Electrohalomethoxylation of Chromone Derivatives

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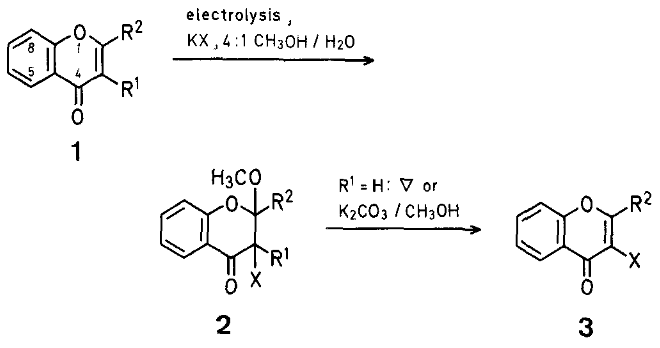
The synthetic utility of the organic electrochemistry has been generally recognized. The following conversions are noteworthy: furan derivatives are converted to the corresponding 2,5-dimethoxy-2,5-dihydrofurans[1] or to ring-opened products[2], carbonyl or aromatic compounds are converted to halogenated products[3], and olefins are converted to a variety of products[4]. We now report on the electrohalomethoxylation of chromone derivatives **1**[5].



A mixture of the chromone **1** in 4:1 methanol/water containing the potassium halide as a 0.1 molar solution was electrolyzed at a graphite anode to afford the halomethoxylated product **2** in good yield (Table 1).

The chromanones **2** having a hydrogen atom at C-3 ($R^1 = H$) are unstable and decompose slowly on standing and rapidly on heating to the chromones **3**. Products **3a** and **3c** were identified by comparison with authentic samples[6]. These products **2a–d** can be converted quantitatively to **3a–d** by treatment with potassium carbonate in methanol.

This ready conversion of **2a–d** to **3a–d** is indicative that regioselective attack of halo and methoxy groups is involved in the formation of **2**. Furthermore the coupling constants $J_{H\text{-}2,H\text{-}3} = 3$ Hz) in **2a** and **2b** suggest that the halo and methoxy groups are *cis*[7].

Many synthetic methods for chromones bearing halogen atoms at C-3 have been reported[8], but only few start from C-2 unsubstituted chromones[9]. Our electrochemical method is thus very useful to synthesize C-3 halogenated chromones.

Electrolysis of Chromones 1; General Procedure:

A mixture of the chromone **1** (1 mmol) in 4:1 methanol/water (70 ml) containing potassium halide (7 mmol) is electrolyzed in a divided cell at graphite anode under a constant current of 10 mA at room temperature for ~6 h. After 2.2 F/mol has been passed, the reaction mixture is concentrated to one-third of its original volume under reduced pressure below 40 °C and extracted with ether (40 ml). The ether layer is washed with sodium chloride solution (20 ml), dried with magnesium sulfate, and concentrated. The residue is subjected to preparative thin layer chromatography (Kieselgel 60 PF_{254}) or column chromatography (Kieselgel 60, 70–230 mesh) eluting with chloroform to afford the 3-halo-2-methoxychromanone **2** (Table 1).

3-Halochromones 3a–d; General Procedure:

A mixture of the 3-halo-2-methoxychromanone **2** (50 mg), potassium carbonate (50 mg) and methanol (5 ml) is heated at 50 °C for 2 h. The reaction mixture is poured into water (5 ml) and extracted with ether (3 × 10 ml). The ether layer is washed with sodium chloride solution (10 ml), dried with magnesium sulfate, and evaporated to give the crystalline 3-halochromone **3** quantitatively (Table 2).

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Table 1. 3-Chloro-2-methoxychromanones **2a–f**

Product No.	R^1	R^2	X	Yield [%]	m.p. [°C]	Molecular formula[a]	I.R. (neat or KBr) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]	M.S. *m/e*
2a	H	H	Cl	70[b]	—	—	1702; 1603; 1580	3.54 (s, 3H, OCH_3); 4.26 (d, 1H, H-3, $J_{H-3,H-2}$ = 3 Hz); 5.34 (d, 1H, H-2, $J_{H-2,H-3}$ = 3 Hz); 7.06 (dd, 1H, H-8, $J_{H-8,H-7}$ = 8 Hz, $J_{H-8,H-6}$ = 2 Hz); 7.13 (dt, 1H, H-7, $J_{H-7,H-6} = J_{H-7,H-8}$ = 8 Hz, $J_{H-7,H-5}$ = 2 Hz); 7.60 (dt, 1H, H-6, $J_{H-6,H-5} = J_{H-6,H-7}$ = 8 Hz, $J_{H-6,H-8}$ = 2 Hz); 7.95 (dd, 1H, H-5, $J_{H-5,H-6}$ = 8 Hz, $J_{H-5,H-7}$ = 2 Hz)	214 (M^+ + 2); 212 (M^+)
2b	H	CH_3	Cl	97[b]	—	—	1705; 1610; 1580	1.76 (s, 3H, CH_3); 3.27 (s, 3H, OCH_3); 4.11 (s, 1H, H-3); 6.9–7.8 (m, 3H, H-6, H-7, H-8); 7.95 (dd, 1H, H-5, $J_{H-5,H-6}$ = 8 Hz, $J_{H-5,H-7}$ = 2 Hz)	—
2c	H	H	Br	86[b]	—	—	1700; 1603	3.40 (s, 3H, OCH_3); 4.18 (d, 1H, H-3, $J_{H-3,H-2}$ = 3 Hz); 5.23 (d, 1H, H-2, $J_{H-2,H-3}$ = 3 Hz); 6.7–6.9 (m, 4H_{arom})	—
2d	H	CH_3	Br	92[b]	—	—	—	—	—
2e	—$(CH_2)_3$—		Cl	61[c]	—	$C_{13}H_{13}ClO_3$ (252.7)	1705; 1608; 1585	1.6–2.6 (m, 6H); 3.18 (s, 3H, OCH_3); 6.9–7.8 (m, 3H, H-6, H-7, H-8); 7.96 (dd, 1H, H-5, $J_{H-5,H-6}$ = 8 Hz, $J_{H-5,H-7}$ = 2 Hz)	—
2f	—$(CH_2)_4$—		Cl	73[c]	62–64° (n-C_6H_{14})	$C_{14}H_{15}ClO_3$ (266.7)	1705; 1608; 1580	1.5–2.4 (m, 8H); 3.16 (s, 3H, OCH_3); 6.8–7.7 (m, 3H, H-5, H-6, H-7); 7.90 (dd, 1H, H-8, $J_{H-8,H-7}$ = 7.5 Hz, $J_{H-8,H-6}$ = 2 Hz)	—

[a] Satisfactory microanalyses obtained for **2e** and **2f**: C ±0.18, H ±0.12.

[b] Yields were obtained after rapid, and short column chromatography since these compounds were converted the corresponding 3-halochromones **3** on prolonged exposure to silica gel.

[c] Yields after preparative thin layer chromatography.

Table 2. 3-Halochromones **3a–d**

Product	Yield [%][a]	m.p. [°C]	Molecular formula[b] or Lit. m.p. [°C]	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]	M.S. *m/e*
3a	92	113–114° (C_6H_6/n-C_6H_{14})	114–115°[6]	1650; 1601	7.3–8.0 (m, 3H, H-6, H-7, H-8); 8.18 (s, 1H, H-2); 8.1–8.4 (m, 1H, H-5)	182 (M^+ + 2); 180 (M^+); 154; 152; 120; 92
3b	90	128–130° (C_6H_6/n-C_6H_{14})	$C_{10}H_7ClO_2$ (194.6)	1650; 1612	2.63 (s, 3H, CH_3); 7.3–7.9 (m, 3H, H-6, H-7, H-8); 8.27 (dd, 1H, H-5, $J_{H-5,H-6}$ = 8 Hz, $J_{H-5,H-7}$ = 2 Hz)	196 (M^+ + 2); 194 (M^+); 166; 159; 120; 92
3c	93	95° (C_6H_6/n-C_6H_{14})	96–97°[6]	1653; 1602	7.0–7.7 (m, 3H, H-6, H-7, H-8); 8.02 (s, 1H, H-2); 8.0–8.2 (m, 1H, H-5)	
3d	95	118–119° (C_6H_6/n-C_6H_{14})	117–118°[10]	1650; 1610	2.67 (s, 3H, CH_3); 7.3–8.0 (m, 3H, H-6, H-7, H-8); 8.27 (dd, 1H, H-5, $J_{H-5,H-6}$ = 8 Hz, $J_{H-5,H-7}$ = 2 Hz)	240 (M^+ + 2); 238 (M^+); 212; 210; 159; 131; 120; 92

[a] Yield of pure, recrystallized product.

[b] Satisfactory microanalyses obtained for **3b** and **3d**: C ±0.12, H ±0.16.

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