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]

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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

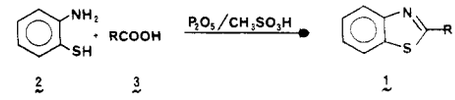

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Table I
Preparation of 2-Substituted Benzothiazoles (1) from 2-Aminothiophenol (2) and Carboxylic Acids (3)

Entry	R	Reaction time (temp, °C)	Yield,[a] %
a	CH_3	1 h (25) 10 h (70)	93[b]
b	$CH_3(CH_2)_5$	1 h (25) 10 h (75–80)	96[c]
c	$PhCH_2$	1 h (25) 10 h (75)	89[c]
d	3-Pyridyl-CH_2	1 h (25) 10 h (75–80)	86[d]
e	Cyclohexyl	1 h (25) 10.5 h (80–85)	88[e]
f	$(CH_3)_2CH$	15 h (25) 8 h (70)	74[c]
g	3-$MeOC_6H_4$	1 h (25) 10 h (95)	85[f]
h	4-ClC_6H_4	10 min (25) 17.5 h (90–95)	83[g]
i	2-Furyl	1 h (25) 10 h (75–80)	84[h]
j	PhCH=CH	1 h (25)[i] 10 h (55)	57[j]
k	$(CH_3)_2C=CH$	1 h (25) 10 h (55)	19[k]
l	$(CH_3)_3C$	1 h (25)[l] 10 h (75–80)	<10

[a] Yield after purification by column chromatography (SiO_2). All products exhibited the reported or expected ^{1}H-NMR, IR, mass spectral characteristics and were identical in all respects to authentic material (when available). [b] Identical in all respects to distilled commercial material (Aldrich). [c] For previous characterization see J. Metzger and H. Plank, *Bull. Soc. Chim. Fr.*, 1692 (1956); R. Guglielmetti, E. J. Vincent, J. Metzger, J. Berger, and R. Garnier, *ibid.*, 4195 (1967). [d] For preparation of authentic material see ref 4a. [e] For preparation of authentic material see ref 5. [f] Mp 81–82 °C (lit. mp 82–83 °C): F. A. Babiehev, L. A. Kirpianova, and T. A. Dashevskaya, *Urk. Khim. Zh. (Russ. Ed.)*, **32,** 706 (1966); *Chem. Abstr.*, **65,** 13682a (1966). [g] Mp 115–116 °C (lit.[4c] mp 117–118 °C). [h] Mp 103–104.5 °C (lit. mp 105 °C): M. T. Bogert and A. Stull, *J. Am. Chem. Soc.*, **47,** 3078 (1925). [i] Weight (g) of P_2O_5/CH_3SO_3H (1/10, w/w): mmol substrate was 2:1. [j] Mp 110–111 °C (lit. mp 112 °C): D. M. Brown and G. A. R. Kon, *J. Chem. Soc.*, 2147 (1948). [k] Mp 78–80 °C (lit. mp 81–82 °C): E. B. Knott, *ibid.*, 3793 (1965). [l] Evolution of gas evident, presumably CO and isobutylene.

(**3l**), appears to decarbonylate under the reaction conditions (evolution of gas).

The ease with which the reagent P_2O_5/CH_3SO_3H (1/10, w/w) may be handled, especially on large preparative scales, is particularly noteworthy.[10] This fact coupled with the reagent's ability to promote the direct condensation of a wide range of carboxylic acids (**3**) with 2-aminothiophenol (**2**) in high yields makes this procedure a particularly convenient and attractive method for the direct preparation of 2-substituted benzothiazoles when compared to related direct condensation methods.[2,6,8,9]

Experimental Section[11]

Preparation of 2-Substituted Benzothiazoles. The General Procedure is Illustrated with 2-Methylbenzothiazole (1a). A 4.5-g solution of P_2O_5/CH_3SO_3H (1/10, w/w)[10] was treated sequentially with 2-aminothiophenol (3.0 mmol, 376 mg) and acetic acid (3.0 mmol, 180 mg). The resulting solution was stoppered and magnetically stirred at 25 (1 h) and 70 °C (10 h). After cooling, the solution was slowly added to ca. 50–75 mL of aqueous 5% $NaHCO_3$[12] and the resulting solution was made basic to pH paper by the addition of aqueous 10% NaOH. Extraction of the aqueous phase ($CHCl_3$) followed by drying of the combined organic phases ($MgSO_4$) and evaporation of the solvent in vacuo afforded the crude product as a yellow oil. Chromatography (20 g SiO_2, 20 × 1.5 cm, CH_2Cl_2 to 20% Et_2O:CH_2Cl_2 gradient elution) afforded 415 mg (447 theoretical, 93%) of pure 2-methylbenzothiazole (**1a**), as a colorless liquid identical in all respects with distilled authentic material (Aldrich).

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Registry No.—**1a,** 120-75-2; **1b,** 65718-88-9; **1c,** 6265-94-7; **1d,** 33928-36-8; **1e,** 40115-03-5; **1f,** 17626-86-7; **1g,** 10002-44-5; **1h,** 6265-91-4; **1i,** 1569-98-8; **1j,** 1483-30-3; **1k,** 1628-61-1; **1l,** 17626-88-9; **2,** 137-07-5; **3a,** 64-19-7; **3b,** 111-14-8; **3c,** 103-82-2; **3d,** 501-81-5; **3e,** 98-89-5; **3f,** 79-31-2; **3g,** 586-38-9; **3h,** 74-11-3; **3i,** 88-14-2; **3j,** 140-10-3; **3k,** 541-47-9; **3l,** 75-98-9.

References and Notes

(1) This work was assisted financially by a grant from the National Science Foundation.
(2) R. C. Elderfield, "Heterocyclic Compounds", Vol. 5, Wiley, New York, N.Y., 1957, pp 484–722.
(3) (a) F. M. Hamer in "The Chemistry of Heterocyclic Compounds", Vol. 18, A. Weissberger, Ed., Interscience, New York, N.Y., 1964, Chapter 6; (b) T. S. Gore, B. S. Jashi, S. V. Sunthankar, and D. B. Tilak, Ed., "Chemistry of Natural and Synthetic Colouring Matters", Academic Press, New York, N.Y., 1962, pp 573–587 and 615–643; (c) A. Dorlars, C. W. Schellhammer, and J. Schroeder, *Angew. Chem., Int. Ed. Engl.*, **14,** 665 (1975).
(4) For the various examples pertaining to the benzothiazole derivatives prepared herein see (a) H. Iwato, N. Nichimura, and J. Nakano, Japanese Patent 71 31 862; *Chem. Abstr.*, **75,** 140831v (1971); (b) B. Prescott and J. M. Webb, *Antibiot. Chemother. (Washington, D.C.)*, **8,** 33 (1958); (c) W. L. Hubbard, R. E. Grahame, Jr., R. A. Covey, and E. H. Jonis, U.S. Patent 3 876 791; *Chem. Abstr.*, **83,** 92409e (1975); (d) H. Schwartz, Netherlands Appl. 6 607 039; *Chem. Abstr.*, **67,** 100132w (1967); (e) L. W. Wattenberg, M. A. Page, and L. J. Leong, *Cancer Res.*, **28,** 2539 (1968); (f) Gh. Miron and Gh. Ripeanu, *Comun. Acad. Repub. Pop. Rom.*, **11,** 241 (1961); *Chem. Abstr.*, **55,** 17985f (1961).
(5) We have recently employed the benzothiazole nucleus as the center of a wide variety of synthetic operations in which the benzothiazole nucleus serves as a masked carbonyl functionality and have applied this chemistry toward the preparation of various annulation products, cf. E. J. Corey and D. L. Boger, *Tetrahedron Lett.*, 5, 9, 13 (1978).
(6) Generally this direct approach requires rather harsh reaction conditions (e.g., high temperatures, sealed tubes) and affords low to modest yields of the desired 2-substituted benzothiazoles; cf. ref 2 and references cited therein.
(7) B. George and E. P. Papadopoulos, *J. Org. Chem.*, **42,** 441 (1977).
(8) D. W. Hein, R. J. Alheim, and J. J. Leavitt, *J. Am. Chem. Soc.*, **79,** 427 (1957).
(9) Y. Kanaoka, T. Hamada, and O. Yonemitsu, *Chem. Pharm. Bull.*, **18,** 587 (1970).
(10) P. E. Eaton, G. R. Carlson, and J. T. Lee, *J. Org. Chem.*, **38,** 4071 (1973); the reagent was prepared as described with the exception that CH_3SO_3H (98%, Aldrich) was not distilled prior to reagent formation.
(11) Melting points are uncorrected. Infrared spectra (IR) were obtained in $CHCl_3$ for solids or as neat films for liquids and recorded on a Perkin-Elmer 267 spectrophotometer. ^{1}H-NMR spectra were obtained on a Varian A-60 or CFT-20/HFT-80 spectrophotometer in $CDCl_3$ with tetramethylsilane as an internal standard. Mass spectra were recorded on an AEI-MS9 spectrophotometer at 70 eV.
(12) When working on large preparative scales workup is facilitated by pouring directly onto aqueous 10% NaOH.

Photoreaction of Hexafluorobenzene with Cyclohexane: Evidence for Substitution and Addition Mechanism

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Light-induced substitution reactions of aryl fluorides have been recently reviewed.[1] Bryce-Smith and co-workers[2] have recently observed cine-substitution by nucleophilic substitution of fluorobenzene and difluorobenzenes with primary and secondary amines and found evidence for the addition–elimination mechanism. Irradiation of solutions of hexafluorobenzene in cyclohexane and cyclooctane gives hydrogen fluoride and a complex mixture containing cyclohexylpentafluorobenzene and other radical coupling products.[3]

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