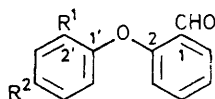


Generation of Xanthenes and Benzoxanthenes from *o*-Aryloxybenzaldehydes by Use of Copper(II) Halides

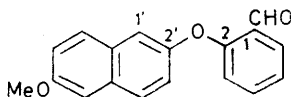
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The reaction of copper(II) halides with *o*-aryloxybenzaldehydes to give xanthenes is shown to be a general one. 2-(6-Methoxy-2-naphthyl)oxy)benzaldehyde undergoes concomitant nuclear bromination to give 4-bromo-3-methoxybenzo[*a*]xanthen-12-one.

RECENTLY we reported¹ that xanthenes are side products in the reaction between salicylaldehydato-copper and aromatic halides and that they may have



- (1) $R^1 = R^2 = H$
- (2) $R^1 = OMe, R^2 = H$
- (3) $R^1 = H, R^2 = OMe$
- (4) $R^1 = H, R^2 = Me$
- (5) $R^1 = H, R^2 = NO_2$



(6)

arisen from the action of copper(II) on the aldehydes formed during the reaction. We now demonstrate that phenoxybenzaldehydes in general react with copper(II) chloride or bromide to give xanthenes.

The aldehydes (1)–(6) were produced by the reaction² between salicylaldehydato-copper and the appropriate aryl halides. In the reaction leading to the aldehyde (6), the corresponding benzo[*a*]xanthone (7) was isolated. Its spectra were similar to those of benzo[*a*]xanthone (8), easily obtained from the reaction³ between salicylic acid and 2-naphthol.

All the aldehydes (1)–(5) yielded the corresponding xanthenes on treatment with copper(II) chloride or bromide. The aldehyde (6), however, with copper(II) bromide gave 4-bromo-3-methoxybenzo[*a*]xanthen-12-one (9). The bromo-substituent was placed at C-4 on n.m.r. evidence: the H-5 signal suffered a paramagnetic shift from δ 7.9 in the spectrum of (7) or (8) to 8.6 in the spectrum of (9) due to the *peri*-effect of the bromo-substituent. The H-1 signal also suffered a slight shift from 9.9 in the spectrum of (7) to 10.1 in that of (9).

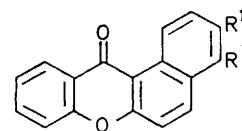
It appears that the first step of the cyclisation reaction is the decomposition of copper(II) halide to copper(I) halide and a halogen radical. The halogen radical attacks the formyl group to form the acyl radical^{1,4} (10), which cyclises oxidatively to give the xanthone. In the process hydrogen bromide is formed.

¹ J. I. Okogun and K. S. Okwute, *J.C.S. Chem. Comm.*, 1975, 8.

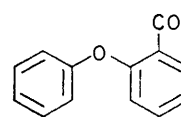
² R. H. F. Manske and A. E. Ledingham, *J. Amer. Chem. Soc.*, 1950, **72**, 4797.

The amount of hydrogen bromide released in the reaction between 2-phenoxybenzaldehyde and copper(II) bromide was estimated by absorbing the acid in an excess of sodium carbonate solution. Estimation showed that *ca.* 1 mol of hydrogen bromide was formed per mol of aldehyde. This suggested that, as expected, the solvent nitrobenzene probably participated in the second step of the reaction. That nitrobenzene is involved was supported by the following facts: (i) other experiments⁵ have led to the formation of anthraquinones from methylbenzophenones and copper(II) bromide, and (ii) the oxidative cyclisation reaction was hardly observed when chlorobenzene, diphenyl ether, or ethyl benzoate was used as the reaction medium.

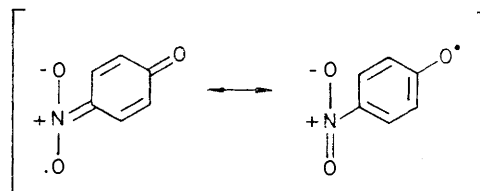
The reaction is however a complex one. For example, 2-(4-nitrophenyl)benzaldehyde, on treatment with copper(II) bromide gave a mixture from which bis-4-nitrophenyl ether was isolated as well as the expected xanthone. This suggested various possibilities, including the formation from the starting material of the intermediate (11).



- (7) $R^1 = OMe, R^2 = H$
- (8) $R^1 = R^2 = H$
- (9) $R^1 = OMe, R^2 = Br$



(10)



(11)

This reaction constituted a new method of generating xanthenes from aldehydes in a Friedel-Crafts-like

³ Ng. P. Buu-Hoi and Ng. D. Xuong, *J. Org. Chem.*, 1951, **16**, 1633.

⁴ W. H. Urry, D. J. Trecker, and H. D. Hartzler, *J. Org. Chem.*, 1964, **29**, 1663 and references therein.

⁵ J. I. Okogun, in preparation.

manner⁶ and should be effective where substituents in the starting phenoxybenzaldehyde are unaffected by bromine atoms.

EXPERIMENTAL

For general experimental details see reference 7. N.m.r. spectra were obtained with a Varian T60A instrument.

Salicylaldehydato-copper⁸ was formed by following the first steps in the purification procedure for salicylaldehyde, and was stored in a desiccator. Copper(II) chloride was left in an oven at 60 °C for 72 h; copper(II) bromide was left in the same oven for 36 h before use.

2-Phenoxybenzaldehyde (1) and *2-(2-methoxyphenoxy)benzaldehyde* (2) were prepared as described in reference 2.

2-(4-Methylphenoxy)benzaldehyde (4).—A mixture of *p*-bromotoluene (13 g) and salicylaldehydato-copper (20 g) was heated under nitrogen at reflux (240 °C) for 3 h. The resulting mixture was extracted with ether by decantation (3 × 60 cm³). The extract was washed with dilute aqueous sodium hydroxide, washed with water, dried (MgSO₄), and evaporated to leave an oil, which was chromatographed on activated alumina. Hexane eluted unchanged bromotoluene and salicylaldehyde dimer. Ether-hexane (1 : 9) eluted the *aldehyde* (4) as an oil (1.5 g), which crystallized from benzene-hexane; m.p. 46–48°; ν_{\max} . 3 100, 1 690, 1 600, 1 500, 1 230, 875, 840, 830, and 760 cm⁻¹; λ_{\max} . 210 (ϵ 20 400), 226 (19 000), 245 (14 000), 287 (3 900), and 316 nm (5 000); δ 2.35 (3 H, s, CH₃), 6.8–7.62 (7 H, m, aromatic), 7.9 (1 H, dd, *J* 7 and 2 Hz, H-6), and 10.4 (1 H, s, CHO); *m/e* 212 (*M*⁺), 211, 210, 197, 120, 92, 91, 77, and 76 (Found: C, 79.15; H, 5.75). C₁₄H₁₂O₂ requires C, 79.2; H, 5.7%), followed by 2-methylxanthone, m.p. 119–122°, ν_{\max} . 1 650, 1 600, 860, 820, and 760 cm⁻¹, λ_{\max} . 233 (ϵ 32 900), 241 (33 900), 261 (11 400), 290 (3 500), and 340 nm (5 800); δ 2.48 (3 H, s, CH₃), 7.2–7.82 (5 H, m, aromatic), 8.1br (1 H, s, H-1), and 8.3 (1 H, dd, *J* 7 and 2 Hz, H-8).

The following aldehydes were prepared by the above general procedure.

2-(4-Methoxyphenoxy)benzaldehyde (3). Salicylaldehydato-copper (6 g) and *p*-bromoanisole (10 g) were heated at reflux for 4.5 h and the mixture was worked up as above. The product was distilled and then chromatographed on silica gel to give the *aldehyde* (3) as an oil (1.1 g), ν_{\max} . (neat) 1 695, 1 600, 1 225, 880, 840, 830, 800, and 760 cm⁻¹; λ_{\max} . 210 (ϵ 20 400), 220 (15 200), 230 (11 400), 250 (9 500), 274 (2 200), 282 (1 900), and 315 nm (3 500); δ 3.9 (1 H, s, OCH₃), 6.75–7.7 (7 H, m, aromatic), 7.95 (1 H, dd, *J* 7 and 2 Hz, H-6), and 10.2 (1 H, s, CHO); *m/e* 228 (*M*⁺), 227, 120, and 108 (Found: C, 73.8; H, 5.2). C₁₄H₁₂O₃ requires C, 73.4; H, 5.3%); followed by 2-methoxyxanthone (10 mg), m.p. 129–131°, ν_{\max} . 1 650, 1 605, 875, 865, and 820 cm⁻¹, λ_{\max} . 234 (ϵ 33 200), 248 (28 300), 302 (3 500), and 358 nm (5 700).

2-(4-Nitrophenoxy)benzaldehyde (5). Salicylaldehydato-copper (5 g) and *p*-bromonitrobenzene (10 g) were heated at reflux (200–208 °C) for 5 h and the reaction was worked up as usual. The product was chromatographed on silica gel. Hexane eluted unchanged bromonitrobenzene and salicylaldehyde dimer. Ether-hexane (1 : 9) eluted bis-4-nitrophenyl ether (100 mg), m.p. 137–140°, followed by the *aldehyde* (5) (600 mg), m.p. 101–103° (from benzene-

hexane); ν_{\max} . (Nujol) 3 100, 1 690, 1 600, 1 580, 1 510, 1 480, 1 450, 1 345, 1 240, 1 160, 1 100, 880, 865, 760, and 750 cm⁻¹; λ_{\max} . 211 (ϵ 23 000), 227 (13 000), 245 (9 200), and 302 nm (14 700); *m/e* 243 (*M*⁺), 242, 226, 196, 150, 121, 104, 93, 92, and 76 (Found: C, 64.15; H, 3.8; N, 5.4). C₁₃H₉NO₄ requires C, 64.2; H, 3.7; N, 5.8%).

Ether-hexane (1 : 1) eluted 2-nitroxanthone (40 mg) (see below).

2-(6-Methoxy-2-naphthylloxy)benzaldehyde (6) and *3-methoxybenzo[a]xanthen-12-one* (7).—Salicylaldehydato-copper (3 g) and 2-bromo-6-methoxynaphthalene (4.9 g) were heated at reflux (205–208 °C) for 5 h and the mixture was worked up as usual. The product on chromatography on silica gel gave the *aldehyde* (6) (1.1 g), m.p. 101–104° (from ether); ν_{\max} . (Nujol) 1 670, 1 601, and 1 505 cm⁻¹; λ_{\max} . 210 (ϵ 34 400), 219 (68 000), 268 (8 800), 278 (5 500), and 320br nm (5 500); δ 4.0 (3 H, s, OCH₃), 6.8–7.7 (8 H, m, aromatic), 7.8 (1 H, d, *J* 8 Hz, H-8'), 8.0 (1 H, dd, *J* 8 and 2 Hz, H-6), and 10.3 (1 H, s, CHO); *m/e* 278 (*M*⁺), 277, 205, 185, 158 (base peak), and 115 (Found: C, 77.45; H, 5.2). C₁₈H₁₄O₃ requires C, 77.7; H, 5.05%); followed by the *xanthone* (7), m.p. 188–190° (from benzene-petroleum), ν_{\max} . (Nujol) 1 640 (CO), 1 601, and 1 590 cm⁻¹; λ_{\max} . 212 (ϵ 26 500), 236 (25 000), 260 (25 300), 300 (8 800), 318 (8 400), and 368br nm (3 800); δ 3.9 (3 H, s, OCH₃), 7.1–7.7 (6 H, m, aromatic), 7.9 (1 H, d, *J* 9 Hz, H-6), 8.3 (1 H, d with fine structure, *J* 7 Hz, H-1), and 9.9 (1 H, d, *J* 9 Hz, H-10); *m/e* 276 (*M*⁺), 261 (*M* - CH₃), 233 (*M* - CH₃ - CO), 205, and 176 (Found: C, 78.4; H, 4.65). C₁₈H₁₂O₃ requires C, 78.3; H, 4.4%).

Conversion of the Aldehydes into Xanthenes.—The following procedure was followed generally. 2-Phenoxybenzaldehyde (0.5 g) and copper(II) chloride (1 g) in nitrobenzene (15 cm³) were heated at reflux for 1 h, with nitrogen bubbling through the mixture 15 min before heating was begun and throughout the reaction. White fumes of hydrochloric acid were observed about 10 min after heating started. At the end of the reaction (t.l.c.) a grey precipitate of copper(I) chloride was observed in the dark brown mixture. Nitrobenzene was distilled off under reduced pressure. The residue was taken up in ether and washed with sodium hydrogen carbonate solution and then water. The extract was dried (MgSO₄) and distilled, and the residue was chromatographed on activated alumina. Ether-hexane (1 : 9) eluted xanthone (0.25 g), m.p. and mixed m.p. 173–175° (from benzene-petroleum), ν_{\max} . (Nujol) 1 650, 1 601, and 760 cm⁻¹; λ_{\max} . 230 (ϵ 37 000), 236 (39 200), 260 (12 700), 285 (5 100), and 334 nm (7 600).

A ratio of one part by weight of aldehyde to two of copper(II) bromide was used for all the other aldehydes except the nitro-derivative (5), for which a ratio of 1 : 1 by weight was used.

4-Methoxyxanthone. 4-Methoxyxanthone (40 mg) was isolated from the reaction of the methoxy-aldehyde (2) (240 mg) with copper(II) bromide (510 mg); m.p. 174–175°; ν_{\max} . (Nujol) 1 650, 1 610, 1 560, 965, 750, and 730 cm⁻¹; λ_{\max} . 212 (ϵ 10 500), 232 (24 000), 246 (29 000), 275 (4 900), 288 (3 200), and 345 nm (4 600).

2-Methoxyxanthone. 2-Methoxyxanthone (250 mg) was isolated from the reaction between the methoxy-aldehyde (3) (500 mg) and copper(II) bromide (1 g); m.p. 129–131°.

2-Methylxanthone. 2-Methylxanthone (100 mg) was isolated from the reaction between the methyl derivative

⁶ D. Y. Curtin and J. C. Kauer, *J. Org. Chem.*, 1960, **25**, 880.

⁷ D. E. U. Ekong, J. I. Okogun, and B. L. Sondengam, *J.C.S. Perkin I*, 1975, 2118.

⁸ A. I. Vogel, 'Practical Organic Chemistry,' Longmans, London, 1959, p. 704.

(4) (400 mg) and copper(II) bromide (610 mg), the temperature of the bath being kept at 192–196 °C during the reaction. The product had m.p. 119–122°.

2-Nitroxanthone. The nitro-aldehyde (5) (0.6 g) reacted with copper(II) bromide (0.6 g) to give an unidentified compound (130 mg), m.p. 125–127°, bis-4-nitrophenyl ether (80 mg), m.p. 138–140° (identified by i.r., u.v., n.m.r., and mass spectra), and 2-nitroxanthone (62 mg), m.p. 204–206° (from ethanol); $\nu_{\max.}$ (Nujol) 1 650, 1 600, 1 530, 770, 745, and 715 cm^{-1} ; $\lambda_{\max.}$ 217 (ϵ 20 300), 250 (21 700), 272 (15 100), 280 (14 700), 305 (8 300), and 330 nm (3 800); δ 7.3–8.2 (4 H, m, aromatic), 8.4 (1 H, d with fine structure, J 7 Hz, H-8), 8.6 (1 H, dd, J 7 and 3 Hz, H-3), and 9.2 (1 H, d, J 3 Hz, H-1); m/e 241 (M^+), 211, 195, 155, 139, and 112.

4-Bromo-3-methoxybenzo[a]xanthone (9).—The naphthyl-oxybenzaldehyde (6) (400 mg) reacted with copper(II) bromide (800 mg) to give, after isolation and purification as usual, 4-bromo-3-methoxybenzo[a]xanthone-12-one (140 mg), m.p. 225–227° (from chloroform–methanol); $\nu_{\max.}$ (Nujol) 1 640, 1 605, 1 580, 1 500, 840, 820, 810, 790, 760, and 745 cm^{-1} ; $\lambda_{\max.}$ 220 (ϵ 21 400), 238 (24 900), 255 (22 300), 262 (21 700), 275 (12 800), 302 (8 600), 325 (8 700), and 372 nm (3 900); δ 4.1 (3 H, s, OCH_3), 7.2–7.8 (5 H, m,

aromatic), 8.4 (1 H, d with fine structure, J 7 Hz, H-10), 8.6 (1 H, d, J 9 Hz, H-5), and 10.1 (1 H, d, J 9 Hz, H-1); m/e 356/354 (M^+), 341/339 ($M - \text{CH}_3$), 313/311 ($M - \text{CH}_3 - \text{CO}$), and 285/283 (Found: C, 60.7; H, 3.05; Br, 22.65. $\text{C}_{18}\text{H}_{11}\text{BrO}_3$ requires C, 60.8; H, 3.1; Br, 22.5%).

Estimation of Hydrogen Bromide Released during the Cyclization Reaction.—The reaction between 2-phenoxybenzaldehyde (0.2 g) and copper(II) bromide (0.45 g) in nitrobenzene (10 cm^3) was carried out in such a way that the hydrogen bromide released was flushed with nitrogen into standard sodium carbonate solution. Neutralization of the unchanged carbonate with standard hydrochloric acid showed that 0.82 mol of hydrogen bromide was released per mol of aldehyde consumed. T.l.c. showed that there was no starting material left after 1 h.

Other Solvents.—2-Phenoxybenzaldehyde was heated as above with copper(II) bromide in each of the solvents chlorobenzene, diphenyl ether, and ethyl benzoate. There was hardly any reaction in chlorobenzene after 3 h. There was reaction in diphenyl ether and in ethyl benzoate, as indicated by the evolution of hydrogen bromide, but the amount of xanthone formed in each case was too small to be isolated and the reaction was incomplete after 1½ h.

[6/408 Received, 1st March, 1976]