**Ethyl 2-Butyl-1-nitrocyclopropenecarboxylate (5j).** Ethyl nitrodiazoacetate[5] (700 mg, 4.4 mmol) was added to 3 mL of 1-hexyne containing 30 mg of catalyst at 20 °C. The mixture was stirred for 30 min, ether and saturated sodium carbonate were added, and this solution was stirred for 10–15 min. Separation of the organic layer followed by drying with magnesium sulfate and concentration afforded 800 mg (3.8 mmol, 87%) of 95% pure cyclopropenecarboxylate. While stable to air, this material was sensitive to acid, base, and silica gel: $^1$H NMR $\delta$ 0.85 (t, $J$ = 7.1 Hz, 3 H), 1.21 (t, $J$ = 7.2 Hz, 3 H), 1.30 (m, 2 H), 1.49–1.59 (m, 2 H), 2.58 (dt, $J$ = 1.0, 9 Hz, 2 H), 4.23 (q, $J$ = 7.1 Hz, 2 H), 6.67 (s, 1 H); $^{13}$C NMR $\delta$ 13.4, 13.9, 22.0, 23.1, 28.0, 62.2, 69.6, 98.3, 119.4, 166.1; IR 3160, 1740, 1550 cm$^{-1}$.

***anti*-3-Nitro-2-(trimethylsilyl)-*endo*-tricyclo[3.2.1.0$^{2,4}$]-oct-6-ene (9a).** (Trimethylsilyl)nitrocyclopropene (**5d**) (40 mg, 0.23 mmol) and cyclopentadiene (100 mg, 1.5 mmol) were heated in 0.5 mL of toluene under an inert atmosphere in a 10 mL round-bottom flask on an oil bath at 70 °C for 4 h. The entire reaction mixture was then chromatographed over a short silica gel column (0–20% ether/pentane) to afford 50 mg (0.21 mmol, 91%) of colorless oil: $^1$H NMR $\delta$ 0.08 (s, 9 H), 1.48 (m, 2 H), 2.58 (m, 1 H), 3.05 (m, 2 H), 3.37 (m, 1 H), 5.76 (m, 1 H), 5.87 (m, 1 H); $^{13}$C NMR $\delta$ -1.2, 21.2, 29.3, 43.5, 48.7, 62.4, 71.5, 131.2, 132.1; IR 1550, 1370 cm$^{-1}$; HRMS ($M^+$ + $NH_4$) 241.141, calcd for $C_{11}H_{21}N_2O_2$ 241.137.

***anti*-3-Nitro-*endo*-tricyclo[3.2.1.0$^{2,4}$]oct-6-ene-3-*syn*-carbonitrile (9b).** Nitrocyanocyclopropene (**7**) (60 mg, 0.54 mmol) and cyclopentadiene (150 mg, 2 mmol) were heated in 0.5 mL of toluene in a sealed flask for 2 h in an oil bath at 70 °C. Chromatography of the entire reaction mixture over silica gel (0–20% ether/hexane) afforded 70 mg (0.40 mmol, 74%) of white solid: $^1$H NMR $\delta$ 1.81 (d, $J$ = 7.6 Hz, 1 H), 2.06 (d, $J$ = 7.6 Hz, 1 H), 3.08 (t, $J$ = 2.1 Hz, 2 H), 3.36 (br, 2 H), 6.23 (t, $J$ = 2.1 Hz, 2 H); $^{13}$C NMR $\delta$ 38.0, 45.0, 66.8, 70.0, 112.7, 136.4; IR 2160, 1570, 1340 cm$^{-1}$; HRMS ($M^+$ + H) 177.068, calcd for $C_9H_{10}N_2O_2$ 177.066; mp 111–112 °C. Anal. Calcd for $C_9H_8N_2O_2$: C, 61.34; H, 4.58. Found: C, 61.20, H, 4.59.

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**Supplementary Material Available:** $^1$H and $^{13}$C NMR spectra for compounds **5a–d,f,g,j**, **7**, and **9a** and crystallographic data for **9b** (23 pages). Ordering information is given on any current masthead page.

## Optimizations in the Preparation of the First Benzimidazolyl Salicylic Acid Derivative. An Efficient One-Pot Synthesis of 2-[(2′-Carbomethoxyphenoxy)methyl]benzimidazole†

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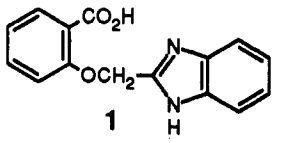
*Received June 26, 1990*

### Introduction

Considerable interest has been directed toward modeling active sites of enzymes, especially those of the serine proteases.[1] Most of these studies involve reconstructing the *charge-relay* system on a small framework.[2] Quite recently, models with the syn lone pair of carboxylate oriented toward the imidazole have appeared.[3,4] Such models allow an evaluation of our hypothesis that the syn lone pairs of carboxylate are more basic than the anti.[5]

Our interest in *biomimetic*[6] chemistry focuses in part on the design and synthesis of biomodels with two or more functional groups with defined spatial arrangement between these groups. In particular, we desire chemical models that possess both syn- and anti-oriented carboxylates in addition to other functionalities. We have prepared the acid derivative, **1**, of the title compound as an *intra*molecular model for hydrogen bonding between carboxyl and imidazole. The crystal structure exhibits a strong *inter*molecular syn-oriented hydrogen bond between the carboxyl and the benzimidazolyl instead of an *intra*molecular anti-oriented hydrogen bond.[7] We describe herein the preparation of **1** by optimized procedure, which has general applicability to the synthesis of functionalized benzimidazoles.[8] Benzimidazoles are commercially important as pharmaceuticals, veterinary anthelminitics, fungicides, and insecticides.[9] Furthermore, they are established inhibitors of cytochrome P-450 mediated enzyme activity of various species.[10]




**1**

### Results and Discussion

**Williamson's Route.** Initially, we attempted to prepare **1** via the Williamson ether synthesis by coupling methyl salicylate and 2-(chloromethyl)benzimidazole. Bahadur and Pandey[11] had synthesized the para analogue of **1** by

† Presented in part at the 197th National Meeting of the American Chemical Society, Dallas, TX, Apr 9–14, 1989; Abstract ORG 168.

(1) D'Souza, V.; Bender, M. *Acc. Chem. Res.* **1987**, *20*, 146–152. Rogers, G.; Bruice, T. *J. Am. Chem. Soc.* **1974**, *96*, 2473–2480. Jones, J.; Taylor, K. *Can. J. Chem.* **1977**, *55*, 1653–1657.

(2) For recent reviews of the charge-relay mechanism in serine proteases, see: Dugas, H. In *Bioorganic Chemistry, A Chemical Approach to Enzyme Action*, 2nd ed.; Cantor, C. R., Ed.; Springer-Verlag: New York, 1989, Chapter 4. Schowen, R. L. In *Mechanistic Principles of Enzyme Activity, Molecular Structure and Energetics*, Vol. 9; Liebman, J. F., Greenburg, A., Eds.; VCH Publishers: Wienheim, FRG, 1988, Chapter 4. Steitz, T. A.; Shulman, R. G. *Ann. Rev. Biophys. Bioeng.* **1982**, *11*, 419–444.

(3) Huff, J.; Askew, B.; Duff, R.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 5908–5909.

(4) Zimmerman, S. C.; Cramer, K. D. *J. Am. Chem. Soc.* **1988**, *110*, 5906–5908.

(5) Gandour, R. D. *Bioorg. Chem.* **1981**, *10*, 169–176.

(6) The term "biomimetic", introduced by R. Breslow, refers to any aspect in which a chemical process mimics that of a biochemical reaction. Cf: Breslow, R. *Chem. Soc. Rev.* **1972**, *1*, 553–580.

(7) Gandour, R. D.; Nabulsi, N. A. R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1990**, *112*, 7816–7817.

(8) For reviews, see: Potts, T. In *Comprehensive Heterocyclic Chemistry*, Vol. 5; Pergamon Press: Elmsford, New York, 1970; pp 457–498. Preston, P. In *The Chemistry of Heterocyclic Compounds, Benzimidazoles and Congeneric Tricyclic Compounds*, Vol. 40, Part 1; John Wiley & Sons: New York, 1981; pp 1–285. Preston, P. *Chem. Rev.* **1974**, *74*, 279–314. Grimmmet, M. R. *Adv. Heterocycl. Chem.* **1970**, *12*, 103–183; **1980**, *27*, 241–326. Pozharskii, A.; Garnovskii, A.; Simnov, A. *Russ. Chem. Rev.* **1966**, *35*, 122–144.

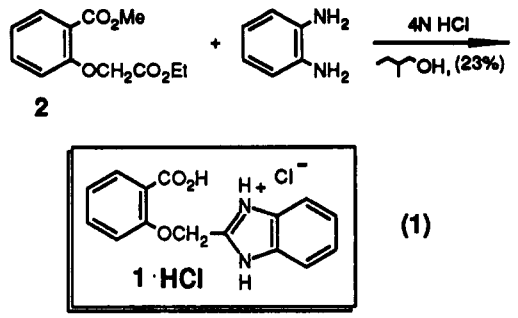
(9) Preston, P. In *The Chemistry of Heterocyclic Compounds, Benzimidazoles and Congeneric Tricyclic Compounds*, Vol. 40, Part 2; John Wiley & Sons: New York, 1980; Chapter 10.

(10) Murray, M.; Ryan, A. J.; Little, P. J. *J. Med. Chem.* **1982**, *25*, 887–892 and references therein.

0022-3263/91/1956-2260$02.50/0 

this method. In our hands, however, all attempts[12] to prepare 1 by this method failed.[13-15]

**Method of Phillips.** Once the Williamson method proved unsuccessful, we turned to the conventional method of Phillips[16] (reaction 1). Accordingly, the desired ester




(1)

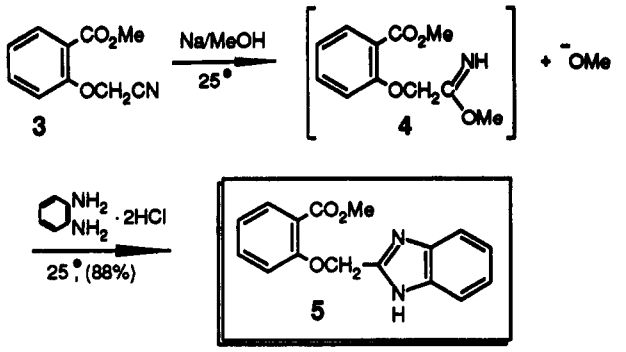
precursor 2 was prepared in 81% isolated yield from the reaction of methyl salicylate with ethyl bromoacetate and potassium carbonate in refluxing acetone. Refluxing a solution of 2 and phenylenediamine in 2-methyl-1-butanol in the presence of dilute aqueous HCl gave the hydrochloride salt of 1 in 23% crude yield. The reaction was repeated under milder conditions but without success.[17]

**Method of King and Acheson.** The problems encountered in the preparation of 1 have led us to explore alternative procedures. We prepared 1, in good overall yields, by two independent routes following the method of King and Acheson[18] for the preparation of benzimidazoles.[19-22]

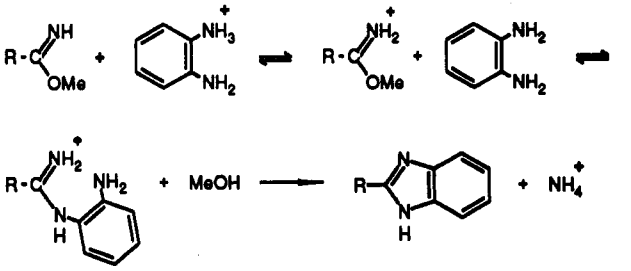
We have developed a one-pot reaction (Scheme I) for the preparation of 5 in order to avoid handling the hygroscopic imidates. This method affords 5 in higher yields than the traditional two-step procedure described by King and Acheson.[18] It involves condensation of phenylenediamine dihydrochloride with the basic imidate 4 that is generated in situ by the method of Schaefer and Peters.[23]

The success of this single-pot procedure depends on regulating the base and acid that are required for the two steps. Conversion of nitriles into basic imidates requires a catalytic amount of base.[23] Formation of benzimidazoles, however, occurs most readily with the reaction of phenylenediamine and an imidinium ion.[18] We have used 1 equiv of base to produce 4, and the resulting methoxide is neutralized with phenylenediamine dihydrochloride, thus

**Scheme I**




**Scheme II**




producing methanol and *o*-phenylenediamine monohydrochloride in situ. The second equivalent of HCl is necessary for generating the reactive imidinium salt, 4·HCl, which subsequently condenses with phenylenediamine to give 5.[24] The latter step likely proceeds via the amidinium intermediate, which undergoes facile *intra*molecular condensation.[25] The overall reaction mechanism is acid-catalyzed (Scheme II). Hydrolysis of 5 to 1 is accomplished by treatment with dilute HCl followed by neutralization with $NH_4OH$. The structures of 1,[7] 1·HCl,[26] and 5[26] have been established by single-crystal X-ray analysis.

**Summary.** We have outlined the synthetic methods employed in the preparation of the first benzimidazolium salicylate derivative. We have also developed a one-pot method, which complements the method of King and Acheson, for the preparation of the ester derivative of the title compound. This procedure gives higher yields and obviates the necessity for isolating the otherwise hygroscopic imidates.

## Experimental Section

**General Procedures.** Melting points were measured on Fisher

(11) Bahadur, S.; Pandey, K. K. *Pharm.* **1979**, *34*, 570.

(12) The following conditions have been employed for the reaction of methyl salicylate with 2-(chloromethyl)benzimidazole: (a) EtOH/EtO$^-$; (b) THF/NaH; (c) THF:HMPA (80%, v/v)/NaH; (d) acetone/$K_2CO_3$. In a typical experiment, the chloride (6.0 mmol) was added to a stirring solution of methyl salicylate (6.0 mmol) at 0–5 °C under $N_2$ atmosphere and the resulting mixture was refluxed for 24 h. In each case only salts of methyl salicylate were isolated in addition to gummy materials, which was assumed to be linear polymers formed from self-condensation of 2-(chloromethyl)benzimidazole. Self-condensation of 2-(chloroalkyl)-benzimidazoles has been reported. Cf: Siegart, W.; Day, A. *J. Am. Chem. Soc.* **1957**, *79*, 4391–4394.

(13) Failure of the substitution reaction is likely due to chelation of the alkali metal cation with the oxygen atoms of methyl salicylate.[14] Such chelation is analogous to that involving β-keto enolates, which is known to hinder O-alkylation.[15]

(14) Sidgwick, N. V.; Brewer, F. M. *J. Chem. Soc.* **1925**, *127*, 2379–2387.

(15) Olmstead, W. N.; Bordwell, F. G. *J. Org. Chem.* **1980**, *45*, 3299–3305 and references therein.

(16) Phillips, M. *J. Chem. Soc.* **1928**, 172–177; **1928**, 2393–2399.

(17) No product was obtained when equivalent amounts of phenylenediamine and 2 were refluxed in MeOH, DMF, and dioxane in the presence or absence of a catalytic amount of aqueous HCl. Similar results were obtained when the reaction was carried out in refluxing toluene in the presence or absence of toluenesulfonic acid as catalyst.

(18) King, F. E.; Acheson, R. M. *J. Chem. Soc.* **1949**, 1396–1400.

(19) The first route involved conversion of 3 into its imidinium derivative[20] according to the method of Pinner,[21] followed by condensation with phenylenediamine and subsequent acid hydrolysis. In the second route, 1 was prepared directly from the reaction of the diamine with the imidinium derivative of (2-carboxyphenoxy)acetonitrile.[27] The later acetimidinium derivative[22] also was prepared according to Pinner's method. Full characterization of 1 was carried out for both methods, including elemental analyses, which were satisfactory.

(20) (2-Carbomethoxyphenoxy)acetimidate hydrochloride: 99% yield; mp 148 °C (sealed tube). Anal. Calcd for $C_{11}H_{14}ClNO_4$: C, 50.88; H, 5.43. Found: C, 50.64; H, 5.61.

(21) Pinner, A. *Ber.* **1883**, *16*, 352–363; 1643–1659.

(22) (2-Carboxyphenoxy)acetimidate hydrochloride: 66.5% yield; mp 221.5–222 °C dec. Anal. Calcd for $C_{10}H_{12}ClNO_4$: C, 48.89; H, 4.92; Cl, 14.43; N, 5.70. Found: C, 48.50; H, 4.91; Cl, 14.03; N, 5.62.

(23) Schaefer, F.; Peters, G. *J. Org. Chem.* **1961**, *26*, 412–418.

(24) Condensation of phenylenediamine with basic imidate gives the amidine derivative but not the benzimidazole. Cf: Unangst, P. C.; Southwick, P. L. *J. Heterocycl. Chem.* **1973**, *10*, 399–402.

(25) Others have postulated N-substituted imidates as the reactive intermediate in the formation of benzimidazoles.[18,23] For a discussion on the mechanism of the reaction of imidates with amines, see: Hand, E. S.; Jencks, W. P. *J. Am. Chem. Soc.* **1962**, *84*, 3505–3514.

(26) Nabulsi, N. A. R.; Fronczk, F. R.; Gandour, R. D. To be submitted to *Acta Crystallogr. C.*

Johns or Electrothermal melting point apparatus and are uncorrected. $^1H$ and $^{13}C$ NMR spectra were recorded with IBM AF 100, Bruker AC 200, or Bruker AM 400 FTNMR spectrometers. Proton chemical shifts are expressed in parts per million (ppm) downfield from internal tetramethylsilane (TMS). $^{13}C$ chemical shifts are also expressed in ppm relative to the solvent chemical shift. Infrared data (IR and FTIR) are reported in reciprocal centimeters and were recorded either with a Perkin-Elmer 283B spectrophotometer or an IBM IR/44 FTIR spectrophotometer. Mass spectra were obtained with a Hewlett-Packard 5985A mass spectrometer. Elemental analyses were performed either by Desert Analytics of Tuscon, AZ, or by Oneida Research Services of Whitesboro, NY.

Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. Dioxane and tetrahydrofuran (THF) were distilled from a mixture of sodium and potassium. Reagent grade dimethyl sulfoxide (DMSO) was stored over molecular sieves (4 Å) for 24 h before use. Phenylenediamine was recrystallized from hexane and sublimed under vacuum before use. Phenylenediamine dihydrochloride and methyl salicylate were used as received. Chloroacetonitrile was distilled and stored over molecular sieves before use.

**(2-Carbomethoxyphenoxy)acetonitrile (3).** Under nitrogen, a solution of methyl salicylate (6.5 mL, 50.0 mmol) in 50 mL of DMSO was added dropwise over a period of 2 and 1/4 h to a stirring solution of anhydrous $K_2CO_3$ (7.0 g, 55.0 mmol) in 50 mL of DMSO at room temperature, and the resulting solution was stirred for 1 h. Then a solution of chloroacetonitrile (4.7 mL, 75.0 mmol) in 100 mL of DMSO was added dropwise over a period of 5 and 1/4 h at room temperature. After completion of the addition, the reaction mixture was stirred for 1 h. The resulting mixture was filtered, and the filtrate was poured into 300 mL of cold water. The precipitate that formed was filtered, washed with cold water, and air dried, giving 7.13 g (76%) of **3** as a white powder with a melting point of 53.0–54.0 °C. Recrystallization from hexane yielded colorless needles with mp 54.5–55.0 °C (lit.[27] mp 53–54 °C): IR (KBr) 1725 (C=O), 1599 (C=C), 1276, 1232, and 1090 $cm^{-1}$ (alkyl and/or aryl C–O); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.89 (s, $CO_2CH_3$, 3 H), 4.86 (s, $OCH_2CN$, 2 H), 7.10–7.20 (m, Ar H, 2 H), 7.47–7.56 (m, Ar H, 1 H), 7.83–7.88 (m, Ar H, 1 H); $^{13}C$ NMR (100.61 MHz, $CDCl_3$) $\delta$ 52.26 (s), 55.66 (s), 115.18 (s), 116.45 (s), 122.15 (s), 123.62 (2), 132.16 (s), 133.82 (s), 156.14 (s), 165.76 (s); MS, *m/e* (rel intensity) 191 ($M^+$, 3.8), 176 (18.2), 160 (58.4), 159 (14.8), 149 (10.2), 148 (20.6), 135 (6.5), 120 (57.9), 105 (55.1), 95 (19.5), 92 (100.0), 77 (35.7), 65 (22.4), 64 (56.0), 63 (85.9), 62 (23.6), 51 (21.0), 50 (19.9). Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33; O, 25.11. Found: C, 62.71; H, 4.52; N, 7.27; O, 25.09.

**2-[(2'-Carbomethoxyphenoxy)methyl]benzimidazole (5).** Under nitrogen, sodium (0.35 g, 15.0 mmol) was added to a stirring solution of **3** (3.0 g, 15.7 mmol) in 50 mL of anhydrous methanol at room temperature. The resulting warm solution was stirred at ambient temperature for 40 min. To this colorless solution was added phenylenediamine dihydrochloride (2.72 g, 15.0 mmol), and the resulting solution turned yellow followed by formation of a precipitate. Stirring was continued for 2 h. The salts that formed were filtered, and the filtrate was treated with decolorizing charcoal. After removal of the charcoal, water (about 70–75 mL) was added to the alcoholic solution until cloudiness developed, and the resulting mixture was allowed to stand at room temperature for several hours. The precipitate that formed was filtered, washed with water, and air dried, giving 3.66 g (88%) of **5** as colorless plates with mp 159–159.5 °C: FTIR (KBr, $cm^{-1}$) 3300–2200 (br, N–H, H-bonded), 1727 (Ar—C=O, with a shoulder at 1680), 1599, 1588, 1491 (aryl C=C and N heterocycl. combination of C=C and C=N), 1433 (aryl multiple C=C), 1242, 1086, 1045 (alkyl and/or aryl C–O), 761, 752, 741 (Ar–H def.); $^1H$ NMR (100 MHz, $CDCl_3$, ppm) 3.93 (s, $CO_2CH_3$, 3 H), 5.47 (s, $ArOCH_2$, 2 H), 6.96–7.91 (m, Ar H, 8 H), 11.54 (br, =NH, 1 H); $^{13}C$ NMR (50.33 MHz, $CDCl_3$, ppm) 52.29 (s), 65.93 (s), 111.38 (s), 114.56 (s), 119.25 (s), 119.85 (s), 121.73 (s), 122.02 (s), 122.72 (s), 131.95 (s), 133.49 (s), 134.37 (s), 143.65 (s), 150.80 (s), 158.15 (s), 166.46 (s); MS, *m/e* (rel intensity) 282 ($M^+$, 14.7), 253 (21.7), 131 (100.0), 104 (10.4), 77 (17.5). Anal. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.93. Found: C, 68.18; H, 5.00; N, 9.95.

**2-[(2'-Carboxyphenoxy)methyl]benzimidazole (1).** A suspension of **5** (4.0 g, 14.0 mmol) in 100 mL of 0.5 N HCl was refluxed for 15 h. Cooling to room temperature resulted in formation of a precipitate. The resulting mixture was warmed until complete dissolution of the precipitate, followed by neutralization with concentrated $NH_4OH$. After being cooled to room temperature, the precipitate that formed was filtered, washed with water, and air dried, giving 3.33 g (85%) of **1** as a white solid with mp 200–203.5 °C. Recrystallization from a mixture of 1:2 water/absolute ethanol gave tan needles with mp 212.5–213 °C. A second recrystallization from 80% aqueous dioxane yielded white solid with mp 201.5–202 °C. A suitable single crystal for X-ray analysis was obtained by slow evaporation from dioxane: FTIR (KBr) 3454 ($R_2N$–H), 3330–2680 (H-bonded O=C—O—H centered at 3194), 3069 (Ar–H), 1680 (Ar—C=O), 1601, 1489 (aryl C=C and N heterocycl. C=C and C=N), 1452, 1439 (aryl multiple C=C), 1271, 1095, 1049 (alkyl and/or aryl C–O), 735 $cm^{-1}$ (Ar–H def.); $^1H$ NMR (100 MHz, $d_6$-DMSO) $\delta$ 5.47 (s, $ArOCH_2$, 2 H), 6.99–7.72 (m, Ar H, 8 H); $^{13}C$ NMR (25.16 MHz) $d_6$-DMSO, ppm) 64.80 (s), 114.78 (s), 115.03 (s), 121.30 (s), 122.05 (s), 122.61 (s), 130.75 (s), 132.86 (s), 138.14 (s), 150.14 (s), 156.59 (s), 167.17 (s); MS, *m/e* (rel intensity) 268 ($M^+$, 34.3), 239 (10.2), 223 (11.0), 131 (100.0), 104 (17.5), 92 (10.2), 77 (28.8), 65 (11.8), 64 (12.6), 63 (14.9). Anal. Calcd for $C_{15}H_{12}N_2O_3 \cdot {}^1/_2H_2O$: C, 64.98; H, 4.36; N, 10.10. Found: C, 65.22; H, 4.50; N, 10.16. Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51. Found: C, 66.87; H, 4.49.

**Acknowledgment.** We thank the National Institutes of Health (Grant GM35818) for financial support of this work. We also thank the referees for their suggestions and comments.

(27) Wormser, H.; Lieu, S. *J. Pharm. Sci.* **1976**, *65*, 397–400.

## A Facile and Highly Stereoselective Synthesis of (*R*)- and (*S*)-[2-(Phenylmethoxy)ethyl]oxirane

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In the course of research on stereochemically defined inhibitors of polyamine biosynthesis,[1] we had need for a highly stereoselective synthesis of the *R* and *S* enantiomers of 1,8-dichlorooctan-3-ol.[2] Following unsatisfactory results with an approach based on asymmetric induction,[3] we pursued an enantiomeric synthesis using (*R*)- or (*S*)-malic acid as starting materials. We envisioned using procedures described in the literature[4-6] to afford the desired enantiomerically pure oxiranes **5**, which could then be further elaborated to the desired 1,8-dichlorooctanol.

Conversion of the free malic acids or their dimethyl esters to a 9:1 mixture of the 1,2 and 1,3 cyclic ketals of 1,2,4-butanetriol was done by the procedure described previously.[7] The mixture of cyclic ketals was benzylated at the remaining free hydroxyl group and the ketal removed by mild acid hydrolysis to provide a mixture of the desired 4-benzyloxy diol **1** (Scheme I) and the 1-benzyloxy regioisomer (9:1). Conversion of the primary alcohol of **1** to a good leaving group (e.g., sulfonate ester) followed by treatment with base should result in cyclization to the desired oxirane with retention of configuration at the chiral center of interest. We anticipated that formation of the corresponding oxetane from the 1-benzyloxy regioisomer

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