid solution of sulphuric acid, zinc chloride, or hydrochloric acid, obtained phenylchrysofluorene. In offering the above suggestion, it is appreciated that phenyl groups exhibit less tendency than naphthyl groups to formation of fluorene linkages.

It was not found possible to prepare the oxime from 2-*o*-carboxybenzoyldi-*p*-tolyl ether (I), and the phenylhydrazone was only obtained under drastic conditions. These appear to be cases of steric hindrance by substituents in the two ortho-positions with respect to the carbonyl group. 2-Benzoyldi-*p*-tolyl ether, under identical conditions, did not give a phenylhydrazone, the reaction proceeding in a different direction.

Contrary to the generally accepted view that the reaction between benzoyl chloride and phenols in presence of aluminium chloride results in poor yields of hydroxybenzophenones unless the hydroxyl group has been previously protected (compare Fries and Finck, *Ber.*, 1908, **41**, 4276; Heller, *Ber.*, 1913, **46**, 1498), it is now found that with acetylene tetrachloride as solvent 2-hydroxy-5-methylbenzophenone is obtained in good yield from *p*-cresol and benzoyl chloride.

EXPERIMENTAL.

2-o-*Carboxybenzoyldi*-p-*tolyl Ether* (I).—A mixture of di-*p*-tolyl ether (8 g.) and phthalic anhydride (6 g.) was slowly added to anhydrous aluminium chloride (9 g.), covered with dry carbon disulphide and protected from moisture. After 12 hours, the product was poured on ice, the carbon disulphide and other volatile products were removed in steam, and the colourless residue was repeatedly dissolved in aqueous sodium hydroxide and precipitated by dilute acid. The product then crystallised from aqueous ethyl alcohol in long, hexagonal prisms (yield, 70%), m. p. 155° (Found : C, 76·2; H, 5·5; *M*, cryoscopic in naphthalene, 360. $C_{22}H_{18}O_4$ requires C, 76·3; H, 5·2%; *M*, 346).

Repetition of the above experiment, twice the quantities of phthalic anhydride and aluminium chloride being used, gave the same product, namely, 2-o-*carboxybenzoyldi*-p-*tolyl ether*, in approximately the same yield, no diketonic derivative being isolated.

Synthesis of 2-o-*Carboxybenzoyldi*-p-*tolyl Ether.*—*p*-Bromotoluene (10 g.), the dipotassium derivative (10 g.; dried at 120° in a vacuum) of 2-hydroxy-5-methylbenzophenone-2′-carboxylic acid prepared by Ullmann's method (*Ber.*, 1919, **52**, 2102), and a trace of copper bronze (Naturkupfer C, washed with ether to remove oily impurities) were heated in absolute-alcoholic solution in a sealed tube for 10 hours at 200°. The product was distilled in steam; unchanged *p*-bromotoluene passed over, followed by di-*p*-tolyl ether (1 g.). The residual oil was extracted with hot dilute sodium hydroxide solution, the extract acidified, and the viscous precipitate obtained crystallised from acetic acid (80%); 2-*o*-carboxybenzoyldi-*p*-tolyl ether slowly separated in colourless prisms, m. p. 154—155°, identical with the ether described above.

2-*o*-Carboxybenzoyldi-*p*-tolyl ether is readily soluble in glacial acetic acid, absolute alcohol or ether and very sparingly soluble in light petroleum (b. p. 60—80°) or water. It dissolves in concentrated sulphuric acid to an orange solution exhibiting a greenish fluorescence; the colour is discharged on dilution with water. Its *silver* salt is sparingly soluble in water, but readily soluble in dilute aqueous ammonia (Found : Ag, 23·9. $C_{22}H_{17}O_4Ag$ requires Ag, 23·8%). The ether, on fusion with potassium hydroxide, is decomposed into di-*p*-tolyl ether and phthalic acid. It unites with anhydrous aluminium chloride to give an orange-coloured solid.

The formation of di-*p*-tolyl ether in the above reaction was at first suspected to result from hydrolysis of the 2-*o*-carboxybenzoyldi-*p*-tolyl ether formed, but on heating *p*-bromotoluene and alcoholic potassium hydroxide under identical conditions di-*p*-tolyl ether was isolated in small quantity.

2-*o*-Carboxybenzoyldi-*p*-tolyl ether was recovered unchanged after being heated with hydroxylamine hydrochloride in strongly alkaline solution for 8 hours on the water-bath. The *phenylhydrazone* was obtained only by heating the ether (1 mol.) and phenylhydrazine (2 mols.) for 3 hours at 160—170°. The cooled product was extracted with very dilute hydrochloric acid; from an alcoholic solution of the residue, the *phenylhydrazone* separated in pale yellow needles, m. p. 156° (Found: N, 6·6. $C_{28}H_{24}O_3N_2$ requires N, 6·4%).

Action of Sulphuric Acid on 2-o-*Carboxybenzoyldi*-p-*tolyl Ether*.—The ether (1 g.) and concentrated sulphuric acid (8 c.c.) were heated on a boiling water-bath for 3 hours. The solution was then cooled and mixed with ice, and the precipitate obtained was collected and digested with aqueous sodium hydroxide solution; the extract was purple, owing probably to the presence of an anthraquinone derivative. The part insoluble in alkali was crystallised from absolute ethyl alcohol, 2 : 7-dimethylfluoran being obtained in colourless, glistening prisms (yield, 90%), m. p. 254° (Drewsen, *loc. cit.*, gives m. p. 246°) (Found: C, 80·6; H, 5·1. Calc. for $C_{22}H_{16}O_3$: C, 80·5; H, 4·9%).

The nature of this substance was established by fusion with potassium hydroxide at 220—240°. The dark yellow aqueous extract of the product was acidified and then boiled with sufficient alcohol to give a clear solution; on standing, yellow needles of 2 : 2′-dihydroxy-5 : 5′-dimethylbenzophenone separated which, after one recrystallisation from alcohol, had m. p. 104—106°. Distillation in steam of the filtrate from the fusion product gave benzoic acid.

Equal weights of 2-*o*-carboxybenzoyldi-*p*-tolyl ether and phosphorus pentachloride were heated in benzene solution until evolution of hydrogen chloride ceased. To the cooled, light orange solution was added the same weight of anhydrous aluminium chloride; hydrogen chloride was then again evolved. The deep red solution was finally refluxed for a short time and poured on ice; the product, isolated in the usual way, was 2 : 7-dimethylfluoran.

Constitution of Heller and Schulke's Ketone (III).—A mixture of the potassium salt of Heller and Schulke's ketone (*loc. cit.*) (1 mol.), potassium *p*-tolyloxide (1·5 mols.), *p*-cresol (solvent), and a trace of copper bronze was slowly heated, with stirring, to 200°; at 160° potassium chloride separated. After being heated for an hour at 190—200°, the product was dissolved in water, and the solution was extracted with ether, acidified, and extracted with chloroform. The chloroform was evaporated, and the residue dissolved in hot acetic acid (80%); 2-*o*-carboxybenzoyldi-*p*-tolyl ether slowly crystallised in short, colourless prisms, m. p. 153—154°.

2-*Benzoyldi*-p-*tolyl Ether* (formula as I).—The preparation from di-*p*-tolyl ether (7 g.), benzoyl chloride (5 g.), and aluminium chloride (12 g.) is very similar to that of the carboxylic acid (I) described above. The residue obtained after the steam-distillation set to a crystalline mass which separated from boiling, absolute ethyl alcohol in colourless, glistening rhombohedra (5·5 g.), m. p. 185—186° (Found: C, 83·1; H, 6·3. $C_{21}H_{18}O_2$ requires C, 83·4; H, 6·0%). A viscous oil (4 g.) obtained from the mother-liquor resisted all attempts to crystallise it.

A second experiment with di-*p*-tolyl ether (7 g.), benzoyl chloride (10 g.), and aluminium chloride (24 g.) was carried out under identical conditions, but the same monobenzoyl compound was obtained (7·8 g.) and no dibenzoyl compound was isolated.

2-*Benzoyldi*-p-*tolyl ether* is readily soluble in chloroform, acetone or benzene, much less soluble in ethyl alcohol, and insoluble in light petroleum (b. p. 60—80°). It dissolves in concentrated sulphuric acid to a bright yellow solution with a green fluorescence; dilution with water discharges the fluorescence but not the colour. It combines with anhydrous aluminium chloride to form a bright orange solid which immediately decomposes in contact with water.

Glacial acetic acid in contact with 2-benzoyldi-*p*-tolyl ether is coloured yellow; it becomes orange on heating and reddish-orange on boiling. On cooling, 9-phenyl-2 : 7-dimethylxanthen separates in colourless, glistening needles which, alone or mixed with an authentic specimen, melt at 195—196° (Found: by the micro-method, C, 87·8; H, 6·2; *M*, cryoscopic in camphor, 312. Calc. for $C_{21}H_{18}O$: C, 88·1; H, 6·3%; *M*, 286. Calc. for $C_{21}H_{16}O$: C, 88·7; H, 5·6%; *M*, 284). The same xanthen was obtained when 2-benzoyldi-*p*-tolyl ether was heated with phenylhydrazine at 160° for 2 hours.

2-*Hydroxy*-5-*methylbenzophenone*.—To *p*-cresol (10 g.) and benzoyl chloride (14·1 g.), dissolved in dry acetylene tetrachloride and protected from moisture, anhydrous aluminium chloride (26·7 g.) was added during 1 hour. The mixture was then heated for 4 hours at 100—110°, hydrogen chloride being copiously evolved. After cooling, the dark brown solution was poured into water, a dark oil separating. On distillation in steam, acetylene tetrachloride passed over, followed slowly by a light yellow oil which quickly solidified and was highly pure 2-hydroxy-5-methylbenzophenone (yield, 80%), m. p. 84·5° (Cox, *J. Amer. Chem. Soc.*, 1927, **49**, 1029, gives m. p. 87°).

2-p-*Tolyloxy-5-methylacetophenone*, prepared in the usual manner, was obtained as a red oil which was purified by distillation; the fraction, b. p. 320—340°, set to a crystalline solid which separated from alcohol in colourless, glistening plates, m. p. 168° (Found: C, 79·6; H, 7·0; *M*, cryoscopic in naphthalene, 251. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%; *M*, 240). This ketone has the characteristic odour of acetophenone and is readily soluble in ether, benzene, or hot alcohol. It dissolves in sulphuric acid to a yellow solution.

Addendum.—Since the above work was completed, a paper by Rosenmund and Schulz has appeared (*Arch. Pharm.*, 1927, **265**, 308), in which it is stated that the reaction between phenols and acid chlorides with aluminium chloride in nitrobenzene solution, giving phenolic ketones, is of general applicability. The unique behaviour of nitrobenzene is ascribed to its solvent action on the aluminium chloride complexes. Monohydric phenols react readily except when the *p*-position to the hydroxyl group is occupied. We have observed that acetylene tetrachloride also can be used as solvent in the preparation of phenolic ketones, and this holds even when the *p*-position to the hydroxyl group is occupied (*e.g.*, the yield of 2-hydroxy-5-methylbenzophenone is 80%).

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