hexane gave needles, m.p. 177–179°; λ_{max} 235 mμ (log ϵ 4.40) 249 sh (4.14), 296 sh (3.94), 307 (4.03), 318 (3.98); acid: λ_{max} 233 mμ (log ϵ 4.72), 239 sh (4.58), 288 (4.13), 300 sh (4.09), 313 sh (3.86).

Anal. Calcd. for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 74.14; H, 7.04; N, 5.58.

1-Methyl-3-(2-hydroxy-3-methylbutyl)-4-hydroxy-2-quinolone.—A solution of 0.08 g. of demethoxylunacrine in 5 ml. of 10% ethanolic potassium hydroxide was heated under reflux for 11 hr. The ethanol was removed by distillation and water was added simultaneously to keep a volume of no less than 5 ml. After the ethanol had been removed, the solution was diluted and extracted with chloroform. The aqueous layer was saturated with carbon dioxide and extracted three times with chloroform. Evaporation of the organic extracts and crystallization of the residue from methanol–water gave 0.06 g. (70%) of white plates, m.p. 166–168°.

Anal. Calcd. for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 69.16; H, 7.45; N, 5.14.

Acknowledgment.—This work was supported by Grant GM-8731 from the Division of General Medical Sciences of the National Institutes of Health. We would like to thank Mr. Kenneth I. Burke for technical assistance.

Anthocyanins and Related Compounds. III. Oxidation of Substituted Flavylium Salts to 2-Phenylbenzofurans

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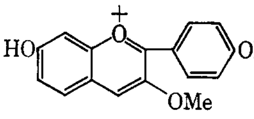
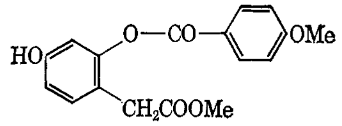
Flavylium salts with an alkyl, alkoxy, or phenoxy grouping in the 3-position are oxidized by hydrogen peroxide in aqueous methanol at pH 5–7 to yield 3-acyl-, 3-carboalkoxy-, and 3-carbophenoxy-2-phenylbenzofuran derivatives, respectively.

Hydrogen peroxide oxidation[1] or ozonolysis[2] of 3-methoxyflavylium salts in acetic acid solutions yields substituted *o*-benzoyloxyphenylacetic acids, *e.g.*, I → II. Structurally similar products were also reported by Karrer and his associates[3,4] to be formed by oxidation of natural anthocyanidin 3-glycosides in aqueous solutions. The constitution of these anthocyanin products, *e.g.*, malvone, however, has not yet been established with certainty.[5] On the basis of these early observations it has been suggested[6] that benzoyl esters of the malvone type may be formed in oxidative decoloration of anthocyanin pigments in plant juices. The rate of anthocyanin destruction, however, is pH dependent[7] and thus it seemed desirable to examine the oxidation of flavylium salts at a pH (5–7) commonly occurring in plant extracts. At these pH values it has now been determined that the major oxidation products of 3-alkyl- and 3-alkoxyflavylium salts are 3-acyl- and 3-carboalkoxy-2-phenylbenzofuran derivatives.



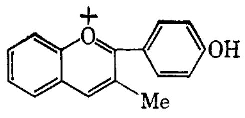
I



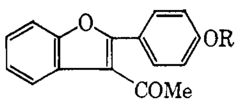
II

Thus, 3-methyl-4'-hydroxyflavylium chloride (III) rapidly reacts with hydrogen peroxide in aqueous methanol or in methanol buffered to pH 5.8 to give a cream-colored, blue fluorescent (in ultraviolet light) monohydroxy ketone, $C_{16}H_{12}O_3$, in 54% yield. This product is not easily hydrolyzed by alkalies and its λ_{max} in ethanol (314 mμ, log ϵ 4.15) undergoes a pronounced bathochromic shift of 50 mμ in the presence of sodium ethylate. A benzoyl ester linkage is thus excluded. The constitution of the product as 3-acetyl-2-(4-hydroxyphenyl)benzofuran (IV, R = H) was established by the formation of a benzal derivative and the reaction of its methyl ether (IV, R = Me) with iodine and alkali to give iodoform and, in small quantity, an acid, $C_{16}H_{12}O_4$ (V). Decarboxylation of this acid gave the known 2-(4-methoxyphenyl)benzofuran (VI). VI was also obtained directly from the ketone (IV, R = Me) by prolonged alkaline hydrolysis. The identity of the benzofuran VI was confirmed by direct comparison with an authentic specimen, prepared by alkaline degradation of 2-ethyl-3-anisoylbenzofuran.[8]

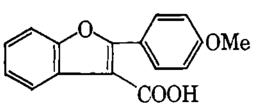
Peroxide oxidation of 3-aryloxy- and 3-methoxyflavylium salts similarly gave good yields (about 50%) of the aryl and methyl esters of the corresponding 2-phenylbenzofuran-3-carboxylic acids; *e.g.*, 3-phenoxy-4'-methoxyflavylium chloride and 3,4'-dimethoxyflavylium chloride gave the phenyl and methyl ester of V, respectively. Structures were assigned to these esters on the basis of their alkaline hydrolysis to yield the free acid. Benzofurans have now been obtained from about twenty flavylium salts. Some of these are listed in Tables I and II. In view of the ready availability of flavylium salts this oxidation process offers a very favorable synthetic route to diffi-



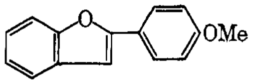
III



IV



V



VI

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[1] W. Dilthey and W. Hoschen, *J. prakt. Chem.*, **138**, 42 (1933).

[2] R. L. Shriner and R. B. Moffett, *J. Am. Chem. Soc.*, **62**, 2711 (1940).

[3] P. Karrer, R. Widmer, A. Helfenstein, W. Hürliman, O. Nievergelt, and P. Monsarrat-Thoms, *Helv. Chim. Acta*, **10**, 729 (1927).

[4] R. Robinson and A. R. Todd, *J. Chem. Soc.*, 2293 (1932).

[5] P. Karrer and R. Widmer, *Helv. Chim. Acta*, **10**, 758 (1927); P. Karrer and Cr. de Meuron, *ibid.*, **15**, 507, 1212 (1932).

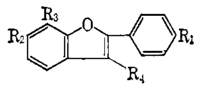
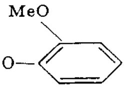
[6] E. Sondheimer and Z. I. Kertesz, *Food Research*, **17**, 288 (1952).

[7] A. Lukton, C. O. Chichester, and G. Mackinney, *Food Technol.*, **10**, 427 (1956).

[8] R. Royer and E. Bisagni, *Bull. soc. chim. France*, 395 (1960).

TABLE I

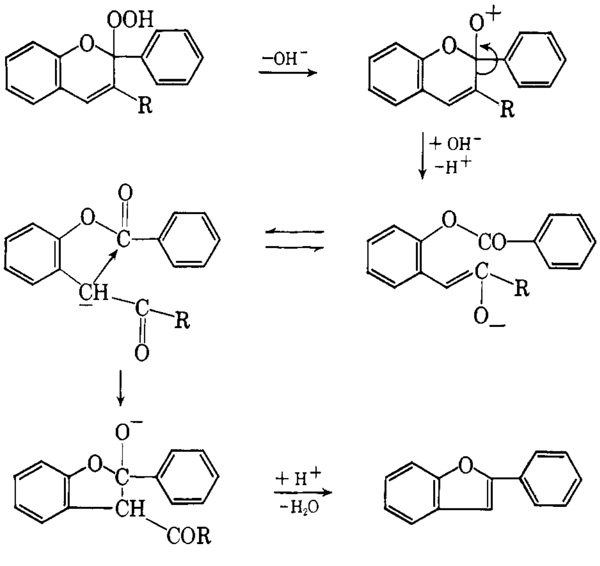
BENZOFURANS OBTAINED FROM FLAVYLIUM SALTS BY OXIDATION

Flavylium salt[a]	Benzofuran 	M.p., °C.	Formula	Calcd., % C	Calcd., % H	Calcd., % MeO	Calcd., % N	Found, % C	Found, % H	Found, % MeO	Found, % N
1	R_1 = OH, R_2 = R_3 = H, R_4 = COC_2H_5[b]	170	$C_{17}H_{14}O_3$	76.7	5.30			76.9	5.26		
	Acetate	108	$C_{19}H_{16}O_4$	74.0	5.23			74.0	5.35		
2	R_1 = OH, R_2 = H, R_3 = OMe, R_4 = $COCH_3$	222	$C_{17}H_{14}O_4$	72.3	5.00	11.0		72.4	5.01	10.8	
	Acetate	117	$C_{19}H_{16}O_5$	70.4	4.98	9.57		70.3	5.00	9.43	
	Benzoate	155	$C_{24}H_{18}O_5$	74.6	4.70			74.6	4.71		
	Benzyl ether	153–154	$C_{24}H_{20}O_4$	77.4	5.41			77.5	5.44		
	Methyl ether	98	$C_{18}H_{16}O_4$	73.0	5.44	20.9		73.0	5.50	20.6	
	Oxime	134'	$C_{17}H_{15}NO_4$	68.7	5.08		4.71	68.5	5.01		4.67
	Oxime of methyl ether	158	$C_{18}H_{17}NO_4$	69.4	5.50		4.50	69.2	5.44		4.46
	Benzal derivative of methyl ether	116	$C_{26}H_{20}O_4$	78.1	5.24			78.0	5.25		
3	R_1 = R_2 = H, R_3 = OMe, R_4 = $COCH_3$	107	$C_{17}H_{14}O_3$	76.7	5.30	11.6		76.8	5.28	11.3	
	Oxime	154	$C_{17}H_{15}NO_3$	72.6	5.37		4.98	72.5	5.35		4.97
	Benzal derivative	139.5	$C_{24}H_{18}O_3$	81.3	5.12			81.3	5.14		
4	R_1 = OMe, R_2 = OH, R_3 = H, R_4 = $COCH_3$	150–151	$C_{17}H_{14}O_4$	72.3	5.00	11.0		72.4	4.98	10.9	
	Acetate	93	$C_{19}H_{16}O_5$	70.4	4.98			70.3	5.01		
5	R_1 = OMe, R_2 = R_3 = H, R_4 = COO— 	126	$C_{23}H_{18}O_5$	73.8	4.85	16.6		73.9	4.88	16.7	
6	R_1 = R_3 = OMe, R_2 = H, R_4 = COOPh	161	$C_{23}H_{18}O_5$	73.8	4.85	16.6		73.6	4.87	16.4	
	R_1 = R_3 = OMe, R_2 = H, R_4 = COOH	203–204	$C_{17}H_{14}O_5$	68.5	4.73	20.8		68.5	4.68	20.7	
	R_1 = R_3 = OMe, R_2 = H, R_4 = COOMe	101	$C_{18}H_{16}O_5$	69.2	5.16	29.8		69.3	5.1	29.8	
	R_1 = R_3 = OMe, R_2 = R_4 = H	82	$C_{16}H_{14}O_3$	75.6	5.55	24.4		75.5	5.62	24.4	

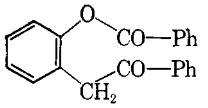
[a] See Table II. [b] This is a known compound, lit.[1] m.p. 171°.

cultly accessible 2-phenylbenzofurans.[9] The oxidation of natural anthocyanidin 3-glycosides has not yet been reinvestigated. However, the reported reactions[3,5] of malvone and its method of preparation do not appear to exclude a possible 2-phenylbenzofuran-3-carboxylic acid structure for this compound.

A plausible mechanism[10] for this oxidative ring contraction involves initial formation of a hydroperoxide and its subsequent rearrangement along these lines.

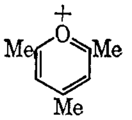


This mechanism is supported by an early observation of Dilthey and Quint[11] that KOH hydrolysis of the benzoyl ester VII, obtained by oxidation of 3-phenylflavylium perchlorate in acetic acid, yields 2-phenylbenzofuran.

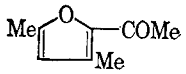


VII

In contrast with the oxidative scission of 3-substituted flavylium salts between C-2 and C-3 to yield benzoyl esters in acid solution or 2-phenyl-3-acylbenzofurans at pH 5–7, it is noteworthy that Balaban and Nenitescu[12] recently reported that peroxide oxidation of 2,4,6-trialkylpyrylium salts in dilute aqueous perchloric acid yields 2-acyl-3-alkylfurans, *e.g.*, VIII → IX. In the case of these pyrylium salts, unsubstituted in the C-3 position, oxidative scission occurs between C-2 and the oxygen atom of the pyrylium ring.



VIII



IX

Experimental

3-Methyl-4'-hydroxyflavylium Chloride.—A solution of salicylaldehyde (24.4 g.) and 4-hydroxypropiophenone (30.0 g.) in ethyl acetate (200 ml.) and ethanol (50 ml.) was saturated with hydrogen chloride gas and allowed to stand overnight. The orange-red, crystalline flavylium salt was collected, washed with ether, and air-dried (53.0 g.). The chloride (15 g.) was recrystallized by adding concentrated hydrochloric acid (50 ml.) to its solution in boiling 1% aqueous HCl (150 ml.). 3-Methyl-4'-hydroxyflavylium chloride thereby separated as brick red prisms, (12.0 g.) m.p. 213–215°; $\lambda_{\max}^{\mathrm{EtOH-0.5\%\ HCl}}$ 448, 251, 306 (infl.), and 269 mμ.[13]

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(9) C. A. F. Wagner, A. N. Wilson, and K. Folkers, *J. Am. Chem. Soc.*, **81**, 5441 (1959); D. M. X. Donnelly, J. F. K. Eades, E. M. Philbin, and T. S. Wheeler, *Chem. Ind.* (London), 1453 (1961); B. Cummins, D. M. X. Donnelly, J. F. X. Eades, N. Fletcher, F. O'Cinneide, E. M. Philbin, J. Swirski, T. S. Wheeler, and R. K. Wilson, *Tetrahedron*, **19**, 499 (1963); S. Kawai, T. Nakamura, and N. Sugiyama, *Chem. Ber.*, **72**, 1146 (1939).

(10) T. A. Geissman, private communication.

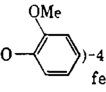
(11) W. Dilthey and F. Quint, *J. prakt. Chem.*, **131**, 1 (1931).

(12) A. T. Balaban and C. D. Nenitescu, *Chem. Ber.*, **93**, 599 (1960).

(13) The procedure used in the preparation of this and other flavylium salts is in accordance with the general methods described by Robinson and his co-workers [D. D. Pratt, R. Robinson, and P. N. Williams, *J. Chem. Soc.*, 199 (1924); A. Robertson and R. Robinson, *ibid.*, 1526 (1928); W. H. Perkin, R. Robinson and M. R. Turner, *ibid.*, **93**, 1085 (1908)] and structures are assigned to the salts on this basis. In view of the known unreliability of analytical data in this field (due to hydration, decomposition with loss of HCl in drying, etc.) many of these flavylium salts have not been analyzed.

TABLE II

FLAVYLIUM SALTS OXIDIZED TO BENZOFURANS

No.	Flavylium salt	Form, recrystn. solvent	M.p., °C.	Formula	Calcd., % C	Calcd., % H	Found, % C	Found, % H
1	3-Et-4′-HO-, chloride	Orange needles, 5% aq. HCl	219–221	$C_{17}H_{15}ClO_2$	71.1	5.28	71.3	5.30
2	3-Me-4′-HO-8-MeO-, chloride	Orange needles, 10% aq. HCl	213	$C_{17}H_{15}ClO_3$	67.4	5.00	68.2	5.11
	3-Me-4′-HO-8-MeO-, ferrichloride	Yellow needles, HOAc	159	$C_{17}H_{15}Cl_4FeO_3$	43.9	3.25	44.7	3.38
3	3-Me-8-MeO-, chloride	Could not be purified without decomposition						
4	3-Me-4′-MeO-7-HO-, chloride	Brown needles, MeOH–10% aq. HCl	234–236					
5	3-(O )-4′-MeO-, ferrichloride	Orange needles, HOAc	167	$C_{23}H_{19}Cl_4FeO_4$	49.6	3.44	49.7	3.49
6	3-PhO-4′,8-diMeO-, ferrichloride	Red needles, HOAc	165–165	$C_{23}H_{19}Cl_4FeO_4$	49.6	3.44	50.1	3.35

The ferrichloride was prepared by adding a concentrated solution of ferric chloride in hydrochloric acid to a solution of the flavylium chloride in the minimum quantity of hot glacial acetic acid. It was recrystallized from glacial acetic acid to form yellow-orange prisms, m.p. 143–144°.

Anal. Calcd. for $C_{16}H_{13}Cl_4FeO_2$: C, 44.2; H, 3.01. Found: C, 45.1; H, 3.19.

3-Acetyl-2-(4-hydroxyphenyl)benzofuran (IV, R = H).—A solution of 3-methyl-4′-hydroxyflavylium chloride (30 g.) in warm methanol (300 ml.) was diluted with water (300 ml.) or aqueous buffer, pH 5.8, and 30% hydrogen peroxide (60 ml.). Rapid decoloration occurred and within a minute of mass of almost colorless crystals separated. After standing 1 hr., water was added and the solid was collected and recrystallized from methanol. 3-Acetyl-2-(4-hydroxyphenyl)benzofuran separated as cream-colored needles (15.0 g., 54%, theory) m.p. 173–173.5°; $\lambda_{\max}^{\mathrm{EtOH}}$ 314 (log ε 4.15), 233 mμ (4.21); $\lambda_{\max}^{\mathrm{EtOH\text{-}NaOEt}}$ 363 (4.29), 267 (4.20), and 249 (4.24) mμ.

Anal. Calcd. for $C_{16}H_{12}O_3$: C, 76.2; H, 4.80. Found: C, 76.2; H, 4.83.

The **acetate** of the product, prepared by brief heating with acetic anhydride and sodium acetate, crystallized from methanol as colorless felted needles, m.p. 132°, $\lambda_{\max}^{\mathrm{EtOH}}$ 302 and 240 mμ.

Anal. Calcd. for $C_{18}H_{14}O_4$: C, 73.5; H, 4.80; 1 CH_3CO–, 14.6. Found: C, 73.7; H, 4.88; CH_3CO–, 14.7.

The **benzyl ether** of the oxidation product, prepared by reaction with benzyl chloride, potassium carbonate, and acetone, separated from methanol as colorless needles, m.p. 102°.

Anal. Calcd. for $C_{23}H_{18}O_3$: C, 80.7; H, 5.30. Found: C, 80.7; H, 5.34.

3-Acetyl-2-(4-methoxyphenyl)benzofuran (IV, R = Me).—The above oxidation product (10.0 g.) was refluxed with dimethyl sulfate (10 ml.) and anhydrous potassium carbonate (20 g.) in dry acetone (200 ml.) for 3 hr. The filtered acetone solution was concentrated and diluted with aqueous K_2CO_3 solution. The solid residue was collected and recrystallized from methanol. 3-Acetyl-2-(4-methoxyphenyl)benzofuran was obtained as colorless needles, m.p. 73°, $\lambda_{\max}^{\mathrm{EtOH}}$ 311 and 233 mμ.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.7; H, 5.30; 1 MeO–, 11.65; mol. wt., 266. Found: C, 76.6; H, 5.32; MeO–, 11.8; mol. wt., 263.

3-Cinnamoyl-2-(4-hydroxyphenyl)benzofuran.—Ten per cent aqueous sodium hydroxide (5.0 ml.) was added to a warm solution of 3-acetyl-2-(4-hydroxyphenyl)benzofuran (1.26 g.) and benzaldehyde (1.0 g.) in ethanol (10.0 ml.). The red solution was allowed to stand for 20 hr., then warmed, and acidified with HCl. The yellow solid was recrystallized from methanol. 3-Cinnamoyl-2-(4-hydroxyphenyl)benzofuran was obtained as yellow plates, m.p. 169°.

Anal. Calcd. for $C_{23}H_{16}O_3$: C, 81.2; H, 4.74. Found: C, 81.2; H, 4.82.

Acetylation of the cinnamoyl derivative gave an **acetate** which separated from acetone–methanol as pale yellow, glistening prisms, m.p. 148°.

Anal. Calcd. for $C_{25}H_{18}O_4$: C, 78.5; H, 4.74. Found: C, 78.5; H, 4.65.

Methylation of the cinnamoyl derivative with methyl iodide and potassium carbonate in the usual way gave **3-cinnamoyl-2-(4-methoxyphenyl)benzofuran**, which crystallized from wet acetone–methanol in large, pale yellow prisms, m.p. 110°. The same product was obtained by reaction of 3-acetyl-2-(4-methoxyphenyl)benzofuran with benzaldehyde in warm aqueous ethanolic NaOH for 20 min.

Anal. Calcd. for $C_{24}H_{18}O_3$: C, 81.3; H, 5.12. Found: C, 81.4; H, 5.15.

3-Carboxy-2-(4-methoxyphenyl)benzofuran (V).—3-Acetyl-2-(4-methoxphenyl)benzofuran (2.66 g.) and iodine (7.62 g.) in methanol (60 ml.) were treated with a solution of KOH (3.42 g.) in water (4.0 ml.). A heavy, yellow solid separated at once. After 5 min. an excess of water was added and the solid was filtered (discarded). The pale yellow filtrate, treated with a little $NaHSO_3$ and acidified, precipitated a cream solid. This was recrystallized from acetone–methanol. 3-Carboxy-2-(4-methoxyphenyl)benzofuran was thus obtained as colorless, felted needles, m.p. 217°, $\lambda_{\max}^{\mathrm{EtOH}}$ 311 mμ (0.2 g.).

Anal. Calcd. for $C_{16}H_{12}O_4$: C, 71.6; H, 4.51; MeO–, 11.6. Found: C, 71.5; H, 4.47; MeO–, 11.5.

The **methyl ester** of the acid, formed by reaction with excess ethereal diazomethane, crystallized from methanol as colorless, felted needles, m.p. 81°.

Anal. Calcd. for $C_{17}H_{14}O_4$: C, 72.3; H, 5.00. Found: C, 72.2; H, 5.04.

2-(4-Methoxyphenyl)benzofuran (VI). A. **Decarboxylation of 3-Carboxy-2-(4-methoxyphenyl)benzofuran.**—The previous carboxylic acid (1.0 g.) was heated in an oil bath at 235–245° until evolution of carbon dioxide ceased (10 min.). The decarboxylated product crystallized on cooling. It was suspended in 5% aqueous NaOH and filtered, and the undissolved solid was recrystallized from acetone–methanol. 2-(4-Methoxyphenyl)benzofuran was obtained as colorless prisms (0.6 g.), $\lambda_{\max}^{\mathrm{EtOH}}$ 307 mμ, m.p. 148–149°, undepressed on admixture with an authentic specimen prepared below (C).

Anal. Calcd. for $C_{15}H_{12}O_2$: C, 80.3; H, 5.40; 1 MeO–, 13.8. Found: C, 80.2; H, 5.58; MeO–, 13.9.

B. **Alkaline Hydrolysis of 3-Acetyl-2-(4-methoxyphenyl)benzofuran.**—The methyl ether (1.0 g.) of the peroxide oxidation product was dissolved in ethanol (5.0 ml.), treated with 40% aqueous NaOH (1.0 ml.), and heated under reflux for 1 hr. Excess of water was then added and the mixture was extracted with ether. The ether extract was washed with aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated. The residue was dissolved in methanol containing a few drops of concentrated HCl and heated for 5 min. Colorless crystals then began to separate. Water was added and the crystalline product was collected. Recrystallized from acetone–methanol, 2-(4-methoxyphenyl)benzofuran, m.p. and m.m.p. 148–149°, $\lambda_{\max}^{\mathrm{EtOH}}$ 307 mμ, was obtained (0.13 g.).

C. **Alkaline Hydrolysis of 3-Anisoyl-2-ethylbenzofuran (Royer and Bisagni[8]).**—A solution of 3-anisoyl-2-ethylbenzofuran (3 g.) and sodium hydroxide (1.2 g.) in ethanol (10 ml.) and water (2.0 ml.) was refluxed for 4 hr., diluted with water (60 ml.) and concentrated HCl (5 ml.), and heated for a further 10 min. The oily product rapidly solidified on cooling. It was suspended in aqueous alkali and filtered. The undissolved solid was recrystallized from acetone-methanol to give authentic 2-(4-methoxyphenyl)benzofuran (1.4 g.), $\lambda_{\max}^{\mathrm{EtOH}}$ 307 mμ, m.p. 148–149° [lit.[8] m.p. 151° (148°)].

Cochromatographed on silicic acid the 2-(4-methoxyphenyl)benzofuran prepared by each of the above procedures migrated as a single, blue fluorescent compound, R_f 0.74 in ether–Skellysolve F (7:3, v./v.), R_f 0.66 in ethyl acetate–Skellysolve F (1:4, v./v.).

3-Phenoxy-4'-methoxyflavylium Chloride.—A solution of salicylaldehyde (1.22 g.) and ω-phenoxy-4-methoxyacetophenone[8] (2.42 g.) in glacial acetic acid (5.0 ml.) was saturated with hydrogen chloride and kept overnight. Ether (50 ml.) was added. The oily product rapidly crystallized on scratching to a mass of orange needles, λ_{max} 462 mμ (3.5 g.).

The flavylium salt was characterized as its **ferrichloride.** This crystallized from glacial acetic acid as orange-red, glistening prisms, m.p. 165–167°.

Anal. Calcd. for $C_{22}H_{17}Cl_4FeO_3$: C, 50.1; H, 3.25. Found: C, 50.2; H, 3.39.

3-Carbophenoxy-2-(4-methoxyphenyl)benzofuran.—The above crude phenoxyflavylium chloride (2.0 g.) was dissolved in warm methanol (40 ml.) and treated with aqueous buffer, pH 5.8 (5.0 ml.) and 30% hydrogen peroxide (5.0 ml.). Decoloration occurred almost instantly and an oily precipitate separated. After 5 min. water was added, whereupon the oil solidified. Recrystallized from methanol, 3-carbophenoxy-2-(4-methoxyphenyl)benzofuran was obtained as long, colorless needles, m.p. 92°, λ_{max}^{EtOH} 319, 228 mμ.

Anal. Calcd. for $C_{22}H_{16}O_4$: C, 76.7; H, 4.68; 1 MeO–, 9.01. Found: C, 76.7; H, 4.78; MeO–, 8.97.

The carbophenoxy compound (4.0 g.) was heated on a steam bath with acetone (100 ml.) and 5% aqueous NaOH (50 ml.) for 15 min. Acidification of the solution with concentrated HCl (20 ml.) then precipitated a crystalline solid. Recrystallized from acetone–methanol, 3-carboxy-2-(4-methoxyphenyl)benzofuran was obtained as colorless needles (3.0 g.), λ_{max}^{EtOH} 311 and 224 mμ, m.p. 217°, undepressed on admixture with the previously described acid.

Anal. Found: C, 71.7; H, 3.55; MeO–, 11.7.

The methyl ester of the acid had m.p. and m.m.p. 81°.

3-Methoxy-4'-hydroxyflavylium Chloride.—Hydrogen chloride was passed into a solution of salicylaldehyde (1.5 g.) and ω-methoxy-4-hydroxyacetophenone (1.9 g.) in ethyl acetate (10 ml.) and ethanol (2.0 ml.) for 5 min. Red crystals rapidly separated from the reaction mixture. After 2 hr. the flavylium salt was collected (3.1 g.) and recrystallized from 5% aqueous hydrochloric acid. 3-Methoxy-4'-hydroxyflavylium chloride was obtained as red-brown, glistening needles with a green reflex, m.p. 135–137° dec.

3-Carbomethoxy-2-(4-hydroxyphenyl)benzofuran.—A solution of the above flavylium salt (2.0 g.) in methanol (40 ml.) and aqueous buffer, pH 5.8 (30 ml.), was treated with 30% hydrogen peroxide (4.0 ml.). Colorless crystals rapidly separated. After 5 min. water was added and the product was collected and recrystallized from methanol. 3-Carbomethoxy-2-(4-hydroxyphenyl)benzofuran was obtained as colorless, glistening needles, m.p. 187°, λ_{max}^{EtOH} 316 mμ (1.0 g.).

Anal. Calcd. for $C_{16}H_{12}O_4$: C, 71.6; H, 4.51; MeO–, 11.6. Found: C, 71.7; H, 4.62; MeO–, 11.5.

Acetylation of the product gave **3-carbomethoxy-2-(4-acetoxyphenyl)benzofuran** which crystallized from methanol as colorless, felted needles, m.p. 135°, λ_{max}^{EtOH} 303 and 224 mμ.

Anal. Calcd. for $C_{18}H_{14}O_5$: C, 69.7; H, 4.55. Found: C, 69.5; H, 4.59.

Methylation of the oxidation product gave the previously described 3-carbomethoxy-2-(4-methoxyphenyl)benzofuran, m.p. and m.m.p. 81°, λ_{max}^{EtOH} 314 and 227 mμ. This methyl ether methyl ester was also obtained by hydrogen peroxide oxidation of 3,4'-dimethoxyflavylium chloride. On alkaline hydrolysis the 3-carboxy-2-(4-methoxyphenyl)benzofuran, m.p. and m.m.p. 217°, was obtained.

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Furazan Oxides. IV. Extensions of the Scope of the Haloalkoxy Substitution Reaction[1a,b]

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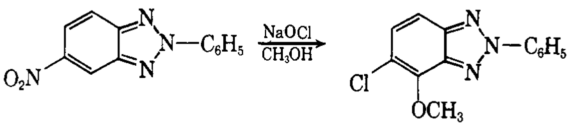
Additional examples are given of the recently described reaction in which an aromatic nitro group and an adjacent ring hydrogen are replaced by a halogen and an alkoxy group, respectively, by treatment of certain aromatic nitro compounds with aqueous sodium hypohalite in alkaline alcohol solution. Improved conditions are given for the reduction of benzofurazan oxides by copper and acid to give *o*-nitroanilines.

In a previous paper in this series[1a] a novel aromatic substitution reaction was described in which the overall result was the replacement of a nitro group by a chloro group and also the replacement of an adjacent ring hydrogen by a methoxy group as a consequence of the treatment of certain aromatic nitro compounds with aqueous sodium hypochlorite in alkaline methanol solution at about 50°. Since this reaction, which we designate as a haloalkoxy substitution reaction, is potentially useful as a means of synthesizing certain aromatic compounds that have several adjacent ring substituents and that are difficult to prepare by other methods, we have investigated the scope and generality of the reaction.

It was reported earlier[1a] that the reaction unfortunately was found not to occur with some of the more common aromatic nitro compounds such as *m*-dinitrobenzene. In the work done thus far, successful haloalkoxy substitution reactions have been achieved only with molecules having a nitrogen heterocycle fused to the ring bearing the replaceable nitro group as in the 4- and 5-nitrobenzofurazans and the corresponding N-oxides; the two new examples of nitro compounds that undergo haloalkoxy substitution that have been found in the present work, 5-nitro-2-phenylbenzotri-



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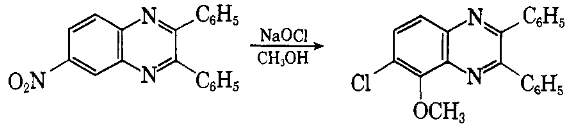

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