179 (1969); (c) C. Anselmi, B. Macchia, F. Macchia, and L. Monti, *Chem. Commun.*, 1152 (1971); (d) I. L. Knunyantis, M. V. Urushadze, and E. M. Rokhlin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1364 (1971); *Chem. Abstr.*, **75**, 88031t (1971); (e) C. Anselmi, G. Berti, B. Macchia, F. Macchia, and L. Monti, *Tetrahedron Lett.*, 1209 (1972); (f) A. J. Bates, I. J. Galpin, A. Hallet, D. Hudson, G. W. Kenner, R. Ramage, and R. C. Sheppard, *Helv. Chim. Acta*, **58**, 688 (1975); (g) S. Arimatsu, R. Yamaguchi, and M. Kawanisi, *Bull. Chem. Soc. Jpn.*, **48**, 741 (1975); (h) B. Castro, J.-R. Dormoy, B. Dourtoglov, G. Evin, C. Selve, and J.-C. Ziegler, *Synthesis*, 751 (1976).
(10) I. M. Downie, J. B. Lee, and M. F. S. Matough, *Chem. Commun.*, 1350 (1968); B. Castro and C. Selve, *Bull. Soc. Chim. Fr.*, 2296, 4368 (1971); B. Castro, Y. Chapleur, and B. Gross, *Tetrahedron Lett.*, 2313 (1974).
(11) D. Brett, I. M. Downie, J. B. Lee, and M. F. S. Matough, *Chem. Ind. (London)*, 1017 (1969); B. Castro, Y. Chapleur, B. Gross, and C. Selve, *Tetrahedron Lett.*, 5001 (1972); B. Castro, Y. Chapleur, and B. Gross, *Bull. Soc. Chim. Fr.*, 3034 (1973); B. Castro, M. Ly, and C. Selve, *Tetrahedron Lett.*, 4455 (1973); B. Castro and C. Selve, *ibid.*, 4459 (1973); R.-A. Boigegrain, B. Castro, and B. Gross, *Bull. Soc. Chim. Fr.*, 2623 (1974); B. Castro and C. Selve, *ibid.*, 3009 (1974); B. Castro, Y. Chapleur, and B. Gross *ibid.*, 875 (1975); R. Boigegrain, B. Castro, and C. Selve, *Tetrahedron Lett.*, 2529 (1975); I. M. Downie, H. Heaney, and G. Kemp, *Angew. Chem., Int. Ed. Engl.*, **14**, 370 (1975); I. M. Downie, H. Heaney, and G. Kemp, *Tetrahedron Lett.*, 3951 (1975); R. Boigegrain and B. Castro, *Tetrahedron*, **32**, 1283 (1976); Y. Chapleur, B. Castro, and B. Gross, *ibid.*, **33**, 1609, 1615 (1977); Y. Chapleur, B. Castro, and B. Gross, *Synth. Commun.*, **7**, 143 (1977).
(12) T. Gramstad and R. N. Haszeldine, *J. Chem. Soc.*, 4069 (1957).
(13) R. Mayer and E. Alder, *Chem. Ber.*, **88**, 1866 (1955).
(14) D. M. Pond and R. L. Cargill, *J. Org. Chem.*, **32**, 4064 (1967).

An Improved Synthesis of α-Methylene γ-Lactones by Electrolysis of α-Carboxy-α-phenylthiomethyl-γ-butyrolactones

Sigeru Torii.* Tsutomu Okamoto, and Takahide Oida

Department of Industrial Chemistry, School of Engineering, Okayama University, Okayama, Japan 700

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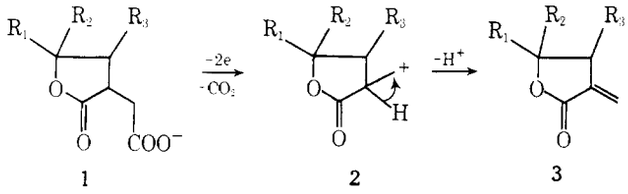
α-Methylene γ-lactone function, an important structural feature of biologically active natural products,[1] has received much attention and its synthetic attempts have been well documented in a recent publication.[2a,b] The reported methods for the preparation of α-methylene γ-lactone analogues[2] have been shown to employ largely severe conditions such as strong acids, bases, and heat in the crucial steps of the formation of the exo double bond. Recently, Ronald reported an interesting method for the preparation of *trans*-α-methylene-β,γ-tetramethylene-γ-butyrolactone from the corresponding α-carboxy-α-methylthiomethyl γ-lactone by three steps.[3] In this paper, we describe an improved one-step synthesis of α-methylene γ-lactones from α-carboxy-α-phenylthiomethyl-γ-butyrolactones, involving electrolytic elimination of both sulfenyl and carboxyl groups at room temperature.

Our preliminary challenges for the synthesis of the α-methylene γ-lactone group by electrodecarboxylation of the primary carboxylic acids **1** in pyridine–water–triethylamine (9:1:0.3 v/v)[4] at a current of 0.01–0.06 A/cm^2 (applied voltage 50–60 V) afforded **3** in 30–35% yields[5] via the intermediate **2**, indicating that the desired product **3**, which was exposed to a high applied voltage and also a high oxidation potential,[6] would undergo further anodic oxidation, causing decrease of the yield. This result suggests that the electrolysis at lower potential than that of **1** would promise a more favorable result. Besides, it is desirable that the product **3** should be removed immediately from the electrolysis solution. The advantage of allowing the anodic oxidation of the phenyl sulfide derivatives



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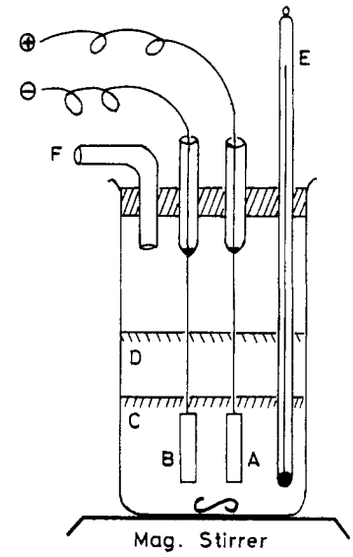
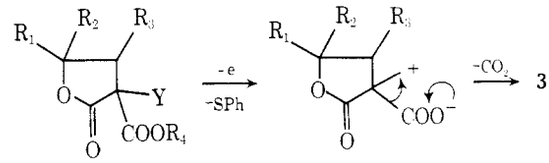


Figure 1. Electrolysis cell: (A) anode Pt plate (3 cm^2); (B) cathode Pt plate (3 cm^2); (C) aqueous phase; (D) organic phase; (E) thermometer; (F) gas lead pipe.

at the lower potential[7] rather than those of the carboxylic acids[6] led us to choose α-carboxy-α-phenylthiomethyl-γ-butyrolactone analogues **5** as a suitable compound for our synthetic purpose, since elimination of phenyl thiyl radical would be expected by one-electron oxidation on the sulfur atom of **5**,[7] affording the intermediate **7**, and subsequent loss of carbon dioxide would provide the desired **3**.



7

4, Y = H; R_4 = H
5, Y = CH_2SPh; R_4 = H
6, Y = H; R_4 = Et

Improvement of the electrolysis for the continuous extraction of the products was made by employing a two-phase system, consisting of water and organic solvents as shown in Figure 1. By this procedure, the products are expected to move from the aqueous layer to the organic layer, while the substrates are electrolyzed in the aqueous phase. Electrolysis of the ammonium salt of **5** to the desired **3** was carried out in an aqueous layer, dissolving an excess amount of triethylamine and lithium perchlorate as supporting electrolytes (Table II). The aqueous layer as depicted in Figure 1 was covered with a mixed solution of ether and benzene (3:2) as an extracting solvent. The aqueous solution was electrolyzed in an undivided beaker under a current of 16–7 mA/cm^2 with applied voltage of 3.2–3.5 V (1.3–1.5 V vs. SCE) at 38–40 °C for 4–12 h using platinum electrodes (3 cm^2). Successfully, the desired **3** was obtained only by evaporation of the extracting solvent as a sole product along with diphenyl disulfide after 40–80 Faradays/mol of electricity were passed. The electrolysis conditions of **5** as well as the yields of **3** are shown in Table II.

Experimental Section

Melting points and boiling points are uncorrected. IR spectra were determined with a JASCO Model IRA-1 grating spectrometer. ^{1}H-NMR spectra were determined at 60 MHz with a Hitachi Model R-24 and ^{13}C-NMR spectra were determined at 25.05 MHz with a JEOL Fourier transform spectrometer, Model FX-100 with a JEC-980-16K memory computer. The chemical shift values are expressed in δ values

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Table I. Physical Properties, Yields, and Combustion Analyses of α-Carboxy-α-phenylthiomethyl γ-Lactones 5

Product 5			Registry	Mp,	IR, C=O cm^{-1}		^{1}H NMR, δ –CH_2S–	Yield,	Anal., % Calcd		Found	
R_1	R_2	R_3	no.	°C	Lactone	Acid	(multiplicity)	%[a]	C	H	C	H
n-C_8H_{17}	H	H	65651-96-9		1772	1710	3.52 (q, J = 7.5 Hz)	94	65.92	7.74	65.97	7.92
–$(CH_2)_5$–		H	65651-97-0		1765	1718	3.52 (q, J = 6.5 Hz)	92	63.74	6.29	63.58	6.57
H	–$(CH_2)_5$–		65651-98-1	124.2	1776	1722	3.51 (broad s)	94	63.74	6.29	63.72	6.47
H	–$(CH_2)_4$–		65651-99-2	141.4	1770	1698	3.56 (broad s)	95	62.74	7.92	62.72	6.07

[a] The yield is based on isolated **5**.

Table II. Electrolysis Conditions[a] of 5 and Yields of α-Methylene γ-Lactones 3

Substrate 5			Registry	Amt added,	Solvent and electrolyte H_2O,	Et_3N,	$LiClO_4 \cdot 3H_2O$,	Current density,	Electricity, Faradays/	Time,	Yield of 3,
R_1	R_2	R_3	no.	mmol	mL	mg	mg	mA/cm^2	mol	h	%
n-C_8H_{17}	H	H	65651-99-8	0.193	15	182	200	16–10	80	12	92[c]
–$(CH_2)_5$–		H	52978-85-0	0.178	10	109	200	13–10	42	4	82
H	–$(CH_2)_5$– (β,γ-cis)		3725-04-0	0.093	15	109	120	13–7	48	4	77[d]
H	–$(CH_2)_4$– (β,γ-trans)		3727-53-5	0.147	10	109	200	13–7	30	5	73[e]

[a] The electrolysis was carried out at 38–40 °C. [b] Applied voltages were adjusted at 3.2–3.5 V. [c] Diphenyl disulfide was also obtained in 91% yield. [d] Physical data are as follows: bp 70–73 °C (0.015 mm, Kugelrohr) (lit.[11] bp 60–70 °C (0.05 mm)); ^{13}C NMR ($CDCl_3$) δ_C 24.3 (t), 27.4 (t), 30.7 (t), 31.2 (t), 31.8 (t), 43.1 (d), 82.3 (d), 122.0 (t), 140.3 (s), 170.3 (s). [e] Physical data are as follows: bp 70–72 °C (0.015 mm, Kugelrohr) (lit.[11] 70 °C (0.01 mm)); ^{13}C NMR ($CDCl_3$) δ_C 24.1 (t), 24.9 (t), 25.8 (t), 30.5 (t), 48.9 (d), 83.1 (d), 117.1 (t), 139.6 (s), 170.6 (s).

(ppm) relative to Me_4Si as an internal standard. Elemental analyses were performed in our laboratory.

α-Ethoxycarbonyl-γ-*n*-octyl γ-lactone (**6**, R_1 = n-C_8H_{17}, R_2 = R_3 = H) was prepared by the reaction of ethyl sodiomalonate (3.8 mmol) with 1,2-epoxydecane (4 mmol) in dry EtOH (2 mL) at 70 °C for 12 h. After workup in the usual manner, there was obtained 770 mg (75%) of **6** (R_1 = n-C_8H_{17}, R_2 = R_3 = H): bp 88–90 °C (0.015 mm, Kugelrohr); IR (neat) 1780 (lactone), 1735 cm^{-1} (ester); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 5 Hz, 3, CH_3), 1.28 (t, J = 7 Hz, 3, CH_3), 1.30 (br s, 14, CH_2), 1.80–2.90 (m, 2, CH_2), 3.31–3.80 (m, 1, CH), 4.26 (q, J = 7 Hz, 2, CH_2), 4.00–4.80 (m, 1, CH–O). Anal. Calcd for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.42; H, 9.80.

α-Carboxy-γ-*n*-octyl γ-lactone (**4**, R_1 = n-C_8H_{17}, R_2 = R_3 = H) was obtained by hydrolysis of **6** (R_1 = n-C_8H_{17}, R_2 = R_3 = H, 2.64 mmol) with NaOH (5.5 mmol) in aqueous 20% EtOH at room temperature for 15 h in 95% yield as a white solid: mp 63.5–64.5 °C (lit.[9] mp 58–59 °C); IR (Nujol) 1775 (lactone), 1718 cm^{-1} (COOH); ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 3, CH_3), 1.27 (br s, 14, CH_2), 1.90–2.90 (m, 2, CH_2), 3.50–3.87 (m, 1, CH), 4.14–4.80 (m, 1, CH–O), 6.87 (br s, 1, COOH).

Similarly, **α-carboxy-γ,γ-pentamethylene γ-lactone** (**4**) was obtained in 98% yield by hydrolysis of **6** (R_1, R_2 = –$(CH_2)_5$–, R_3 = H) with aqueous ethanolic NaOH: mp 135–136 °C (lit.[10] 136 °C); IR (Nujol) 1757 (lactone), 1716 cm^{-1} (COOH); ^{1}H NMR ($CDCl_3$) δ 1.62 (br s, 10, CH_2), 2.37 (d, J = 10 Hz, 2, CH_2), 3.75 (t, J = 10 Hz, 1, CH), 7.99 (br s, 1, COOH).

α-Carboxy-β,γ-*cis*-pentamethylene γ-lactone (**4**, R_2, R_3 = –$(CH_2)_5$–, R_1 = H) was prepared by the reaction of β,γ-*cis*-pentamethylene γ-lactone[11] (1.4 mmol) with excess CO_2 using i-Pr_2NLi (2.5 mmol) in dry THF (5 mL) at –40 °C for 30 min. After workup in the usual manner, there was obtained 267 mg (96%) of **4** (R_2, R_3 = –$(CH_2)_5$–, R_1 = H) as a pasty oil: IR (neat) 1780 (lactone), 1720 cm^{-1} (COOH); ^{1}H NMR ($CDCl_3$) δ 1.10–2.30 (m, 10, CH_2), 2.75–3.48 (m, 1, CH), 3.37 (d, J = 8 Hz, 1, CH), 4.74 (t, d, J = 8, 4 Hz, 1, CH), 9.14 (br s, 1, COOH). Anal. Calcd for $C_{10}H_{14}O_4$: C, 60; 59; H, 7.12. Found: C, 60.76; H, 7.22.

Similarly, **α-carboxy-β,γ-*trans*-tetramethylene γ-lactone**[13] (**4**, R_2, R_3 = –$(CH_2)_4$–, R_1 = H) was obtained in 97% yield from β,γ-*trans*-tetramethylene γ-lactone:[12] IR (neat) 1775 (lactone), 1720 cm^{-1} (COOH); ^{1}H NMR ($CDCl_3$) δ 1.10–2.60 (m, 9, CH_2, CH), 3.38 (d, J = 13 Hz, 1, CH), 2.60–3.50 (m, 1, CH–O), 9.52 (br s, 1, COOH).

α-Ethoxycarbonyl-α-ethoxycarbonylmethyl-γ-*n*-octyl γ-Lactone (8). To a mixture of EtONa (1.5 mmol) and **6** (R_1 = n-C_8H_{17}, R_2 = R_3 = H, 0.9 mmol) in dry EtOH (1.5 mL) $BrCH_2CO_2Et$ (1.2 mmol) was added. After stirring for 48 h at room temperature, the white slurry was quenched with cold water and taken up in ether–benzene (1:1). The organic layer was washed with brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed (SiO_2, hexane–ether 4:1) to give 270 mg (84%) of **8**: bp 136–138 °C (0.015 mm, Kugelrohr); IR (neat) 1775 (lactone), 1735 cm^{-1} (ester); ^{1}H NMR ($CDCl_3$) δ 0.90 (t, 3, CH_3), 1.27 (t, 6, CH_3), 1.30 (br s, 14, CH_2), 2.40–3.53 (m, 4, CH_2), 4.16 (q, 2, CH_2), 4.24 (q, 2, CH_2), 4.40–4.90 (m, 1, CH–O). Anal. Calcd for $C_{19}H_{32}O_6$: C, 64.02; H, 9.05. Found: C, 64.14; H, 9.10.

Similarly, **α-ethoxycarbonyl-α-ethoxycarbonylmethyl-γ,γ-pentamethylene γ-lactone** (**9**) was obtained in 82% yield by the reaction of **6** (R_1, R_2 = –$(CH_2)_5$–, R_3 = H) with $BrCH_2CO_2Et$: bp 103–104 °C (0.015 mm, Kugelrohr); IR (neat) 1768 (lactone), 1735 cm^{-1} (ester); ^{1}H NMR ($CDCl_3$) δ 1.25 (t, 3, CH_3), 1.28 (t, 3, CH_3), 1.20–2.10 (m, 10, CH_2), 2.59 (ABq, J = 14 Hz, 2, CH_2), 3.05 (ABq, J = 18 Hz, 2, CH_2), 4.02 (q, 2, CH_2), 4.27 (q, 2, CH_2). Anal. Calcd for $C_{16}H_{24}O_6$: C, 61.52; H, 7.74. Found: C, 61.71; H, 7.89.

α-Carboxymethyl-γ-*n*-octyl γ-Lactone (**1**, R_1 = n-C_8H_{17}, R_2 = R_3 = H). A mixture of **8** (300 mg, 0.84 mmol), aqueous 48% HBr (3 mL), and AcOH (6 mL) was stirred at 130 °C for 10 h. The volatile materials were rotoevaporated and the residue was recrystallized from benzene to give 162 mg (75%) of **1** (R_1 = n-C_8H_{17}, R_2 = R_3 = H): mp 91–92 °C; IR (Nujol) 1780 (lactone), 1705 cm^{-1} (COOH); ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 3, CH_3), 1.28 (br s, 14, CH_2), 1.98–2.30 (m, 4, CH_2), 4.10–4.70 (m, 1, CH–O), 9.05 (br s, 1, COOH). Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44. Found: C, 65.80; H, 9.51.

Similarly, **α-carboxymethyl-γ,γ-pentamethylene γ-lactone** (**1**, R_1, R_2 = –$(CH_2)_5$–, R_3 = H) was obtained in 77% yield by hydrolysis of **9** with aqueous 48% HBr: mp 133.5–134.5 °C; IR (Nujol) 1764 (lactone), 1730 cm^{-1} (COOH); ^{1}H NMR ($CDCl_3$) δ 1.64 (br s, 10, CH_2), 2.26–3.30 (m, 5, CH_2, CH), 9.30 (br s, 1, COOH). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.27; H, 7.59.

Electrolysis apparatus used for the electrolysis of **1** and **5** is outlined in Figure 1. A simple undivided cell, 2 cm in diameter and 10 cm high, fitted with a gas lead pipe, a thermometer, a magnetic stirrer bar, and too smooth platinum electrodes (1.5 × 2 cm^2), being placed parallel to each other 5 mm apart was used.

Electrochemical Synthesis of 3 from 1 in a Homogenious Pyridine–Water Solution. A stirred solution of **1** (R_1 = n-C_8H_{17}, R_2 = R_3 = H, 150 mg, 0.6 mmol), Et_3N (0.3 mL), and water (1.0 mL) in pyridine (9.0 mL) was electrolyzed in a beaker (35 mL) fitted with platinum electrodes (3 cm^2) at 50–60 V (0.01–0.06 mA/cm^2) at 32–39 °C for 5 h. The reaction mixture was acidified with cold aqueous 10% tartaric acid and extracted with ether–benzene (1:1). The organic layer was washed with brine, dried (Na_2SO_4), and concentrated. The resi-

due was chromatographed (SiO_2, hexane–ether 4:1) to give 38 mg (30%) of **3** (R_1 = n-C_8H_{17}, R_2 = R_3 = H) as an oil: bp 98 °C (0.015 mm, Kugelrohr); IR (neat) 1768 (lactone), 1666 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 0.87 (t, 3, CH_3), 1.29 (br s, 14, CH_2), 2.27–3.32 (m, 2, CH_2), 4.49 (q, J = 7 Hz, 1, CH–O), 5.59 (t, J = 3 Hz, 1, HC=C), 6.18 (t, J = 3 Hz, 1, HC=C); ^{13}C NMR ($CDCl_3$) δ_C 14.1 (q), 22.7 (t), 29.2 (t, 2), 29.3 (t), 29.4 (t), 31.8 (t), 33.6 (t), 36.3 (t), 77.6 (d), 121.8 (t), 134.7 (s), 170.3 (s). Anal. Calcd for $C_{13}H_{22}O_2$: C, 72.24; H, 10.54. Found: C, 72.39; H, 10.48.

α-Methylene-γ,γ-pentamethylene γ-lactone[2d] (**3**, R_1, R_2 = $-(CH_2)_5-$, R_3 = H) was obtained in 35% yield by the electrolysis of **1** (R_1, R_2 = $-(CH_2)_5-$, R_3 = H) in the same manner as described in the preceding experiment: bp 73 °C (0.02 mm, Kugelrohr); IR (neat) 1762 (lactone), 1663 cm^{-1} (C=C); ^1H NMR ($CDCl_3$) δ 1.73 (br s, 10, CH_2), 2.74 (t, J = 3 Hz, 2, CH_2), 5.45 (t, J = 3 Hz, 1, HC=C), 6.06 (t, J = 3 Hz, 1, HC=C); ^{13}C NMR ($CDCl_3$) δ_C 22.5 (t, 2), 24.8 (t), 37.5 (t, 3), 36.6 (t), 38.4 (s), 122.1 (t), 135.5 (s), 169.9 (s).

α-Carboxy-α-phenylthiomethyl-γ-*n*-octyl γ-Lactone (**5**, R_1 = n-C_8H_{17}, R_2 = R_3 = H). To a cooled (−70 °C) solution of i-Pr_2NLi (161 mg, 1.50 mmol) in dry THF (1.0 mL) was added dropwise a solution of **4** (R_1 = n-C_8H_{17}, R_2 = R_3 = H, 122 mg, 0.5 mmol) in dry THF (1.5 mL). After stirring for 15 min at −70 °C, the dry ice bath was removed and the mixture was allowed to stand for several minutes until the temperature reached 0 °C. Then, to the mixture cooled with an ice–water bath at 0 °C, a solution of freshly prepared phenylthiomethyl iodide[14] (254 mg, 1.02 mmol) in dry THF (1.5 mL) was added dropwise with stirring and the mixture was stirred for 3 h. The mixture was quenched with cold water and acidified with cold aqueous 10% HCl. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2. The combined extracts were washed with cold brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (SiO_2, hexane–AcOEt 2:1) to give 172 mg (94%) of **5** (R_1 = n-C_8H_{17}, R_2 = R_3 = H) as a pasty oil.

Physical constants together with elemental analyses of the analogous compounds **5** prepared from the corresponding γ-lactone-α-carboxylic acids **4** are shown in Table I.

A General Procedure for Electrochemical Synthesis of 3 from 5 in a Two-Layer System. A stirred solution of **5** (R_1 = n-C_8H_{17}, R_2 = R_3 = H, 69 mg, 0.19 mmol), $LiClO_4 \cdot 3H_2O$ (1.3 mmol), and Et_3N (1.8 mmol) in water, being covered with 5 mL of ether and benzene (3:2), was electrolyzed in a beaker fitted with platinum electrodes (3 cm^2) at a constant applied voltage of 3.5 V (ca. 1.4 V vs. SCE), current density 10–16 mA/cm^2, for 12 h (ca. 80 Faradays/mol). The organic phase that separated was washed with brine and dried (Na_2SO_4). Removal of the solvent and the following chromatography (SiO_2, hexane–ether 4:1) of the residue gave 37 mg (92%) of **3** (R_1 = n-C_8H_{17}, R_2 = R_3 = H) as an oil. The electrolysis conditions of **5** as well as the yield of the α-methylene γ-lactone **3** are shown in Table II.

Registry No.—**1** (R_1 = n-C_8H_{17}; R_2 = R_3 = H), 65652-01-9; **1** (R_1, R_2 = $(CH_2)_5$; R_3 = H), 65652-02-0; **4** (R_1 = n-C_8H_{17}; R_2 = R_3 = H), 65652-03-1; **4** (R_1, R_2 = $(CH_2)_5$; R_3 = H), 65652-04-2; **4** (R_2, R_3 = $(CH_2)_5$; R_1 = H), 65652-05-3; **4** (R_2, R_3 = $(CH_2)_4$; R_1 = H), 4354-68-1; **6** (R_1 = n-C_8H_{17}; R_2 = R_3 = H), 14872-59-4; **6** (R_1, R_2 = $(CH_2)_5$; R_3 = H), 58022-89-2; **8**, 65701-65-7; **9**, 65652-06-4; ethyl sodiomalonate, 996-82-7; 1,2-epoxydecane, 2404-44-6; β,γ-*cis*-pentamethylene γ-lactone, 3724-99-0; β,γ-*trans*-tetramethylene γ-lactone, 34905-87-8.

References and Notes

(1) E. Rodriguez, G. H. N. Towers, and J. C. Mitchell, *Phytochemistry*, **15**, 1573 (1976), and references cited therein.
(2) (a) P. A. Grieco, *Synthesis*, 67 (1975); (b) R. B. Gammill, C. A. Wilson, and T. A. Bryson, *Synth. Commun.*, **5**, 245 (1975); (c) J. R. Norton, K. E. Shenton, and J. Schwartz, *Tetrahedron Lett.*, 51 (1975); (d) L. S. Hegedus, S. D. Wagner, E. L. Waterman, and K. Siirala-Hansen, *J. Org. Chem.*, **40**, 593 (1975); (e) R. E. Damon and R. H. Schlessinger, *Tetrahedron Lett.*, 1561 (1976); (f) S. M. Ali and S. M. Roberts, *J. Chem. Soc., Perkin Trans. 1*, 1934 (1976); (g) J. P. Marino and J. S. Farina, *J. Org. Chem.*, **41**, 3213 (1976); (h) R. M. Carlson and A. R. Oyler, *ibid.*, **41**, 4065 (1976); (i) J. Haslouin and F. Rouessac, *Tetrahedron Lett.*, 4651 (1976); (j) S. Danishefsky, T. Kitahara, R. McKee, and P. F. Schuda, *J. Am. Chem. Soc.*, **98**, 6715 (1976); (k) J. L. Roberts, P. S. Borromeo, and C. D. Poulter, *Tetrahedron Lett.*, 1621 (1977); (l) N. L. Holy and Y. F. Wang, *J. Am. Chem. Soc.*, **99**, 946 (1977); (m) R. K. Boeckman, Jr., and M. Ramaiah, *J. Org. Chem.*, **42**, 1581 (1977).
(3) R. C. Ronald, *Tetrahedron Lett.*, 3831 (1973).
(4) Anodic decarboxylation in pyridine–water: S. Torii, T. Okamoto, and H. Tanaka, *J. Org. Chem.*, **39**, 2486 (1974).
(5) Oxidation of α-carboxymethyl γ-lactones with lead tetraacetate has been shown to give the corresponding α-methylene γ-lactones in 30–50% yields: (a) K. J. Divakar, P. P. Same, and A. S. Rao, *Tetrahedron Lett.*, 399 (1974); (b) T.-L. Ho and C. M. Wang, *Synth. Commun.*, **4**, 133 (1974).
(6) Anodic oxidation of primary carboxylic acids have been shown to occur generally over 2.0 V vs. SCE: L. Eberson, "Organic Electrochemistry", M. M. Baiser, Ed., Marcel Dekker, New York, N.Y., 1973, p 469.
(7) Phenyl sulfide derivatives are oxidaized at 1.45 V vs. SCE in acetonitrile: S. Torii, K. Uneyama, K. Iida, and K. Sasaki, *Tetrahedron Lett.*, 4513 (1972).
(8) K. Uneyama and S. Torii, *Tetrahedron Lett.*, 329 (1971).
(9) Firmenich & Co., French Patent 1 319 516 (March 1, 1963); *Chem. Abstr.*, **59**, 9808c (1963).
(10) M. Mousseron and F. Winternitz, *Bull. Soc. Chim. Fr.*, 604 (1946).
(11) J. A. Marshall and N. Cohen, *J. Org. Chem.*, **30**, 3475 (1965).
(12) P. A. Grieco and K. Hiroi, *Chem. Commun.*, 500 (1973).
(13) M. S. Newman and C. A. Vander Werf, *J. Am. Chem. Soc.*, **67**, 233 (1945).
(14) B. M. Trost and R. A. Kunz, *J. Org. Chem.*, **39**, 2648 (1974).

A Convenient Preparation of 2-Substituted Benzothiazoles[1]

Dale L. Boger

Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138

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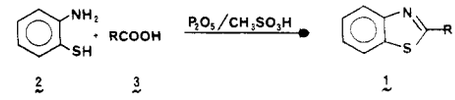
The availability of 2-substituted benzothiazoles (**1**) depends on preparative routes in which the fused thiazole ring is constructed from acyclic reactants.[2] Since many compounds containing this heterocyclic nucleus are of industrial[3] or biological[4] interest, methods for the preparation of 2-substituted benzothiazoles have been extensively studied.[2] Recently we have become interested in benzothiazoles as synthetically useful units[5] and required a broad and facile entry to this ring system.

Though in principle the direct condensation of 2-aminothiophenol (**2**) with the appropriate carboxylic acid (**3**) provides the most direct route to the 2-substituted benzothiazoles (**1**), in practice this direct route has been difficult to carry out conveniently in the laboratory.[6] Generally a reactive carboxylic acid derivative, e.g., an acid chloride,[2] acid anhydride,[2] imino ester,[2] or *N*-ethoxycarbonylthioamide,[7] has been employed, and obviously this method requires an extra step. Although polyphosphoric acid (PPA)[8] and more recently polyphosphate ester (PPE)[9] have been employed for the direct condensation of carboxylic acids with 2-aminothiophenol, both methods afford variable yields of the 2-substituted benzothiazoles (**1**) and the former requires high reaction temperatures (ca. 200 °C).

We would like to report that 2-substituted benzothiazoles (**1**) are obtainable directly from 2-aminothiophenol (**2**) and the corresponding carboxylic acid (**3**) by treatment with P_2O_5/CH_3SO_3H (1/10, w/w)[10] and warming (Scheme I). The reaction as illustrated by the examples in Table I is generally effective for a wide range of aliphatic and aromatic carboxylic acids. The general procedure involves treating a mixture of P_2O_5/CH_3SO_3H (1/10, w/w) and **2** (ratio of 1.5 g/1.0 mmol) with 1 equiv of the required carboxylic acid and warming for ca. 10 h followed by aqueous basic workup.

The reaction does not appear to be useful for α,β-unsaturated carboxylic acids. Whereas 2-styrylbenzothiazole (**1j**) was obtained in 57% from *trans*-cinnamic acid and **2**, less than 20% of 2-(2-methylpropenyl)benzothiazole (**1k**) was obtained from 3,3-dimethylacrylic acid and **2** under the described conditions. Furthermore, the α-trialkylated carboxylic acid, pivalic acid

Scheme I



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