Synthesis of 9-Oxoxanthen-2-carboxylic Acids

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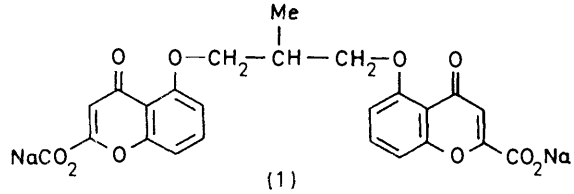
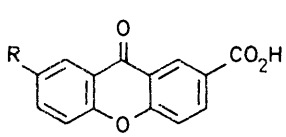
7-Substituted 9-oxoxanthen-2-carboxylic acids can be prepared in good yield from hydroxylated benzophenones. Oxidative coupling of 4-hydroxy-3-(3-hydroxybenzoyl)benzoic acid using potassium ferricyanide gave 7-hydroxy-9-oxoxanthen-2-carboxylic acid (8: R = H). Cyclisation of 3-(5-chloro-2-methoxybenzoyl)-4-hydroxybenzoic acid took place in alkaline solution to give 7-chloro-9-oxoxanthen-2-carboxylic acid. Both these ring closure reactions when carried out in potassium hydrogen carbonate or in potassium hydroxide solutions respectively gave the conveniently isolated insoluble potassium salt of the 9-oxoxanthen-2-carboxylic acid.

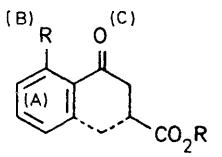
THE success of sodium chromoglycate (1) in the treatment of certain types of bronchial asthma [1] and the recognition that the structural requirements for activity in this field may involve the grouping O–C=C–C=O [2] has led to a spate of investigations into compounds containing this and related structural features. One of the first of the new types of compounds found to possess anti-allergic activity were 9-oxoxanthen-2-carboxylic acids [3] (2)



(1)



(2)



(3) (D)

and this type of compound has been much modified to give enhanced activity.[4-8] Activity has also been found in tetrahydroxanthones [9] and tetrazol-2-yl-substituted xanthones.[10] The observation that oxo-anthracene- [11] and -acridine-2-carboxylic acids [12,13] also possess anti-allergic activity suggests that the original structural requirement (above) could usefully be modified to include the structural features present in these latter types of compounds. In 1975 the more general structural requirement (3) was proposed to account for activity in oxanilic acids; [14] four active centres were related to each other, (A) an aromatic ring containing a substituent preferably OMe (B) *peri* to a carbonyl function (C), and an acid or its derivative located at (D). This structural requirement can be used to account for the activity found in 2-carboxy-benzopyrones,[15] -xanthones,[3] -anthrones,[11] and -acridones.[12,13]

The synthesis of 9-oxoxanthen-2-carboxylic acids has been extensively reported in patents abstracted by *Chemical Abstracts*. In all cases the method has involved prior formation of the diphenyl ether by Ullman condensation of a halogenobenzene with the appropriate phenol, a reaction well known for its 'unpractical' yields. The resulting 2-carboxydiphenyl ether is consequently cyclised to the xanthone.

Our previously described biomimetic synthesis of 2-hydroxyxanthones [16,17] has been extended to give 7-hydroxy-9-oxoxanthen-2-carboxylic acids.[16,17] The synthesis of 4-hydroxy-3-(3-hydroxybenzoyl)benzoic acid was carried out † to assess the viability of its cyclisation under oxidative conditions. Condensation of 3-methoxybenzoyl chloride with methyl 4-hydroxyben-

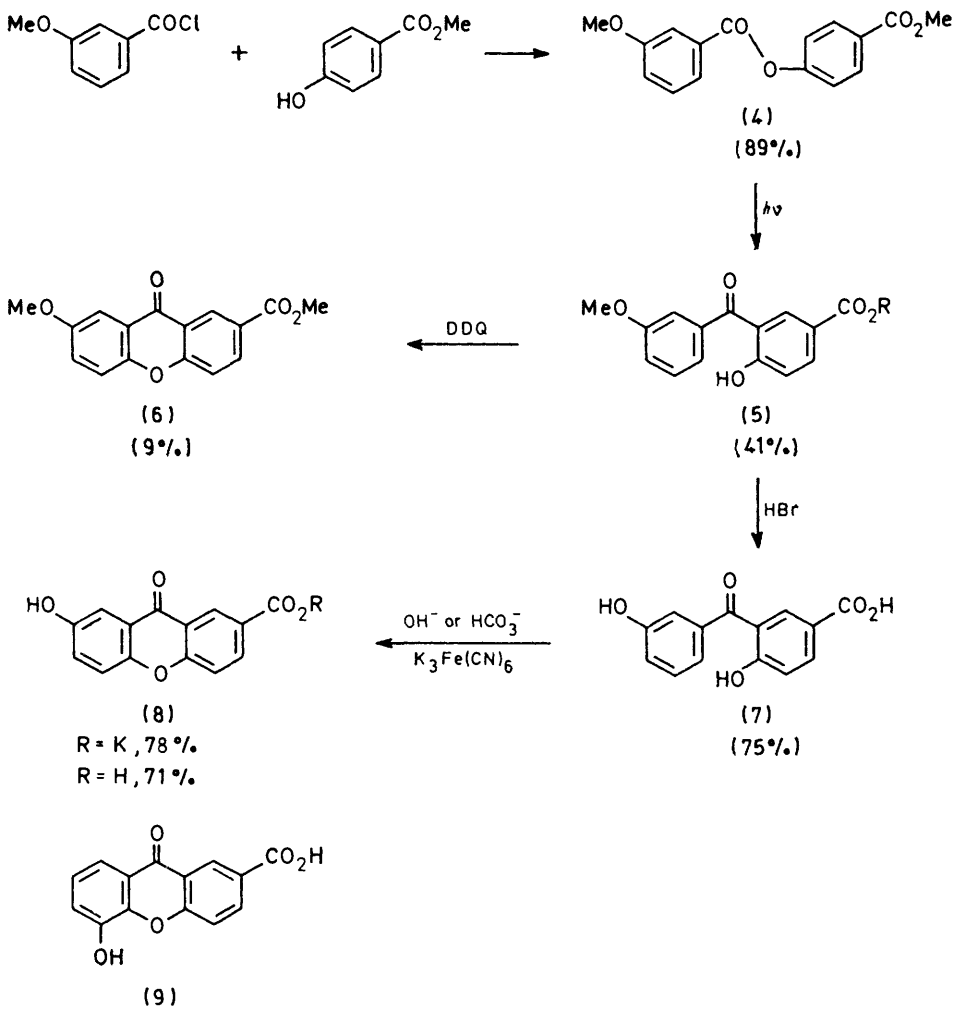
† The synthesis of phenolic benzophenones can be achieved by direct condensation of the benzoic acid with a phenolic substrate usually in polyphosphoric acid or trifluoroacetic anhydride,[18] by Friedel-Crafts condensation of an acid [19] or acid chloride with a phenol,[20] or by Fries rearrangement of the ester.[21] Our preliminary experiments indicated that the last approach gives maximum yields of the required benzophenone.

[1] J. S. G. Cox, *Nature*, 1967, **216**, 1328.
[2] H. Cairns, C. Fitzmaurice, D. Hunter, P. B. Johnson, J. King, T. B. Lee, G. H. Lord, R. Minshull, and J. S. G. Cox, *J. Medicin. Chem.*, 1972, **15**, 583.
[3] J. R. Pfister, K. W. Ferraresi, I. T. Harrison, W. H. Rooks, A. P. Roszkowshi, A. Van Horn, and J. H. Fried, *J. Medicin. Chem.*, 1972, **15**, 1032.
[4] J. R. Pfister, I. T. Harrison, and J. H. Fried, U.S.P. 3,821,251 (*Chem. Abs.*, 1974, **81**, 135,956).
[5] J. R. Pfister, I. T. Harrison, and J. H. Fried, Ger. Offen., 2,265,052 (*Chem. Abs.*, 1976, **82**, 135,472).
[6] A. C. Barnes, P. W. Hairsine, P. J. Rainin, and J. B. Taylor, Ger. Offen., 2,530,466 (*Chem. Abs.*, 1976, **84**, 135,473).
[7] J. R. Pfister, I. T. Harrison, and J. H. Fried, U.S.P. 3,988,352 (*Chem. Abs.*, 1977, **86**, 106,387).
[8] L. D. Jones, W. L. Albrecht, N. L. Munro, and K. T. Stewart, *J. Medicin. Chem.*, 1977, **20**, 594.
[9] S. Klutchko, M. van Strandtmann, and J. Shand, jun., U.S.P. 3,862,141 (*Chem. Abs.*, 1975, **82**, 170,675).
[10] E. S. K. Assem, *Proc. Roy. Soc. Medicin.*, 1973, **66**, 1191 (*Chem. Abs.*, 1974, **80**, 128,407).
[11] J. R. Pfister, U.S.P. 3,835,167 (*Chem. Abs.*, 1975, **82**, 16,617).
[12] J. R. Pfister, I. T. Harrison, and J. H. Fried, U.S.P. 3,835,139 (*Chem. Abs.*, 1975, **82**, 16,711).
[13] J. R. Pfister, I. T. Harrison, and J. H. Fried, U.S.P. 3,886,162 (*Chem. Abs.*, 1975, **83**, 131486).
[14] J. H. Sellstedt, C. J. Guinosso, A. J. Begany, S. C. Bell, and M. Rosenthale, *J. Medicin. Chem.*, 1975, **18**, 926.
[15] G. Doria, P. N. Girandi, F. Lauria, M. L. Corno, P. Sberze, and M. Tibolla, Ger. Offen., 2,461,670 (*Chem. Abs.*, 1975, **83**, 178827).
[16] J. R. Lewis and B. H. Warrington, *J. Chem. Soc.*, 1964, 5074.
[17] J. A. Atkinson and J. R. Lewis, *J. Chem. Soc.* (*C*), 1969, 281.
[18] T. R. Kasturi and K. M. Dausodaran, *Canad. J. Chem.*, 1969, **47**, 1529.
[19] D. Taub, C. H. Kuo, and N. L. Wendler, *Chem. and Ind.*, 1962, 557.
[20] A. C. Day, J. Nabney, and A. I. Scott, *J. Chem. Soc.*, 1961, 4067.
[21] D. Taub, C. H. Kuo, H. L. Slates, and N. L. Wendler, *Tetrahedron*, 1963, **19**, 1.

zoate gave the ester (4) in 89% yield. Photochemical Fries rearrangement of this ester in benzene gave the acidic benzophenone (5; R = H) in 41% yield or in dioxan the methyl ester (5; R = Me) in 34% yield. Conversion of the benzophenone (5; R = Me) to xanthone (6) was attempted using DDQ as oxidising agent as it had been reported that hydroxybenzophenones were easily oxidised to 2-hydroxyxanthones [22] and Scheme 1 outlines the reaction pathways. The overall yield in this Scheme was *ca.* 21%.

It is interesting to note that in these oxidative coupling experiments (Scheme 1) no cyclisation occurred *ortho* to the activating group, to give (9) although this direction of cyclisation has been observed in other cases.[16,17]

The second route to 9-oxoxanthen-2-carboxylic



SCHEME 1 Overall yield 21%

methoxybenzophenones were converted to 2-methoxyxanthones.[23] After prolonged reaction (5; R = Me) was converted into (6) but in low yield (9%). Scheme 1 outlines this sequence. Demethylation of the benzophenone (5; R = H) gave the dihydroxy-acid (7) which on treatment with potassium ferricyanide in alkaline solution was converted into 7-hydroxy-9-oxoxanthen-2-carboxylic acid (8; R = H) in excellent yield (71%). When the oxidative coupling reaction was carried out in potassium hydroxide the 9-oxoxanthen-2-carboxylic acid precipitated as its potassium salt (8; R = K).

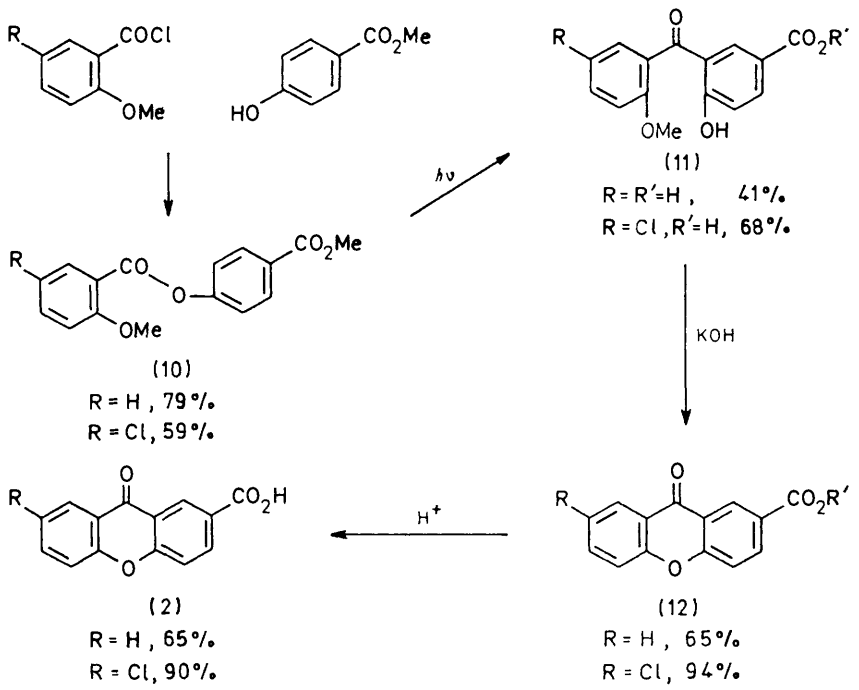
[22] R. C. Ellis, W. B. Whalley, and K. Ball, *Chem. Comm.*, 1967, 803.

acid involved intramolecular cyclisation of 2-hydroxy-2'-methoxybenzophenones with concomitant loss of methanol. For our first example 2-methoxybenzoyl chloride was condensed with methyl 4-hydroxybenzoate to give the ester (10; R = H) which on photoFries rearrangement gave 4-hydroxy-3-(2-methoxybenzoyl)-benzoic acid (11; R = R' = H). Treatment of this benzophenone with aqueous potassium hydroxide gave the easily isolated and insoluble potassium salt of 9-oxoxanthen-2-carboxylic acid (12; R = H) in overall yield 21%. When the reaction sequence was repeated

[23] J. W. A. Findlay, P. Gupta, and J. R. Lewis, *J. Chem. Soc.* (*C*), 1969, 2761.

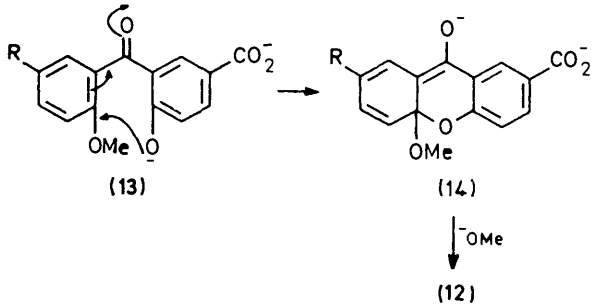
starting with 5-chloro-2-methoxybenzoyl chloride, 7-chloro-9-oxoxanthen-2-carboxylic acid was obtained (as the potassium salt) in 38% overall yield. Scheme 2 indicates the relevant steps in this synthesis.

A simplified method for the synthesis of 7-chloro-9-oxoxanthen-2-carboxylic acid involved the photochemical Fries reaction on ester (10; R = Cl) followed by direct extraction of the phenolic products from the



SCHEME 2 Overall yield for R = H 21%, for R = Cl 38%

In the cyclisation reactions involving the elimination of methanol (Scheme 2) the previously reported intramolecular nucleophilic displacement of a methoxy-group from a 2-amino-2'-methoxybenzophenone resulting in acridone formation gives a possible explanation as to the mechanism of cyclisation [24] whereby the anion (13)



is capable of attacking the neighbouring ring, through participation of the carbonyl group [as in (13) → (12)] with subsequent loss of methoxide to give the product (12).

Of a practical development is the observation that in the presence of potassium ions the 9-oxoxanthen-2-carboxylic acids can be easily isolated as their insoluble salts, the overall yields being in the region of 21—38%.

[24] J. H. Adams, P. Gupta, M. S. Khan, and J. R. Lewis, *J. Chem. Soc.* (*C*), 1976, 2089.
[25] A. A. Goldberg and A. W. Wragg, *J. Chem. Soc.*, 1958, 4227.

photolysed solution and *in situ* cyclisation of them to the potassium salt of the xanthone (12; R = Cl). The yield from the sequence was 40%.

7-Chloro-9-oxoxanthen-2-carboxylic acid can be converted into the appropriate 7-oxygenated derivatives by analogy to published methods [25] or upon treatment with sodium methanethiolate to 7-methylthio-9-oxoxanthen-2-carboxylic acid (2; R = SMe).[26]

EXPERIMENTAL

All irradiation experiments were carried out with a medium pressure u.v. lamp in a quartz reaction vessel. Satisfactory elemental analyses were obtained for new compounds.

3-Methoxybenzoyl Chloride.—3-Methoxybenzoic acid (25 g) was dissolved in dry benzene (200 ml) and treated with PCl_5 (42 g) under reflux for 1 h. The solution was cooled and evaporated to dryness and excess of $POCl_3$ removed on an oil pump. The residue was distilled at 66° and 0.15 mmHg to give the acid chloride as an oil (17.7 g, 70%) and was used as such for subsequent reactions.

Methyl 4-Hydroxybenzoate.—4-Hydroxybenzoic acid (20 g) was esterified with methanol (300 ml) and concentrated sulphuric acid (10 ml) to give the ester (19.0 g) which crystallised from aqueous ethanol, m.p. 125—126° (17.4 g, 79%) (lit.,[27] 131°), $\lambda_{max.}$ (MeOH) 210 (log ε 3.90) and 257 nm (4.01), $\nu_{max.}$ (KBr) 3 300 (OH) and 1 680 cm^{-1} (CO), δ($CDCl_3$)

[26] J. R. Pfister, I. T. Harrison, and J. H. Friend, Ger. Offen., 2,234,251 (*Chem. Abs.*, 1974, **80**, 27,104).
[27] N. V. Sidgwick and N. S. Baylis, *J. Chem. Soc.*, 1930, 2027.

3.90 (3 H, s, CO_2Me), 6.55 (1 H, s, OH), and 6.82—8.04 (4 H, q, ArH).

Methyl 4-(3-*Methoxybenzoyloxy*)*benzoate* (4).—3-Methoxybenzoyl chloride (10.3 g) was added to methyl 4-hydroxybenzoate (9.2 g) in dry acetone (300 ml) containing anhydrous K_2CO_3 (20 g) and the mixture refluxed for 2 h. The acetone was removed under reduced pressure and the remaining solid extracted with ethyl acetate (100 ml) which was subsequently washed with NaOH and water, dried, and evaporated to give a solid (16.35 g). This solid was crystallised from aqueous ethanol to give the *ester* (15.3 g, 89%), m.p. 99—100°, $\lambda_{max.}$ (MeOH) 214 (log ε 4.41), 243 (4.29), and 303 nm (3.48), $\nu_{max.}$ (KBr) 1 735 (ester CO) and 1 725 cm^{-1} (phenyl ester CO), δ($CDCl_3$) 3.86 (3 H, s, OMe), 3.91 (3 H, s, CO_2Me), and 7.20—8.30 (8 H, m, ArH), *m/e* 286(89%), 285(63), 271(5), 256(13), 255(100), 227(25), 189(45), 147(20), 139(4), 136(10), and 135(25).

4-*Hydroxy*-3-(3-*methoxybenzoyl*)*benzoic Acid* (5; R = H) *and Methyl Ester* (5; R = Me).—The ester (4) (1.4 g) was dissolved in AnalaR dioxan (500 ml) in a quartz reactor and the solution irradiated with a medium pressure mercury lamp for 6 h. The solution was extracted with NaOH (2M; 5 × 50 ml) and the extract acidified followed by extraction with ethyl acetate; subsequent extraction of the organic layer with $NaHCO_3$, followed by drying and evaporation gave the crude ester (0.7 g) (5; R = Me). Crystallisation from ether gave the pure *ester* (0.55 g, 34%), m.p. 98—99°, $\lambda_{max.}$ (MeOH) 236 (log ε 4.46) and 325 nm (3.69), $\nu_{max.}$ (KBr) 1 735 (CO_2Me) and 1 635 cm^{-1} (OH bonded CO), δ($CDCl_3$) 3.87 (6 H, s, 20Me), 7.03—8.45 (7 H, m, ArH), and 12.35 (1 H, s, OH), *m/e* 286(79%), 285(56), 271(6), 255(100), 179(45), 147(18), 135(25), 108(10), 107(13), 92(16), and 77(13). A repeat photolysis of the ester (4) (4.3 g) in AnalaR benzene (500 ml) for 11 h and direct extraction of the solution with $NaHCO_3$ solution followed by isolation of the acidic component gave a crude product (2.5 g). Crystallisation from ethyl acetate gave the pure *acid* (5; R = H) (1.7 g, 41%), m.p. 214—217°, $\lambda_{max.}$ (MeOH) 236 (log ε 4.37) and 325 nm (3.66), $\nu_{max.}$ (KBr) 1 690 (COOH) and 1 625 cm^{-1} (OH bonded CO), δ[$^2H_6$]-(DMSO) 3.78 (3 H, s, OMe) and 6.9—8.1 (7 H, m, ArH), *m/e* 272(100%), 271(50), 257(5), 255(5), 242(9), 241(79), 165(45), 135(32), 108(13), 107(16), 92(13), and 77(14).

DDQ Oxidation of (5; R = Me).—The benzophenone (45 mg) was dissolved in dioxan (3 ml), DDQ (50 mg) dissolved in dioxan (3 ml) added, and the mixture heated on a steam-bath for 72 h. T.l.c. examination of the reaction media showed mostly starting material together with a trace of a fluorescent blue product. Isolation of this product by preparative t.l.c. gave a brown oil (5 mg, 9%) which eventually crystallised from methanol. Accurate mass measurement gave 284.068 5 and indicated it to be the xanthone (6), *m/e* 284(100%), 283(11), 269(37), 254(13), 253(50), 225(11), 213(5), 183(8), 154(4), and 126(6). T.l.c. behaviour compared favourably with that of the authentic xanthone, m.p. 280—281° (lit.,[28] 297—297.5°).

4-*Hydroxy*-3-(3-*hydroxybenzoyl*)*benzoic Acid* (7).—The methoxy acid (5; R = H) (821 mg) was dissolved in glacial HOAc (30 ml) and refluxed with HBr (60%; 15 ml) for 6 h whence the solution was cooled, diluted with water, and extracted with ethyl acetate (2 × 50 ml). The organic layer was washed with $NaHCO_3$, water, dried, and evaporated to give a solid (636 mg) which crystallised from aqueous methanol as the *hydroxy-acid* (7) (587 mg, 75%), m.p. 256—260° (sublim.), $\lambda_{max.}$ (MeOH) 238 (log ε 4.52) and 327 nm (3.66), $\nu_{max.}$ (KBr) 1 680 (CO_2H) and 1 625 cm^{-1} (OH-bonded CO), δ(CD_3OD) 7.0—7.5 (5 H, complex, ArH), 8.10 (1 H, q, *J* 2 and 8 Hz, H-4), 8.25 (1 H, d, *J* 2 Hz, H-2), *m/e* 258(100%), 257(79), 256(14), 255(10), 242(10), 241(89), 239(11), 213(6), 166(6), 165(94), 164(14), 121(71), 120(11), and 92(32).

Oxidation of Hydroxy-acid (7).—(a) $K_3Fe(CN)_6$ *in aqueous sodium hydroxide*. The benzophenone (7) (106 mg) was dissolved in NaOH (25 ml, 2M) containing $K_3Fe(CN)_6$ (532 mg) and the solution stirred at room temperature for 1 h. The solution was acidified with dilute HCl and extracted with ethyl acetate (100 ml) to give after the usual work-up, a yellow solid (95 mg) which crystallised from acetone as 7-hydroxy-9-oxoxanthen-2-carboxylic acid (8) (75 mg, 71%), m.p. >310° (lit.,[28] >300°). No isomeric 5-hydroxy-9-oxoxanthen-2-carboxylic acid (9) could be detected.

(b) $K_3Fe(CN)_6$ *in aqueous potassium hydrogen carbonate*. The benzophenone (7) (101 mg) was dissolved in $KHCO_3$ solution (15 ml, 2M) containing $K_3Fe(CN)_6$ (1.03 g); after 10 min a solid gradually formed, after a further 2 h the solid (88 mg) was filtered off and acidified with dilute HCl, taken up in ethyl acetate, and isolated in the usual way to give the xanthone (8) (61 mg, 61%). The oxidation media on acidification and extraction with ethyl acetate yielded a further quantity of xanthone (8) (17 mg, 17%), total yield 78%

Methyl 4-(2-*Methoxybenzoyloxy*)*benzoate* (10; R = H).—2-Methoxybenzoyl chloride (3.7 g, prepared from the acid and distilled at 76—77° and 0.1 mmHg) was dissolved in dry acetone (150 ml), methyl 4-hydroxybenzoate (3.38 g) and anhydrous K_2CO_3 (7 g) added, and the mixture refluxed for 2 h, cooled, and filtered. The filtrate was evaporated to dryness under reduced pressure and the residue dissolved in ethyl acetate (100 ml) and this solution was washed with NaOH, water, dried, and evaporated to give a solid (5.1 g) which crystallised from ether as the *ester* (11; R = H, R′ = CH_3) (4.88 g, 79%), m.p. 105—107°, $\lambda_{max.}$ (MeOH) 213 (log ε 4.10), 243 (4.23), and 300 nm (3.56), $\nu_{max.}$ (KBr) 1 760 (phenyl ester CO) and 1 725 cm^{-1} (CO_2Me), δ($CDCl_3$) 3.95 (6 H, s, Me) and 6.95—8.20 (8 H, m, ArH), *m/e* 286(0.3%), 285(0.3), 255(0.3), 152(1), 151(1), 136(5), 135(100), 121(1), 120(1), 106(1), and 105(3).

4-*Hydroxy*-3-(2-*methoxybenzoyl*)*benzoic Acid* (11; R = R′ = H).—The ester (10; R = H) (4.3 g) was dissolved in AnalaR benzene (500 ml) and the solution irradiated for 11 h. The mixture was washed with dilute NaOH (3 × 50 ml, 2M) and the alkaline washings acidified with dilute HCl, and extracted with ethyl acetate (100 ml), after washing the organic layer with water and drying evaporation yielded a brown solid (3.1 g) which crystallised from ethyl acetate to give the *acid* (11; R = R′ = H) (1.7 g, 41.5%), m.p. 210—213°, $\lambda_{max.}$ (MeOH) 234 (log ε 4.34) and 328 nm (3.57), $\nu_{max.}$ (KBr) 1 685 (CO_2H) and 1 630 cm^{-1} (OH bonded CO), δ[$^2H_6$](DMSO) 3.72 (3 H, s, OMe) and 7.10—8.20 (7 H, m, ArH), *m/e* 272(14%), 257(11), 241(100), 165(10), 135(25), and 77(16).

Cyclisation of Acid (11; R = R = H).—(a) NaOH. The acid (11; R = R′ = H) (100 mg) was dissolved in NaOH solution (20 ml, 2M) and the solution left at 50° for 3 days. On acidification a precipitate was produced which was extracted into ethyl acetate solution and isolated in the normal way to give a solid (98 mg) which crystallised from

[28] D. E. Bays, Patent Specification 1,312,620, April 1973, (*Chem. Abs.*, 1969, **75**, 98,447).

methanol as 9-oxoxanthen-2-carboxylic acid (2; R = H) (54 mg, 60%), m.p. 303—304° (sublim.) (lit.,[29] 305°), $\lambda_{max.}$ (MeOH) 217 (log ε 3.95), 246 (4.45), 290sh (3.14), and 336 nm (3.64), $\nu_{max.}$ (KBr) 1 700 (CO_2H) and 1 660 cm^{-1} (aryl CO), δ([$^2H_6$]DMSO) 7.30—8.40 (6 H, m, ArH) and 8.63 (1 H, d, *J* 2 Hz, 1-H), *m/e* 240(100%), 233(45), 196(11), 195(14), 168(4), 167(3), and 159(32).

(b) KOH. A repeat reaction of the acid (202 mg) in KOH solution (40 ml, 2M) at 100° for 3 h gave a precipitate, the solution was cooled, the precipitate filtered off and dissolved in hot water, acidified with dilute HCl, and extracted into ethyl acetate whence work-up in the usual way gave 9-oxoxanthen-2-carboxylic acid (2; R = H) (116 mg, 65%) which crystallised from methanol to give the xanthone (92 mg), m.p. and mixed m.p. 303—304° (sublim.).

(c) NaH. Treatment of the acid (99 mg) with NaH (76 mg, 60%) in DMSO (5 ml) at 50° for 3 days followed by acidification of the solution with dilute HCl and extraction with ethyl acetate (30 ml) gave in the usual way a solid (82 mg) which crystallised from methanol to give 9-oxoxanthen-2-carboxylic acid (59 mg, 68%).

5-Chloro-2-methoxybenzoyl Chloride.—The chloro-acid was prepared from 2-methoxybenzoic acid by chlorination in acetic acid to give the product, m.p. 70—72° (lit.,[30] 72—74°), which upon treatment with PCl_5 gave the acid chloride (2.76 g) which was carefully evacuated under reduced pressure to remove $POCl_3$. This acid chloride was used without further purification.

Methyl 4-(5-Chloro-2-methoxybenzoyloxy)benzoate (10; R = Cl).—The crude acid chloride (2.76 g) was dissolved in dry acetone (50 ml) containing methyl 4-hydroxybenzoate (2.05 g) and anhydrous $KHCO_3$ (5 g) and the mixture refluxed for 1 h. The solution was filtered and the filtrate evaporated to dryness to give an oil which was redissolved in ether and the ethereal solution washed with NaOH solution, water, dried ($MgSO_4$), and evaporated to leave an oil (3.3 g) which crystallised from methanol to give the *ester* (10; R = Cl) (2.8 g, 59%), m.p. 87—89°, $\lambda_{max.}$ (MeOH) 211 (log ε 3.67), 234 (3.50), and 313 nm (2.81), $\nu_{max.}$ (KBr) 1 750 (CO_2Me) and 1 720 cm^{-1} (phenyl ester), δ($CDCl_3$) 3.90 (6 H, s, CO_2Me, OMe), 7.95 (1 H, d, *J* 2 Hz, 6-H), 7.30 (2 H, d, *J* 8 Hz, 2'- and 6'-H), 7.46 (1 H, dd, *J* 2 and 8 Hz, 4'-H), 6.95 (1 H, d, *J* 8 Hz, 3-H), 8.1 (2 H, d, *J* 8 Hz, 3'- and 5'-H), *m/e* 320(5), 288(1), 171(22), 170(4), 169(100), 126(6), and 111(6).

3-(5-Chloro-2-methoxybenzoyl)-4-hydroxybenzoic Acid (11; R = Cl, R' = H).—The ester (10; R = Cl) (3.6 g) was dissolved in AnalaR benzene (600 ml) and irradiated for 9 h in the presence of nitrogen. The solution was evaporated to dryness under reduced pressure, the residue dissolved in ether (200 ml), and this solution extracted with $NaHCO_3$ (3 × 50 ml, 3M) followed by NaOH (5 × 50 ml, 3M); the residual ethereal layer was washed with water, dried, and evaporated to give starting material (850 mg). Both the $NaHCO_3$ and NaOH extracts upon acidification yielded the *acid* (11; R = Cl, R' = H) (total yield 2.46 g, 68%), which crystallised from methanol, m.p. 220—222° (sublim. at 234°), $\lambda_{max.}$ (MeOH) 205 (log ε 4.18), 229 (4.48), 260sh (3.99), and 337 nm (3.56), $\nu_{max.}$ (KBr) 3 400 (OH), 1 687 (ester CO), and 1 620 cm^{-1} (bonded CO), δ([$^2H_6$]acetone) 3.80 (3 H, s, OMe), 7.10 (1 H, d, *J* 8 Hz, 3-H), 7.24 (1 H, d, *J* 8 Hz, 3'-H), 7.45 (1 H, d, *J* 2 Hz, 6'-H), 7.58 (1 H, dd, *J* 8 and 2 Hz, 4'-H), 8.03 (1 H, d, *J* 2 Hz, 6-H), and 8.16 (1 H, dd, *J* 8 and 2 Hz, 4-H), *m/e* 306(5%), 277(11), 275(100), 171(2), 169(10), 165(13), 142(10), 126(3), and 111(3).

Methyl 3-(5-Chloro-2-methoxybenzoyl)-4-hydroxybenzoate (11; R = Cl, R' = Me).—In a repeat photolysis the ester (10; R = Cl) (1.5 g) was dissolved in AnalaR benzene (500 ml) and irradiated for 11 h, the solution was cooled, concentrated under reduced pressure, and extracted repeatedly with $NaHCO_3$ (10 × 50 ml, 2M) followed by NaOH washing (6 × 20 ml, 4M). The NaOH extract was acidified with dilute HCl and extracted with ether (200 ml) to yield the *ester* (11; R = Cl, R' = Me) (0.66 g) which crystallised from benzene–light petroleum (b.p. 40—60°), m.p. 109—110°, $\lambda_{max.}$ (MeOH) 205 (log ε 3.20), 231 (3.49), 259sh (3.07), and 329 nm (2.60), $\nu_{max.}$ (KBr) 1 730 (CO_2Me) and 1 635 cm^{-1} (CO), δ($CDCl_3$) 3.74 (3 H, s, OMe or CO_2Me), 3.84 (3 H, s, OMe or CO_2Me), 6.96 (1 H, d, *J* 8 Hz, 3-H), 7.06 (1 H, d, *J* 8 Hz, 3'-H), 7.28 (1 H, d, *J* 2 Hz, 6-H), 7.46 (1 H, dd, *J* 2 and 8 Hz, 4-H), 8.02 (1 H, d, *J* 2 Hz, 6'-H), 8.11 (1 H, dd, *J* 2 and 8 Hz, 4'-H), and 12.36 (1 H, s, OH), *m/e* 322(2), 320(9), 291(22), 289(100), 179(13), 171(3), 169(13), 147(13), and 142(16).

Cyclisation of Acid (11; R = Cl, R' = H).—The foregoing acid (0.59 g) was dissolved in aqueous KOH (20 ml, 2M) and heated in a steam-bath for 10 min, the solution was cooled, and the precipitate filtered off (0.52 g, 91%). This solid was acidified and extracted with ethyl acetate to give after washing and evaporation 7-chloro-9-oxoxanthen-2-carboxylic acid (0.45 g, 90%), m.p. >300°, recrystallisation from ethyl acetate gave m.p. >320° (lit.,[28] 349.5°), $\lambda_{max.}$ (MeOH) 209 (log ε 4.32), 248 (4.98), 283sh (3.52), 297 (3.44), 330sh (3.69), and 346 nm (3.74), $\nu_{max.}$ (KBr) 3 420 (OH), 1 685 (COOH), and 1 660 cm^{-1} (CO), δ([$^2H_6$]DMSO) 7.68br (1 H, s, 4-H), 7.78br (1 H, s, 5-H), 7.87 (1 H, d, *J* 2 Hz, 6-H), 8.09 (1 H, d, *J* 2 Hz, 8-H), 8.32 (1 H, dd, *J* 8 and 2 Hz, 3-H), and 8.67 (1 H, d, *J* 2 Hz, 1-H), *m/e* 274(100%), 259(6), 257(25), 230(6), and 173(8).

Direct Cyclisation of Phenolic Products from Fries Rearrangement.—The ester (10; R = Cl) (1.5 g) was dissolved in AnalaR benzene (500 ml) and the solution irradiated for 11 h; after cooling the organic layer was washed with KOH (8 × 50 ml, 4M) and the alkaline washings heated to 100° for 1 h. On cooling the potassium salt of 7-chloro-9-oxoxanthen-2-carboxylic acid precipitated (0.63 g, 43%) which after acidification and extraction with ethyl acetate gave the xanthone (0.51 g, 40%), m.p. *ca.* 228°. The original basic solution upon acidification and extraction with ethyl acetate gave a further quantity of xanthone (0.25 g, 19%), total yield 0.76 g, 59%. The overall yield of the reactions was 40%.

7-Methylthio-9-oxoxanthen-2-carboxylic Acid (12; R = SMe).—Sodium hydride (300 mg) was dissolved in DMSO (20 ml) and MeSH bubbled through slowly for 10 min whence the chloroxanthone (12; R = Cl) (58 mg) was added and the mixture heated to 100° for 2 h. The reaction was shown to be complete by t.l.c. monitoring and the mixture was poured into water, acidified with dilute HCl, and extracted with ethyl acetate (2 × 50 ml); the organic layer was washed with water, dried, and evaporated to give a yellow solid (35 mg, 43%) which crystallised from acetic acid to give a solid with m.p. 304—310° (sublim.), $\lambda_{max.}$ (MeOH) 211 (log ε 4.41), 230sh (4.40), 251 (4.49), 258 (4.49), 278sh (4.29), and 343 nm (3.49), $\nu_{max.}$ (KBr) 1 680 (carboxy CO) and 1 655 cm^{-1} (CO), δ(CF_3COOD) 2.52 (3 H, s, SMe), 7.5—8.0 (3 H, m ArH), 8.12 (1 H, d, *J* 2 Hz, 8-H),

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8.56 (1 H, dd, J 2 and 8 Hz, 3-H), 9.16 (1 H, d, J 2 Hz, H-1) (Found: M^+, 286.029 60. $C_{15}H_9O_4S$ requires M, 286.029 97), *m/e* 286(100%), 271(20), 253(22), 240(45), and 223(14).

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