Cleavage of Halogenobenzophenones by Potassamide in Ammonia; New Routes to Xanthen- and Thioxanthen-9-ones

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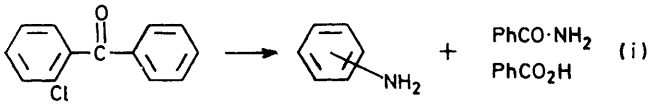
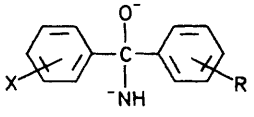
Treatment with potassamide in ammonia cleaved 2-chloro-4'-methoxy- and -4'-methylthio-benzophenones to give 4-methoxy- and 4-methylthio-benzoic acids respectively, but 2-chloro-4'-hydroxybenzophenone was largely unchanged. Similar treatment of 2'-fluoro-2-hydroxy-5-methylbenzophenone gave mainly 2-methylxanthen-9-one; the 2'-chloro- and 2'-bromo-analogues gave the xanthenone and the corresponding 2'-aminobenzophenone. 3'-Fluoro-2-hydroxy-5-methylbenzophenone was largely unchanged under these conditions, but the 3'-chloro- and 3'-bromo-analogues gave 2-methylxanthen-9-one and the corresponding 3'-aminobenzophenone. 2-Methylthioxanthen-9-one was prepared by two routes: (i) from 2-chlorobenzoyl chloride, 4-methylthiotoluene, and aluminium chloride; and (ii) from 3'-chloro-5-methyl-2-methylthiobenzophenone and potassamide in ammonia.

QUILLINAN and SCHEINMANN have recently reported a synthesis of xanthones which involves elimination of methanol from 2-hydroxy-2'-methoxybenzophenones in the presence of base; an attractive feature of the method is the ready access to a variety of naturally occurring xanthones which were not readily available by previous synthetic methods.[1] We have approached the synthesis of xanthones from a different viewpoint, using 2- and 3-halogeno-2'-hydroxybenzophenones as intermediates. Our work has origins in a publication [2] on the cleavage of halogenobenzophenones by potassamide in ammonia: various 2-halogenobenzophenones were extensively cleaved to the halogenobenzene or aniline and a mixture of the benzamide and benzoic acid from the other portion of the molecule [*e.g.* equation (i)]. With 4-chlorobenzophenone, cleavage was barely perceptible



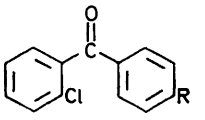
(i)

(1·6%), and with the 3-isomer the occurrence of cleavage was not firmly established but the extent was judged in any event to be less than 6%; the major products from these two compounds were aminobenzophenones, formed *via* arynes, though material balance was perhaps less than desirable. The cleavage reactions were considered to proceed *via* the dianions (1), and the ease of



R = H or Me
X = Cl or F

(1)



(2) R = OMe
(3) R = OH
(4) R = SMe

cleavage of *ortho*-compounds was attributed to the relative stability of *ortho*-halogenobenzenide ions, although the relative ease of formation of (1) because of greater electron deficiency at the carbonyl carbon atom in the *ortho*-compounds may also be a factor. The mechanism of formation of carboxylic acid was not finally established.

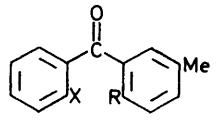
In the present work, it was necessary first to determine the extent to which cleavage of 2-halogenobenzophenones could be limited by incorporating electron-releasing substituents *ortho* or *para* to the carbonyl group. The three ketones (2)—(4) were prepared. Ketones (2) and (4) were obtained by Friedel–Crafts acylation of anisole and of thioanisole respectively by 2-chlorobenzoyl chloride in the presence of aluminium chloride; in the former case, heating the reaction mixture to 150° did not result in significant demethylation of (2) to (3), in agreement with other observations.[1] Ketone (3) was prepared by Fries rearrangement of phenyl 2-chlorobenzoate.

Ketone (2) was treated with potassamide in ammonia for 4 h and the mixture was separated into neutral, acidic, and basic fractions. Ketone (2) was recovered (28%) from the neutral fraction. The acidic fraction gave 4-methoxybenzoic acid (60%), and aniline, though not isolated, was detected in the basic fraction. Ketone (2) is thus markedly less reactive than 2-chlorobenzophenone, though cleavage remains a significant reaction. When ketone (3) was subjected to similar conditions, it remained largely unchanged, though a small amount of cleavage to 4-hydroxybenzoic acid and aniline occurred. Ketone (4), treated in this way, gave 4-methylthiobenzoic acid (51%) and presumably aniline; some ketone was recovered. With ketones (2) and (4), tarry material was also produced and, as in Bunnett and Hrutfiord's experiments,[2] the material balance was less satisfactory than desired, but the main course of the reaction was clear. In each case, reactivity of the ketone towards cleavage by potassamide in ammonia was depressed, markedly so for (3), relative to 2-chlorobenzophenone. The way thus seemed open for a xanthone synthesis from 2-halogeno-2'-hydroxybenzophenones and potassamide and, by inference, for a parallel synthesis of thioxanthen-9-ones.

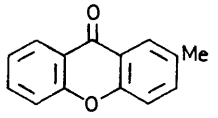
[1] A. J. Quillinan and F. Scheinmann, *J.C.S. Perkin I*, 1973, 1329.

[2] J. F. Bunnett and B. F. Hrutfiord, *J. Org. Chem.*, 1962, **27**, 4152.

To simplify synthetic problems, the 5-methyl derivatives were chosen. These were prepared by Fries rearrangement of the appropriate 4-tolyl 2-halogenobenzoates or, if rearrangement was incomplete, by Friedel–Crafts acylation of 4-methoxytoluene followed by demethylation of the initially formed methoxyketone *in situ*. Ketone (5) was prepared by the latter method and ketones (6) and (7) by the former.



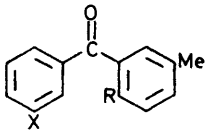
(5) X = Br, R = OH
(6) X = Cl, R = OH
(7) X = F, R = OH
(8) X = NH_2, R = OH
(9) X = Cl, R = SMe



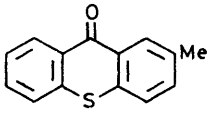
(10)

Ketone (5) was treated with potassamide in redistilled ammonia and the mixture was separated into acidic, neutral, and basic fractions. The acidic fraction contained 2-hydroxy-5-methylbenzoic acid (1·7%), indicating that ketone cleavage had been largely but not entirely suppressed, and unchanged ketone (5). The neutral fraction provided 2-methylxanthone (10) (14%) and the basic fraction gave the amino-ketone (8), isolated as its hydrochloride. The formation of (8) recalls the formation of 2′-amino-2,5-dimethylbenzophenone, albeit in only 2% yield, from 2′-chloro-2,5-dimethylbenzophenone.[2] In the present case, amide ion was competing for the substitution site with anionic oxygen of the phenolic group, suggesting that the yield of xanthone might be improved at higher dilution. In a similar experiment at higher dilution in undistilled ammonia, the yield of the xanthone was increased to 35% and ketone (5) was again recovered; the basic fraction could not be recovered as crystalline hydrochloride.

Ketone (6), similarly treated, gave 2-methylxanthone (10) and the amino-ketone (8) together with some unchanged (6). 2-Methylxanthone was also obtained in a relatively clean reaction from ketone (7); some of (7) was recovered, but the basic fraction yielded a negligible amount of material.



(11) X = Br, R = OH
(12) X = Cl, R = OH
(13) X = F, R = OH
(14) X = NO_2, R = OH
(15) X = NH_2, R = OH
(16) X = Cl, R = SMe



(17)

Attention was next directed to the 3-halogenobenzophenones (11)—(13), where cleavage by potassamide was expected to be insignificant. Ketones (11) and (13) were prepared by the Friedel–Crafts route with subsequent demethylation *in situ*, and ketone (12) was prepared by Fries rearrangement.

Treatment of (11) with potassamide in redistilled ammonia at fairly high dilution gave 2-methylxanthone (66%). The acidic fraction gave unchanged ketone (11) (39%) and the basic fraction gave a small amount of the amino-ketone (15); this was recovered as the hydrochloride and identified by comparison with a sample prepared by reduction of (14). Treatment of the chloroketone (12) with potassamide at higher concentration gave a lower yield of (10) with correspondingly higher yield of (15); again, some of (12) was recovered. These reactions of (11) and (12) evidently proceed *via* aryne intermediates, though whether the carbonyl group has undergone addition of amide ion [2] or whether the electron density at the carbonyl carbon atom is sufficiently lowered by conjugation to inhibit this is not known. Interestingly, ketone (13) is largely unchanged under these conditions, reflecting the relative difficulty of generating arynes from aromatic fluoro-compounds.

The feasibility of similar routes to thioxanthen-9-ones, exemplified by (17), was next considered. Attempted preparation of 2-(2-chlorobenzoyl)-4-methylbenzenethiol by Fries rearrangement of 4-tolyl 2-chlorothiobenzoate was abandoned because extensive decomposition occurred. An alternative approach involving Friedel–Crafts acylation of 4-methylthiotoluene with 2-chlorobenzoyl chloride, followed by demethylation of the first-formed sulphide (9) *in situ*, was pre-empted when serendipitous formation of 2-methylthioxanthen-9-one (17) occurred in 17% yield. It is not clear whether demethylation precedes or follows ring closure.

Finally, 3-chlorobenzoyl chloride and 4-methylthiotoluene were condensed in the presence of aluminium chloride to give ketone (16). Since cleavage by potassamide is not as significant for 3-chloro- as for 2-chlorobenzophenones, no attempt was made to demethylate (16) with aluminium chloride. Instead, (16) was treated with potassamide in ammonia under the usual conditions and, from the tarry mixture, (17) was isolated in 17% yield.

These procedures provide new routes to xanthen- and thioxanthen-9-ones and augment limited instances of preparations of xanthones from 2-chloro-2′-hydroxybenzophenones reported previously.[3]

EXPERIMENTAL

Ammonia was dried and distilled before use for reactions in liquid ammonia unless otherwise stated; yields for reactions conducted in liquid ammonia are based on starting material consumed.

2-Chloro-4′-methoxybenzophenone (2); *Treatment with Potassamide.*—(i) A solution of 2-chlorobenzoyl chloride [from 2-chlorobenzoic acid (7·8 g, 0·05 mol) and thionyl chloride] and anisole (4·8 g, 0·05 mol) in carbon disulphide

[3] (*a*) R. Hanssen, J. Meisenheimer, and A. Wachterowitz, *J. prakt. Chem.*, 1928, **119**, 315; (*b*) M. Kulka, *J. Amer. Chem. Soc.*, 1954, **76**, 5469.

(25 ml) was added during 30 min to a stirred suspension of powdered aluminium chloride (5 g, 0·038 mol) in carbon disulphide (25 ml) at room temperature. After 2 h, the mixture was evaporated and the residue was heated at 150° for 1 h to give a red tar. This was cooled and taken up in ethanol (25 ml), and the solution was poured into 2M-hydrochloric acid (100 ml). The resulting suspension was extracted with chloroform.

The chloroform solution was extracted with 1M-sodium carbonate; acidification of this aqueous phase gave slightly impure 2-chlorobenzoic acid (0·8 g, *ca.* 10%) (mixed m.p.). The resulting chloroform solution was extracted with 2M-sodium hydroxide; acidification of this aqueous phase gave a small amount of sticky brown oil apparently containing 2-chloro-4′-hydroxybenzophenone (t.l.c.). The remaining chloroform solution was washed with water, dried, and evaporated to give 2-chloro-4′-methoxybenzophenone (2) (7·0 g, 75%), m.p. 80—81° (from hexane) (lit.,[4] 80°).

(ii) Ketone (2) (2·5 g, 0·01 mol) was added during 20 min to a stirred solution of potassamide [from potassium (0·8 g, 0·02 g atom)] in liquid ammonia (250 ml). After 4 h, ammonium chloride (2·5 g) and ether (100 ml) were added, and the ammonia was allowed to evaporate.

The ether solution was extracted with 2M-hydrochloric acid; basification of this aqueous phase gave a small amount of brown oil which apparently contained aniline (t.l.c. of derived hydrochloride). The resulting ether solution was extracted with 2M-sodium hydroxide; acidification of this aqueous phase gave a solid (0·75 g) which crystallized from water to give 4-methoxybenzoic acid (0·6 g, 60%), m.p. and mixed m.p. 183—184°. The remaining ether solution was washed with water, dried, and evaporated to give a brown solid (1·4 g); extraction with boiling hexane left a residual tar and the extracts on cooling afforded starting material (2) (0·7 g, 28%), m.p. 76—78·5° (identity confirmed by t.l.c., i.r. spectrum, and mixed m.p.).

2-Chloro-4′-hydroxybenzophenone (3); *Treatment with Potassamide.*—(i) Fries rearrangement of phenyl 2-chlorobenzoate in dry nitrobenzene at 60° gave the ketone (3) (31%), m.p. 119—121° (from benzene) (lit.,[5] 128°).

(ii) Ketone (3) (2·9 g, 0·012 mol) in dry tetrahydrofuran (100 ml) was added to a stirred solution of potassamide [from potassium (1·4 g, 0·035 g atom)] in liquid ammonia (300 ml). After 4 h, the mixture was worked up as for (2) above. The ether solution containing the products was extracted with 2M-hydrochloric acid; basification gave a small amount of oil which was converted into the hydrochloride (15 mg) (using HCl in dry ether) and hence identified as aniline [i.r. spectrum; mass spectrum *m/e* 93 (M^+)]. Extraction of the ether solution with 2M-sodium hydroxide left nothing in the ether. The alkaline solution was acidified and extracted with ether; the extract was washed, dried, and evaporated to give starting material (3) (2·7 g, *ca.* 93%), contaminated with a second minor substance, presumably 4-hydroxybenzoic acid (t.l.c.). Crystallization from benzene gave (3) (still slightly contaminated), identified by mixed m.p. and i.r. spectrum.

2-Chloro-4′-methylthiobenzophenone (4); *Treatment with Potassamide.*—(i) A solution of thioanisole (14·9 g, 0·12 mol) in methylene chloride (15 ml) was added during 15 min to a stirred suspension of aluminium chloride (18 g, 0·135 mol) in a solution of 2-chlorobenzoyl chloride [from the acid (28·1 g, 0·20 mol)] in methylene chloride (60 ml), maintained at 0—5°. A precipitate formed and hydrogen chloride was evolved. After 1·5 h, the mixture was poured onto crushed ice and concentrated hydrochloric acid (150 ml) and the yellow organic phase was separated; the acid phase was extracted with chloroform. The combined organic extracts were washed with sodium hydrogen carbonate solution and water, dried, and evaporated. The residual oil was chromatographed on Florisil, eluted with ether–pentane (1 : 4), and crystallized at low temperature from methanol; *2-chloro-4′-methylthiobenzophenone* (4) (5·5 g, 18%) formed needles, m.p. 43—45° (Found: C, 64·0; H, 4·2; Cl, 13·7. $C_{14}H_{11}ClOS$ requires C, 64·0; H, 4·2; Cl, 13·5%).

(ii) Ketone (4) (4·0 g, 0·015 mol) was added to a stirred solution of potassamide [from potassium (1·2 g, 0·03 g atom)] in liquid ammonia (500 ml). After 4 h, the mixture was worked up as for (2) above. The ether solution containing the products was extracted with 2M-hydrochloric acid; basification and attempted conversion into hydrochlorides gave a tar (1·05 g) whose components were not identified. The resulting ether solution was extracted with 2M-sodium hydroxide; acidification and isolation by means of ether gave 4-methylthiobenzoic acid (0·95 g, 51%), m.p. 190—192°; crystallization from aqueous ethanol gave needles, m.p. 194—196° (lit.,[6] 192°) (Found: C, 56·9; H, 4·8; S, 19·2. Calc. for $C_8H_8O_2S$: C, 57·1; H, 4·8; S, 19·1%). The remaining ether solution was washed with water, dried, and evaporated to give a brown oil (1·1 g); this contained starting material (4) (t.l.c.), some of which (0·5 g; m.p. and mixed m.p. 40—43°) was recovered by low temperature crystallization, and tarry impurities.

2′-Bromo-2-hydroxy-5-methylbenzophenone (5) *and 2-Methylxanthone* (10).—(i) A solution of 2-bromobenzoyl chloride [from the acid (20 g, 0·1 mol)] and 4-methoxytoluene (11 g, 0·102 mol) in carbon disulphide (50 ml) was added during 30 min to a stirred suspension of aluminium chloride (10 g, 0·076 mol) in carbon disulphide (50 ml) at room temperature. After 2 h, the mixture was evaporated and the residue was heated at 150° for 1 h, and then cooled. The resulting golden-brown foam was powdered and added to 2M-hydrochloric acid, and the mixture was extracted with ether. The ether solution was washed with dilute sodium carbonate solution and water, dried, and evaporated. Crystallization from ethanol gave ketone (5) (16·2 g, 68%) as yellow prisms, m.p. 75·5° (lit.,[3a] 78·5°).

(ii) Ketone (5) (5·0 g, 0·017 mol) was added during 15 min to a stirred solution of potassamide [from potassium (1·9 g, 0·049 g atom)] in liquid ammonia (150 ml). After 3·5 h, ammonium chloride (5 g) and ether (100 ml) were added, and the ammonia was allowed to evaporate.

The ether solution was extracted with 2M-hydrochloric acid and the ether solution was retained. The acidic extract was basified with dilute sodium carbonate solution and extracted with ether (3 × 50 ml); addition of 2M-hydrochloric acid (2 ml) to the latter ether solution precipitated a yellow solid which was collected, and the ether phase was discarded. Crystallization from 2M-hydrochloric acid gave *2′-amino-2-hydroxy-5-methylbenzophenone hydrochloride* (8) (0·56 g. 19%) as platelets, m.p. 175—179° (opaque liquid, resolidifying at 220—225° as plates,

[4] B. Jones, *J. Chem. Soc.*, 1936, 1854.
[5] L. H. Thomas and T. Vlismas, *J. Chem. Soc.*, 1963, 612 and references cited therein.
[6] Th. Zincke and P. Jorg, *Ber.*, 1910, **43**, 3443.

decomp. 338—340°) (Found: C, 63·1; H, 5·3; N, 5·3. $C_{14}H_{14}ClNO_2$ requires C, 63·7; H, 5·3; N, 5·3%).

The ether solution retained above was extracted with aqueous 40% sodium hydroxide until no more yellow solid precipitated; the ether solution was retained. The alkaline suspension was acidified with concentrated hydrochloric acid and extracted with ether; this ether solution was washed with water, dried, and evaporated. The gummy yellow solid was dissolved in boiling light petroleum (b.p. 100—120°). As the solution cooled, colourless needles separated which were collected and recrystallized to give 2-hydroxy-5-methylbenzoic acid (30 mg, 1·7%), m.p. 147° (lit.,[7] 151°) (Found: C, 63·3; H, 5·3. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·3%). When concentrated, the mother liquor deposited starting material (5); recrystallization gave prisms (1·51 g, 30%), m.p. and mixed m.p. 75°.

The ether solution remaining from the alkaline washing was washed with water, dried, and evaporated. Crystallization from light petroleum (b.p. 100—120°) gave 2-methylxanthone (10) (0·34 g, 14%), m.p. 121—123° (lit.,[3a] 125·5°), not depressed on admixture with an analytical sample from the following experiment.

(iii) The foregoing experiment was repeated in undistilled liquid ammonia (250 ml), dried *in situ*. The same work-up procedure was used. The basic fraction gave a brown amorphous hydrochloride fraction (0·7 g) which could not be crystallized. The phenolic fraction gave starting material (5) (1·28 g, 26%), m.p. and mixed m.p. 75°. The neutral fraction gave 2-methylxanthone (10) (0·95 g, 35%) as buff needles, m.p. 122—123° (Found: C, 80·0; H, 4·6. Calc. for $C_{14}H_{10}O_2$: C, 80·0; H, 4·8%); $\nu_{max.}$ (Nujol) 1658 cm^{-1} (C=O); $\lambda_{max.}$ (EtOH) 240 (log ε 4·56), 263 (3·91), 290sh (3·18), and 340—344 nm (3·59). The xanthone exhibited a turquoise fluorescence in concentrated sulphuric acid.

2′-Chloro-2-hydroxy-5-methylbenzophenone (6) *and* 2-*Methylxanthone* (10).—Ketone (6) (4·13 g, 0·017 mol) [prepared by a known method;[8] m.p. 75—77° (lit.,[8] 76·3—77·2°)] was added during 15 min to a stirred solution of potassamide [from potassium (2·0 g, 0·051 g atom)] in liquid ammonia (300 ml). After 4 h, ammonium chloride (5 g) and ether were added. The above procedure for (5) was followed: basic material was extracted with 2M-hydrochloric acid and 2′-amino-2-hydroxy-5-methylbenzophenone hydrochloride (8) (0·4 g, 12%) was subsequently isolated by using dry hydrogen chloride in ether. The melting characteristics differed slightly from those of the previous sample, but i.r. correlations confirmed identity (melting commenced at 166°; resolidification as before; charring occurred at *ca.* 360°).

Phenolic and acidic materials were next extracted with 40% sodium hydroxide solution; acidification and extraction (ether) gave a red oil containing ketone (6). Isolated by chromatography on Florisil, ketone (6) (0·87 g, 21%) was obtained as yellow prisms, m.p. and mixed m.p. 75—77°.

The final ether solution gave 2-methylxanthone (10) (1·5 g), m.p. 113—117°, which crystallized from hexane as prisms (1·1 g, 40%), m.p. 120—121°.

2′-Fluoro-2-hydroxy-5-methylbenzophenone (7) *and* 2-*Methylxanthone* (10).—(i) Application of a standard procedure [8] to 2-fluorobenzoyl chloride [from the acid (10 g, 0·072 mol)] and 4-cresol (14·3 g, 0·15 mol) gave a brown solid; crystallization from ethanol and then from pentane gave *4-tolyl 2-fluorobenzoate* (11·9 g, 73%), m.p. 35—36° (from pentane) (Found: C, 73·5; H, 4·9; F, 8·6. $C_{14}H_{11}FO_2$ requires C, 73·0; H, 4·8; F, 8·3%).

A mixture of the ester (11 g, 0·045 mol) and aluminium chloride (8·5 g, 0·064 mol) was heated (oil-bath) till the internal temperature reached 120°. The temperature was slowly raised to 140°; an exothermic reaction then occurred which carried the temperature to 160°. After 10 min, the mixture was cooled and the resulting yellow foam was stirred into crushed ice and concentrated hydrochloric acid (25 ml). Extraction with ether, washing, drying, and evaporation gave the isomeric *2′-fluoro-2-hydroxy-5-methylbenzophenone* (7), which crystallized from hexane as yellow prisms (4·0 g, 36%), m.p. 72—73° (Found: C, 72·9; H, 4·8; F, 8·3%).

(ii) Ketone (7) (3·0 g, 0·013 mol) was treated with a solution of potassamide [from potassium (1·6 g, 0·041 g atom)] in liquid ammonia (300 ml) for 4 h, after which ammonium chloride (5 g) and ether were added. Extraction with 2M-hydrochloric acid removed only a trace of material. Extraction with 40% sodium hydroxide solution resulted in incomplete separation, and the ketone (7) (1·5 g, 50%), m.p. and mixed m.p. 69—70°, and 2-methylxanthone (10) (0·8 g, 58%), m.p. and mixed m.p. 121—123°, were separated by chromatography on Florisil. Final elutions gave tarry material (total 0·3 g).

3′-Bromo-2-hydroxy-5-methylbenzophenone (11) *and* 2-*Methylxanthone* (10).—(i) A solution of 3-bromobenzoyl chloride [from the acid (6·3 g, 0·03 mol)] and 4-methoxytoluene (3·66 g, 0·034 mol) in carbon disulphide (10 ml) was added gradually to a stirred suspension of aluminium chloride (10 g, 0·076 mol) in carbon disulphide (20 ml). After 1 h under reflux, the mixture was evaporated and the residue was heated at 150° for 1 h and then cooled. The resulting black solid was powdered and added to 2M-hydrochloric acid, and the mixture was extracted with ether. The ether solution was washed with dilute sodium carbonate solution; acidification of the aqueous phase gave 3-bromobenzoic acid (2 g), m.p. 155° (after crystallization). The ether solution was washed with water, dried, and evaporated. The red-brown oil was extracted with 20% sodium hydroxide solution, insoluble material being discarded. The alkaline extract was acidified and extracted with ether; this ether solution was washed with water, dried, and evaporated and the solid was crystallized from ethanol to give *3′-bromo-2-hydroxy-5-methylbenzophenone* (11) (1·0 g, 20%) as golden needles, m.p. 88—89° (Found: C, 57·7; H, 3·8; Br, 27·9. $C_{14}H_{11}BrO_2$ requires C, 57·7; H, 3·8; Br, 27·5%).

(ii) The foregoing procedure for (5) was applied to ketone (11) (1·0 g, 0·0034 mol) [with potassium (0·4 g, 0·01 g atom) and ammonia (100 ml)] and the foregoing method of separation of fractions was employed. The basic fraction in dry ether was treated with dry hydrogen chloride and the precipitated solid (5 mg) was sublimed *in vacuo* to give *3′-amino-2-hydroxy-5-methylbenzophenone* (15) *hydrochloride* as fine yellow needles, m.p. and mixed m.p. 163—165° (see below). The phenolic fraction afforded starting material (11) (0·39 g, 39%), m.p. and mixed m.p. 86—87°. The neutral fraction afforded 2-methylxanthone (10) (0·27 g, 65%), m.p. and mixed m.p. 121—123°.

3′-Amino-2-hydroxy-5-methylbenzophenone (15) *Hydrochloride; Alternative Preparation.*—(i) A solution of 3nitro-

[7] H. I. Hall and S. G. P. Plant, *J. Chem. Soc.*, 1933, 232.
[8] R. C. Huston and K. R. Robinson, *J. Amer. Chem. Soc.*, 1951, **73**, 2483.

benzoyl chloride [from the acid (10 g, 0·06 mol)] and 4-methoxytoluene (6 g, 0·05 mol) in carbon disulphide (30 ml) was added gradually to a stirred suspension of aluminium chloride (5 g, 0·038 mol) in carbon disulphide (20 ml). After 2 h at room temperature, the mixture was evaporated. The residue was heated at 140° for 30 min, cooled, and digested with 40% sodium hydroxide solution at 80°. Tar was discarded; the clear solution was acidified and the product collected by means of ether. Crystallization from aqueous ethanol gave ketone (14) as yellow leaflets (2·0 g, 11%), m.p. 98—100° (lit.,[9] 104—105°).

(ii) Aqueous ammonia (*d* 0·88) was added in portions with vigorous shaking to a mixture of ketone (14) (0·5 g), iron(II) sulphate (20 g), water (200 ml), and ethanol (50 ml) at 80—85°. When the black mass was permanently alkaline, the mixture was boiled for 5 min and filtered. The residue was washed thoroughly with boiling ethanol and the combined extracts were extracted with ether. The bases were concentrated by extracting the ether solution with 2M-hydrochloric acid, basifying, and extracting with ether; the final extract was dried and treated with dry hydrogen chloride. The precipitated solid (0·17 g, 33%) was crystallized from 2M-hydrochloric acid and then sublimed *in vacuo* to give 3′-amino-2-hydroxy-5-methylbenzophenone (15) hydrochloride, m.p. 165—167° (Found: C, 64·1; H, 5·7; N, 5·2. $C_{14}H_{14}ClNO_2$ requires C, 63·7; H, 5·3; N, 5·3%).

3′-Chloro-2-hydroxy-5-methylbenzophenone (12) *and 2-Methylxanthone* (10).—Ketone (12) (4·5 g, 0·018 mol) [prepared by a known method;[8] m.p. 70—71·5° (lit.,[8] 70·5—71·5°)] was treated with a solution of potassamide [from potassium (2·2 g, 0·056 g atom)] in liquid ammonia (300 ml) for 4 h, after which ammonium chloride (5 g) and ether were added. The normal separation procedure was followed: 40% sodium hydroxide solution was used for extraction of phenolic and acidic materials. 3′-Amino-2-hydroxy-5-methylbenzophenone hydrochloride (15) (0·77 g, 20%), after crystallization from 2M-hydrochloric acid and sublimation *in vacuo*, was obtained as yellow prisms, m.p. 163—166°. The separation of phenolic and acidic products from neutral material was incomplete (t.l.c.), and each fraction was chromatographed on Florisil to give eventually ketone (12) (1·15 g, 22%), m.p. and mixed m.p. 69—71°, and 2-methylxanthone (10) (1·0 g, 34%), m.p. and mixed m.p. 122—123°. Final elutions gave tarry material (total 0·95 g).

3′-Fluoro-2-hydroxy-5-methylbenzophenone (13).—(*a*) 3-Fluorobenzoyl chloride [from the acid (5·0 g, 0·036 mol)] and 4-cresol (7·15 g, 0·076 mol), treated as before, gave *4-tolyl 3-fluorobenzoate*, which crystallized from methanol as needles (5·5 g, 67%), m.p. 40—43°. Sublimation *in vacuo* gave a sample of m.p. 40·5—41·5° (Found: C, 73·2; H, 4·8; F, 8·5%).

Attempted Fries rearrangement of the ester was unsuccessful; the oily reaction mixtures contained much starting material (t.l.c. and i.r. spectrum).

(*b*) A solution of 3-fluorobenzoyl chloride [from the acid (12·5 g, 0·09 mol)] and 4-methoxytoluene (10·5 g, 0·086 mol) in methylene chloride (50 ml) was added during 20 min to a stirred suspension of aluminium chloride (11·43 g, 0·086 mol) in methylene chloride (50 ml). After 2·5 h, the solvent was evaporated off and the residue was heated at 150° for 1·5 h and then cooled. The resulting golden foam was powdered and added to crushed ice and concentrated hydrochloric acid (150 ml), and the mixture was extracted with ether. The ether solution was washed with aqueous sodium hydrogen carbonate solution; acidification of the aqueous phase gave 3-fluorobenzoic acid (0·2 g), m.p. and mixed m.p. 120—122°. The ether solution was then shaken with 40% sodium hydroxide solution. The precipitated sodium salt was collected and decomposed with 2M-hydrochloric acid; extraction with ether then gave crude *3′-fluoro-2-hydroxy-5-methylbenzophenone* (13) (13·8 g, 70%) as a pale yellow oil. The ketone was purified by reconversion into the sodium salt, which was crystallized (acetonitrile) and decomposed with 2M-hydrochloric acid; extraction with ether and distillation gave the pure (t.l.c.) benzophenone (13) (4·13 g) as a pale yellow oil, b.p. 70—74° at 15 mmHg, $n_D^{27\cdot4}$ 1·5946, which slowly crystallized as yellow prisms, m.p. 31—34° (Found: C, 73·2; H, 4·8; F, 8·3%).

Treatment of the sodium salt with bromine in aqueous potassium bromide solution gave *3-bromo-3′-fluoro-2-hydroxy-5-methylbenzophenone*, which crystallized from ethanol as pale yellow needles, m.p. 130—131° (Found: C, 54·4; H, 3·3; Br, 26·2; F, 5·4. $C_{14}H_{10}BrFO_2$ requires C, 54·4; H, 3·2; Br, 25·9; F, 6·2%).

Ketone (13) (2 g) in tetrahydrofuran was treated with potassamide in ammonia in the normal way. The bulk of the ketone was subsequently recovered *via* the sodium salt and isolated as the bromo-derivative (2·2 g, 82%), m.p. 129—131°; a small amount (0·1 g) was recovered from other fractions (t.l.c. and i.r. spectrum). No evidence (t.l.c.) was obtained for presence of 2-methylxanthone.

Attempted Preparation of 2′-Chloro-5-methyl-2-methylthiobenzophenone (9); *2-Methylthioxanthen-9-one* (17).—(*a*) A mixture of 2-chlorobenzoyl chloride [from the acid (12·7 g, 0·085 mol)], 4-thiocresol (10 g, 0·08 mol), and 10% sodium hydroxide solution (150 ml) was shaken for 45 min. The solid (18·0 g, 85%) was filtered off, washed with water, dried, and crystallized from ethanol to give *S-4-tolyl 2-chlorothiobenzoate*, m.p. 92·5—94·5° (Found: C, 64·0; H, 4·2; Cl, 13·6; S, 12·2. $C_{14}H_{11}ClOS$ requires C, 64·0; H, 4·2; Cl, 13·5; S, 12·2%).

Attempted Fries rearrangement resulted in extensive decomposition.[9]

(*b*) A solution of 2-chlorobenzoyl chloride [from the acid (15·6 g, 0·1 mol)] and 4-methylthiotoluene (12·5 g, 0·09 mol) in carbon disulphide (50 ml) was added during 1 h to a stirred suspension of aluminium chloride (10 g, 0·075 mol) in carbon disulphide (50 ml). After 2 h, the solvent was evaporated off and the residue was heated at 145° for 1 h and then cooled. The red tar was treated with 2M-hydrochloric acid and extracted with ether. The ether solution was washed with aqueous sodium hydrogen carbonate and water, and was then dried and evaporated. The residue was chromatographed on Florisil; elution with chloroform gave 2-methylthioxanthen-9-one (17), which crystallized from ethanol as brown prisms (2·8 g, 17%), m.p. 122—124°, raised by recrystallization to 124—125° (lit.,[10] 123°) (Found: C, 73·5; H, 4·5; S, 14·3. Calc. for $C_{14}H_{10}OS$: C, 74·3; H, 4·4; S, 14·2%).

3′-Chloro-5-methyl-2-methylthiobenzophenone (16) *and 2-Methylthioxanthen-9-one* (17).—(i) A solution of 3-chlorobenzoyl chloride [from the acid (15·6 g, 0·01 mol)] and 4-methylthiotoluene (10 g, 0·073 mol) in carbon disulphide

[9] G. S. Saharia and B. R. Sharma, *J. Indian Chem. Soc.*, 1956, **33**, 788; D. S. Tarbell and A. H. Herz, *J. Amer. Chem. Soc.*, 1953, **75**, 1668.

[10] F. Mayer, *Ber.*, 1910, **43**, 584.

(50 ml) was added during 15 min to a stirred suspension of aluminium chloride (10·9 g, 0·082 mol) in carbon disulphide (50 ml). After 2 h, the mixture was poured onto crushed ice and concentrated hydrochloric acid (100 ml). The organic phase was separated and the aqueous phase was extracted with ether. The organic phases were combined, washed with sodium hydrogen carbonate solution and water, dried, and evaporated. The residual oil was chromatographed on Florisil with ether–pentane (1 : 9) and finally ether as eluant; the chromatography was monitored by t.l.c. First eluted was 4-methylthiotoluene, followed by the major fraction which was collected and distilled to yield *3′-chloro-5-methyl-2-methylthiobenzophenone* (16) (5 g, 26%), b.p. 85—90° at 15 mmHg, as an oil which slowly crystallized. Crystallization from methanol gave yellow prisms, m.p. 46·5—47·5° (Found: C, 64·9; H, 4·8; Cl, 12·8; S, 11·6. $C_{15}H_{13}ClOS$ requires C, 65·1; H, 4·7; Cl, 12·8; S, 11·6%).

(ii) Ketone (16) (1·38 g, 0·005 mol) was treated with a solution of potassamide [from potassium (0·6 g, 0·015 g atom)] in liquid ammonia (200 ml) for 4 h. Ammonium chloride (2·5 g) and ether were added and the mixture was separated into basic, acidic, and neutral fractions in the usual way. The basic fraction (0·2 g) was a brown oil which contained three components (t.l.c.); no solid hydrochloride could be obtained. The acidic fraction was negligible (3 mg). The neutral fraction (1·13 g) was chromatographed on Florisil; elution with chloroform gave 2-methylthioxanthen-9-one (17) (0·2 g, 17%) as pale yellow prisms, m.p. and mixed m.p. 123—124°. Further elution gave tars (0·9 g).

We thank Professor R. F. Smith (Geneseo) for advice on acylation procedures for thioanisole.

[4/1431 *Received*, 15*th July*, 1974]