HETEROCYCLIC FLUORINE COMPOUNDS—III* MONOFLUOROXANTHONES

F. L. ALLEN, P. KOCH and H. SUSCHITZKY

The Department of Chemistry and Biology, West Ham College of Technology, London and

The Department of Chemistry and Applied Chemistry, Royal Technical College, Salford, Lancs

(Received 25 November 1958)

Abstract—The four monofluoroxanthones substituted in the benzene ring have been prepared by two different routes, namely by cyclisation of the appropriate carboxyfluorodiphenyl ether and by a Balz-Schiemann reaction with the corresponding aminoxanthone.

1-FLUORO-, 2-fluoro-, 3-fluoro-, and 4-fluoroxanthone (as I; R = H) have been made by cyclisation of the requisite carboxyfluorodiphenyl ether obtained by an Ullman type of condensation between a fluorophenol and o-chlorobenzoic acid. The crude diphenyl acid was purified by conversion into its methyl ester followed by hydrolysis. Concentrated sulphuric acid proved the best cyclising agent for fluoroxanthone formation. Cyclisation of 2-carboxy-3'-fluorodiphenyl ether (II; $R_1 = R_2 = H$, $R_3 = F$) gave a mixture of 1-fluoro- and 3-fluoroxanthone in a ratio of 1 : 3. The formation of a large excess of the 3-fluoroisomer is probably due to the strong paradirecting influence of fluorine which has also been observed with the fluoroindoles.¹ The mixture was readily separated by fractional crystallisation from boiling ethanol followed by chromatography. 1-Fluoroxanthone needed as a reference compound



was made unambiguously from 1-fluoro-4-methylxanthone (I; R = Me) obtained by cyclisation of 2-carboxy-5'-fluoro-2'-methyldiphenyl ether (II; $R_1 = H$, $R_2 = Me$, $R_3 = F$) in which the methyl group prevents ring closure from occurring in two directions. Attempts to oxidise the methylgroup with alkaline potassium permanganate or sodium dichromate in sulphuric acid resulted in destruction of the xanthone ring, but were successful when chromium trioxide dissolved in a mixture of acetic and sulphuric acid at 40° was employed. Decarboxylation of the resulting 4-carboxy-1-fluoroxanthone (I; $R = CO_2H$) occurred readily on heating the acid to its melting point. Authentic 3-fluoroxanthone was prepared from 2-carboxy-5-fluorodiphenyl ether in the usual way.

Another route to the monofluoroxanthones was by a Balz-Schiemann reaction with the monoaminoxanthones. The required nitroxanthones resulted from cyclisation of nitrodiphenyl ethers of type II ($R_1 = R_2 = H$, $R_3 = NO_2$). When the 3'-substituted diphenyl ether was ringclosed, a mixture of two xanthones (1-nitro and

* Part II was published in J. Chem. Soc. 1283 (1955).

¹ F. L. Allen, J. C. Brunton and H. Suschitzky, J. Chem. Soc. 1283 (1955).

3-nitro) was obtained, from which 1-nitroxanthone was separable by fractional crystallisation. This nitrocompound was also prepared unambiguously from 2-carboxy-3-nitrodiphenyl ether.

Absorption spectra of the fluorine substituted xanthones are given in the accompanying table.

Xanthones	λ,	ε ₁	λ,	ε _s	λ ₃	£3	λ.	ε.
1-F	238	42,000	263	11,800			336	6170
2-F	230 240	31,900 30,400	259	11,200	290	4200	342	7200
3-F	233	44,800	258	11,550	283	7220	329	6450
4-F	238	41,000	262	12,400	327	5800	337	6400
1-F-4-Me	241	40,400	268	9600	I	i —	340	5900
				1	i		· · ·	1

TABLE 1. ULTRA-VIOLET ABSORPTION MAXIMA ($m\mu$) in methanol

EXPERIMENTAL

Fluoromethoxycarbonyldiphenyl ethers. Sodium (2 moles) was dissolved in 40 times its weight of methanol and to this solution was added the requisite fluorophenol (1 mole), o-chlorobenzoic acid (1 mole) and a trace of copper powder. After driving off the methanol the reaction mixture was kept at 150° for 2 hr and finally heated to 200° for 20 min. Extraction of the reaction mixture with boiling water followed by acidification of the filtrate yielded a crude carboxyfluorodiphenyl ether which was esterified with methanol and sulphuric acid by refluxing for 8 hr. The excess of methanol was distilled off, the residue poured into ice and the crude ester extracted with ether and finally purified by fractional distillation.

2'-Fluoro-2-methoxycarbonyldiphenyl ether (40%), b.p. 146°/3 mm (Found: C, 68·2; H, 4·5; $C_{14}H_{11}O_{3}F$ requires: C, 68·3; H, 4·5%).

3'-Fluoro-2-methoxycarbonyldiphenyl ether (32.5%), b.p. 145°/4 mm (Found: C, 68.2; H, 4.4%).

4'-Fluoro-2-methoxycarbonyldiphenyl ester (44%), b.p. 154°/4 mm (Found: C, 68 0; H, 44%).

 \hat{S} -Fluoro-2-methoxycarbonyldiphenyl ether was obtained by condensation of 2-chloro-4-fluorobenzoic acid² and phenol with sodium as a pale-yellow oil (30%) b.p. 158°/6 mm (Found: C, 68.2; H, 4.4%).

5'-Fluoro-2-methoxycarbonyl-2'-methyldiphenyl ether. A solution of 2-amino-4-fluorotoluene (10 g) in concentrated sulphuric acid (30.6 g) and water (93 ml) was diazotised and then added in small portions to a boiling, saturated solution of copper sulphate (150 ml). Steam distillation of the reaction mixture gave 4-fluoro-2-hydroxytoluene as a light-amber oil (90%), b.p. 66°/4 mm. (Found: C, 66.4; H, 5.4. C₂H₇OF requires: C, 66.7; H, 5.5%). Its p-nitrobenzoyl ester made in pyridine had m.p. 113° (Found: C, 61.0; H, 3.8. C₁₄H₁₀O₄NF requires: C, 61.1; H, 3.6%). Condensation of the phenol with o-chlorobenzoic acid as described above gave 5'-fluoro-2-methoxycarbonyl-2'-methyldiphenyl ether (35%) b.p.128°/2 mm (Found: C, 69.5; H, 5.2; C₁₆H₁₃O₃F requires: C, 69.2; H, 5.0%).

Carboxyfluorodiphenyl ethers were obtained pure in high yield by hydrolysis of the above esters (5 g) with N-potassium hydroxide (100 ml). The compounds thus prepared and their p-nitrobenzyl esters are listed in Table 2.

Fluoroxanthones

Method A: The requisite carboxyfluorodiphenyl ether was cyclised by heating with about 15 times its weight of concentrated sulphuric acid on a water-bath for 0.5 hr. The reaction mixture was poured onto ice and the precipitated fluoroxanthone washed with caustic soda and recrystallised from ethanol.

² O. Yu. Magidson and A. I. Travin, J. Gen. Chem. (U.S.S.R.) 11, 243 (1941).

Method B: The requisite aminoxanthone³ prepared from 1-nitro,^{3,4}, 2-nitro,^{3,5} 3-nitro,^{3,5} and 4-nitroxanthone⁶ was converted into its diazonium borofluoride which was decomposed in the usual way⁷ to give a fluoroxanthone.

1-Fluoroxanthone

Method A: This compound was unambiguously made by cyclisation of 2-carboxy-5'-fluoro-2'methyldiphenyl ether which gave 1-fluoro-4-methylxanthone ($66\cdot5\%$), m.p. 156-157° (Found: C, 73·3; H, 4·0. C₁₄H₉O₁F requires: C, 73·7; H, 4·1%). The methylxanthone (2·4 g) dissolved in a mixture of acetic acid (50 ml) and concentrated sulphuric acid (25 ml) was oxidised by slow addition of an aqueous solution (30 ml) of chromium trioxide (6 g) at 40°. When the reaction mixture was

Substituent	M.P. C°	Found (%) C H		Formula	Required (%) C H	
		<u>. </u>		!	<u> </u>	
2'-Fluoro	140	67-2	4 ·1	C13H9O3F	67-2	3.9
3'-Fluoro	130	∣ 66 [.] 8	3.7	C ₁ ,H ₉ O ₃ F	67·2	3.9
4'-Fluoro	142	67.3	4 ·1	C ₁₃ H ₉ O ₃ F	67-2	3.9
5-Fluoro	122	67·2	4.0	C ₁₃ H ₂ O ₃ F	67.2	3.9
5'-Fluoro-2'-methyl	108 ,	68-6	4.6	$C_{14}H_{11}O_3F$	68-3	4∙5
р-1	Nitrobenzy	L ESTERS O	F 2-CARBO	XYDIPHENYL ETHERS		
2'-Fluoro	75	65-3	3-8	C ₂₀ H ₁₄ O ₅ NF	65-4	3.8
3'-Fluoro	54	65.6	4.3	C ₁₀ H ₁₄ O ₅ NF	65.4	3.8
4'-Fluoro	76	65-4	4 ·1	C ₂₀ H ₁₄ O ₅ NF	65-4	3.8
5'-Fluoro	112	65-5	4·1	C ₂₀ H ₁₄ O ₅ NF	65.4	3.8
5' Eluoro 2' methyl	87	66-0	4.3	C.H.O.NE	66-1	4.7

TABLE 2. 2-CARBOXYDIPHENYL ETHERS

poured onto ice, 4-carboxy-1-fluoroxanthone precipitated as white crystals (92%), m.p. 252° (dec) (Found: C, 64.9; H, 2.9. $C_{14}H_2O_4F$ requires: C, 65.1; H, 2.7%). Its p-nitrobenzyl ester had m.p. 170–172° (Found: C, 63.7; H, 3.2; N, 3.9. $C_{21}H_{12}O_6NF$ requires: C, 64.1; H, 3.1; N, 3.6%). On heating the acid (0.5 g) in an ignition tube until gas evolution ceased and extraction of the residue with petroleum ether (b.p. 60–80°) 1-fluoroxanthone was obtained as white needles (6%), m.p. 147° (Found: C, 72.6; H, 3.6. $C_{13}H_7O_4F$ requires: C, 72.9; H, 3.3%). Ring-closure of 2-carboxy-3'-fluorodiphenyl ether gave a mixture of 1-fluoro- (1 part) and 3-fluoroxanthone (3 parts) separable by fractional crystallisation from ethanol in which 3-fluoroxanthone is less soluble. Purification of the constituents was carried out by chromatography on an alumina column with petroleum ether (b.p. 60–80°) as solvent.

Method B: Decomposition of xanthone-1-diazonium borofluoride, m.p. 154° (dec) gave 1-fluoroxanthone (50%), m.p. and mixed m.p. 147° .

2-Fluoroxanthone

Method A gave 2-fluoroxanthone (83%) as white, feathery needles, m.p. 156° (Found: C, 72.6; H, 3.5%).

Method B: Xanthone-2-diazonium borofluoride, m.p. 181° (dec) gave 2-fluoroxanthone (58%) on decomposition.

- ³ A. A. Goldberg and H. A. Walker, J. Chem. Soc. 1348 (1953).
- 4 C. F. Koelsch and F. J. Lucht, J. Amer. Chem. Soc. 71, 3556 (1949).
- ⁵ F. G. Mann and J. H. Turnbull, J. Chem. Soc. 747 (1951).
- ⁶ R. Q. Brewster and F. Strain, J. Amer. Chem. Soc. 56, 117 (1934).
- 7 F. L. Allen and H. Suschitzky, J. Chem. Soc. 3845 (1953).

3-Fluoroxanthone

Method A: 5-Fluoro-2-methoxycarbonyldiphenyl ether yielded authentic 3-fluoroxanthone (75.5%), m.p. 158° (Found: C, 72.7; H, 3.2). This xanthone was also obtained from 2-carboxy-3'-fluorodiphenyl ether (cf. 1-fluoro-xanthone).

Method B: A yield of 45.5% resulted from pyrolysis of xanthone-3-diazonium borofluoride, m.p. 161° (dec).

4-Fluoroxanthone

Method A: Ring-closure of 2-carboxy-2'-fluorodiphenyl ether gave 4-fluoroxanthone, m.p. 177° in 76% yield (Found: C, 72.9; H, 3.4%).

Method B: A Balz-Schiemann reaction with xanthone-4-diazonium borofluoride, m.p. 204° (dec) yielded impure fluoroxanthone (21%) which was purified by chromotography.