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Electrolytic α-Bromination of Some α-Substituted Active Methylene Compounds

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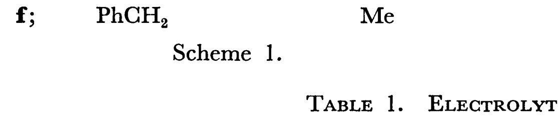
Synopsis. Electrolytic α-bromination of methyl α-substituted malonates and methyl α-substituted acetoacetates was accomplished in 73—84% yields in dichloromethane containing tetraethylammonium bromide as an electrolyte and sodium methoxide as an enolizing reagent.

Electrolytic bromination and bromohydrination of olefins proceed *via* electrophilic attack by electrochemically generated bromonium ion or bromine.1) Enolate **2** would be brominated in principle by electrolysis to give the corresponding bromo compounds **3**. Reports have appeared on the electrolytic α-halogenation of acetone,2) cyclohexanone, acetophenone,3) and acetic acid4) in a strong acidic medium such as hydrochloric acid. However, α-bromonation of active methylene and methine of malonates and acetoacetates dose not seem to have been studied.5,6) During the course of studies on the reaction by electrochemically generated halonium ion, we found a typical electrolytic condition which enables us to trap the electrochemically generated bromonium ion with active methylene compounds and also prevents oxidation of the enolate **2**, leading to dimerization. Although direct bromination with bromine gives the corresponding bromo compounds, active methylene compounds bearing an olefinic functional group may suffer bromination of the carbon-carbon double bond in the reaction. In this article we describe an electrolytic α-bromination of **1** which is characterized by (1) bromination without use of molecular bromine or hydrobromic acid and (2) selective bromination at α-possition of olefinic active methylene compounds.



1a—f **2a—f** **3a—f**

	R_1	R_2
a;	R_1=*n*-Bu	R_2=MeO
b;	$PhCH_2$	MeO
c;	$(Me)_2C=CH\text{-}CH_2$	MeO
d;	H	MeO
e;	*n*-Bu	Me
f;	$PhCH_2$	Me

Scheme 1.

Compounds **1a**—**1f** were prepared by the alkylation of methyl malonate and methyl acetoacetate.7) The reaction conditions and results of electrolysis of **1** are given in Table 1. The compounds gave α-brominated products **3** in 73—84% yields. Alkenylated substrate **1c** gave **3c** in 83% yield without modifying the carbon-carbon double bond. Dichloromethane was found to be a useful solvent for most of the substrates. Methanol and a mixed solvent of MeCN–H_2O were chosen for **1b** and **1d**, respectively, to attain the optimum yields of **3b** and **3d**. The quantity of sodium methoxide required for the electrolysis seems to be variable depending on the acidity of the substrate and polarity of the solvent.8)

A characteristic feature of the electrolysis is that high current densities are required (87—133 mA/cm^2) to terminate the reaction within a few minutes for the mili mole scale experiment. The yield of **3a** was unsatisfactory (42%) at lower current densities and several byproducts being obtained, one of which was the corresponding dimeric malonate (21%).9) A soluble brominating reagent (electrolyte) was used. The behavior of **1d** in CH_2Cl_2 differed electrolysis with use of Et_4NBr (10—20 eq) affording *ca.* 50% of **3d** along with methyl α-chloromalonate (10—20%) as a byproduct. The yield of the chloro compound reached 50—60% at a lower concentration of Et_4NBr (1—2 eq). The use of sodium bromide in methanol resulted in a poor yield of **3d**. In contrast, electrolysis using Mg(II) or Cu(II) bromide in a mixed solvent of MeCN/H_2O (1/7 v/v) was successful.

Experimental

IR spectra were obtained with a JASCO IRA-1 spectrometer, and ^1H NMR spectra with a JNM FX-100 fourier

Table 1. Electrolytic bromination of **1a**—**f**

Substrate	Solvent	Supportinga) electrolyte (eq)	MeONaa) (eq)	Current mA	Electricityb) F mol^{-1}	Temp °C	Yield of **3** %
1a	CH_2Cl_2	Et_4NBr (35)	5	260	3.5	0—5	84
1b	MeOH	NaBr (20)	5	400	30	20	78c)
	CH_2Cl_2	Et_4NBr (35)	10	260	5	20	64
1c	CH_2Cl_2	Et_4NBr (35)	5	260	5	6—8	83
1d	MeCN/H_2Od)	$MgBr_2$ (1.2)	1.8	400	3	2—3	77
		$CuBr_2$ (0.8)	1.8	400	4	2—3	72
1e	CH_2Cl_2	Et_4NBr (23)	2	260	6	−30	82
1f	CH_2Cl_2	Et_4NBr (28)	3	260	4	−30	73

a) Equivalent amount to substrate. b) Two Pt foils (2×1.5 cm^2) were used for electrode. c) 12% of starting material **1b** was recovered. d) MeCN/H_2O=1/7 (v/v).

transform spectrometer at 100 MHz in $CDCl_3$ using Me_4Si as an internal standard.

*Methyl α-(3-Methyl-2-butenyl)malonate (**1c**).* Compound **1c** was prepared by alkylation of methyl malonate with 1-chloro-3-methyl-2-butene: IR (neat) 2960, 1760, 1740, 1460, 1246, 1155 cm^{-1}; NMR δ 1.63 (3H, s, CH_3), 1.68 (3H, s, CH_3), 2.58 (2H, t, J=7.4 Hz, CH_2), 3.36 (1H, t, J=7.7 Hz, CH), 3.73 (6H, s, CH_3O), 5.03 (1H, t, J=7.3 Hz, CH=). Found: C, 59.70; H, 8.25%. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05%.

*Methyl α-Bromo-α-butylmalonate (**3a**) (Electrolysis of **1a**).* A mixture of **1a** (30 mg), Et_4NBr (850 mg), and MeONa (45 mg) dissolved in dry CH_2Cl_2 (7 ml) was electrolyzed using Pt foils (2×1.5 cm^2) at 6—8 °C with a constant current (260 mA) for 3.5 min. On passing electricity, the mixture turned yellow. After evaporating the solvent, the residue was mixed with water and acidified with 5% HCl. The organic substances were extracted with ether, treated with CH_2N_2, and chromatographed (SiO_2, benzene) to give **3a** (37 mg, 84%) as a colorless oil; IR (neat) 2966, 2880, 1743, 1435, 1254, 1130 cm^{-1}; NMR δ 0.92 (3H, t, J=6.5 Hz, CH_3), 1.10—1.52 (4H, m, CH_2), 2.10—2.40 (2H, m, CH_2), 3.82 (6H, s, CH_3). Found: C, 40.34; H, 5.38%. Calcd for $C_9H_{15}O_4Br$: C, 40.47; H, 5.66%.

*Methyl α-Bromo-α-(3-methyl-2-butenyl)malonate (**3c**)*: IR (neat) 2945, 1747, 1434, 1243 cm^{-1}; NMR δ 1.64 (3H, s, CH_3), 1.73 (3H, d, J=1.2 Hz, CH_3), 3.01 (2H, d, J=7.3 Hz CH_2), 3.81 (6H, s, CH_3O), 5.10 (1H, t, J=7.3 Hz, CH=). Found: C, 42.83; H, 5.47%. Calcd for $C_{10}H_{15}O_4Br$: C, 43.03; H, 5.42%.

*Methyl 2-Acetyl-2-bromohexanoate (**3e**)*: IR (neat) 2960, 1730, 1439, 1250 cm^{-1}; NMR δ 0.92 (3H, t, J=6.5 Hz, CH_3), 1.10—1.50 (4H, m, CH_2), 2.08—2.32 (2H, m, CH_2), 2.40 (3H, s, CH_3), 3.82 (3H, s, CH_3O). Found: C, 43.25; H, 5.73%. Calcd for $C_9H_{15}O_3Br$: C, 43.05; H, 6.02%.

*Methyl 2-Benzyl-2-bromo-3-oxobutanoate (**3f**)*: IR (neat) 3040, 2965, 1730, 1440, 1255, 705 cm^{-1}; NMR δ 2.35 (3H, s, CH_3), 3.47 (1H, d, J=17.0 Hz, CH_2), 3.64 (1H, d, J=17.0 Hz, CH_2), 3.75 (3H, s, CH_3O), 7.24 (5H, m, ArH). Found: C, 50.70; H, 4.76%. Calcd for $C_{12}H_{13}O_3Br$: C, 50,55; H, 4.60%.

Bromo compound **3b** has been reported.[10]

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