Synthesis and Herbicidal Activity of Xanthones

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Several substituted xanthones have been synthesized and tested for herbicidal activity. Both the classical Michael–Kostanecki method and a new regioselective method were used to prepare starting 1-hydroxyxanthones from which several 1-alkoxyxanthones were prepared. Among the compounds tested, herbicidal activity was greatest for 1-methoxyxanthone and 1-(allyloxy)xanthone. Some species specificity was observed, particularly for 1-methoxy-3-methylxanthone, which was more toxic to grasses than to broadleaf species.

INTRODUCTION

In the course of earlier work on the synthesis of a xanthone analogue of an anthracycline, 1-hydroxy- and 1-methoxy-3-methylxanthone (**1a** and **1b**, respectively) had been prepared (Sayeed 1982). As part of a routine testing program these compounds were assessed for herbicidal activity in the laboratories of Uniroyal Chemicals Ltd. While the 1-hydroxy derivative showed no significant activity, the 1-methoxy derivative showed significant herbicidal activity with some species specificity (see Table II).

To assess the potential of this class of compounds as herbicides, several analogues were prepared and tested for activity. In this paper we describe the synthesis of these derivatives and report on their herbicidal activity.

EXPERIMENTAL PROCEDURES

^{1}H NMR spectra were recorded on a Bruker AM-300 instrument using tetramethylsilane as internal standard. IR spectra were recorded on a Perkin-Elmer 881 spectrometer. Merck Kieselgel 60 was used for all chromatography. Exact mass/mass spectra were obtained on an Analytical VG 7070E-HF instrument. Melting points were measured on a hot-stage instrument and are uncorrected.

1-Hydroxy-3-methylxanthone (1a). Salicylic acid (24.0 g, 0.173 mol), orcinol monohydrate (24.0 g, 0.170 mol), and polyphosphoric acid (200 g) were stirred together and heated to 140 °C for 4 h. The mixture was cooled in an ice bath, and ice-cold water was added to make the volume 500 mL; the mixture was then heated to 90 °C for 0.5 h. The suspension was cooled, extracted with chloroform, dried ($MgSO_4$), and evaporated to give yellow crystals. Chromatography on silica (benzene) gave 11.5 g (30%): mp 147 °C [lit. 148 °C (Desai et al., 1960)]; IR (CH_2Cl_2) 1645 cm^{-1}; ^{1}H NMR (60 MHz) ($CDCl_3$) δ 12.25 (1 H, s), 7.3–8.3 (4 H, m), 6.7 (1 H, s), 6.6 (1 H, s), 2.35 (3 H, s); mass spectrum m/e (rel %) 226 (100), 197 (40).

2,6,2′-Trimethoxybenzophenone. *m*-Dimethoxybenzene (25 g, 0.18 mol) and tetramethylethylenediamine (TMEDA, 21 g, 0.18 mol) were mixed with dry tetrahydrofuran (THF, 70 mL) under nitrogen. *n*-BuLi (75 mL of a 2.5 N solution in hexane, 0.19 mol) was added slowly at 25 °C. After stirring for 0.5 h, the solution was slowly transferred (0.5 h) under nitrogen into a stirred solution of methyl anisate (32 g, 0.21 mol) in THF (100 mL) which was maintained at 0 °C. Additional THF (200 mL) was added to the mixture to facilitate stirring, and stirring was continued for 3 h. The mixture was then poured into 10% aqueous HCl, extracted with CH_2Cl_2, dried ($MgSO_4$), and evaporated. Recrystallization from benzene/hexane gave 36.8 g (75%): IR (CH_2Cl_2) 1673 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.69_7 (6 H, s), 3.73_7 (3 H, s), 6.57_0 (2 H, d, J = 8.37), 6.9–7.0 (2 H, m), 7.27_0 (1 H, t, J = 8.37), 7.44_7 (1 H, ddd, J = 9.17, 7.26, 1.8), 7.68 (1 H, dd, J = 8.04, 1.8); mass spectrum m/e (rel %) 272 (32), 241 (55), 211 (19), 165 (100), 151 (27), 135 (67). Exact mass calcd for $C_{16}H_{16}O_4$: 272.1054. Found: 272.1051.

1-Hydroxyxanthone (2a). 2,6,2′-Trimethoxybenzophenone (36.8 g, 0.14 mol) was placed in a 1-L flask with toluene (300 mL) and $AlCl_3$ (55 g) cautiously added. The mixture was warmed slowly to reflux (Caution: The reaction may go exothermic and cooling may be required.) and refluxed for 5 h. The solution was cooled in ice and 10% aqueous HCl (200 mL) slowly added with stirring (very exothermic at first). After refluxing 1 h, the mixture was extracted with ethyl acetate, dried ($MgSO_4$), evaporated, and recrystallized from 2-propanol to give 21.5 g (75%) of pale yellow crystals: mp 144–146 °C (lit. 147 °C); IR (CH_2Cl_2) 1649 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.78_9 (1 H, dd, J = 8.31, 0.8), 6.95_0 (1 H, dd, J = 8.39, 0.8), 7.39_8 (1 H, br t, $J \cong 7.5$), 7.47_6 (1 H, br d, $J \cong 8.4$), 7.59_2 (1 H, t, J = 8.33), 7.75_4 (1 H, ddd, J = 8.69, 6.95, 1.7), 8.28_1 (1 H, dd, J = 8.03, 1.7), 12.64 (1 H, s); mass spectrum m/e (rel %) 213 (14), 212 (100), 184 (10).

5-Chloro-2,2′,6′-trimethoxybenzophenone. The benzophenone was prepared in a manner identical with that used for trimethoxybenzophenone, above, using *m*-dimethoxybenzene (0.76 g, 5.5 mmol), TMEDA (0.64 g, 5.5 mmol), and *sec*-BuLi (2.2 mL of 2.5 M hexane solution, 5.5 mmol). The product was filtered through a short silica gel column with CH_2Cl_2 and recrystallized from benzene/hexane to give 0.76 g (45%): IR (CH_2Cl_2) 1677, 1664 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.68_8 (3 H, s), 3.70_4 (6 H, s), 6.57_0 (1 H, d, J = 8.38), 6.86_8 (1 H, d, J = 8.81), 7.30_2 (1 H, d, J = 8.38), 7.38_4 (1 H, dd, J = 8.81, 2.73), 7.64_2 (1 H, d, J = 2.73); mass spectrum m/e (rel %) 308 (3), 306 (10), 275 (9), 169 (11), 165 (41), 151 (12), 150 (14), 149 (100). Exact mass calcd for $C_{16}H_{15}O_4{}^{35}Cl$: 306.0629. Found: 306.0644.

7-Chloro-1-hydroxyxanthone (3a). The 5-chloro-2,2′,6′-trimethoxybenzopheneone (5 g) was treated with $AlCl_3$ (7.5 g) in 100 mL of benzene in a manner identical with that described for trimethoxybenzophenone, above. The product was

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Table I. Synthesis of 1-Alkoxyxanthones

product	made from	RX	K_2CO_3, g	DMSO, mL	time	yield, g
1c	1a, 1 g	EtI, 3 mL	1.75	6	1 h	0.98 (85%)
1d	1a, 1 g	nBuBr, 3 mL	2.0	6	1 h	1.1 (88%)
1e	1a, 1 g	nOctI, 3 mL	2.0	6	0.75 h	1.3 (87%)
2b	2a, 1 g	MeI, 1 mL	2.0	6	0.5 h	0.81 (76%)
2c	2a, 1 g	EtI, 3 mL	2.0	6	1 h	0.81 (72%)
2d	2a, 1 g	nBuBr, 3 mL	2.0	6	0.5 h	0.89 (70%)
2e	2a, 1 g	nOctI, 3 mL	2.0	6	2 h	1.2 (79%)
2f	2a, 1 g	BzCl, 3 mL	2.0	6	3 h	0.93 (65%)
2g	2a, 1 g	allylBr, 3 mL	2.0	6	2 h	1.0 (84%)
2h	2a, 0.5 g	R_1Br, 0.45 mL	1.0	4	10 min	0.54 (73%)
2i	2a, 0.5 g	R_2Br, 0.45 mL	1.0	4	10 min	0.52 (74%)
3b	3a, 1.3 g	MeI, 2 mL	2.0	6	10 min	1.2 (87%)

refluxed in toluene (20 mL) containing toluenesulfonic acid (400 mg) for 8 h, passed through a short silica gel column (1 in.) with CH_2Cl_2, and evaporated to give 3.2 g (90%) of the xanthone: IR (CH_2Cl_2) 1649 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.79_4 (1 H, dd, J = 8.33, 0.88), 6.90_3 (1 H, dd, J = 8.33, 0.88), 7.40_5 (1 H, d, J = 8.96), 7.58_6 (1 H, t, J = 8.33), 7.66_2 (1 H, dd, J = 8.96, 2.61), 8.19_2 (1 H, d, J = 2.61), 12.38 (1 H, s); mass spectrum m/e (rel %) 248 (4), 246 (11), 149 (23), 137 (12), 129 (16). Exact mass calcd for $C_{13}H_7O_3{}^{35}Cl$: 246.0067. Found: 246.0075.

2-Methoxyxanthone (4). *p*-Methoxyphenol (31.04 g, 0.25 mol), *o*-chlorobenzoic acid (31.3 g, 0.2 mol), and copper powder (2.6 g) were added sequentially to a solution of sodium methoxide in methanol (prepared from 9.2 g of sodium, 0.4 mol, and 140 mL of methanol). The open mixture was slowly heated with stirring to 200 °C, resulting in the evaporation of the methanol to leave an amorphous black mass. This was cooled and dissolved in water whose pH was adjusted to 7.0 by addition of NaOH. After extraction with CH_2Cl_2, the solution was acidified and extracted with CH_2Cl_2 and the extract dried ($MgSO_4$) and evaporated to leave 44.7 g of crude 2-(*p*-methoxyphenoxy)-benzoic acid. NMR indicated the presence of about 10% *o*-chlorobenzoic acid. The crude 2-(*p*-methoxyphenoxy)benzoic acid (32.8 g, 0.13 mol) was dissolved in polyphosphoric acid and heated to 92 °C for 8 h. The mixture was cooled, diluted with ice water, and extracted with ethyl acetate, and the extract was washed with 5% aqueous $NaHCO_3$ (removing any remaining starting material and the *o*-chlorobenzoic acid), dried ($MgSO_4$), and evaporated to give 23.1 g (76%): IR (CH_2Cl_2) 1654 cm^{-1}; ^1H NMR ($CDCl_3$) δ $3..2_2$ (3 H, s), 7.32_6 (1 H, dd, J = 9.13, 3.08), 7.37_1 (1 H, m), 7.43_8 (1 H, d, J = 9.13), 7.48_2 (1 H, dd, J = 8.33, 0.69), 7.70_9 (2 H, m), 8.34_7 (1 H, dd, J = 8.05, 1.6); mass spectrum m/e (rel %) 226 (100), 225 (35), 211 (30), 197 (15), 196 (18), 155 (23), 149 (24). Exact mass calcd for $C_{14}H_{10}O_3$: 226.0630. Found: 226.0630.

Alkylation of the 1-Hydroxyxanthones. General Procedure. *1-Ethoxy-3-methylxanthone* (1c). The same procedure was used for the preparation of all of the 1-alkoxyxanthones (except for 1b), and the procedure for the preparation of 1-ethoxy-3-methylxanthone (1c) is typical. 1-Hydroxy-3-methylxanthone (1 g, 4.4 mmol), anhydrous K_2CO_3 (1.75 g), dimethyl sulfoxide (DMSO, 6 mL), and ethyl iodide (6 mL) were heated under reflux at 100 °C for 1 h. After cooling and the addition of water, the mixture was extracted with benzene, washed with water, dried ($MgSO_4$), evaporated, and recrystallized from CCl_4/hexane to give 0.98 g (87%).

Table I gives the data for the preparation of the 1-alkoxy derivatives.

In the preparation of **2f**, 0.5 g of KI was also included in the reaction mixture as a nucleophilic catalyst (BzCl is benzyl chloride).

1-Methoxy-3-methylxanthone (1b). 1-Hydroxy-3-methylxanthone (4.0 g, 18 mmol), anhydrous K_2CO_3 (6.0 g, 43 mmol), and dimethyl sulfate (10.0 mL, 59 mmol) were refluxed in dry acetone (150 mL) for 18 h. The cooled solution was poured into water (50 mL) and extracted ($CHCl_3$); the extracts were dried ($MgSO_4$) and evaporated to give 4.3 g of crude product. Chromatography on silica gel (benzene/ether, 1:1) gave 4.1 g (91%) of pure product.

The physical properties of each of the 1-alkoxyxanthones are given below.

1-Methoxy-3-methylxanthone (1b). mp 153.5 °C (CH_2Cl_2/hexane); IR (CH_2Cl_2) 1657 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.46_2 (3 H, s), 4.44_4 (3 H, s), 6.60_4 (1 H, s), 6.87_0 (1 H, s), 7.31_8 (1 H, ddd, J = 0.96, 7.09, 8.05), 7.38_3 (1 H, dd, J = 8.21, 0.59), 7.63_9 (1 H, ddd, J = 8.76, 6.99, 1.77), 8.29_2 (1 H, dd, J = 7.94, 1.47); mass spectrum m/e (rel %) 240 (100), 239 (32), 225 (28), 211 (93), 210 (26), 209 (17), 194 (63), 181 (37). Exact mass calcd for $C_{15}H_{12}O_3$: 240.0786. Found: 240.0783.

1-Ethoxy-3-methylxanthone (1c). mp 129–130 °C (CCl_4/hexane); IR (CH_2Cl_2) 1659 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.59_3 (3 H, t, J = 6.95), 2.44_5 (3 H, s), 4.20_2 (2 H, q, J = 6.97), 6.59_4 (1 H, s), 6.85_0 (1 H, s), 7.31_1 (1 H, ddd, J = 0.95, 7.09, 8.04), 7.37_7 (1 H, dd, J = 8.22, 0.65), 7.63_2 (1 H, ddd, J = 8.78, 7.14, 1.64), 8.29_0 (1 H, dd, J = 7.94, 1.76); mass spectrum m/e (rel %) 254 (59), 240 (17), 239 (100), 235 (17), 226 (40), 211 (35), 210 (62), 192 (31), 181 (24). Exact mass calcd for $C_{16}H_{14}O_3$: 254.0943. Found: 254.0942.

1-*n*-Butoxy-3-methylxanthone (1d). mp 118 °C (CCl_4/hexane); IR (CH_2Cl_2) 1656 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02_5 (3 H, t, J = 7.36), 1.63_9 (2 H, m), 1.95_6 (2 H, m), 2.44_4 (3 H, s), 4.11_8 (2 H, t, J = 7.31), 6.59_3 (1 H, s), 6.84_2 (1 H, s), 7.30_5 (1 H, ddd, J = 1.06, 7.00, 8.06), 7.37_3 (1 H, d, J = 7.57), 7.62_7 (1 H, ddd, J = 1.61, 7.02, 8.63), 8.29_1 (1 H, dd, J = 7.97, 1.72); mass spectrum m/e (rel %) 282 (19), 253 (25), 239 (100), 226 (84), 210 (27), 197 (20), 181 (8.6). Exact mass calcd for $C_{17}H_{15}O_3$: 282.1256. Found: 282.1238.

1-(*n*-Octyloxy)-3-methylxanthone (1e). mp 74.5–75 °C (hexane); IR (CH_2Cl_2) 1657 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88_7 (3 H, t, J = 6.80), 1.20–1.38 (8 H, m), 1.57_4 (2 H, m), 1.97_4 (2 H, p, J = 7.19), 2.44_3 (3 H, s), 4.10_3 (2 H, t, J = 6.80), 6.59_0 (1 H, s), 6.83_9 (1 H, s), 7.30_5 (1 H, ddd, J = 0.94, 7.10, 8.04), 7.37_2 (1 H, dd, J = 8.42, 0.62), 7.62_6 (1 H, ddd, J = 8.59, 7.00, 1.59), 8.28_8 (1 H, dd, J = 7.99, 1.65); mass spectrum m/e (rel %) 338 (15), 253 (24), 239 (100), 227 (26), 226 (98), 210 (22), 197 (14). Exact mass calcd for $C_{22}H_{26}O_3$: 338.1882. Found: 338.1893.

1-Methoxyxanthone (2b). mp 128.5 °C (CH_2Cl_2/hexane); IR (CH_2Cl_2) 1661 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.02_6 (3 H, s), 6.80_2 (1 H, d, J = 8.24), 7.06_1 (1 H, dd, J = 8.39, 0.88), 7.33_4 (1 H, ddd, J = 0.69, 7.11, 8.05), 7.41_1 (1 H, dd, J = 8.49, 0.60), 7.58_5 (1 H, t, J = 8.39), 7.66_2 (1 H, ddd, J = 8.65, 7.02, 1.63), 8.30_4 (1 H, dd, J = 8.00, 1.52); mass spectrum m/e (rel %) 226 (64), 225 (22), 197 (52), 180 (35), 168 (21), 139 (19). Exact mass calcd for $C_{14}H_{10}O_3$: 226.0630. Found: 226.0622.

1-Ethoxyxanthone (2c). mp 100–101 °C (2-propanol/hexane); IR (CH_2Cl_2) 1662 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.60_1 (3 H, t, J = 6.97), 4.22_5 (2 H, q, J = 6.97), 6.78_6 (1 H, d, J = 8.24), 7.03_7 (1 H, dd, J = 8.44, 0.86), 7.33_1 (1 H, ddd, J = 1.04, 7.01, 8.05), 7.40_6 (1 H, dd, J = 0.54, 8.28), 7.57_0 (1 H, t, J = 8.36), 7.65_5 (1 H, ddd, J = 8.63, 7.03, 1.61), 8.30_3 (1 H, dd, J = 7.97, 1.60); mass spectrum m/e (rel %) 240 (65), 226 (16), 225 (100), 221 (19), 212 (53), 197 (35), 196 (61), 184 (19), 168 (26), 139 (18), 128 (21), 127 (18). Exact mass calcd for $C_{15}H_{12}O_3$: 240.0786. Found: 240.0780.

1-*n*-Butoxyxanthone (2d). mp 126 °C (CCl_4/hexane); IR (CH_2Cl_2) 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02_6 (3 H, t, J = 7.37), 1.63_7 (2 H, m), 1.97_5 (2 H, p, J = 7.07), 4.14_1 (2 H, t, J = 6.56), 6.78_4 (1 H, d, J = 8.23), 7.02_5 (1 H, dd, J = 8.44, 0.84), 7.32_3 (1 H, ddd, J = 1.00, 7.03, 8.03), 7.40_0 (1 H, d, J = 7.76), 7.56_4 (1 H, t, J = 8.36), 7.64_8 (1 H, ddd, J = 8.62, 7.01, 1.61), 8.30_2 (1 H, dd, J = 7.97, 1.67); mass spectrum m/e (rel %) 268 (18), 239

Table II. Postemergence Herbicidal Activities (% Control)

compd	concn, ppm	jim[a]	morn[a]	vellf[a]	barn[a]	gosgr[a]	grfox[a]	swigr[a]	wioat[a]	yefox[a]	corn[a]	cotn[a]	rice[a]	soyn[a]
1a	3000	0	0	0	0		0	0						
1b	3000	65	75	0	50	100	100	100	100	100	70	0	100	10
	2000				10	100	100	100	100	100	50	0	70	10
	1000				45	95	100	95	95	90	75	10	50	15
	500				60	90	100	90	80	80	60	0	50	20
	250				50	50	100	80	80	80	40	0	50	10
1c	3000	0	0	0	74		45	15			0	0	0	0
1d	3000	0	0	0	75		15	15			0	0	0	0
1e	3000	0	0	0	50		20	15			0	0	0	0
2a	3000	0	0	0	5		5	0						
2b	3000	70	100	100	100		100	100	90		100	20	100	100
	2000	70	100		100		100		90		100	0	100	90
	1000	70	100		100		100		90		50	0	100	80
	500	60	80	100	90		100		90		50	0	100	20
	250	50	80		50		90		90		0	0	50	20
	125	50	20		0		60		50		0	0	20	10
2c	3000	90	100	20	0		80	5	0		0	0	40	0
	2000	90	100		0		50		0		0	0	40	0
	1000	80	50		0		20		0		0	0	0	0
2d	3000	0	10	0	0		0	0						
2e	3000	20	10	0	0		40	75	30		0	0	0	0
	2000	0	0		0		20		10		0	0	0	0
2f	3000	10	25	15	70		55	15						
2g	3000	100	100	5	100		100	100	90		20	70	90	40
	2000	100	100		90		10		80		30	50	90	40
	1000	100	50		80		100		20		20	50	60	20
	500	90	50		70		100		20		0	50	60	20
	250	90	50		60		100		20		0	50	60	20
2h	3000	30	30	25	30		20	10						
2i	3000	15	15	20	65		40	5						
3b	3000	0	0	0	5		5	0						
4	3000	0	0	0	5		5	0						

[a] jim = jimsonweed, morn = wild morningglory, vellf = velvetleaf, barn = barnyard grass, gosgr = goosegrass, grfox = green foxtail, swigr = switchgrass, wioat = wild oats, yefox = yellow foxtail, cotn = cotton, soyn = soybean.

(20), 225 (91), 213 (18), 212 (100), 196 (23). Exact mass calcd for $C_{17}H_{16}O_3$: 268.1099. Found: 268.1089.

1-(*n*-Octyloxy)xanthone (2e). mp 54 °C (hexane); IR (CH_2Cl_2) 1661 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88_6 (3 H, t, J = 6.81), 1.33_0 (8 H, m), 1.53_9 (2 H, m), 1.97_9 (2 H, m), 4.12_7 (2 H, t, J = 6.77), 6.78_0 (1 H, d, J = 8.27), 7.02_3 (1 H, dd, J = 8.47, 0.88), 7.32_1 (1 H, ddd, J = 1.07, 6.99, 8.06), 7.39_8 (1 H, dd, J = 8.42, 0.63), 7.56_1 (1 H, t, J = 8.36), 7.64_7 (1 H, ddd, J = 8.59, 7.00, 1.59), 8.30_0 (1 H, dd, J = 7.95, 1.52); mass spectrum m/e (rel %) 324 (12), 239 (16), 226 (21), 225 (80), 213 (23), 212 (100), 197 (13), 196 (17). Exact mass calcd for $C_{21}H_{24}O_3$: 324.1725. Found: 324.1712.

1-(Benzyloxy)xanthone (2f). mp 134 °C (ethyl acetate/hexane); IR (CH_2Cl_2) 1662 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.32_0 (2 H, s), 6.84_1 (1 H, d, J = 8.08), 7.06_7 (1 H, dd, J = 0.74, 8.47), 7.3–7.7 (9 H, m), 8.33_2 (1 H, dd, J = 1.70, 7.93); mass spectrum m/e (rel %) 302 (29), 196 (28), 91 (100), 65 (12). Exact mass calcd for $C_{20}H_{14}O_3$: 302.0943. Found: 302.0935.

1-(Allyloxy)xanthone (2g). mp 101 °C (2-propanol); IR (CH_2Cl_2) 1657 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.65_8 (2 H, dt, J = 5.29, 1.40), 5.33_2 (1 H, dd, J = 10.48, 1.35), 5.47_1 (1 H, dd, J = 15.75, 1.50), 6.10_0 (1 H, m), 7.3–7.8 (6 H, m), 8.34_8 (1 H, dd, J = 1.61, 7.97); mass spectrum m/e (rel %) 252 (59), 237 (18), 223 (14), 212 (22), 211 (100), 155 (28), 149 (11), 127 (15). Exact mass calcd for $C_{16}H_{12}O_3$: 252.0786. Found: 252.0776.

1-(Carbethoxymethoxy)xanthone (2h). mp 128–129 °C (2-propanol); IR (CH_2Cl_2) 1759, 1662 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29_7 (3 H, t, J = 7.13), 4.28_5 (2 H, q, J = 7.13), 4.84_4 (2 H, s), 6.72_0 (1 H, d, J = 8.22), 7.13_3 (1 H, dd, J = 8.44, 0.71), 7.34_5 (1 H, ddd, J = 0.96, 7.05, 8.02), 7.41_7 (1 H, d, J = 7.95), 7.57_0 (1 H,t, J = 8.37), 7.67_1 (1 H, ddd, J = 8.62, 7.03, 1.59), 8.30_9 (1 H, dd, J = 7.95, 1.67); mass spectrum m/e (rel %) 298 (2.4), 226 (16), 225 (100), 97 (12), 196 (42), 139 (20). Exact mass calcd for $C_{17}H_{14}O_3$: 298.0841. Found: 298.0857.

1-(1-Carbethoxyethoxy)xanthone (2i). mp 133 °C (2-propanol); IR (CH_2Cl_2) 1749, 1662 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23_2 (3 H, t, J = 7.13), 1.81_1 (3 H, d, J = 6.76), 4.22_0 (2 H, q, J = 3.15), 4.86_2 (1 H, q, J = 6.77), 6.72_2 (1 H, d, J = 7.48), 7.11_4 (1 H, dd, J = 8.49, 0.92), 7.33_9 (1 H, ddd, J = 1.23, 7.38, 8.61), 7.41_6 (1 H, dd, J = 8.39, 0.70), 7.53_9 (1 H, t, J = 8.36), 7.66_8 (1 H, ddd, J = 8.64, 7.02, 1.61), 8.30_2 (1 H, dd, J = 8.01, 1.69); mass spectrum m/e (rel %) 312 (10), 239 (100), 223 (41), 212 (35), 196 (83), 139 (22). Exact mass calcd for $C_{18}H_{16}O_3$: 312.0998. Found: 312.0980.

7-Chloro-1-methoxyxanthone (3b). mp 164.5–165 °C (hexane); IR (CH_2Cl_2) 1662 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.02_7 (3 H, s), 6.81_6 (1 H, d, J = 8.28), 7.05_3 (1 H, dd, J = 8.42, 0.84), 7.37_5 (1 H, d, J = 8.87), 7.58–7.65 (2 H, m), 8.24_3 (1 H, d, J = 2.60); mass spectrum m/e (rel %) 262 (33), 261 (25), 260 (100), 259 (34), 246 (12), 233 (28), 232 (19), 231 (84), 230 (24), 216 (17), 214 (51), 202 (23), 149 (39). Exact mass calcd for $C_{14}H_9O_3$: 260.0240. Found: 260.0239.

Herbicide Tests. Compounds **1a–e**, **2a–i**, **3b**, and **4** were tested as postemergence (foliage applied) and preemergence (soil applied) herbicides against nine weed species and four crop species including jimson weed (*Datura stramonium* L.), wild morningglory [*Ipomoea purpurea* (L. Roth)], velvetleaf (*Abutilon theophrasti* Medic), barnyard grass [*Echinochloa crus-galli* (L.) Beauv.], goosegrass [*Eleusine indica* (L.) Gaertn], green foxtail [*Setaria viridis* (L.) Beauv.], switchgrass (*Panicum virgatum* L.), wild oats (*Avena fatua* L.), yellow foxtail [*Setaria glauca* (L.) Beauv.], corn (*Zea mays* L.), cotton (*Gossypium hirsutum* L.), rice (*Oryza sativa* L.), and soybean [*Glycine max* (L.) Merr.], respectively.

In preparation for application to the plant foliage, 0.3 g of each compound was dissolved in 10 mL of acetone; 100 mg of ethoxylated sorbitan monolaurate Tween 20 was added to the mixture, which was agitated vigorously with an ultrasonic probe. Distilled water was then added to the mixture, making 100 mL of each 3000 ppm solution. The solutions were applied to the drip point on the plant foliage 7 days after emergence by using a No. 152 DeVilbiss atomizer.

At the time of treatment, the dicotyledonous species were in the cotyledon to first true leaf stages and the monocots were in the one and one-half to two and one-half leaf stage. The heights of the plants measured from the tip of the tallest leaves to the soil line were as follows: jimson weed, 4 cm; morninglory, 10 cm; velvetleaf, 9 cm; barnyard grass, 15 cm; goosegrass, 3 cm;

Table III. Preemergence Herbicidal Activities (% Control)

compd[a]	concn, lb/acre	jim[b]	morn[b]	vellf[b]	barn[b]	gosgr[b]	grfox[b]	swigr[b]	wioat[b]	yefox[b]	rice[b]
2b	10	0	0	0	70	30	90	50	40	30	0
	5				30	0	0	0	0	0	0
	2				0	0	0	0	0	0	0

[a] All other compounds showed no activity at 10 lb/acre. [b] jim = jimsonweed, morn = wild morningglory, vellf = velvetleaf, barn = barnyard grass, gosgr = goosegrass, grfox = green foxtail, swigr = switchgrass, wioat = wild oats, yefox = yellow foxtail.

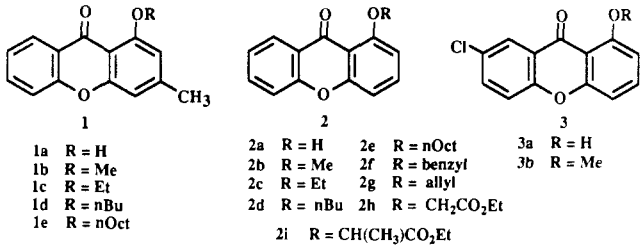

Figure 1.

green foxtail, 7 cm; switchgrass, 3 cm; wild oats, 10 cm; yellow foxtail, 10 cm; corn, 30 cm; cotton, 16 cm; rice, 15 cm; soybean, 16 cm. Tests involving dosage rates of less than 3000 ppm were conducted by dilution of the 3000 ppm solution with water prior to application to the foliage. The postemergence data are given in Table II.

The preemergence tests at 11.2 kg/ha, 10 lb/acre, were conducted by drenching 46 mL of a 250 ppm solution, prepared by dilution of the 3000 ppm solution with distilled water, onto the soil surface in 11.4-cm pots containing the aforementioned seeds. Only compound 2a showed any activity, and the data are given in Table III.

In all tests, the percentage control of each species was estimated by visual comparison with untreated controls 2 weeks after treatment. Within a species, the amount of necrotic tissue determined the percent control rating.

RESULTS AND DISCUSSION

Synthetic Methods. The xanthones **1**, **2** and **3** (Figure 1), as well as 2-methoxyxanthone **4**, were prepared in this study, and details regarding preparation and characterization are given under Experimental Procedures.

Many general methods for the synthesis of xanthones are known and have been reviewed (Afzal and Al-Hassan, 1980; Roberts, 1961). Among the most popular methods is the Michael–Kostanecki method, which was later modified by Grover et al. (1955) and still later by Muchali et al. (1985) and Nevrekar et al. (1983). This method involves the reaction of an *o*-hydroxybenzoic acid with a polyhydric phenol in the presence of a dehydrating agent such as polyphosphoric acid, acetic anhydride, phosphorus oxychloride, or mixtures of these reagents. Using this general method, Desai et al. (1960) have carried out a synthesis of 1-hydroxy-3-methylxanthone (**1a**) from *o*-hydroxybenzoic acid and orcinol monohydrate by heating in polyphosphoric acid. Even though the yield was low, the same method, due to its simplicity, was used for the preparation of **1a** in this work.

Although 1-hydroxyxanthone has been synthesized by the Michael–Kostanecki method (Muchali et al., 1985; Nevrekar et al. 1983), the yields are low and the possibility of contamination by 3-hydroxyxanthone exists. For these reasons we chose to carry out a regioselective synthesis of both the 1-hydroxy- and 7-chloro-1-hydroxyxanthones via the procedure shown in Figure 2.

o-Dimethoxybenzene was lithiated specifically between the two methoxy substituents (Gilman et al., 1940) and added to the appropriately substituted methyl benzoates to prepare the trimethoxybenzophenones (R = H, 75%; R = Cl, 45%). The benzophenones were then treated

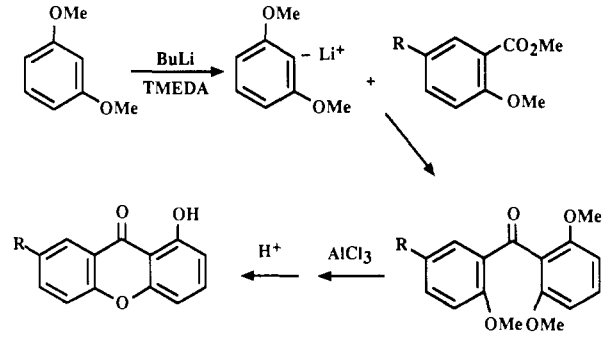

Figure 2.

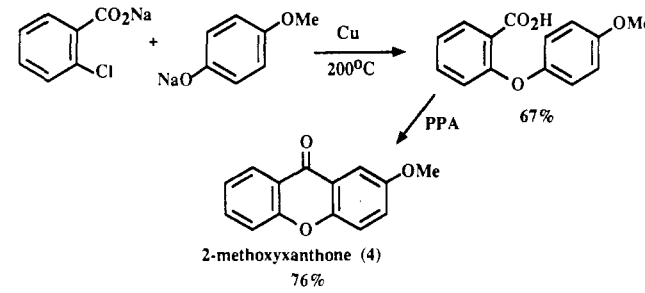

Figure 3.

with $AlCl_3$ to deblock the phenolic groups and form the xanthones (R = H, 75%). In the case of the chlorobenzophenone (R = Cl), the product of the $AlCl_3$ treatment, which appeared to be largely the triol, had to be treated with toluenesulfonic acid in refluxing toluene to dehydrate it to give 7-chloro-1-hydroxyxanthone (**3a**) (90% overall yield from the benzophenone).

2-Methoxyxanthone was synthesized by the Ullman procedure shown in Figure 3 (Ullman and Zlokasoff, 1905).

Alkylation of **1a**, **2a**, and **3a** to form the 1-alkoxy derivatives was accomplished by heating the corresponding 1-hydroxyxanthone in DMSO with anhydrous K_2CO_3 and an excess of the alkyl halide. For benzylation of **2a**, benzyl chloride was used as the alkyl halide and potassium iodide added as a nucleophilic catalyst.

All new compounds were characterized by 300-MHz NMR, high-resolution mass spectrometry (with exact mass for elemental composition), and infrared spectroscopy (see Experimental Procedures).

Herbicide Testing. As the data in Table II show, some of the 1-alkoxyxanthones prepared in this study show quite strong herbicidal activity. Both the series **1b–e** and **2b–e** show that herbicidal activity decreases with the chain length of the alkoxy substituent at the 1-position. The 1-hydroxy compounds **1a** and **2a** show no activity at all. Some crop specificity is observed, particularly for **1b**, where there is somewhat greater activity against the grass species. This specificity is diminished in **2b**, even at the lowest application levels. The 1-allyloxy compound **2g** is the only compound with a larger 1-alkoxy substituent with significant broad activity. Placing a chlorine substituent at the 7-position of **2b** (to produce **3b**) reduces the herbicidal activity to almost zero. Moving the alkoxy sub-

stituent to the 2-position, as in **4**, also reduces the herbicidal activity to zero.

Few conclusions about the relationship of herbicidal activity to structure can be made from the limited series of compounds tested. The activity appears to be dependent on the presence of a small 1-alkoxy substituent, although the 1-allyloxy compound **2g** is also active. With the synthesis of other analogues we hope to further elucidate the steric and electronic factors required to optimize the herbicidal activity of this interesting class of compounds.

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LITERATURE CITED

Afzal, M.; Al-Hassan, J. M. Synthesis and Biosynthesis of Phytoxanthones. *Heterocycles* **1980**, *14*, 1173.

Desai, B. M.; Desai, P. R.; Desai, R. D. Heterocyclic Compounds (XXXIII) Synthesis of Xanthones. *J. Indian Chem. Soc.* **1960**, *37*, 53.

Gilman, H.; Willis, B.; Cook, T. H.; Webb, F. J.; Meals, R. N. Dibenzofuran. XVII. Isomeric Metalation Products of Some Phenols and their Methyl Ethers. *J. Am. Chem. Soc.* **1940**, *62*, 667.

Grover, P. K.; Shah, G. D.; Shah, R. C. A New Synthesis of Hydroxyxanthones and Hydroxybenzophenones. *J. Chem. Soc.* **1955**, 3982.

Muchali, M. V. R.; Kudav, N. A. *o*-Hydroxybenzoyl Ureas in the Synthesis of 1-Hydroxyxanthones. *Chem. Ind.* **1985**, 31.

Nevrekar, N. B.; Lele, S. V.; Muchali, M. V. R.; Kudav, N. A. A Novel Reagent system: A Mixture of Phosphorus Oxychloride, *o*-Phosphoric Acid and Anhydrous Zinc Chloride for the Synthesis of 1-Hydroxyxanthones. *Chem. Ind.* **1983**, 479.

Roberts, J. C. Naturally Occurring Xanthones. *Chem. Rev.* **1961**, *61*, 591.

Sayeed, V. A. Xanthocycline Synthesis. Ph.D. Dissertation, The University of Manitoba, Winnipeg, Canada, 1982.

Ullman, F.; Zlokasoff, M. Uber Arylsalicylsäuren und deren Ueberfüren in Xanthone. *Ber. Dtsch. Chem. Ges.* **1905**, *38*, 2111.

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