JOC Note
pubs.acs.org/joc

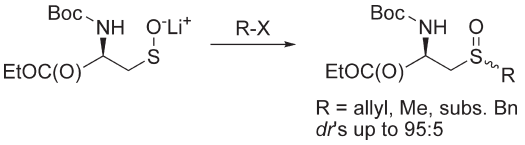
Diastereoselective Alkylations of a Protected Cysteinesulfenate

Adrian L. Schwan,* Marcus J. Verdu, Suneel P. Singh, Jennifer S. O'Donnell, and Amir Nasser Ahmadi

Department of Chemistry, University of Guelph, Guelph, Ontario, Canada, N1G 2W1

schwan@uoguelph.ca

Received May 26, 2009



To further understand stereoselection in the alkylation of sulfenate anions, a protected cysteinesulfenate was generated in THF solution at low temperature. Introduction of a reactive alkylating agent brings about a cysteinyl sulfoxide in 51−75% yield, with diastereomeric ratios at the sulfinyl group ranging from 83:17 to 95:5. An internally complexed lithium counterion is proposed to account for the stereoselectivity.

Sulfenate anions (**1**)[1] represent the conjugate base of sulfenic acids (**2**) (Figure 1).[2] Like sulfenic acids, the anions are inherently unstable and their study is based principally on their reactivity. In recent years, a variety of routes have been developed for the generation of sulfenate anions including oxidation reactions,[3] base induced retro-Michael fragmentations,[4−6] addition−elimination chemistry,[7−9] desilylation methods[10,11] and selected specialized protocols.[12,13]

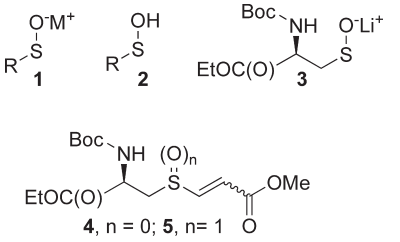


FIGURE 1. Sulfenates and related structures.

The growth in the number of sulfenate preparations has been mirrored by an increase in studies pertaining to stereoselective sulfur functionalization reactions. Calling on the prochiral nature of the sulfur's lone pairs, Madec and Poli[14] reported the enantioselective palladium-catalyzed preparation of aryl sulfoxides in the presence of chiral ligands. With the assistance of internal chirality, diastereoselective alkylation reactions have also been achieved.[4,13,15,16] On the basis of these latter results, we investigated diastereoselective alkylations of protected cysteinesulfenate derivative **3**, wherein the substituents on the amino acid α-carbon may be positioned to influence the alkylations. Exploration of this chemistry will enhance our knowledge of factors that govern sulfenate reactivity and selectivity.

This study may also assist in understanding the role of reactive cysteinesulfenate residues in proteins, which have been implicated as catalysts for a number of enzymes[17] including nitrile hydratase.[18] In addition, cysteinesulfenate alkylation chemistry is expected to amplify the available synthetic procedures to analogues of *Allium*-based naturally occurring sulfoxides.[19,20]

(1) O'Donnell, J.; Schwan, A. *J. Sulfur Chem.* **2004**, *25*, 183–211.
(2) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Giannetto, P. *Curr. Org. Chem.* **2007**, *11*, 1034–1052.
(3) (a) Sandrinelli, F.; Perrio, S.; Beslin, P. *J. Org. Chem.* **1997**, *62*, 8626–8627. (b) Sandrinelli, F.; Boudou, C.; Caupene, C.; Averbuch-Pouchot, M.-T.; Perrio, S.; Metzner, P. *Synlett* **2006**, 3289–3293. (c) Sandrinelli, F.; Fontaine, G.; Perrio, S.; Beslin, P. *J. Org. Chem.* **2004**, *69*, 6916–6919. (d) Boudou, C.; Berges, M.; Sagnes, C.; Sopkova-de Oliveira Santos, J.; Perrio, S.; Metzner, P. *J. Org. Chem.* **2007**, *72*, 5403–5406.
(4) Lohier, J.-F.; Foucoin, F.; Jaffres, P.-A.; Garcia, J. I.; Sopkova-de Oliveira Santos, J.; Perrio, S.; Metzner, P. *Org. Lett.* **2008**, *10*, 1271–1274.
(5) Caupene, C.; Boudou, C.; Perrio, S.; Metzner, P. *J. Org. Chem.* **2005**, *70*, 2812–2815.
(6) (a) Maitro, G.; Prestat, G.; Madec, D.; Poli, G. *J. Org. Chem.* **2006**, *71*, 7449–7454. (b) Maitro, G.; Vogel, S.; Prestat, G.; Madec, D.; Poli, G. *Org. Lett.* **2006**, *8*, 5951–5954.
(7) O'Donnell, J. S.; Schwan, A. L. *Tetrahedron Lett.* **2003**, *44*, 6293–6296.
(8) Furukawa, N.; Konno, Y.; Tsuruoka, M.; Ogawa, S. *Heteroat. Chem.* **1992**, *3*, 495–503.
(9) Furukawa, N.; Konno, Y.; Tsuruoka, M.; Fujihara, H.; Ogawa, S. *Chem. Lett.* **1989**, 1501–1504.
(10) Foucoin, F.; Caupene, C.; Lohier, J.-F.; Santos, J. S. d. O.; Perrio, S.; Metzner, P. *Synthesis* **2007**, 1315–1324.
(11) Keerthi, K.; Gates, K. S. *Org. Biomol. Chem.* **2007**, *5*, 1595–1600.
(12) (a) Refvik, M. D.; Froese, R. D. J.; Goddard, J. D.; Pham, H. H.; Pippert, M. F.; Schwan, A. L. *J. Am. Chem. Soc.* **1995**, *117*, 184–192. (b) Schwan, A. L.; Lear, Y. *Sulfur Lett.* **2000**, *23*, 111–119. (c) Schwan, A. L.; Roche, M. R.; Gallagher, J. F.; Ferguson, G. *Can. J. Chem.* **1994**, *72*, 312–324. (d) Maezaki, N.; Yagi, S.; Yoshigami, R.; Maeda, J.; Suzuki, T.; Ohsawa, S.; Tsukamoto, K.; Tanaka, T. *J. Org. Chem.* **2003**, *68*, 5550–5558. (e) Maezaki, N.; Yagi, S.; Maeda, J.; Yoshigami, R.; Tanaka, T. *Heterocycles* **2004**, *62*, 263–277. (f) Maezaki, N.; Yoshigami, R.; Maeda, J.; Tanaka, T. *Org. Lett.* **2001**, *3*, 3627–3629.
(13) Maezaki, N.; Yagi, S.; Ohsawa, S.; Ohishi, H.; Tanaka, T. *Tetrahedron* **2003**, *59*, 9895–9906.
(14) Maitro, G.; Vogel, S.; Sadaoui, M.; Prestat, G.; Madec, D.; Poli, G. *Org. Lett.* **2007**, *9*, 5493–5496.
(15) Sandrinelli, F.; Perrio, S.; Averbuch-Pouchot, M.-T. *Org. Lett.* **2002**, *4*, 3619–3622.
(16) Maezaki, N.; Yagi, S.; Ohsawa, S.; Ohishi, H.; Tanaka, T. *Tetrahedron: Asymmetry* **2002**, *13*, 1961–1964.
(17) Kovacs, J. A. *Chem. Rev.* **2004**, *104*, 825–848.
(18) (a) Hashimoto, K.; Suzuki, H.; Taniguchi, K.; Noguchi, T.; Yohda, M.; Odaka, M. *J. Biol. Chem.* **2008**, *283*, 36617–36623. (b) Heinrich, L.; Li, Y.; Vaissermann, J.; Chottard, J.-C. *Eur. J. Inorg. Chem.* **2001**, 1407–1409. (c) Lugo-Mas, P.; Dey, A.; Xu, L.; Davin, S. D.; Benedict, J.; Kaminsky, W.; Hodgson, K. O.; Hedman, B.; Solomon, E. I.; Kovacs, J. A. *J. Am. Chem. Soc.* **2006**, *128*, 11211–11221.
(19) Block, E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1135–1178.
(20) One unoptimized example of this work has been reported previously, see ref 7. Herein we significantly expand upon that contribution, with optimizations, more examples, complete characterizations, and alkylation models.

DOI: 10.1021/jo901021r Published on Web 08/11/2009

In a previous communication, we introduced the use of sulfinyl acrylates as a source of sulfenate anions through addition−elimination reactions with nucleophiles.[7] This was viewed as a safe choice given the alkaline protocols for accessing some sulfenates and the base sensitivity of protected cysteinyl sulfoxides.

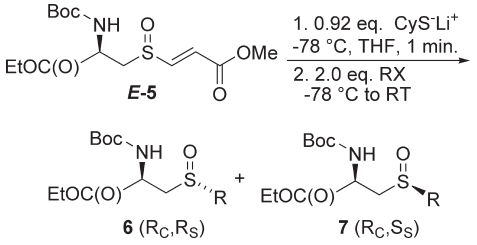
The logical means to prepare the requisite cysteinesulfinyl acrylate **5** would be through conjugate addition of Boc-Cys-OEt (derived from (*R*)-(+)-cysteine) to methyl propiolate and oxidation. Similar reactions of protected cysteine derivatives have been reported in the past as problematic, since the products are obtained in low yields and unwanted byproducts are formed.[21] We have demonstrated an alternative approach to 2-*Z*-carbomethoxyethenyl cysteinyl sulfides such as *Z*-**4**,[22] but still sought an efficient preparation of *E*-**4** or *E*-**5**.

For direct access to the *E*-isomer of **5** without the intermediacy of *E*-**4**, we evaluated the chemistry employed by Aversa to generate cysteinesulfenic acids.[23] That protocol generates a sulfenic acid that in our case would conveniently add in a syn fashion to create exclusively *E*-**5**. We evaluated that chemistry and could access *E*-**5** in approximately 60% yield over three steps, but the process incurred consumption of excess and expensive methyl propiolate and diethyl isopropylidenemalonate.

Revisiting the conjugate addition of thiol to methyl propiolate, several experiments were performed to optimize the addition reaction for *E*-selectivity and to improve the yield of *E*-**4**. A key finding was that short reaction times were vital. Hence, this reaction was terminated after 3−5 min and taken directly to MCPBA oxidation. The overall two-step preparation could be achieved in 60% yield (1.2:1 dr) in one afternoon without the need for excess amounts of expensive coreactants.[24]

Several nucleophiles were evaluated for release of cysteinesulfenate **3** from *E*-**5**, but only thiolates proved successful, presumably because of their highly nucleophilic and weakly basic nature. From those experiments, lithium cyclohexanethiolate was adopted as the nucleophile. Other optimizations provided the following experimental protocol for the release and alkylation of cysteinesulfenate **3**. A prepared solution of 0.90−0.95 equiv of lithium cyclohexanethiolate was added to sulfoxide *E*-**5** at −78 °C.[25] After 1 min, the electrophile was added, and the reaction was allowed to stir for 16 h, while warming slowly to rt. Direct concentration and flash chromatography provided diastereomeric mixtures of sulfoxides with chemical yields as shown in Table 1.[26] The yields are fair-to-good and are thought to be reflective of the sensitivity and lability of the cysteine-based substrates at all stages of the reaction sequence.

TABLE 1. Sulfenate Anion Trapping, Using Various Electrophiles



	RX	product	yield[a]	dr[b]
1	$PhCH_2Br$	**6**/**7a**	60 (65)	92:8
2	*p*-$MeC_6H_4CH_2Br$	**6**/**7b**	69 (75)	92:8
3	*p*-$BrC_6H_4CH_2Br$	**6**/**7c**	66 (72)	92:8
4	*m*-$MeOC_6H_4CH_2Br$	**6**/**7d**	48 (52)	91:9
5	*m*-$O_2NC_6H_4CH_2Br$	**6**/**7e**	61 (66)	89:11
6	*p*-$NCC_6H_4CH_2Br$	**6**/**7f**	68 (74)	89:11
7	*o*-$NCC_6H_4CH_2Br$	**6**/**7g**	49 (53)	89:11
8	*o*-$BrC_6H_4CH_2Br$	**6**/**7h**	67 (73)	95:5
9	*o*-$HC(O)C_6H_4CH_2Br$	**6**/**7i**	53 (58)	93:7
10	MeI	**6**/**7j**	47 (51)	83:17[c]
11	Allyl bromide	**6**/**7k**	54 (60)	83:17[c]

[a]First value is the yield based on the sulfur-containing substrate. Parenthesized value is the yield based on the limiting reagent. [b]Dr values based on peak integrations unless otherwise noted. See text and the Supporting Information for additional detail. [c]Dr calculated by NMR spectroscopy.

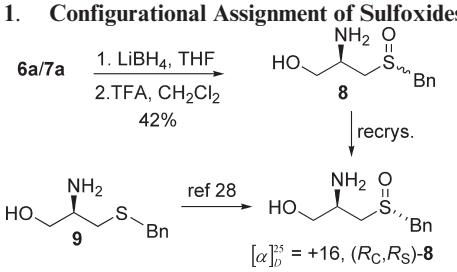
The dr values of cysteinyl benzyl sulfoxides **6/7a**−**i** were measured by HLPC on a CHIRACEL-OJ chiral HPLC column. Authentic samples of each diastereomer were obtained by MCPBA oxidation of the corresponding sulfide and were used to establish separations and retention times. The assigned structures were fully consistent with their infrared and ^1H and ^{13}C NMR spectra. Recrystallization of the diastereomeric mixtures gave major sulfoxide **6** in pure form (HPLC and elemental analysis).

The configuration of the sulfinyl stereocenter of the major diastereomer was assigned to be *R* on the following basis. As indicated, all the benzyl sulfoxides could be separated on a CHIRACEL-OJ chiral HPLC column and the major isomer always eluted second under consistent elution conditions. Allyl and methyl sulfoxides **6**/**7j**/**k** could not be assessed by HPLC, but crystals of **6k** were grown and successfully analyzed by X-ray crystallography, wherein the sulfinyl configuration was established to be *R*.[27]

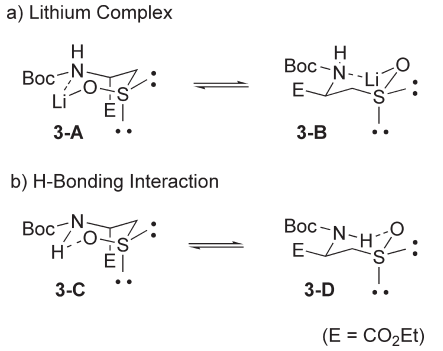
The benzyl sulfoxides did not provide suitable crystals for X-ray analysis, so chemical adaptations were performed. A 92:8 mixture of **6a**/**7a** was reduced to the alcohol with $LiBH_4$/THF and the Boc group was removed with TFA/CH_2Cl_2. The resulting amino alcohols **8** were obtained as a diastereomeric mixture (ca. 92:8), whose 600 MHz ^1H NMR spectra could be assigned to those spectra reported in the literature for (R_C,R_S) and (R_C,S_S) examples of **8**, previously prepared through sulfoxidation of the corresponding R_C-sulfide **9**.[28] To complete the comparison, recrystallization of a diastereomeric mixture a **8** provided the major diastereomer only, which gave an optical rotation of +16.2, matching that reported

(21) Crisp, G. T.; Millan, M. J. *Tetrahedron* **1998**, *54*, 637–648.
(22) O'Donnell, J. S.; Singh, S. P.; Metcalf, T. A.; Schwan, A. L. *Eur. J. Org. Chem.* **2009**, 547–553.
(23) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Giannetto, P. *J. Org. Chem.* **2005**, *70*, 1986–1992.
(24) Full experimental detail including a reaction equation are part of the Supporting Information.
(25) The use of excess base brought about lower yields and increased byproducts including protected dehydroalanine and dibenzyl sulfoxides, when the alkylation was performed with a benzyl bromide.
(26) To confirm the sulfoxides were kinetic products arising directly from alkylation chemistry, selected sulfoxides were thermolyzed to determine if the observed dr value were caused by (a) selective thermal breakdown of one diasteromer or (b) thermal conversion of one isomer to the other. No evidence in support of either of these processes was observed. See: Rich, D. H.; Tam, J. P. *J. Org. Chem.* **1977**, *42*, 3815–3820.
(27) Singh, S. P.; Verdu, M. J.; Lough, A. J.; Schwan, A. L. *Acta Crystallogr.* **2009**, *E65*, o1385–o1386.
(28) Petra, D. G. I.; Kamer, P. C. J.; Spek, A. L.; Schoemaker, H. E.; van Leeuwen, P. W. N. M. *J. Org. Chem.* **2000**, *65*, 3010–3017.

SCHEME 1. Configurational Assignment of Sulfoxides 6a/7a



SCHEME 2. Possible Sulfenate Conformations



for the (R_C,R_S) isomer of **8** previously obtained (+16).[28] Based on Scheme 1, it follows that the sulfinyl configuration of the major isomer of the **6a**/**7a** isomeric pair is *R*.

The key features uniting all of the sulfoxides are their chemical shift trends in both their ^{1}H and ^{13}C NMR spectra. In the ^{1}H NMR spectra of every sulfoxide, the NH peak of the major isomer of **6** was 0.04−0.15 ppm downfield from that of the minor isomer. Moreover, in the ^{13}C NMR spectra, the amino acid α and *β* carbon atoms of the major diastereomer resonated downfield by 0.11−0.81 and 0.55−1.59 ppm, respectively, in every example. It has previously been established that like isomers of cysteinyl sulfoxides demonstrate consistent trends for related NMR spectroscopic data.[29,30]

Following the lead of Perrio, who invoked internal complexation of the lithium counterion,[15] it is suggested that sulfenate **3** adopts a chair conformation from which the diastereoselection arises. The chair conformations of **3** may be held through either lithium complexation (**3-A**/**3-B**, Scheme 2) or by way of internal hydrogen bonding (**3-C**/**3-D**).

To investigate if the lithium plays a prominent role in the coordination of the intermediate, several alkylations of **3** with benzyl bromide were performed in the presence of varying amounts of 12-crown-4 (12-c-4), which was anticipated to sequester the lithium counterion.[31] The reaction afforded the same major diastereomer (R_C,R_S) as previous alkylations, but progressively lower dr values were observed as the 12-c-4 concentration was increased (Table 2). The interpretation is that under the reaction conditions, 12-c-4 competitively strips sulfenate **3** of some its stoichiometric lithium leaving the uncomplexed sulfenate to alkylate with reduced stereoselectivity.

TABLE 2. Influence of 12-Crown-4 on the Diastereoselectivity of Benzylations of Sulfenate 3

	equiv of 12-crown-4[a]	dr [b]
1	0	92:8
2	0.3	91:9
3	0.6	90:10
4	1	88:12
5	1.5	86:14
6	2.5	85:15

[a] 12-Crown-4 was introduced immediately after sulfenate generation. [b] Dr values based on peak integrations. See text and the Supporting Information for additional detail.

These results provide evidence that the lithium counterion is indeed an important component of the stereoselection step and directs further scrutiny to conformational isomers **3-A**/**3-B** of Scheme 2. Both conformations hold the potential to add electrophiles at their axial or equatorial positions. The population of complex **3-B** is believed to be insignificant due to an unfavorable interaction of the ester and carbamate groups in adjacent equatorial positions. Focusing on **3-A**, the ester group in the axial form further inhibits the already undesirable axial alkylation, allowing preferential equatorial alkylation. Indeed the (R_C,R_S) configuration of the product is consistent with equatorial alkylation of **3-A** (Scheme 2). Some of the highest dr values were observed with ortho-substituted benzyl bromides, where the alkylation reaction is expected to encounter additional steric encumbrances.

The diastereoselectivity of the benzylation reactions represents a significant contribution to the growing field of asymmetric sulfenate functionalization. The ratios are competitive or superior to a number of *S*-alkylations in the literature.[13,15,16] The chemistry creates products complementary to those accessed through cysteinesulfenic acid addition chemistry,[23] and the functionalization occurs with superior stereoselectivity.

As a final note, it is worth mentioning that the ^{1}H NMR spectra of the crude sulfoxide-containing reaction mixtures displayed chemical shifts of some hydrogen atoms that strayed as far as 0.6 ppm from the chemical shifts of the pure products. While puzzling for a period of time, this observation was eventually found to be a result of the sulfoxide coordinating to lithium in $CDCl_3$ solution.[32] This complexation is consistent with the high affinity that some amino acids have for alkali metals,[33] but it also parallels the behavior of cysteinesulfenate **3**, whose anionic form is expected to demonstrate an even higher affinity for lithium ion. Given the competitiveness for the lithium ion that cysteinesulfenate **3** shares with 12-c-4, this and related sulfenates should be further explored for their strong affinity for alkali metals. Further, the cysteinesulfenato[34] and related complexes[17,35]

(29) Aversa, M. C.; Bonaccorsi, P.; Faggi, C.; Lamanna, G.; Menichetti, S. *Tetrahedron* **2005**, *61*, 11902–11909.
(30) Nakamura, S.; Goto, K.; Kondo, M.; Naito, S.; Tsuda, Y.; Shishido, K. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 2033–2036.
(31) Power, P. P. *Acc. Chem. Res.* **1988**, *21*, 147–153.
(32) This conclusion was established by introducing LiBr to pure sulfoxide and obtaining similar NMR spectra comparable to those of the crude mixtures in $CDCl_3$.
(33) (a) Aziz, E. F.; Ottosson, N.; Eisebitt, S.; Eberhardt, W.; Jagoda-Cwiklik, B.; Vacha, R.; Jungwirth, P.; Winter, B. *J. Phys. Chem. B* **2008**, *112*, 12567–12570. (b) Deeying, N.; Sagarik, K. *Biophys. Chem.* **2007**, *125*, 72–91. (c) Feng, W. Y.; Gronert, S.; Lebrilla, C. *J. Phys. Chem. A* **2003**, *107*, 405–410. (d) Talley, J. M.; Cerda, B. A.; Ohanessian, G.; Wesdemiotis, C. *Chem.—Eur. J.* **2002**, *8*, 1377–1388. (e) Feng, W. Y.; Gronert, S.; Lebrilla, C. B. *J. Am. Chem. Soc.* **1999**, *121*, 1365–1371.
(34) Park, H.; Yang, J. S.; Jun, M.-J. *Bull. Korean Chem. Soc.* **2002**, *23*, 500–502.
(35) Kung, I.; Schweitzer, D.; Shearer, J.; Taylor, W. D.; Jackson, H. L.; Lovell, S.; Kovacs, J. A. *J. Am. Chem. Soc.* **2000**, *122*, 8299–8300.

explored in organometallic studies have arisen through oxidation of thiolato ligands. The chemistry herein may serve as an alterative synthetic strategy for this important area of chemistry.

To summarize, protected cysteinesulfenate **3** has been shown to alkylate with high diastereoselectivity, possibly through an internal complexation with the lithium counterion. From this result, we plan to create new sulfenates and electrophiles based on an amino acid foundation in order to fully evaluate the identity and role of the substituent groups in governing this important alkylation process.

Experimental Section

General Preparation of Sulfoxides via Sulfenate Anion Alkylation. A solution of cyclohexyl mercaptan (0.95 equiv) and *n*-BuLi (0.92 equiv) in anhydrous THF (2 mL), under N_2 gas, was stirred at rt for 5 min and was then cooled to −78 °C. The CySLi solution was transferred via syringe into the solution of the α,β-unsaturated sulfoxide *E*-**5** (1 equiv) with stirring in anhydrous THF (10 mL) at −78 °C, under N_2 gas. The reaction was stirred for 1 min and electrophile (RX, 2 equiv) was added. If the electrophile was a solid, it was dissolved in THF (1 mL) then added. The reaction was left to stir overnight, slowly warming to room temperature. The solution was evaporated under vacuum or concentrated by N_2 gas and the residue was purified by flash chromatography. Yields are based on *n*-BuLi as the limiting reagent.

Sample Procedure and Data for Boc-Cys((*O*)-Bn)-OEt (6a/7a). Sulfoxide *E*-**5** (327 mg, 0.934 mmol) in anhydrous THF (10 mL) was treated with a CySH (112 μL, 0.888 mmol)/*n*-BuLi (102 μL, 0.859 mmol) solution, followed by the addition of benzyl bromide (222 μL, 1.87 mmol). Sulfoxides **6a**/**7a** (200 mg, 65%) were recovered as a white solid after flash chromatography (EtOAc/hexanes 90:10 to 50:50) as a mixture of diastereomers (dr 92:8). Recrystallization from EtOAc/hexanes yielded the major diastereomer. Major diastereomer: mp 126−127 °C; $[\alpha]^{25}_D$ −69.0 (*c* 0.45, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 5H), 5.79 (br d, J = 7.6 Hz, 1H), 4.68 (br d, J = 3.2 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 4.07 (AB_q, J = 11.6 Hz, 2H), 3.11 (ABX, J_{AX} = 7.8 Hz, J_{BX} = 3.6 Hz, J_{AB} = 13.0 Hz, 2H), 1.42 (s, 9H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 155.2, 130.0, 129.2, 129.0, 128.5, 80.2, 61.9, 58.9, 51.9, 50.1, 28.2, 14.0; IR (CH_2Cl_2) cm^{-1} 3270, 2979, 1734, 1715, 1497, 1367, 1216, 1166, 1026; HPLC (10% *i*PrOH/hexanes, 0.4 mL/min flow rate, OJ-H column) 23.1 min. Anal. Calcd for $C_{17}H_{25}NO_5S$: C, 57.44; H, 7.03. Found: C, 57.66; H, 7.17. Minor diastereomer: partial ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73 (br d, J = 6.6 Hz, 1H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.9, 155.1, 130.0, 129.4, 128.8, 128.3, 80.1, 61.8, 57.9, 52.6, 49.5, 28.1, 13.9; HPLC (10% *i*PrOH/hexanes, 0.4 mL/min flow rate, OJ-H column) 20.4 min.

Acknowledgment. The authors wish to thank the Natural Sciences and Engineering Research Council of Canada for partial funding of this research. Acknowledgment is also made to the Donors of the American Chemical Society Petroleum Research Fund for partial support of this research. J.S.O. thanks the Ontario Government for Science and Technology Graduate Fellowship.

Supporting Information Available: Detailed descriptions of experimental procedures and characterization of compounds and ^{1}H NMR and ^{13}C NMR spectra of compounds **6** (37 pages). This material is available free of charge via the Internet at http://pubs.acs.org.