recorded on Varian Associates 220-MHz and Nicolet 360-MHz spectrometers operating at 33 and 55.4 MHz, respectively. Product yields were determined by comparison of peak areas by using either the cut and weigh technique or by using a programmed curve-fitting routine. Estimated errors using these methods is 2–3%. Chemical shifts (δ) were determined relative to tetramethylsilane-d_{12} and were as follows: 3-methylcyclopentene-2-*d* (**6**-2-*d*), 5.9; 1-methylcyclopentene-2-*d* (**7**-2-*d*), 5.6; 3-methylcyclopentene-3-*d* (**6**-3-*d*), 3.0; 1-methylcyclopentene-5-*d* (**7**-5-*d*), 2.5; *cis*-2-methylcyclopentanol-1-*d* (*cis*-**5**-1-*d*), 4.3; *cis*-2-methylcyclopentyl-1-*d* ethyl ether (*cis*-**5**-1-*d*), 4.0; *cis*-2-methylcyclopentyl-1-*d* 2,2,2-trifluoroethyl ether (*cis*-**5**-1-*d*), 4.1; *trans*-2-methylcyclopentanol-1-*d* (*trans*-**5**-1-*d*), 4.0; *trans*-2-methylcyclopentyl-1-*d* ethyl ether (*trans*-**5**-1-*d*), 3.7; *trans*-1-methylcyclopentanol-2-*d* (**8**-*trans*-2-*d*), 1.8; *cis*-1-methylcyclopentanol-2-*d* (**8**-*cis*-2-*d*), 2.1; 2-methylcyclopentanol-2-*d* (**5**-2-*d*), and 2-methylcyclopentyl-2-*d* ethyl ether (**5**-2-*d*), 1.8–2.1.

Solvent Preparation. UV and Conductance Kinetic Procedures. The procedures were the same as those that have been previously reported.[8b,31]

Acknowledgment. This material is based upon work supported by the National Science Foundation under grants CHE 85-06682 (project support) and CHE 81-05004 (Nicolet 360 NMR). M.A.I. also wished to acknowledge The Robert A. Welch Foundation and the W. M. Keck Foundation (HP 5995 GC/MS) for support.

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Vinyl Sulfonyl Esters and Amides in the Synthesis of Substituted δ-Sultams and δ-Sultones

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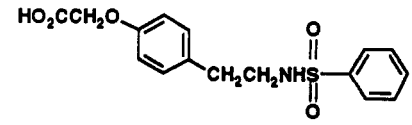
Received October 19, 1990

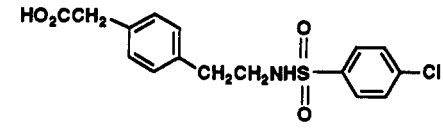
The Michael reaction of phenyl vinyl sulfonate (**3**) or vinyl sulfonamide **12** with phenylacetic esters was the key step in a general synthesis of 4-phenyl-substituted 1,2-thiazane 1,1-dioxides (sultams) and 5-phenyl-1,2-oxathiane 1,1-dioxides (sultones). This methodology was applied to the synthesis of some cyclic sulfonamide and sulfonate derivatives (I and II) of the potent TXA_2 receptor antagonists BM.13177 and BM.13505.

Vinyl sulfonyl esters and amides have served as substrates in a variety of reactions analogous to their carbonyl counterparts including epoxidation,[1] aziridination,[2] and Diels–Alder[3] and nitrone[4] cycloadditions. In addition, these versatile compounds have been utilized as acceptors in Michael reactions, primarily with oxygen and nitrogen nucleophiles.[5] Very few examples of Michael reactions of vinyl sulfonyl derivatives with active methylene compounds have been reported.[5]

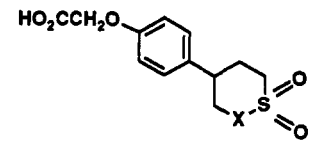
As part of a search for novel antithrombotic agents related to the thromboxane A_2 (TXA_2) receptor antagonists BM.13177 and BM.13505,[6] we were led to propose a series of cyclic sulfonamides and sulfonates as potential substrates.[7] Herein, we describe the utilization of the Michael reactions of vinyl sulfonates and sulfonamides with phenylacetic esters as the key steps in a general synthesis of 4-phenyl-substituted 1,2-thiazane 1,1-dioxides (δ-sultams) and 5-phenyl-1,2-oxathiane 2,2-dioxides (δ-sultones).[8] The application of this methodology to the synthesis of some derivatives (sultams and sultones, I and II) of these potent TXA_2 antagonists is also presented.



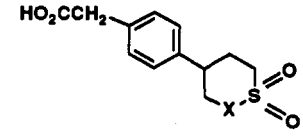
BM.13177



BM.13505



I X = NH, O



II X = NH, O

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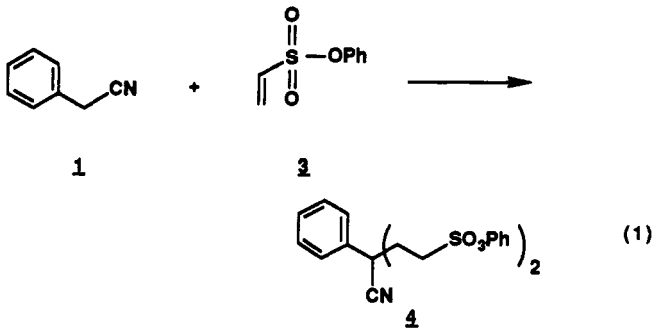
Results and Discussion

Vinyl Sulfonates in the Synthesis of the Sultam and Sultone Ring. Our initial strategy toward the development of an efficient synthesis of 4- and 5-phenyl-substituted sultams and sultones, respectively, called for a Michael reaction between phenyl vinyl sulfonate (3) and benzyl cyanide (1).[5] Reduction of the nitrile to the corresponding amine and subsequent N–S cyclization was expected to yield the desired sultam. In the event, reaction of benzyl cyanide with 3[5a] using a variety of phase-transfer conditions afforded the bis Michael adduct 4 as the sole product along with an equivalent amount of recovered 1 (eq 1).



1 3 4 (1)

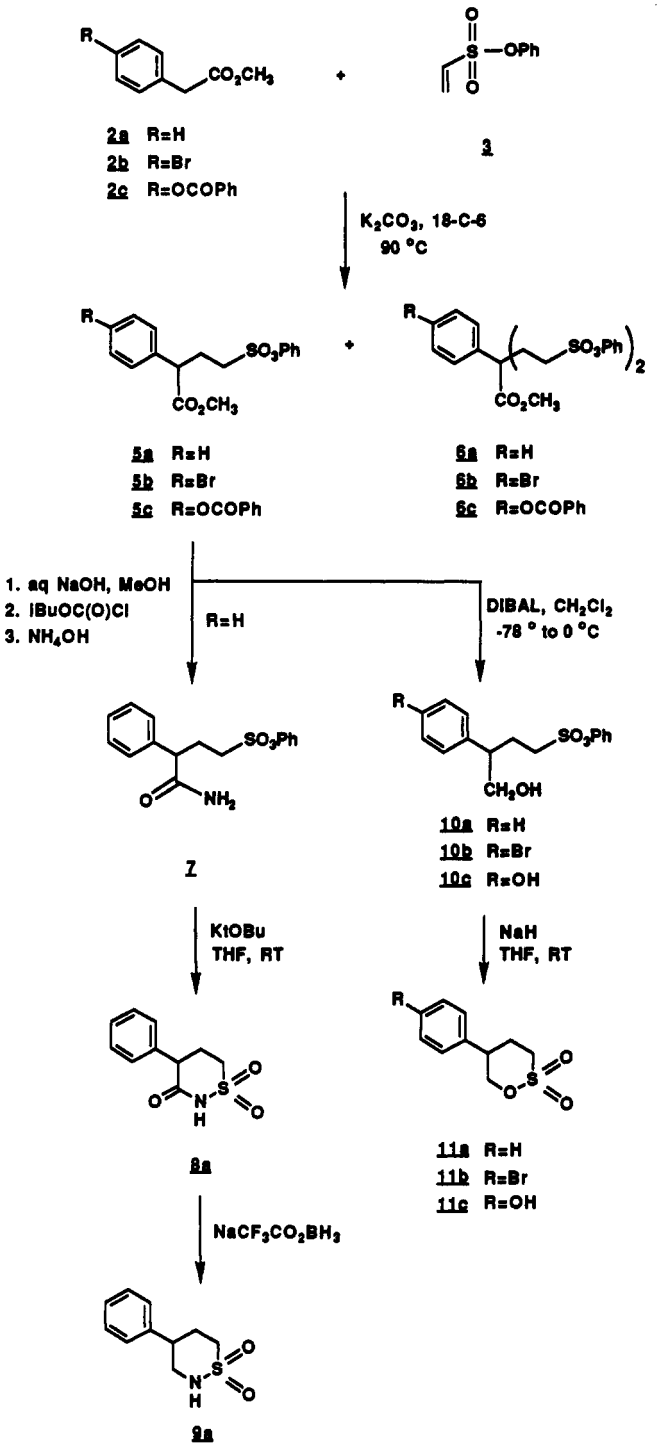
Although disappointed by the exclusive formation of the bis adduct, we were sufficiently encouraged by the reactivity of the vinyl substrate to attempt the Michael reaction with the corresponding ester, methyl phenylacetate (2a). Happily, reaction of sulfonate 3 with 2a (K_2CO_3, 18-crown-6, 90 °C) provided a 4.5:1 ratio of 5a/6a, from which the desired mono Michael adduct 5a was isolated in 48% yield.

The transformation of ester sulfonate 5a to the corresponding sultam was readily accomplished as follows (Scheme I). Hydrolysis of ester 5a was followed by conversion of the corresponding acid to carboxamide 7 in 76% overall yield.[9] Cyclization of 7 to sulfimide 8a was achieved in 45% yield by treatment with potassium *tert*-butoxide. Finally, reduction of 8a ($NaCF_3CO_2BH_3$) cleanly afforded the 4-phenyl sultam 9a (82%).[10]

Alternatively, ester sulfonate 5a could be utilized as a source for the sultone ring system. Reduction of ester 5a (DIBAL) afforded alcohol 10a in 93% yield. Treatment of 10a with sodium hydride produced a smooth cyclization to give an 86% yield of sultone 11a. This methodology served well for the synthesis of the target sultone precursors to 19 and 21 using substituted phenyl acetates. The reaction of 2b with 3 was uneventful, affording a 50% yield of mono Michael adduct 5b (along with 30% 6b).[11] By use of the corresponding 4-benzoylphenyl derivative 2c, the Michael reaction proved somewhat sluggish, producing a modest 20% yield of 5c as well as a 13% yield of the bis adduct 6c.[11,12] Ester reduction of the Michael adducts 5b and 5c (as well as benzoate deprotection in the case of 5c) followed by cyclization of resultant alcohols 10b and 10c cleanly afforded sultones 11b and 11c, respectively, in high yields.

Vinyl Sulfonamides in the Synthesis of Sultams. The low yield of 5c as well as the relatively lengthy conversion of the vinyl sulfonate Michael adduct 5a to sultam 9a prompted us to explore an alternate approach to this ring system. We decided on a strategy that incorporated the sultam nitrogen from the outset by utilizing a suitably protected vinyl sulfonamide as the Michael acceptor. We felt that such a substrate would prove to be more robust than its sulfonate counterpart. The *p*-methoxybenzyl (PMB) group was chosen to mask the sulfonamide functionality because of its stability to base and its ready removal under oxidative conditions.[13] Bis(4-methoxybenzyl)amine was reacted with chloroethanesulfonyl chloride to afford vinyl sulfonamide 12 in 82% yield. Reaction of 2a with 12 afforded the mono Michael adduct

Scheme I



(9) Rzeszotarska, B.; Makowski, M.; Kubica, Z. *OPPI Briefs* **1984**, *16*, 136–139.

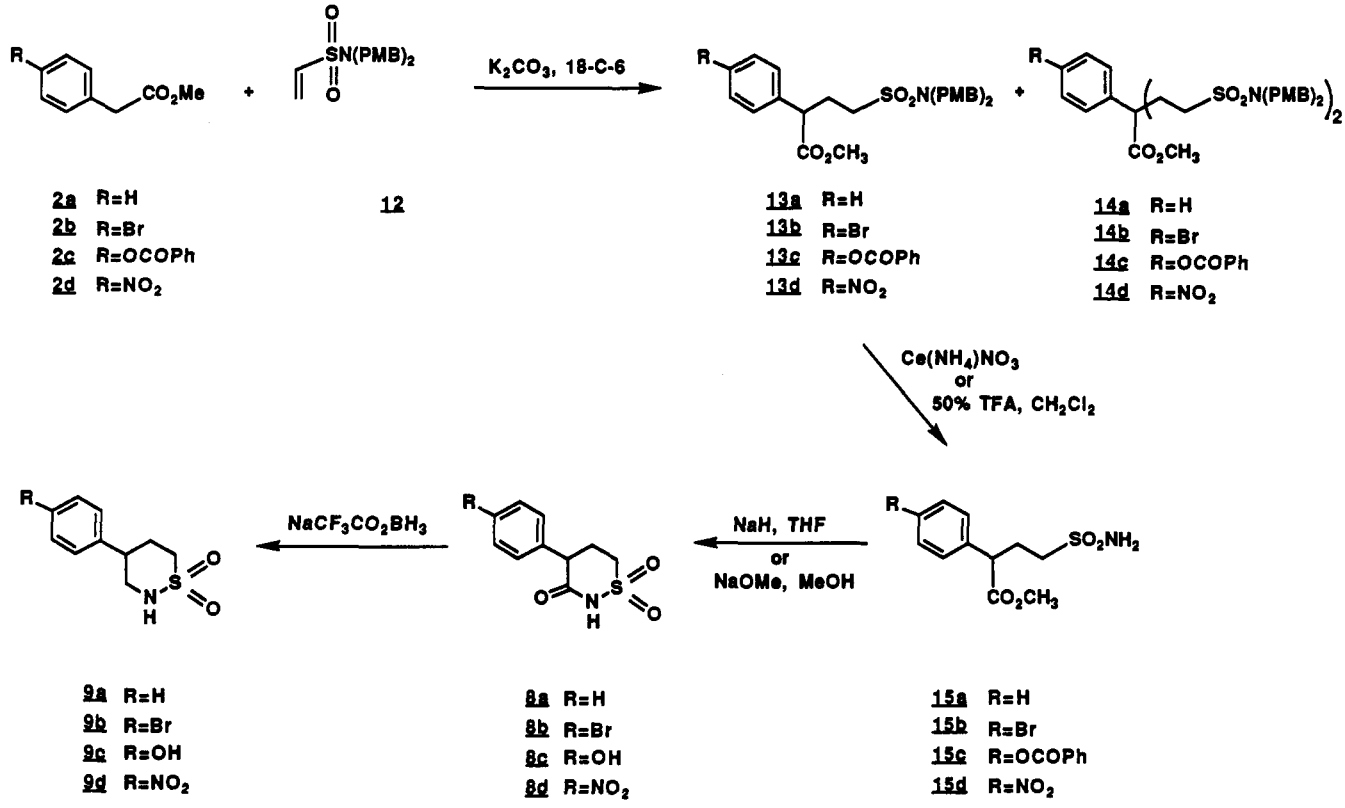
(10) Umino, N.; Iwakuma, T.; Itoh, N. *Tetrahedron Lett.* **1976**, 763–766.

(11) The yields reported for the bis adducts are of isolated products and are based on the vinyl sulfonyl ester or amide.

(12) Increasing the yield of this reaction with longer reaction times was impractical due to the relatively unstable nature of the vinyl sulfonate under the reaction conditions.

(13) Yoshimura, J.; Yamaura, M.; Suzuki, T.; Hashimoto, H. *Chem. Lett.* **1983**, 1001–1002.

Scheme II

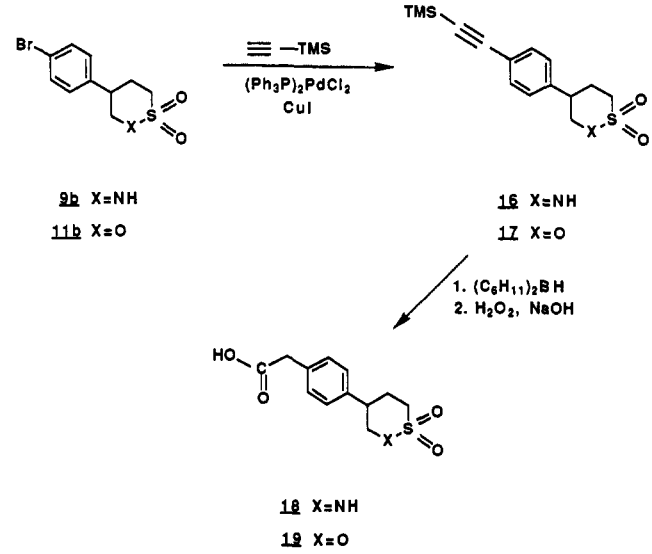


13a in 65% yield in addition to the bis adduct 14a (7%)[11] (Scheme II). Treatment of 13a with ceric ammonium nitrate provided a 66% yield of the primary sulfonamide 15a. Finally, treatment of 15a with sodium hydride produced sulfimide 8a (71%), which upon reduction as in the previous text afforded 4-phenyl sultam 9a in 85% yield.

Scheme II demonstrates the generality of this sultam synthesis utilizing a variety of substituted phenyl acetates. In all cases, the Michael reactions were run under phase-transfer conditions using crown ether catalysis. Although the yields of mono Michael adducts were somewhat higher using a modest excess of the nucleophile, acceptable quantities (44–62%) of material could be obtained utilizing a 1:1 molar ratio of 2/12. Especially noteworthy is the 47% yield of 13c produced from the reaction of 2c and vinyl sulfonamide 12 in contrast to the sequence in which the corresponding vinyl sulfonate 3 is employed as the Michael acceptor. Interestingly, in one example in which the corresponding ethyl ester of the *p*-nitrophenyl acetate 2d was deprotonated with 1 equiv of sodium hydride prior to reaction with 12, the bis Michael adduct was produced as the exclusive product in 70% yield.[14] In contrast, the use of crown ether conditions for this reaction with 2d afforded an amount of the mono adduct (62%) comparable to the other phase-transfer reactions as shown in Scheme II.

Two additional points can be made concerning this reaction sequence. Although removal of the PMB groups from sulfonamides 13a–c was readily accomplished using ceric ammonium nitrate (62–79% yields), the characteristically messy workup conditions associated with this oxidation prompted us to examine an alternate procedure. We have found that treatment of 13c and 13d with 50% trifluoroacetic acid resulted in the smooth removal of the PMB groups, providing primary sulfonamides 15c and 15d in 96 and 97% yields, respectively.[15] In addition, cyclization of the resultant γ-carbomethoxy sulfonamides to the sulfimides was accomplished either with sodium hydride (70%) (as for 15a) or with sodium methoxide (80–98%), which, in the case of 15c, also resulted in the simultaneous deprotection of the phenol. Reduction of 8a–d proceeded cleanly to provide sultams 9a–d in 71–90% yields.

Scheme III

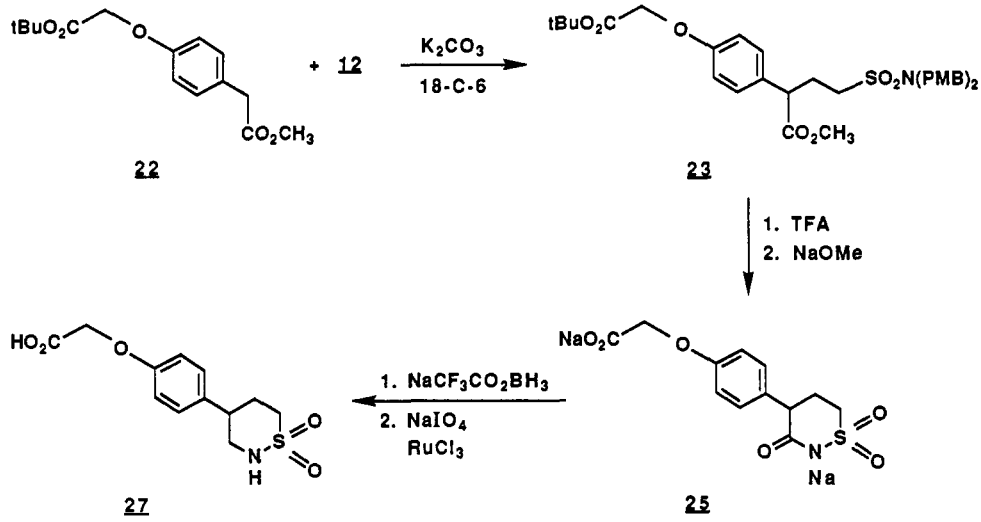


Synthesis of Sultam and Sultone Analogues of TXA_2 Antagonists. The synthesis of the sultam and sultone analogues of the TXA_2 antagonist BM.13505 was accomplished in two steps starting with bromides 9b and 11b, respectively (Scheme III). Reaction of 9b and 11b

(14) The reaction of dimethyl malonate with vinyl sulfonamide 12 using sodium hydride as the base affords a 50% yield of the mono Michael adduct.

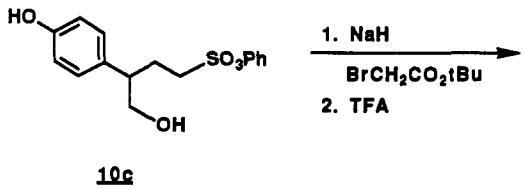
(15) (a) Stewart, F. H. C. *Aust. J. Chem.* **1968**, 2543. (b) Jones, M. I.; Froussios, C.; Evans, D. A. *J. Chem. Soc., Chem. Commun.* **1976**, 472.

Scheme IV

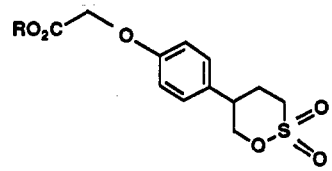


with (trimethylsilyl)acetylene ($(Ph_3P)_2PdCl_2$, CuI) afforded the coupled acetylenes **16** (76%) and **17** (85%)[16] which upon hydroboration ($(C_6H_{11})_2BH$; H_2O_2, NaOH) produced sultam **18** and sultone **19** in 85 and 55% yields, respectively.[17]

The oxyacetic acid sultam and sultone derivatives related to BM.13177 were thought to be available via alkylation of the corresponding phenols **9c** and **11c**, respectively. It was found that sultone **20** could be prepared from a one-pot cyclization/alkylation of **10c** (NaH, $BrCH_2CO_2$-*t*-Bu, 93%; eq 2). Hydrolysis of ester **20** cleanly afforded acid **21** in 84% yield. However, attempts to alkylate phenol **9c** with *tert*-butyl bromoacetate in the presence of a variety of bases (NaH, *n*-BuLi, $KN(TMS)_2$) resulted in low recovery of the *tert*-butyl ester of **27** due to competing alkylation of the sultam nitrogen. Our inability to selectively O-alkylate sultam **9c** led us to incorporate the oxyacetic acid substituent at the beginning of the synthetic sequence (Scheme IV). Methyl 4-[2-(1,1-dimethylethoxy)-2-oxethoxy]phenyl acetate (**22**) was reacted with **12** to provide a 44% yield of the mono adduct **23** in addition to a 48% yield of the corresponding bis adduct.[11] Treatment of **23** with 50% TFA to effect simultaneous debenzylation and removal of the *tert*-butyl group was followed by cyclization of the resulting primary sulfonamide acid **24** (NaOMe) to provide **25** in 68% overall yield. Simultaneous reduction of the sulfimide and carboxylic acid of **25** (82%) followed by oxidation ($NaIO_4$, $RuCl_3$)[18] of the primary alcohol **26** afforded sultam acid **27** in 47% yield.



10c



(2)

20 R-tBu

21 R=H

Sultams **18** and **27** and sultones **19** and **21** were found to have no influence on either arachidonic acid or PGH_2-induced platelet aggregation. In addition, none of the compounds was found to inhibit significantly [^{125}]-PTA-OH (a TXA_2 mimic) binding to washed human platelets. These data suggest that these sultam and sultone derivatives of BM.13177 and BM.13505 are not thromboxane A_2 antagonists.[19]

In summary, we have presented a general synthesis of 4-phenyl sultams and 5-phenyl sultones utilizing the Michael reaction of vinyl sulfonamides and sulfonates with phenylacetic esters. The application of this Michael reaction methodology to other active methylene compounds with these sulfonyl reagents should lead to a variety of substituted sultams and sultones.

Experimental Section

IR spectra were taken as a Nujol mull (unless otherwise indicated). ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ (unless otherwise indicated) at 300 MHz. Melting points are corrected. Thin-layer chromatography was performed on Merck precoated glass TLC plates with silica gel 60-F254 and stained with a solution of 75 g of ammonium molybdate, 2.5 g of ceric sulfate, and 500 mL of 10% sulfuric acid (V/V). Column chromatography was performed with Merck silica gel 60 (230–400 mesh). THF was distilled from sodium/benzophenone ketyl. Reactions were stirred with the aid of a magnetic stirrer unless otherwise indicated. In cases where satisfactory combustion analyses were unavailable, HRMS data along with ^{1}H and ^{13}C NMR spectra were used to establish purity.

Phenyl Vinyl Sulfonate (3).[5a] A mixture of phenol (58 g, 0.61 mol) dissolved in 100 mL of 1,2-dichloroethane and 100 mL of H_2O was mechanically stirred at 0 °C, and 420 mL of 25% aqueous NaOH and 100 g of chloroethanesulfonyl chloride were added simultaneously and slowly while keeping the pH of the reaction between 8.5 and 9.5. The mixture was stirred for another 2 h at 0 °C and then extracted four times with CH_2Cl_2. The combined organics were washed with half-saturated NaCl, dried over Na_2SO_4, filtered, and evaporated in vacuo to afford 85 g of material. Distillation with a Kugelrohr oven at full vacuum at 70 °C gave 70.6 g (62%) of **3**. ^{1}H NMR: δ 7.42–7.21 (m, 5), 6.68

(16) (a) Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627–630. (b) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.

(17) Backlund, S. J.; Zweifel, G. *J. Am. Chem. Soc.* **1977**, *99*, 3184.

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(19) (a) Platelet studies with these compounds, including competitive binding experiments, were performed by Alice H. Lin and Dr. Robert R. Gorman, The Upjohn Co. (b) Mais, D.; Knapp, D.; Halushka, P.; Ballard, K.; Hamenaka, N. *Tetrahedron Lett.* **1984**, 4207.

(dd, J = 9.9, 16.6 Hz, 1), 6.35 (d, J = 16.6 Hz, 1), 6.15 (d, J = 9.9 Hz, 1). ^{13}C NMR: δ 149.4, 132.0, 131.7, 129.9, 127.4, 122.3. IR: 1596, 1587, 1489, 1388, 1376, 1170 cm^{-1}. Anal. Calcd for $C_8H_8SO_3$: C, 52.16; H, 4.38; S, 17.40. Found: C, 51.98; H, 4.48; S, 17.34.

Methyl α-[2-(Phenoxysulfonyl)ethyl]benzeneacetate (5a). A suspension of 1.38 g (10 mmol) of K_2CO_3 in a solution of methyl phenylacetate (**2a**, 2.9 mL, 20 mmol) and 132 mg (0.5 mmol) of 18-crown-6 in 40 mL of toluene was stirred and heated to 85–90 °C as 1.84 g (10 mmol) of **3** in 10 mL of toluene were added over 1 h. After another 1.5 h at 90 °C, the mixture was allowed to cool, diluted with EtOAc, and washed with half-saturated NaCl. The aqueous portion was reextracted with EtOAc, and the combined organics were dried over $MgSO_4$, filtered, and evaporated in vacuo. The crude mixture was chromatographed on silica gel, eluting with 15% EtOAc/hexanes to afford 1.62 g (48%) of **5a** along with 1.12 g (22% based on **3**) of the bis alkylated product **6a**. **5a**. Mp: 30–31 °C. ^{1}H NMR: δ 7.41–7.20 (m, 10), 3.82 (t, J = 7.7 Hz, 1), 3.68 (s, 3), 3.20 (m, 2), 2.69 (m, 1), 2.45 (m, 1). ^{13}C NMR: δ 173.2, 149.4, 137.1, 130.0, 129.1, 128.0, 127.9, 127.3, 122.0, 52.4, 49.2, 48.0, 27.2. R_f: 0.13, 15% EtOAc/hexanes. IR: 1734, 1587, 1376, 1144, 866 cm^{-1}. Anal. Calcd for $C_{17}H_{18}O_5S$: C, 61.06; H, 5.43; S. 9.59. Found: C, 61.07; H, 5.25; S, 9.54. **6a**. Mp: 86–89 °C. ^{1}H NMR: δ 7.43–7.15 (m, 15), 3.78 (s, 3), 3.38 (m, 2), 3.00 (m, 2), 2.67 (m, 4). ^{13}C NMR: δ 173.5, 149.0, 137.9, 130.0, 129.5, 128.3, 127.3, 126.3, 121.9, 52.9, 52.8, 46.7, 31.7. R_f: 0.08, 15% EtOAc/hexanes. IR: 1731, 1460, 1378, 1145 cm^{-1}. Anal. Calcd for $C_{25}H_{26}O_8S_2$: C, 57.90; H, 5.05; S, 12.36. Found: C, 58.06; H, 5.30; S, 12.47.

Methyl 4-bromo-α-[2-(phenoxysulfonyl)ethyl]benzeneacetate (5b) was prepared by the procedure given previously for **5a** except chromatography was with 20% EtOAc/hexane. **5b**. Yield: 5.0 g (48%). Mp: 63–65 °C. ^{1}H NMR: δ 2.32–2.47 (m, 1), 2.61–2.76 (m, 1), 3.13–3.27 (m, 2), 3.67 (s, 3), 3.80 (t, J = 7.7 Hz, 1), 7.13–7.45 (m, 7), 7.47 (d, J = 6.5 Hz, 2). ^{13}C NMR: δ 27.1, 47.8, 48.5, 52.5, 121.9, 122.1, 127.3, 129.6, 130.0, 132.2, 149.0, 172.5. R_f: 0.56, 50% EtOAc/hexane. IR: 2925, 1722, 1381, 1370, 1222, 1152 cm^{-1}. Anal. Calcd for $C_{17}H_{17}BrNO_5S$: C, 49.41; H, 4.15; S, 7.76. Found: C, 49.30; H, 3.97; S, 7.79. **6b**. Yield: 2.2 g (29% based of **3**). Mp: 97–99 °C. ^{1}H NMR: δ 2.50–2.71 (m, 2), 2.92–3.08 (m, 1), 3.27–3.41 (m, 1), 3.80 (s, 3), 7.05 (d, J = 6.6 Hz, 2), 7.15–7.43 (m, 10), 7.52 (d, J = 6.6 Hz, 2). ^{13}C NMR: δ 31.4, 46.4, 52.6, 53.0, 121.9, 122.5, 127.4, 128.1, 130.0, 132.6, 137.0, 148.9, 173.0. R_f: 0.25, 25% EtOAc/hexane. IR (liquid heated): 1736, 1383, 1358, 1244, 1174, 1145 cm^{-1}. MS (HR): calcd for $C_{25}H_{25}BrNO_8S_2$ 596.0175, found 596.0166.

Methyl 4-(benzoyloxy)-α-[2-(phenoxysulfonyl)ethyl]benzeneacetate (5c) was prepared by the procedure given previously for **5a** except chromatography was with 20% EtOAc/hexane. **5c**. Yield: 2.4 g (19%). ^{1}H NMR: δ 2.41–2.53 (m, 1), 2.67–2.81 (m, 1), 3.24 (t, J = 7.7 Hz, 2), 3.70 (s, 3), 3.88 (t, J = 7.7 Hz, 1), 7.19–7.68 (m, 12), 8.20 (d, J = 8.1 Hz, 2). ^{13}C NMR: δ 27.3, 48.0, 48.6, 52.5, 115.6, 122.0, 122.4, 127.3, 128.6, 129.0, 130.0, 130.2, 130.4, 133.8, 134.6, 149.0, 150.6, 165.6, 172.9. R_f: 0.17, 25% EtOAc/hexane. MS (HR): calcd for $C_{24}H_{22}O_7S$ 454.1086, found 454.1087. **6c**. Yield 1.0 g (13%, based on **3**). Mp: 126–128 °C. ^{1}H NMR: δ 2.55–2.78 (m, 2), 3.00–3.12 (m, 1), 3.32–3.48 (m, 1), 3.79 (s, 3), 7.18–7.70 (m, 17), 8.20 (d, J = 8.0 Hz, 2). ^{13}C NMR: δ 31.6, 46.6, 52.5, 53.0, 121.9, 122.7, 127.4, 127.5, 128.7, 129.1, 130.0, 130.2, 133.9, 135.4, 148.9, 150.7, 166.2, 173.2. R_f: 0.10, 25% EtOAc/hexane. IR: 1745, 1725, 1488, 1456, 1372, 1170 cm^{-1}. Anal. Calcd for $C_{32}H_{30}O_{10}S_2$: C, 60.18; H, 4.73; S, 10.04. Found: C, 60.18; H, 4.73; S, 10.05.

Phenyl γ-(Hydroxymethyl)benzenepropanesulfonate (10a). A solution of ester **5a** (3.11 g, 9.3 mmol) in 25 mL of dry CH_2Cl_2 was stirred at −78 °C under N_2 as diisobutylaluminum hydride (1 M CH_2Cl_2, 20 mL, 20 mmol) was added slowly. The reaction mixture was stirred 30 min at −78 °C, warmed to 0 °C, and stirred an additional 30 min. The mixture was carefully quenched with 0.5 mL of MeOH at 0 °C and was stirred vigorously with 35 mL of 0.5 M sodium potassium tartrate overnight. The aqueous layer was diluted with 50 mL of saturated NaCl. The mixture was extracted with 3 × 25 mL of CH_2Cl_2. The combined organics were dried over $MgSO_4$ and were concentrated in vacuo to a pale yellow oil. Purification by chromatography over 82 g of silica gel, eluting with 40% EtOAc/hexane afforded 2.66 g (93%) of alcohol **10a** as a colorless oil. ^{1}H NMR: δ 2.17–2.30 (m, 1), 2.44–2.59 (m, 1), 2.89–2.99 (m, 1), 3.04–3.21 (m, 2), 3.79 (m, 2); 7.13–7.40 (m, 10). ^{13}C NMR: δ 26.1, 46.9, 48.6, 66.9, 122.0, 127.2, 127.6, 127.9, 129.1, 129.9, 139.8, 149.0. IR (liquid): 3560, 1588, 1372, 1192, 1169, 1145 cm^{-1}. Anal. Calcd for $C_{16}H_{18}O_4S$: C, 62.72; H, 5.92; S, 10.46. Found: C, 62.44; H, 6.08; S, 10.40.

Phenyl 4-Hydroxy-γ-(hydroxymethyl)benzenepropanesulfonate (10c). A solution of diester **5c** (1.7 g, 3.3 mmol) in 20 mL of dry CH_2Cl_2 under N_2 at −78 °C was treated slowly dropwise with DIBAL (1.0 M CH_2Cl_2, 15.3 mL, 15.3 mmol), stirred for 30 min at −78 °C, warmed to 0 °C, and stirred an additional 2 h. The mixture was carefully quenched with 0.2 mL of MeOH at 0 °C and was subsequently stirred vigorously with 25 mL of 0.5 M sodium potassium tartrate for 1.5 h. The mixture was diluted with 1 × 25 mL of 10% HCl and was extracted with 2 × 25 mL of CH_2Cl_2. The aqueous layer was filtered to remove 780 mg of a white solid that proved to be phenolic alcohol **10c** (73%). The organics were dried over $MgSO_4$ and were concentrated in vacuo to a pasty oil that provided an additional 160 mg (15%) of **10c** upon trituration with Et_2O. Mp: 165.5–167 °C. ^{1}H NMR (acetone-d_6): δ 2.08–2.21 (m, 1), 2.48–2.62 (m, 1), 2.80–2.93 (m, 1), 3.05–3.19 (m, 1), 3.27–3.40 (m, 1), 3.62–3.79 (m, 2), 6.80 (d, J = 8.5 Hz, 2), 7.11 (d, J = 8.4 Hz, 2), 7.19–7.50 (m, 5). ^{13}C NMR (acetone-d_6): δ 27.5, 47.0, 49.2, 67.0, 116.2, 123.0, 128.0, 129.8, 130.8, 132.7, 150.6, 157.5. IR: 3501, 1597, 1368, 1350, 1258, 1141 cm^{-1}. MS (HR): calcd for $C_{16}H_{18}O_5S$ 322.0875, found 322.0873.

5-Phenyl-1,2-oxathiane 2,2-Dioxide (11a). NaH (50% in oil, 0.286 g, 5.96 mmol) was washed with 2 × 5 mL of pentane under N_2 and was suspended in 25 mL of dry THF. The suspension was cooled to 0 °C and was treated with alcohol **10a** (1.66 g, 5.42 mmol) in 12 mL of dry THF. The mixture was stirred 30 min at 0 °C, warmed to room temperature, and stirred an additional 1.5 h. The reaction was quenched with 10 mL of 1:1 saturated NaCl/NH_4Cl and the THF was removed in vacuo. The solid was collected by filtration and was washed successively with 20 mL of saturated NaCl containing 20% v/v of 2 N NaOH and 20 mL of H_2O. The solid material was air dried to provide 1.00 g (86%) of sultone **11a** as a white crystalline solid. Mp: 116–118 °C. ^{1}H NMR: δ 2.33–2.45 (m, 1), 2.50–2.68 (m, 1), 3.16–3.40 (m, 3), 4.45 (dt, J = 2.5 Hz, 11.5 Hz, 1), 4.69 (t, J = 11.4 Hz, 1), 7.23–7.43 (m, 5). ^{13}C NMR: δ 29.6, 40.5, 47.3, 76.9, 127.4, 128.0, 129.1, 137.4. IR: 2926, 1459, 1359, 1169 cm^{-1}. Anal. Calcd for $C_{10}H_{12}O_3S$: C, 56.58; H, 5.70; S, 15.10. Found: C, 56.23; H, 5.88; S, 15.01.

Phenyl γ-(Aminocarbonyl)benzenepropanesulfonate (7). A solution of ester **5a** (1.34 g, 4.0 mmol) in 15 mL of MeOH was stirred and cooled at 0 °C as 2.4 mL (4.8 mmol) of freshly prepared 2 N NaOH was added. After 10 min at 0 °C, the reaction was stirred at ambient temperature overnight. The mixture was evaporated to dryness, taken up in half-saturated NaCl, acidified to pH 2.5 with 10% HCl, and extracted five times with CH_2Cl_2. The combined organics were dried over $MgSO_4$, filtered, and evaporated in vacuo to afford 1.24 g of the corresponding acid, which was used directly in the next step. ^{1}H NMR: δ 7.38–7.17 (m, 10), 3.82 (t, J = 7.7 Hz, 1), 3.18 (m, 2), 2.68 (m, 1), 2.46 (m, 1). ^{13}C NMR: δ 178.5, 148.9, 136.2, 130.0, 129.2, 128.3, 128.0, 127.3, 122.0, 49.1, 47.9, 26.7. A solution of the acid (1.22 g) and 0.59 mL (4.23 mmol) of Et_3N in 7 mL of dry THF was stirred and cooled at −45 °C, and 0.55 mL (4.23 mmol) of isobutylchloroformate was added all at once. After 10 min, the reaction was cooled to −55 °C and 1.5 mL of concentrated NH_4OH was added. The mixture was warmed to −10 to −15 °C and stirred at that temperature overnight. The mixture was poured into half-saturated NaCl and extracted five times with CH_2Cl_2. The combined organics were dried over $MgSO_4$ and evaporated to give 1.61 g of material. Purification by chromatography on 50 g of silica gel, eluting with 35% acetone/hexanes, afforded 0.97 g (76% from **5a**) of the carboxamide **7**. Mp: 134.5–135.5 °C. ^{1}H NMR: δ 7.39–7.19 (m, 10), 5.97 (br s, 1), 5.65 (br s, 1), 3.70 (t, J = 7.6 Hz, 1), 3.34–3.16 (m, 2), 2.72 (m, 1), 2.38 (m, 1). ^{13}C NMR: δ 174.3, 149.0, 138.1, 130.0, 129.3, 128.1, 128.0, 127.3, 122.0, 49.8, 48.3, 27.1. IR: 3425, 1679, 1664, 1335, 1182 cm^{-1}. Anal. Calcd for $C_{16}H_{17}NSO_4$: C, 60.12; H, 5.31; N, 4.39; S, 10.04. Found: C, 60.12; H, 5.31; N, 4.41; S, 9.87.

***N,N*-Bis[(4-methoxyphenyl)methyl]ethenesulfonamide (12).** A 3000-mL three-necked flask equipped with a mechanical stirrer was charged with 116 g (0.451 mol) of bis(*p*-methoxybenzyl)amine and 720 mL of 1,2-dichloroethane. The solution was layered with 360 mL of H_2O, and the mixture was cooled to

0 °C. The vigorously stirred mixture was treated slowly dropwise with NaOH (48.5 g, 1.21 mol) in 360 mL of H_2O while 2-chloroethanesulfonyl chloride (57 mL, 0.542 mol) in 300 mL of 1,2-dichloroethane was added simultaneously, all the while making sure a slight excess of NaOH was present. The reaction mixture was stirred 30 min at 0 °C and 3 h at rt. The reaction was acidified with 250 mL of 10% HCl, and the precipitated bis(*p*-methoxybenzyl)amine HCl was collected by filtration (23.7 g, 18%). The aqueous layer was extracted with 3 × 500 mL of Et_2O. The combined organics were dried over $MgSO_4$ and concentrated in vacuo to provide 128 g (81%) of **12** as a white solid. The crude material was recrystallized from Et_2O/hexane prior to use. Mp: 70–70.5 °C. ^1H NMR: δ 3.81 (s, 6), 4.19 (s, 4), 5.85 (d, J = 9 Hz, 1), 6.17–6.34 (m, 2), 6.86 (d, J = 9 Hz, 4), 7.20 (d, J = 9 Hz, 4). ^{13}C NMR: δ 48.7, 55.2, 113.9, 126.1, 127.6, 130.1, 136.1, 159.3. IR: 1610, 1511, 1338, 1251, 1177, 1146 cm^{-1}. Anal. Calcd for $C_{18}H_{21}NO_4S$: C, 62.22; H, 6.09; N, 4.03. Found: C, 61.99; H, 6.11; N, 4.07.

Methyl α-[2-[[Bis[(4-methoxyphenyl)methyl]amino]-sulfonyl]ethyl]benzeneacetate (13a). A solution of methyl phenylacetate (**2a**) (10.5 mL, 72.7 mmol) and **12** (14.7 g, 42.2 mmol) was combined with K_2CO_3 (5.8 g, 42.2 mmol) and 18-crown-6 (1.1 g, 4.22 mmol) in 150 mL of dry toluene, and the mixture was heated to reflux for 3 h. The cooled mixture was diluted with 300 mL of EtOAc, washed with 1 × 150 mL of 90% saturated NaCl, and the aqueous layer was backwashed with 3 × 10 mL of EtOAc. The combined organics were dried ($MgSO_4$) and concentrated in vacuo to a pale oil. Purification by chromatography over 527 g silica gel, eluting with 32% EtOAc/hexanes, afforded 13.7 g (65%) of **13a** and 1.1 g (6%) of the bis adduct **14a**. **13a**. Mp: 97–98 °C. ^1H NMR: δ 2.17–2.32 (m, 1), 2.42–2.54 (m, 1), 2.71–2.81 (m, 2), 3.66 (s, 3), 3.72 (t, J = 13 Hz, 1), 3.81 (s, 6), 4.12–4.27 (m, 4), 6.86 (d, J = 9 Hz, 4), 7.17 (d, J = 9 Hz, 4), 7.21–7.39 (m, 5). ^{13}C NMR: δ 27.0, 49.2, 49.5, 51.1, 52.2, 55.3, 114.1, 127.6, 127.8, 127.9, 128.9, 130.1, 136.5, 159.3, 174.2 R_f: 0.53 (50% EtOAc/hexane). IR: 1728, 1610, 1333, 1251, 1146 cm^{-1}. Anal. Calcd for $C_{27}H_{31}NO_6S$: C, 65.17; H, 6.28; N, 2.81. Found: C, 65.23; H, 6.28; N, 2.80. **14a**. ^1H NMR: δ 2.38 (t, J = 8 Hz, 2), 2.54–2.63 (m, 1), 2.70–2.82 (m, 1), 3.67 (s, 3), 3.80 (s, 12), 4.19 (br s, 8), 6.85 (d, J = 8.7 Hz, 8), 7.03–7.07 (m, 2), 7.13–7.21 (d, J = 8.7 Hz, 8), 7.31–7.41 (m, 3). ^{13}C NMR: δ 30.0, 49.1, 52.5, 55.2, 114.1, 126.2, 127.5, 127.7, 129.0, 130.0, 138.8, 159.3, 173.8. R_f: 0.43 (50% EtOAc/hexane). IR: 1731, 1612, 1327, 1249, 1176, 1145 cm^{-1}. Anal. Calcd for $C_{45}H_{52}N_2O_{10}S_2$: C, 63.96; H, 6.20; N, 3.32; S, 7.59. Found: C, 64.17; H, 6.58; N, 3.39; S, 7.47.

Methyl α-[2-[[bis[(4-methoxyphenyl)methyl]amino]-sulfonyl]ethyl]-4-bromobenzeneacetate (13b) was prepared by the procedure given previously for **13a** using 1.1 equiv of **2b**. Purification was by crystallization (EtOAc) and chromatography (25% EtOAc/hexanes) of the mother liquor. **13b**. Yield: 32.3 g (55%). Mp: 113–115 °C. ^1H NMR: δ 2.11–2.26 (m, 1), 2.40–2.52 (m, 1), 2.70 (t, J = 7.5 Hz, 2), 3.63 (s, 3), 3.73 (t, J = 8.3 Hz, 1), 3.80 (s, 6), 4.11–4.30 (m, 4), 6.81–6.86 (d, J = 8.7 Hz, 4), 7.12 (d, J = 8.4 Hz, 2), 7.17 (d, J = 8.7 Hz, 4), 7.47 (d, J = 8.4 Hz, 2). ^{13}C NMR: δ 26.9, 48.8, 49.2, 50.8, 52.4, 55.3, 114.1, 121.6, 127.6, 129.7, 130.1, 132.0, 136.6, 159.4, 172.5. R_f: 0.17 (25% EtOAc/hexane). IR: 1736, 1610, 1512, 1335, 1137 cm^{-1}. MS (HR): calcd for $C_{27}H_{30}BrNO_6S$ 575.0978, found 575.1011. **14b**. Yield: 0.51 g (1%). ^1H NMR: δ 2.28–2.39 (m, 2), 2.44–2.59 (m, 1), 2.51–2.64 (m, 1), 3.66 (s, 3), 3.81 (s, 12), 4.20 (br s, 8), 6.85 (d, J = 8.7 Hz, 8), 6.93 (d, J = 8.4 Hz, 2), 7.16 (d, J = 8.7 Hz, 8), 7.47 (d, J = 8.4 Hz, 2). ^{13}C NMR: δ 29.8, 48.9, 49.2, 52.2, 52.7, 55.3, 114.1, 121.8, 127.5, 128.1, 130.1, 132.1, 138.0, 159.4, 173.3. R_f: 0.08 (40% EtOAc/hexane). IR: 1732, 1612, 1512, 1352, 1145 cm^{-1}. MS (HR): calcd for $C_{45}H_{51}BrN_2O_{10}S_2$ 923.2247, found 923.2216.

Methyl 4-(benzoyloxy)-α-[2-[[bis[(4-methoxyphenyl)-methyl]amino]sulfonyl]ethyl]benzeneacetate (13c) was prepared by the procedure given previously for **13a** using 1.5 equiv of **2c**. Purification was by silica gel chromatography with 30% EtOAc/hexanes. **13c**. Yield: 4.85 g (47%). Mp: 137–138 °C. ^1H NMR: δ 8.19 (m, 2), 7.64 (m, 1), 7.52 (m, 2), 7.32 (m, 2), 7.19 (m, 6), 6.85 (m, 4), 4.23 (m, 4), 3.81 (s, 6), 3.79 (t, J = 8.0 Hz, 1), 3.67 (s, 3), 2.78 (m, 2), 2.49 (m, 1), 2.25 (m, 1). ^{13}C NMR: δ 174.0, 165.0, 159.2, 150.3, 135.0, 133.6, 130.0, 129.9, 129.1, 128.9, 128.5, 127.5, 122.0, 113.9, 55.1, 52.2, 50.8, 49.0, 48.7, 27.0. R_f: 0.095 (25% EtOAc/hexanes). IR: 1732, 1609, 1320, 1309, 1175, 1164 cm^{-1}. Anal. Calcd for $C_{34}H_{35}NO_8S$: C, 66.11; H, 5.71; N, 2.27; S, 5.19. Found: C, 66.16; H, 5.77; N, 2.28; S, 5.21. **14c**. Yield: 2.08 g (24%). ^1H NMR: δ 8.20 (m, 2), 7.66 (m, 1), 7.53 (m, 2), 7.24–7.07 (m, 12), 6.89–6.78 (m, 8), 4.22 (s, 8), 3.80 (s, 12), 3.67 (s, 3), 2.76–2.39 (m, 8). ^{13}C NMR: δ 174.5, 164.9, 159.4, 151.0, 137.0, 134.0, 130.1, 129.5, 129.4, 128.7, 127.6, 122.2, 115.8, 114.1, 60.4, 55.3, 53.6, 53.0, 49.2, 30.4.

Methyl α-[2-(Aminosulfonyl)ethyl]benzeneacetate (15a). A solution of dibenzyl sulfonamide **13a** (3.0 g, 6.03 mmol) and 36 mL of H_2O in 144 mL of CH_3CN under N_2 was treated with $Ce(NH_4)NO_3$ (26.4 g, 48.2 mmol) and stirred 2.5 h at rt. The CH_3CN was removed in vacuo, and the aqueous residue was poured into 150 mL of saturated NaCl and extracted with 5 × 100 mL of Et_2O. The combined organics were washed with 1 × 100 mL saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated in vacuo to a dark oily residue. Purification by chromatography over 100 g of silica gel, eluting with 40% EtOAc/hexane, afforded 1.04 g (67%) of sulfonamide **15a** as a yellow oil that crystallized under high vacuum. Mp: 80–83 °C. ^1H NMR: δ 2.26–2.39 (m, 1), 2.51–2.66 (m, 1), 2.96–3.17 (m, 2), 3.66 (s, 3), 3.76 (t, J = 7.7 Hz, 1), 4.96 (br s, 2), 7.23–7.48 (m, 5). ^{13}C NMR: δ 27.3, 49.2, 52.2, 52.6, 127.6, 128.8, 136.9, 173.1. IR: 3336, 1714, 1349, 1327, 1162, 1148 cm^{-1}. MS (HR): calcd for $C_{11}H_{15}NO_4S$: 257.0722, found 257.0721.

Methyl α-[2-(aminosulfonyl)ethyl]-4-bromobenzeneacetate (15b) was prepared by the procedure given previously for **15a**. Yield was 6.87 g (79%) after recrystallization (40% EtOAc/hexane) and silica gel chromatography of the mother liquor (40% EtOAc/hexane). Mp: 126–129 °C. ^1H NMR: δ 2.25–2.38 (m, 1), 2.50–2.66 (m, 1), 2.96–3.14 (m, 2), 3.68 (s, 3), 3.76 (t, J = 7.7 Hz, 1), 4.65 (br s, 2), 7.16 (d, J = 8.3 Hz, 2), 7.47 (d, J = 8.3 Hz, 2). ^{13}C NMR: δ 28.5, 49.8, 52.7, 53.4, 122.4, 131.0, 132.9, 138.6, 174.5. IR: 3337, 1714, 1349, 1329, 1162 cm^{-1}. MS (HR): calcd for $C_{11}H_{14}BrNO_4S$ 334.9827, found 334.9819.

Methyl α-[2-(aminosulfonyl)ethyl]-4-(benzoyloxy)-benzeneacetate (15c) was prepared by the procedure given previously for **15a**. Yield was 1.89 g (62%) after silica gel chromatography (50% EtOAc/hexane). Alternatively, a solution of **13c** (4.75 g, 7.7 mmol) in 25 mL of dry CH_2Cl_2 under N_2 was treated with trifluoroacetic acid (25 mL) and stirred at rt overnight. The mixture was concentrated in vaeuo to a purple oil and purified by silica gel chromatography over 92 g of silica gel, eluting with 45% EtOAc/hexane to afford 2.8 g (96%) of **15c** as an off-white solid. Mp: 121–122 °C; ^1H NMR: δ 8.16 (m, 2), 7.99 (m, 1), 7.49 (m, 2), 7.35 (m, 2), 7.18 (m, 2), 5.25 (s, 2), 3.83 (t, J = 6.7 Hz, 1), 3.65 (s, 3), 3.10 (m, 2), 2.60 (m, 1), 2.35 (m, 1). ^{13}C NMR: δ 173.3, 165.3, 150.4, 135.1, 133.7, 130.1, 129.1, 128.6, 122.2, 60.4, 52.6, 52.4, 48.7, 27.4, 21.2, 14.1. IR: 3361, 1731, 1710, 1377, 1167 cm^{-1}. Anal. Calcd for $C_{18}H_{19}O_6SN$: C, 57.28; H, 5.07; N, 3.71; S, 8.49. Found: C, 57.08; H, 5.29; N, 3.98; S, 8.21.

Dihydro-4-phenyl-2*H*-1,2-thiazin-3(4*H*)-one 1,1-Dioxide (8a, Method a). A suspension of NaH (50% in oil, 0.493 g, 10.5 mmol, prewashed with 2 × 5 mL pentane) in 30 mL of dry THF at 0 °C was treated slowly with ester **15a** (2.4 g, 9.33 mmol) in 20 mL of dry THF. The mixture was stirred 30 min at 0 °C, warmed to rt, and stirred an additional 3 h. The reaction was concentrated in vacuo to a brown solid (2.4 g), dissolved in 30 mL of MeOH, and stirred with 12 g of Dowex-50W-X8 ion exchange resin (H^+ form) for 1 h at rt. The resin was removed by filtration and washed with copious amounts of MeOH. The filtrate was chilled to −33 °C overnight to provide 1.03 g (49%) of sulfimide **8a** as a fine white solid. The resin bed was washed further with 200 mL of THF, the filtrate was combined with the MeOH mother liquor, and the mixture was concentrated in vacuo to a yellow paste. Purification by chromatography over 20 g of silica gel, eluting with 40% acetone/hexane + 0.25% acetic acid provided an additional 0.52 g (25%) of **8a**.

Method b. A solution of potassium *tert*-butoxide (428 mg, 3.82 mmol) in 10 mL of dry THF at 0 °C was treated slowly with carboxamide **7** (610 mg, 1.91 mmol) in 6 mL of THF. The mixture was stirred at 0 °C for 2 h and at rt for 30 min. The reaction was diluted with 5 mL of MeOH and passed through a column of 5 g of Dowex 50W-X8 (H^+ form) resin. The resin was washed well with THF. The filtrate was evaporated, and the material was purified by chromatography on 20 g of silica gel, eluting with 40% acetone/hexanes/0.25% acetic acid to afford 177 mg (42%) of

8a. Mp: 211–212 °C. ^{1}H NMR (MeOH-d_4): δ 2.38–2.53 (m, 2), 3.46–3.58 (m, 2), 3.90–4.00 (dd, J = 6.4, 10.2 Hz, 1), 7.18–7.40 (m, 5). ^{13}C NMR (acetone-d_6): δ 27.3, 48.4, 48.7, 128.1, 129.5, 140.6, 171.5. IR: 3170, 1700, 1453, 1337, 1147 cm^{-1}. Anal. Calcd for $C_{10}H_{11}NO_3S$: C, 53.32; H, 4.92; N, 6.22. Found: C, 52.97; H, 5.06; N, 6.03.

4-(4-Bromophenyl)dihydro-2*H*-1,2-thiazin-3(4*H*)-one 1,1-Dioxide (8b) was prepared by the procedure (method a) given previously for **8a**. Purification by silica gel chromatography (50% acetone/hexane/0.25% acetic acid) gave 2.8 g (71%). Mp: 189–190.5 °C. ^{1}H NMR (MeOH-d_4): δ 2.40–2.57 (m, 2), 3.52–3.65 (m, 2), 4.01 (dd, J = 6.5, 10.7 Hz, 1), 7.21 (d, J = 8.2 Hz, 2), 7.55 (d, J = 8.2 Hz, 2). ^{13}C NMR (MeOH-d_4): δ 27.3, 122.3, 131.6, 132.8, 139.4, 173.1. IR: 3144, 1697, 1494, 1326, 1161 cm^{-1}. Anal. Calcd for $C_{10}H_{10}BrNO_3S$: C, 39.49; H, 3.31; N, 4.60; S, 10.54. Found: C, 39.43; H, 3.30; N, 4.62; S, 10.64.

Dihydro-4-(4-hydroxyphenyl)-2*H*-1,2-thiazin-3(4*H*)-one 1,1-Dioxide (8c). A solution of benzoate **15c** (2.6 g, 6.9 mmol) in 20 mL of MeOH under N_2 at 0 °C was treated with NaOMe (400 mg, 7.4 mmol) and stirred for 2 h as the cooling bath expired. The mixture was diluted with 25 mL of THF, treated with NaOMe (880 mg, 16.3 mmol), heated to reflux for 2.5 h, and stirred overnight at rt. The mixture was stirred vigorously with 9 g of Dowex 50W-X8 ion exchange resin (H^+ form) for 30 min. The resin was removed by filtration and washed well with 20 mL each of MeOH, acetone, and THF. The filtrate was concentrated in vacuo to a pasty white solid that was throughly washed with Et_2O to provide 1.49 g (90%) of **8c** as a white solid. Mp: 252–254 °C. ^{1}H NMR (DMSO-d_6): δ 6.93 (d, 2), 6.68 (d, 2), 3.79 (dd, J = 6.2, 10.6 Hz, 1), 3.55 (m, 2), 2.33 (m, 1), 2.21 (m, 1). ^{13}C NMR (DMSO-d_6): δ 173.3, 158.1, 131.1, 130.8, 116.9, 49.1, 47.7, 27.8. IR: 3353, 1660, 1615, 1371, 1333, 1190 cm^{-1}. MS (HR): calcd for $C_{10}H_{11}NO_4S$ 241.0409, found 241.0406.

Tetrahydro-4-phenyl-2*H*-1,2-thiazine 1,1-Dioxide (9a). A solution of sulfimide **8a** (100 mg, 0.44 mmol) and $NaBH_4$ (194 mg, 5.13 mmol) in 3 mL of dry dioxane under N_2 at 0 °C was treated slowly with trifluoroacetic acid (0.400 mL, 5.19 mmol). The reaction was stirred for 30 min at 0 °C, heated to reflux for 5 h, and quenched with 2 mL of MeOH at rt. The mixture was concentrated in vacuo, taken up in 25 mL of Et_2O, and washed successively with 2 × 10 mL of 5% HCl and 1 × 10 mL of 8:2 saturated NaCl/$NaHCO_3$. The organics were dried over $MgSO_4$ and concentrated in vacuo to afford 77 mg (82%) of sultam **9a** as a white crystalline solid. Mp: 128–129 °C; ^{1}H NMR δ 2.30–2.39 (m, 1), 2.52–2.67 (ddd, J = 3.7, 12.5, 14.1 Hz, 1), 2.84–2.94 (dddd, J = 3.7, 11.9 Hz, 1), 3.12–3.22 (ddd, J = 4.0, 13.4 Hz, 1), 3.32–3.44 (m, 2), 3.62–3.74 (ddd, J = 9.5, 11.5, 14.5 Hz, 1), 4.52 (br s, 1), 7.21–7.38 (m, 5). ^{13}C NMR: δ 30.5, 41.7, 49.7, 50.9, 67.1, 127.1, 127.4, 128.9, 140.5. IR: 3309, 1584, 1317, 1152 cm^{-1}. Anal. Calcd for $C_{10}H_{13}NO_2S$: C, 56.85; H, 6.20; N, 6.63. Found: C, 56.51; H, 6.10; N, 6.58.

4-(4-Bromophenyl)tetrahydro-2*H*-1,2-thiazine 1,1-dioxide (9b) was prepared by the procedure given previously for **9a**. Yield was 3.5 g (88%) after crystallization ($CHCl_3$) and silica gel chromatograph (35% acetone/hexane) of the mother liquor. Mp 200–202 °C. ^{1}H NMR: δ 2.25–2.37 (m, 1), 2.48–2.62 (m, 1), 2.79–2.92 (m, 1), 3.09–3.21 (m, 1), 3.30–3.42 (m, 2), 3.59–3.73 (m, 1), 4.46 (br s, 1), 7.10 (d, J = 8.4 Hz, 2), 7.46 (d, J = 8.4 Hz, 2). ^{13}C NMR: δ 30.3, 41.4, 49.4, 50.4, 121.3, 128.5, 131.9, 139.1. IR: 3232, 1462, 1320, 1195, 1151, 1137 cm^{-1}. MS (HR): calcd for $C_{10}H_{12}BrNO_2S$ 288.9773, found 288.9790.

Tetrahydro-4-[4-[(trimethylsilyl)ethynyl]phenyl]-2*H*-1,2-thiazine 1,1-Dioxide (16). Two separate 15-mL screw-cap flasks under N_2 were each charged with sultam **9b** (600 mg, 2.06 mmol) and 6 mL of 50% benzene/Et_3N. Each flask was treated successively with $(Ph_3P)_2PdCl_2$ (74 mg, 0.105 mmol) and CuI (10 mg, 0.052 mmol) followed by (trimethylsilyl)acetylene (1.16 mL, 8 mmol). The mixtures were heated at 100–110 °C for 1 h, cooled to room temperature, and treated successively with $(Ph_3P)_2PdCl_2$ (74 mg, 0.105 mmol) and CuI (10 mg, 0.052 mmol) followed by (trimethylsilyl)acetylene (1.16 mL, 8 mmol). The reaction mixtures were heated to 100–110 °C for an additional 1.5 h, cooled to room temperature, and combined. The volatiles were removed in vacuo, and the residue was partitioned between 50 mL of EtOAc and 50 mL of 1:1 saturated NaCl/NH_4Cl. The aqueous layer was extracted with 3 × 50 mL of EtOAc. The combined organics were dried over $MgSO_4$ and concentrated in vacuo to an amber solid. The solid was chromatographed over 100 g of silica gel, eluting with 30% EtOAc/hexane to afford 961 mg (76%) of **16** as a pale tan solid. Mp: 187 °C. ^{1}H NMR: δ 0.28 (s, 9), 2.22–2.35 (m, 1), 2.45–2.61 (m, 1), 2.86–3.00 (m, 1), 3.13–3.28 (m, 1), 3.29–3.41 (m, 2), 3.52–3.67 (m, 1), 5.06 (br s, 1), 7.16 (d, J = 8.3 Hz, 2), 7.45 (d, J = 8.3 Hz, 2). ^{13}C NMR: δ 0.0, 30.4, 41.6, 49.6, 50.7, 94.7, 104.5, 122.3, 127.0, 132.5, 140.9. IR: 3272, 2161, 1317, 1152, 1136 cm^{-1}. MS (HR): calcd for $C_{15}H_{21}NO_2SSi$ 307.1062, found 307.1070.

4-(Tetrahydro-2*H*-1,2-thiazin-4-yl)benzeneacetic Acid *S*,*S*-Dioxide (18). A solution of cyclohexene (1.14 mL, 11.3 mmol) in 3 mL of dry THF under N_2 at 0 °C was treated slowly with BH_3/THF complex (1.0 M THF) (5.65 mL, 5.65 mmol). The mixture was stirred 1 h at 0 °C and treated slowly with a solution of acetylene **16** in 2 × 3 mL of THF. The reaction was stirred 1 h at rt, diluted with 9 mL of MeOH, cooled to 0 °C, and treated successively with 2 N NaOH (2.83 mL, 5.65 mmol) and 30% H_2O_2 (1.73 mL, 17 mmol). After being stirred at 0 °C for 25 min and at 40 °C for 1.5 h, the mixture was cooled to rt and was brought to homogeneity with 2 N NaOH. The organics were removed in vacuo, and the aqueous residue was poured into 20 mL of saturated NaCl. The mixture was extracted with 2 × 20 mL of Et_2O. The aqueous layer was acidified with 30 mL of 10% HCl and was extracted with 4 × 25 mL of EtOAc. The combined EtOAc extracts were dried over $MgSO_4$ and concentrated in vacuo to a white solid (950 mg). Trituration with CH_2Cl_2 provided 670 mg (87%) of acid **17** as a white solid. Mp: 172–173 °C. ^{1}H NMR (MeOH-d_4): δ 2.19–2.29 (m, 1), 2.34–2.51 (m, 1), 2.80–2.94 (m, 1), 3.08–3.32 (m, 3), 3.40–3.51 (m, 1), 3.57 (s, 2), 7.16–7.30 (m, 4). ^{13}C NMR (MeOH-d_4): δ 31.8, 41.5, 42.4, 50.4, 51.9, 128.2, 130.8, 135.0, 141.3, 175.5. IR: 3253, 1709, 1338, 1330, 1147 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.52; H, 5.61; N, 5.20; S, 11.90. Found: C, 53.52; H, 5.54; N, 5.16; S, 11.70.

***tert*-Butyl [4-(1,2-Oxathian-5-yl)phenoxy]acetate *S*,*S*-Dioxide (20).** A suspension of NaH (146 mg, 3.04 mmol; prewashed with 2 × 5 mL of pentane) in 8 mL of dry THF at 0 °C was treated slowly with a solution of alcohol **10c** (445 mg, 1.38 mmol) in 2 × 2 mL of dry THF. The reaction was stirred for 15 min at 0 °C, warmed to rt, and stirred for 1.5 h. The mixture was cooled to 0 °C and treated with *tert*-butyl bromoacetate (0.500 mL, 3.10 mmol), warmed to rt, and stirred for 2 h. The mixture was diluted with 2 mL of saturated $NaHCO_3$, and the THF was removed in vacuo. The aqueous residue was poured into 10 mL of 1:1 saturated NH_4Cl/NaCl, and the mixture was extracted with 4 × 20 mL of Et_2O. The combined organics were dried over $MgSO_4$ and were concentrated in vacuo. Purification by chromatography over 26 g of silica gel, eluting with 30% EtOAc/hexane afforded 438 mg (93%) of **20** as a white crystalline solid. Mp: 127–128 °C. ^{1}H NMR: δ 1.49 (s, 9), 2.31–2.41 (m, 1), 2.48–2.62 (m, 1), 3.09–3.38 (m, 3), 4.38–4.45 (ddd, J = 2.4, 4.5, 11.4 Hz, 1), 4.51 (s, 2), 4.63 (t, J = 11.3 Hz, 1), 6.86 (d, J = 8.7 Hz, 2), 7.17 (d, J = 8.6 Hz, 2). ^{13}C NMR: δ 28.0, 29.7, 39.7, 47.3, 65.6, 82.5, 115.1 128.5, 130.1, 157.6, 167.8. IR: 1749, 1514, 1449, 1350, 1154 cm^{-1}. Anal. Calcd for $C_{16}H_{22}O_6S$: C, 56.12; H, 6.48; S, 9.36. Found: C, 56.08; H, 6.74; S, 9.19.

[4-(1,2-Oxathian-5-yl)phenoxy]acetic Acid *S*,*S*-Dioxide (21). A solution of ester **20** (328 mg, 0.958 mmol) in 11 mL of dry CH_2Cl_2 under N_2 at 0 °C was treated with 3 mL of trifluoroacetic acid. The mixture was stirred for 1 h at rt and concentrated in vacuo to a white solid. The solid was thoroughly washed with Et_2O and was collected by filtration to provide 230 mg (84%) of **21**. Mp: 169.5–170.5 °C. ^{1}H NMR (acetone-d_6): δ 2.30–2.58 (m, 2), 3.22–3.49 (m, 3), 4.37–4.61 (m, 2), 4.72 (s, 2), 6.95 (d, J = 8.6 Hz, 2), 7.30 (d, J = 8.6 Hz, 2). ^{13}C NMR (acetone-d_6): δ 39.9, 47.7, 65.1, 77.5, 115.5, 129.3, 131.6, 158.3, 169.7. IR: 1742, 1709, 1610, 1358, 1162 cm^{-1}. Anal. Calcd for $C_{12}H_{14}O_6S$: C, 50.34; H, 4.93; S, 11.20. Found: C, 49.89; H, 5.12; S, 11.00.

Methyl α-[2-[[bis[(4-methoxyphenyl)methyl]amino]-sulfonyl]ethyl]-4-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-benzeneacetate (23) was prepared by the procedure given previously for **13a** using a 1:1 ratio of **22**/**12**. Yield was 27.0 g (44%) of **23** and 23.5 g (48% based on **12**) of the bis Michael adduct after crystallization (EtOAc) and silica gel chromatography (30% EtOAc/hexane) of the mother liquor. Mp: 140–141 °C. ^{1}H NMR: δ 1.49 (s, 9), 2.13–2.28 (m, 1), 2.40–2.52 (m, 1), 2.74 (t, J = 7.6 Hz, 2), 3.64 (s, 3), 3.67 (m, 1), 3.81 (s, 6), 4.21 (br s,

4), 4.50 (s, 2), 6.80–6.89 (m, 6), 7.14–7.21 (m, 6). ^{13}C NMR: δ 27.0, 28.0, 48.7, 49.2, 51.0, 52.2, 55.3, 65.7, 82.4, 114.1, 115.0, 127.6, 129.0, 130.0, 130.3, 157.5, 159.3, 167.9, 173.4. IR: 1746, 1731, 1612, 1513, 1317, 1185 cm^{-1}. Anal. Calcd for $C_{33}H_{41}NO_9S$: C, 63.14; H, 6.58; N, 2.23; S, 5.11. Found: C, 63.52; H, 6.64; N, 2.43; S, 4.89.

Methyl α-[2-(aminosulfonyl)ethyl]-4-(carboxymethoxy)-benzeneacetate (24) was prepared by the alternate procedure given previously for **15c**. Yield was 9.2 g (85%) after silica gel chromatography (6% MeOH/CH_2Cl_2/0.5% acetic acid). Mp: 115–117 °C dec. ^{1}H NMR (MeOH-d_4): δ 2.16–2.32 (m, 1), 2.42–2.57 (m, 1), 2.87–3.10 (m, 2), 3.62 (s, 3), 3.78 (dd, J = 7.7 Hz, 1), 4.63 (s, 2), 6.90 (d, 2), 7.21 (d, 2). ^{13}C NMR (MeOH-d_4): δ 28.7, 49.7, 52.8, 53.5, 65.9, 116.0, 130.2, 132.1, 158.9, 172.8, 175.3. IR: 3331, 1758, 1713, 1514, 1329, 1163 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_7S$: C, 47.12; H, 5.23; N, 4.17; S, 9.68. Found: C, 46.73; H, 5.32; N, 4.11; S, 9.35.

Disodium [4-(tetrahydro-3-oxo-2*H*-1,2-thiazin-4-yl)phenoxy]acetate *S*,*S*-dioxide (25) was prepared by the procedure given previously for **8c**. Yield 6.4 g (80%). Mp >300 °C. ^{1}H NMR (D_2O): δ 2.21–2.35 (m, 1), 2.41–2.54 (m, 1), 3.20–3.30 (m, 2), 3.70 (dd, J = 5.6, 8.3 Hz, 1), 4.49 (s, 2), 6.95 (d, 2), 7.18 (d, 2). ^{13}C NMR (D_2O): δ 5.6, 22.7, 24.7, 45.2, 93.2, 107.9, 111.7, 135.0, 155.2, 157.6. IR: 1611, 1532, 1300, 1125 cm^{-1}. MS (HR): calcd for $C_{12}H_{11}NO_6SNa_2$ 300.0532, found 300.0542.

2-[4-(Tetrahydro-2*H*-1,2-thiazin-4-yl)phenoxy]ethanol *S*,*S*-dioxide (26) was prepared by the procedure given previously for **9a**. Yield: 127 mg (82%). Mp 130–133 °C, dec. ^{1}H NMR: δ 2.14–2.28 (m, 1), 2.30–4.49 (m, 1), 2.69–2.93 (m, 1), 3.04–3.47 (m, 4), 3.85 (t, J = 2 Hz, 2), 4.00 (t, J = 2 Hz, 2), 6.90 (d, 2), 7.15 (d, 2). ^{13}C NMR: δ 32.1, 42.0, 50.6, 52.2, 61.8, 68.2, 70.6, 116.0, 129.2, 134.9, 159.5. IR: 3506, 3248, 1515, 1317, 1298, 1148 cm^{-1}. Anal. Calcd for $C_{12}H_{17}NO_4S$: C, 53.12; H, 6.32; N, 5.16; S, 11.82. Found: C, 53.24; H, 6.40; N, 5.18; S, 11.79.

[4-(Tetrahydro-2*H*-1,2-thiazin-4-yl)phenoxy]acetic Acid *S*,*S*-Dioxide (27). A vigorously stirred solution of alcohol **26** (210 mg, 0.77 mmol) and 4 mL of H_2O in 4 mL of 50% CH_3CN/CH_2Cl_2 under N_2 at 0 °C was treated successively with $NaHCO_3$ (332 mg, 3.95 mmol), $NaIO_4$ (508 mg, 2.38 mmol), and $RuCl_3$ (17 mg, 0.08 mmol) and stirred for 3 h as the cooling bath expired. The organics were removed in vacuo, and the aqueous residue was diluted with 10 mL of 2 N NaOH. The mixture was extracted with 2 × 10 mL of Et_2O, and aqueous layer was adjusted to pH 2.5 with 5% HCl and extracted with 4 × 15 mL of EtOAc. The combined organics were dried over $MgSO_4$ and concentrated in vacuo (208 mg). Purification by chromatography over 12 g of silica gel, eluting with 10% acetone/EtOAc containing 3% acetic acid, afforded 102 mg (47%) of **27** as a white solid. Mp: 186–188 °C. ^{1}H NMR (MeOH-d_4): δ 2.20–2.30 (m, 1), 2.34–2.51 (m, 1), 2.78–2.91 (m, 1), 3.09–3.50 (m, 4), 4.63 (s, 2), 6.89 (d, 2), 7.19 (d, 2). ^{13}C NMR: δ 32.0, 42.0, 50.6, 52.1, 66.0, 116.0, 129.2, 136.0, 158.6, 173.0. IR: 3217, 1739, 1513, 1318, 1135 cm^{-1}. MS (HR): calcd for $C_{12}H_{15}NO_5S$ 285.0671, found 285.0694.

Supplementary Material Available: ^{1}H and ^{13}C NMR spectra for compounds **5c, 8c, 8d, 9b, 9c, 10c, 13b, 15a, 15b, 15d, 16, 25,** and **27** and spectral and analytical data for compounds **8d, 9c, 9d, 10b, 11b, 11c, 13d, 15c, 15d, 17,** and **19** (29 pages). Ordering information is given on any current masthead page.

Alkylation of 2-Oxy-Substituted 1-Sulfonylallyl and 1-Sulfonylvinyl Anions. New Routes to Functionalized Carbocycles and Dihydrofurans

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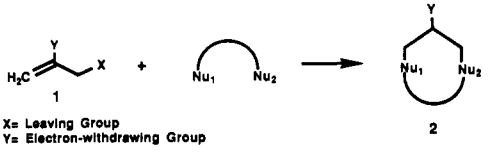
Received November 27, 1990

Alkylation of the anion derived from 2-phenoxy-3-(phenylsulfonyl)-1-propene proceeds α to the phenylsulfonyl group and affords cyclic products from 1,ω-dihalides. Reaction of the monoalkylated products, in which a suitably positioned olefinic or acetylenic unit is present, with sodium benzenesulfinate–acetic acid gives functionalized acetylcyclopentenes and cyclohexenes via C–C bond formation from the allyl cation–sulfinate ion pair. In the vinyl sulfone series, deprotonation of (*E*)- or (*Z*)-2-alkoxyvinyl phenyl sulfones rapidly affords the more stable (*E*)-lithio derivative, an acetaldehyde anion equivalent which reacts normally with aldehydes, ketones, alkyl halides, and epoxides. The latter process may be effected in an intramolecular fashion. Thus, (*E*)-(2-phenylsulfonyl) vinyl ethers of 2,3-epoxy alcohols cyclize on treatment with amide bases to afford dihydrofurans whose stereochemistry is fully defined by that of the starting epoxy alcohol.

For some time, synthetic chemists have sought efficient and stereospecific methods for carbocyclic annulations. Useful annulating reagents should be capable of acting sequentially as an alkylating agent and Michael acceptor.[1] In this context, functionalized allylic reagents of type 1, wherein X is some leaving group and Y is an electron-withdrawing substituent, have been extensively utilized in organic synthesis.[1-11] These substituted 1-propenes have been referred to as multicoupling reagents.[5,12] Recently, we have demonstrated that the closely related 2-



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