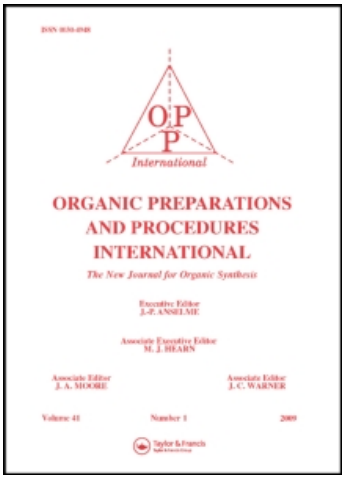

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SYNTHESIS OF SOME NOVEL FUNCTIONALIZED DOUBLE MICHAEL ACCEPTORS BASED ON *bis*(VINYLSULFONYL)METHANE (BVSM)

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SYNTHESIS OF SOME NOVEL FUNCTIONALIZED DOUBLE MICHAEL ACCEPTORS BASED ON *bis*(VINYLSULFONYL)METHANE (BVSM)

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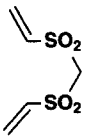
Crosslinking agents have found wide application in the polymer industry. Recently, there has been considerable interest in the site-directed crosslinking of proteins, such as hemoglobin, by bifunctional acylating agents.[1] Bifunctional vinylsulfone compounds have been used extensively to crosslink (harden) gelatin,[2] in particular, *bis*(vinylsulfonyl)methane (BVSM, **1**) has received considerable attention. The hardening property of these compounds is associated with their propensity to undergo double Michael addition with nucleophilic groups of water-permeable, colloid forming, natural or synthetic polymers.[3] Hardening of these polymers is a result of crosslinking between individual polymer chains. This article reports the synthesis of the novel functionalized *bis*(vinylsulfonyl)methane (BVSM) derivatives **8a-8d** and **14**; each bears an electron-withdrawing group in proximity of the vinylsulfone groups and these compounds were found to be useful gelatin hardeners.



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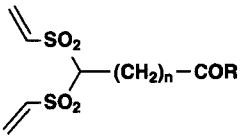
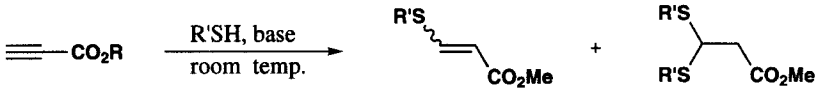


14 n = 0, R = $NHCH_3$

8a-d n = 1, R = OH, OCH_3, NH_2, $NHCH_3$

In general, the addition of thiols or thiolacetic acid to acetylenic esters at room temperature, with or without base catalysis, gives a mixture of E and Z mono-adducts as the major products and varying amounts of the *bis*-adduct (Eq. 1).[4] Reaction of methyl propiolate (**2**) with an excess of mercaptoethanol and a catalytic amount of DBU with heating provided the oily diol **3**, resulting from

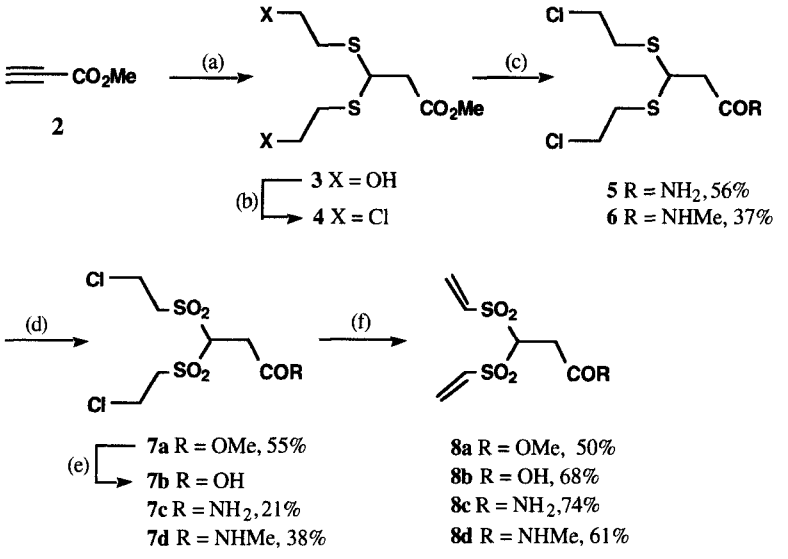


major minor

(1)

R' = Alkyl or CH_3CO

conjugate addition of two mercaptoethanol units. The combination of high temperature as well as amine catalyst (DBU) are necessary to obtain a good yield of the double addition product **3**. The crude diol **3** was not purified further but was converted directly to the corresponding dichloro ester **4** with hexachloroacetone and triphenylphosphine in THF (Scheme 1). Compound **4** was then converted

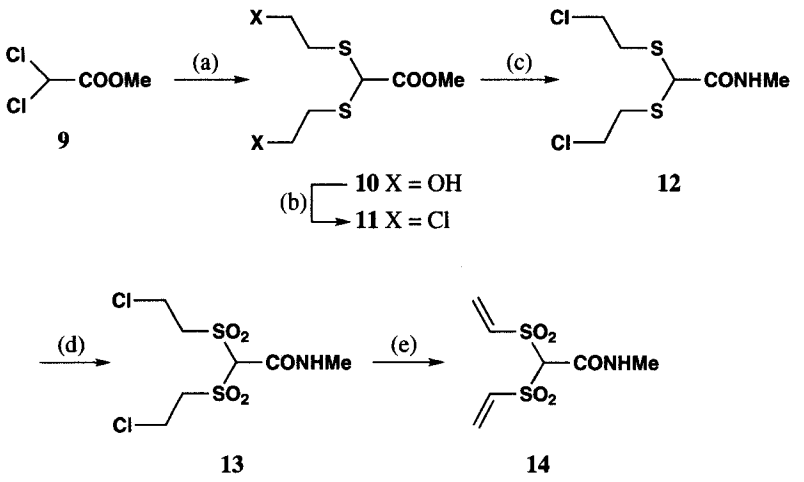


(a) mercaptoethanol, DBU (cat.) 115 - 120°, 100%; (b) PPh_3, hexachloroacetone, THF, r.t., 100%; (c) $MeNH_3Cl$ or NH_4Cl / Me_3Al, C_6H_6, 50°; (d) $R'CO_3H$, CH_2Cl_2, r.t.; (e) concd HCl, HOAc, 50°, 61%; (f) Et_3N, THF, r.t..

Scheme 1

directly to the dichlo-amides **5** and **6** using Weinreb's aluminum amide methodology.[5] The series of thioacetals **4-6** were then converted to their corresponding *bis*-sulfones **7a**, **7c** and **7d** by oxidation with peracid (either *meta*-chloroperoxybenzoic acid or peracetic acid) in methylene chloride. Elimination of HCl from **7a**, **7c** and **7d** was then accomplished by exposure to triethylamine in tetrahydrofuran, providing the expected *bis*-vinylsulfones **8a**, **8c** and **8d** in good yield. In order to prepare the vinylsulfone **8b**, it was necessary to first hydrolyze the methyl ester of **7a**. After a number of unsuccessful attempts at demethylation with trimethylsilyl iodide (TMSI),[6] we found that hydrolysis could be achieved using a conc. hydrochloric/glacial acetic acid mixture with warming, to provide the sulfone-acid **7b**. Elimination of HCl from **7b** with triethylamine in THF followed by acidic workup then afforded *bis*-vinylsulfone acid **8b** in good yield.

The BVSM derivative **14** was prepared by a similar sequence. Reaction of commercially available methyl dichloroacetate **9** with an excess of the sodium salt of mercaptoethanol in acetonitrile at room temperature,[7] afforded crude diol **10**. This diol was not further purified, but directly converted to dichloro ester **11** with hexachloroacetone and triphenylphosphine in THF (Scheme 2). Compound **11** was then converted to the dichloro N-methylamide **12** in one operation, using Weinreb's method.[5]



(a) $HOCH_2CH_2SNa$, CH_3CN, r.t.; (b) Ph_3P, hexachloroacetone, THF, r.t., 21 % (2 steps); (c) $MeNH_3Cl$, Me_3Al, C_6H_6, 50°, 64%; (d) $KMnO_4$, 10% H_2SO_4, $CHCl_3$, 20-25°, 41%; (e) Et_3N, THF, 0°C to r.t., 47%.

Scheme 2

Oxidation of **12** in chloroform with potassium permanganate in the presence of 10% sulfuric acid,[8] then provided the *bis*(sulfone amide) **13**. Elimination of HCl from **13** with triethylamine in THF then afforded *bis*-vinylsulfone **14**.

EXPERIMENTAL SECTION

All reactions involving air and moisture sensitive material were conducted under a dry nitrogen atmosphere using standard syringe/septum techniques. Solvent removal "*in vacuo*" refers to concentration under water aspirator pressure (10-20 mm Hg). THF and benzene were distilled from sodium-benzophenone before use.[9] Triethylamine was distilled over CaH_2 and stored over KOH pellets. All commercial reagents were used without further purification. ^1H NMR and ^{13}C NMR spectra were recorded on a GE QE-300 instrument. IR spectra were recorded on a Perkin Elmer model 1310 spectrophotometer. Compounds **3**, **4**, **5**, **11** and **13** were too unstable to be submitted for combustion analysis.

Methyl 3-*bis*(2'-Hydroxyethylthio)propanoate (3).- A mixture of methyl propiolate (5.00 mL, 51.9 mmol) and mercaptoethanol (10.20 mL, 145.4 mmol) was heated to 100° for 13.5 hrs. At this point, 0.20 mL of DBU was added and the temperature increased to 115-120°. One may also add the DBU initially and then warm to 115-120° without significantly affecting the yield of this reaction. After 4 hrs, the mixture was allowed to cool to room temperature and the remaining mercaptoethanol removed under high vacuum (0.1-0.3 mm Hg) with warming (40-50°) to yield 12.45 g (100%) of diol **3** as a light yellow oil.

IR (film, cm^{-1}): 3100-3700 (b), 1760. ^1H NMR ($CDCl_3$): δ 4.41 (t, J = 8Hz, 1H), 3.84 (t, J = 6Hz, 4H),

3.75 (s, 3H), 2.79-2.99 (m, 4H), 2.10 (bs, 2H). ^{13}C NMR ($CDCl_3$) δ: 170.9, 61.3, 52.2, 47.0, 41.9, 33.8.

Methyl 3-*bis*(2'-Chloroethylthio)propanoate (4).- To a stirred solution of the title diol **3** (3.10g, 12.9 mmol) and triphenylphosphine (8.46g, 32.3 mmol) in 60 mL of THF under nitrogen at room temperature was added hexachloroacetone (4.17 mL, 27.5 mmol) dropwise. At the end of the addition, the mixture was stirred for 45 min. and then concentrated *in vacuo*. The residue was triturated with 100 mL of 4:1 ethyl acetate/hexane and filtered. The filtrate was then concentrated *in vacuo* to give a crude brown oily mass. Flash chromatography on silica gel (eluent: 20% ethyl acetate/hexane) gave 3.99 g (112%) of brown oil. Volatile impurities were then removed under high vacuum for 48 hrs to give 3.55g (100%) of **4** as a dark brown oil.

IR (film, cm^{-1}): 1735, 1435, 1210. ^1H NMR ($CDCl_3$): δ 4.36 (t, J = 7.5 Hz, 1H), 3.75 (s, 3H), 3.70 (t, J = 8Hz, 4H), 2.93-3.11 (m, 4H), 2.83 (d, J = 7.5 Hz, 2H).

Methyl 3-*bis*(2'-Chloroethylsulfonyl)propanoate (7a).- To a stirred solution of the dichloride **4** (600 mg, 0.002 mmol in methylenechloride (20 mL) at 0° was added *m*-chloroperoxybenzoic acid (1.90g, 0.11 mol). The mixture was then allowed to warm up to room temperature. After 48 hrs, the mixture was diluted with CH_2Cl_2 and washed with 20 mL of saturated $NaHCO_3$ solution. The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was recrystallized from ethyl acetate/hexane to give 410 mg (55%) of sulfone **7a**, as a white powder, mp. 64-66 °.

IR ($CHCl_3$, cm^{-1}): 1775, 1380, 1155. ^1H NMR ($CDCl_3$): δ 5.18 (t, J = 6 Hz, 1H), 3.94-4.10 (m, 8H), 3.83 (s, 3H), 3.25 (d, J = 6 Hz, 2H).

Anal. Calcd for $C_8H_{14}O_6S_2Cl_2$: C, 28.16; H, 4.14. Found: C, 28.02; H, 4.04

Methyl 3-*bis*(2'-Vinylsulfonyl)propanoate (8a).- To a stirred solution of the *bis*-sulfone **7a** (1.60 g, 4.69 mmol) in 50 mL of CH_2Cl_2 under nitrogen at room temperature was added triethylamine (1.31 mL, 9.38 mmol) rapidly. After 15 min., the mixture was quenched with 100 mL of 0.1 N HCL and the phases separated. The aqueous layer was further extracted several times with CH_2Cl_2. The combined organic extracts were then dried ($MgSO_4$), filtered and concentrated *in vacuo* to give 1.24 g of crude **8a**. Two recrystallizations from ethyl acetate/hexane, yielded 621 mg (50%) of **8a**, mp. 111-113°.

^1H NMR ($CDCl_3$): δ 7.01-7.09 (dd, J = 10, 17Hz, 2H), 6.57 (d, J = 17 Hz, 2H), 6.38 (d, J = 10 Hz, 2H), 4.93 (t, J = 6 Hz, 1H), 3.80 (s, 3H), 3.07 (d, J = 6 Hz, 2H).

Anal. Calcd for $C_8H_{12}O_6S_2$: C, 35.81; H, 4.50. Found: C, 35.73; H, 4.50

3-*bis*(2'-Chloroethylthio)propionamide (5).- To a stirred suspension of ammonium chloride (2.62 g, 0.049 mmol) in 50 mL of dry benzene under nitrogen at room temperature was added trimethylaluminum solution (Aldrich, 24.5 mL of 2.0 mol/L solution in toluene) dropwise. After 30 min., gas evolution ceased and a solution of the ester **4** (4.50 g, 0.02 mmol in 15 mL of dry benzene) was added. The mixture was then warmed to 50°. After 19h, the mixture was allowed to cool to room temperature and quenched by cautious dropwise addition of 60 mL of 1.0 N HCl. The mixture was then extracted several times with ethyl acetate. The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography on silica gel (eluent: 90% ethyl acetate/hexanes) gave 2.37 g (56%) of **5**, mp. 66-68°.

IR ($CHCl_3$, cm^{-1}): 3510, 3400, 1675. ^1H NMR ($CDCl_3$): δ 5.63 (bm, 2H), 4.37 (t, J = 7 Hz, 1H), 3.68 (m, 4H), 2.90-3.12 (m, 4H), 2.72 (d, J = 7 Hz, 2H).

N-Methyl 3-*bis*(2'-Chloroethylthio)propionamide (6).- To a stirred suspension of methylamine hydrochloride (3.31 g, 0.05 mmol) in 50 mL of dry benzene under nitrogen at room temperature was added trimethylaluminum solution (Aldrich, 24.5 mL of 2.0 mol/L solution in toluene) dropwise. After 30 min., gas evolution ceased and a solution of the ester **4** (4.50 g, 0.02 mmol in 15 mL of dry benzene) was added. The mixture was then warmed to 50°. After 48 hrs, the mixture was allowed to cool to room temperature and quenched by cautious dropwise addition of 60 mL of 1.0 N HCl. The resulting mixture was then extracted several times with ethyl acetate. The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography on silica gel (eluent: 80% ethyl acetate/hexane) gave 2.05 g (37%) of **6** as an oil.

IR ($CHCl_3$, cm^{-1}): 3520, 3390 (b), 1690. ^1H NMR ($CDCl_3$): δ 5.75 (bs, 1H), 4.41 (t, J = 7 Hz, 1H), 3.74-3.64 (m, 4H), 3.13-2.96 (m, 4H), 2.85 (d, J = 5 Hz, 3H), 2.66 (d, J = 6 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 169.2, 48.2, 44.2, 42.9, 33.4, 26.5.

Anal. Calcd for $C_8H_{15}Cl_2NOS_2$: C, 34.78; H, 5.48; N, 5.07. Found: C, 35.18; H, 5.57; N, 4.85

3-*bis*(2'-Chloroethylsulfonyl)propionamide (7c).- To a stirred solution of the amide **5** (3.00 g, 11.6 mmol) in 150 mL of CH_2Cl_2 at room temperature was added acetic acid (6.55 mL, 114 mmol) followed by hydrogen peroxide (7.80 mL of 50% w/w solution). After 45h, the solvent was cautiously removed *in vacuo*. The resulting residue was recrystallized from water and dried *in vacuo* over P_2O_5 to give 790 mg (21%) of the sulfone **7c** as a fine white powder, mp. 135-138°.

^1H NMR (acetone-d_6): δ 7.21 (bs, 1H), 6.70 (bs, 1H), 5.50 (t, J = 6 Hz, 1H), 3.89-4.07 (m, 8H), 3.21 (d, J = 6Hz, 2H).

Anal. Calcd for $C_7H_{13}NO_5S_2$: C, 25.77; H, 4.02; N, 4.29. Found: C, 25.75; H, 4.03; N, 4.08.

N-Methyl-3-*bis*(2'-Chloroethylsulfonyl)propionamide (7d).- To a stirred solution of the amide **6** (3.00 g, 10.8 mmol) in 150 mL of CH_2Cl_2 at room temperature was added acetic acid (6.20 mL, 108 mmol) followed by hydrogen peroxide (7.37 mL of 50% w/w solution). After 45 hrs, the solvent was cautiously removed *in vacuo*. The resulting residue was recrystallized from water and dried *in vacuo* over P_2O_5 to give 1.40 g (38%) of the sulfone **7d** as a fine white powder, mp. 141-143°.

IR ($CHCl_3$, cm^{-1}): 3448, 1675, 1340. ^1H NMR (acetone-d_6): δ 7.41 (bs, 1H), 5.54 (t, J =6 Hz, 1H), 3.86-4.10 (m, 8H), 3.16 (d, J = 6 Hz, 2H), 2.75 (d, J = 4 Hz, 3H).

Anal. Calcd for $C_8H_{15}Cl_2NO_5S_2$: C, 28.24; H, 4.44; N, 4.12. Found: C, 28.01; H, 4.40; N, 3.97

3-*bis*(2'-Chloroethylsulfonyl)propionic Acid (7b).- To a stirred suspension of ester **7a** (320 mg, 0.938 mmol) in 5.0 mL of glacial acetic acid at room temperature was added 6.0 mL of concentrated hydrochloric acid solution. The mixture was then warmed to 50°. After 24h, the mixture was allowed to cool to room temperature and the solution volume concentrated to approx. 1/3 volume *in vacuo* (water pump) and the white solid collected by filtration and washed twice with 2 mL portions of cold water. The resulting powdery solid was then dried over P_2O_5 *in vacuo* to give 188 mg (61%) of **7b**, mp. 140-142°.

^{1}H NMR (acetone-d_6): δ 5.44 (t, J = 6Hz, 1H), 3.95-4.18 (m, 8H), 3.34 (d, J = 6Hz, 2H).

Anal. Calcd for $C_7H_{12}Cl_2O_6S_2$: C, 25.69; H, 3.70. Found: C, 25.62; H, 3.68

3-*bis*(Vinylsulfonyl)propionamide (8c).- To a stirred solution of the *bis*-sulfone **7c** (1.015 gm, 3.11 mmol) in 35 mL of dry THF under N_2 at room temperature was added triethylamine (0.87 mL, 6.22 mmol). After 10 min., the mixture was quenched with 3.0 mL of 1.0 N HCl solution and the solvent removed *in vacuo*. The residue was extracted several times with ethyl acetate and the combined extracts dried ($MgSO_4$) and concentrated *in vacuo*. The residue was subjected to flash chromatography on silica gel (eluent: 90% ethyl acetate/hexane) to give 545 mg (74%) of **8c** mp. 144-146°.

^{1}H NMR (acetone-d_6): δ 7.07 (dd, J = 10, 16 Hz, 2H), 7.06 (bs, 1H), 6.63 (bs, 1H), 6.41 -6.46 (dd, J = 10, 16 Hz, 2H), 5.17 (t, J = 6 Hz, 1H), 2.97 (d, J = 6 Hz, 2H).

Anal. Calcd for $C_7H_{11}NO_5S_2$: C, 33.19; H, 4.39; N, 5.53. Found: C, 33.16, H, 4.41; N, 5.25

N-Methyl-3-*bis*(Vinylsulfonyl)propionamide (8d).- To a stirred solution of the *bis*-sulfone **7d** (1.34 g, 3.93 mmol) in 40 mL of dry THF under N_2 at room temperature was added triethylamine (1.10 mL, 7.86 mmol). After 10 min., the mixture was quenched with 3.0 mL of 1.0 N HCl solution and the solvent removed *in vacuo*. The residue was extracted several times with ethyl acetate and the combined extracts dried ($MgSO_4$) and concentrated *in vacuo*. The residue was subjected to flash chromatography on silica gel (eluent: 80% ethyl acetate/hexane) to give 638 mg (61%) of compound **8d**, mp. 116-119°.

IR ($CHCl_3$, cm^{-1}): 3448, 3405, 1675, 1335. ^{1}H NMR ($CDCl_3$): δ 6.98-7.07 (dd, J = 10, 17 Hz, 2H), 6.55 (d, J = 17 Hz, 2H), 6.34 (d, J = 10 Hz, 2H), 5.87 (bs, 1H), 5.17 (t, J = 6 Hz, 1H), 2.96 (d, J = 6 Hz, 2H), 2.86 (d, J = 5 Hz, 3H).

Anal. Calcd for $C_8H_{13}NO_5S_2$: C, 35.94; H, 4.91; N, 5.24. Found: C, 35.51; H, 4.95; N, 5.06

3-*bis*(Vinylsulfonyl)propionic Acid (8b).- To a stirred solution of acid **7b** (471 mg, 1.44 mmol) in 11 mL of dry THF under nitrogen at room temperature was added triethylamine (0.56 mL, 4.32 mmol). After 10 min., the mixture was filtered through a course glass frit and the filtrate concentrated *in vacuo*. The residue was treated with 13 mL of 1N HCl solution and the resulting mixture extracted several times with ethyl acetate. The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Crude yield = 362 mg. Recrystallization from ethyl acetate/hexane provided 250 mg (68%) of **8b**, mp. 150- 152°.

^{1}H NMR (acetone-d_6): δ 7.05-7.15 (dd, =17, 10Hz, 2H), 6.48 (d, J = 10Hz, 2H), 6.47 (d, J = 17 Hz, 2H), 5.08 (t, J = 6Hz, 1H), 3.06 (d, J = 6Hz, 2H).

Anal. Calcd for $C_7H_{10}O_6S_2$: C, 33.06; H, 3.97. Found: C, 32.72; H, 4.03

Methyl-2-*bis*(2'-Chloroethylthio) Acetate (11).- To a stirred solution of sodium methoxide in methanol (generated by careful dropwise addition of 100 mL of dry methanol to 7.87 g, 0.33 mol of sodium hydride at 0°) at room temperature was added mercaptoethanol (21.0 mL, 0.300 mol). After 10 min., the solvent was removed *in vacuo* and acetonitrile (250 mL) and then methyl dichloroacetate **9** (13.5 mL, 0.130 mol) were added. The mixture was then stirred vigorously for 48 hrs at room temperature. The resulting white suspension was filtered through a bed of celite and the filtrate

concentrated *in vacuo* to give 11.81 g of crude oily **10**. This residue was then dissolved in 150 mL of dry THF at room temperature and triphenylphosphine (31.4 g; 0.12 mol) was added. To this mixture was added hexachloroacetone (16.6 mL, 0.11 mol) dropwise. At the end of the addition, the resulting dark brown mixture was stirred for 30 min. and then concentrated *in vacuo*. The residue was triturated with cold 1:4 ethyl acetate/hexane and filtered. The filtrate was concentrated *in vacuo* and the residue subjected to flash chromatography on silica gel (eluent: 20% ethyl acetate/hexane) to give 4.31 g (21%) of compound **11**as an oil.

IR (film, cm^{-1}): 1762, 1333, 1173. ^1H NMR ($CDCl_3$): δ 4.52 (s, 1H), 3.81 (s, 3H), 3.69-3.77 (m, 4H), 3.07-3.14 (m, 4H).

N-Methyl-2-*bis*(2'-Chloroethylthio)acetamide (12).- To a stirred suspension of methylamine hydrochloride (3.46 g, 0.05 mol) in 60 mL of dry benzene under nitrogen at room temperature was added trimethylaluminum solution (Aldrich, 25.7 mL of 2.0 mol/L solution in toluene) dropwise. After 30 min., gas evolution ceased and a solution of the ester **11** (4.50 g, 0.02 mol in 10 mL of dry benzene) was added. The mixture was then warmed to 50°. After 21 hrs, the mixture was allowed to cool to room temperature and quenched by cautious dropwise addition of 60 mL of 1.0 N HCl. The mixture was then extracted several times with ethyl acetate. The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography on silica gel (eluent: 40% ethyl acetate/hexanes) gave 2.85 g (64%) of compound **12**, mp. 82-84°.

IR ($CHCl_3$, cm^{-1}): 3453, 1705. ^1H NMR ($CDCl_3$): δ 6.51 (bs, 1H), 4.50 (s, 1H), 3.69- 3.73 (m, 4H), 3.04-3.10 (m, 4H), 2.88 (d, J = 5 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 168.7, 53.0, 43.1, 42.9, 33.9, 26.9.

Anal. Calcd for $C_7H_{13}Cl_2NOS_2$: C, 32.06; H, 5.01; N, 5.34. Found: C, 31.83; H, 4.98; N, 5.03

N-Methyl-2-*bis*(2'-Chloroethylthio)acetamide (13).- To a stirring solution of 70 mL of 10% sulfuric acid was added a solution of compound **12** (2.00 g, 7.62 mmol) in 100 mL of chloroform dropwise over a 20 min. period. During this period, potassium permanganate (12.05 g, 76.2 mmol) was added portionwise (exotherm). The internal temperature of the reaction mixture was carefully monitored, and periodic cooling (ice bath) was necessary to maintain a temperature of 20-25°. After 30 min., the mixture was cooled to 0° and 20% sodium *bis*ulfite solution was carefully added dropwise (maintaining the temperature below 25° with external cooling) until the brown color of the reaction mixture discharged. The reaction mixture was then extracted several times with ethyl acetate. The combined extracts were then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was recrystallized from ethyl acetate/hexane to give 1.02 g (41%) of **13**, mp. 173-175°.

^1H NMR (acetone-d_6): δ 7.92 (bs, 1H), 5.73 (s, 1H), 4.01-4.15 (m, 8H), 2.84 (d, J = 5 Hz, 3H).

N-Methyl-3-*bis*(Vinylsulfonyl)propionamide (14).- To a stirred solution of the *bis*-chlorosulfone **13** (600 mg, 1.84 mmol) in 80 mL of THF at 0° was added triethylamine (3.08 mL, 22.1 mmol) rapidly. The mixture was then allowed to warm to room temperature for 50 min. and then quenched with 22 mL of 1N HCl solution. The mixture was then concentrated to about 1/3 volume *in vacuo*. The mixture was then extracted several times with ethyl acetate, the extracts dried ($MgSO_4$) and concentrated *in vacuo*. The residue was then redissolved in 80 mL THF, cooled to 0°, and triethylamine (0.77

mL, 5.52 mmol) was added again. The mixture was allowed to warm to room temperature for 10 min., quenched with 6 mL of 1N HCl. Most of the THF was removed in vacuo and the mixture extracted several times with ethyl acetate. The combined extracts were then dried ($MgSO_4$) and concentrated *in vacuo*.. The resulting crude residue was recrystallized from ethyl acetate/hexane to give 220 mg (47%) of **14** mp. 143-147°.

IR ($CHCl_3$, cm^{-1}): 3400, 1690, 1340. ^1H NMR ($CDCl_3$): δ 6.94-7.03 (dd, J = 16.5, 10 Hz, 2H), 6.71 (bs, 1H), 6.59 (d, J = 16.5 Hz, 2H), 6.39 (d, J = 10 Hz, 2H), 5.04 (s, 1H), 2.97 (d, J = 5 Hz, 3H).

Anal. Calcd for $C_7H_{11}NO_5S_2$: C, 33.19; H, 4.39; N, 5.53. Found: C, 33.13; H, 4.36; N, 5.26

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