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S_N2-Type Nucleophilic Opening of β-Thiolactones (Thietan-2-ones) as a Source of Thioacids for Coupling Reactions

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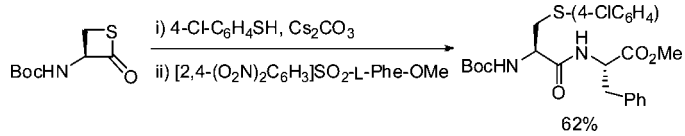
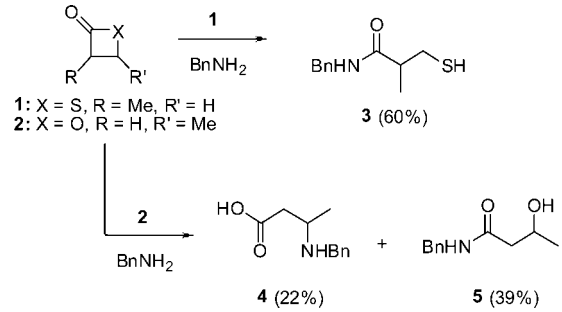


β-Thiolactones monosubstituted in the 3-position by alkyl and carbamoyl groups undergo nucleophilic ring opening by arenethiolates through a process involving an S_N2-type attack at the 4-position leading to 3-arylthiopropionates substituted in the 2-position. These thiocarboxylates can be trapped in situ by Mukaiyama's reagent or Sanger's reagent through a nucleophilic aromatic substitution process leading to highly activated thioesters that are then allowed to react further with primary or secondary amines leading, overall, to one-pot, three-component syntheses of 3-arylthiopropionamides carrying various substituents in the 2-position. Alternatively, the trapping combination of an electron deficient aryl halide and an amine may be replaced by a 2,4-dinitrobenzenesulfonamide, resulting in the formation of the same products overall with the incorporation of the latent amine in the sulfonamide into the final amide product. In another embodiment, the thiocarboxylate intermediate is allowed to react with a sulfonyl azide, resulting overall in *N*-arenesulfonyl 3-arylthiopropionamide derivatives.

Introduction

Unlike the widely appreciated β-lactones,[1] the β-thiolactones (thietan-2-ones) have seen little use in synthesis. We speculated that one of the lesser employed facets of β-lactone chemistry, ring opening by an S_N2-type attack at the 4-position by soft nucleophiles,[2] might be extended to the β-thiolactones when it would provide a novel entry to thioacids, a functional group whose chemistry is of current interest.[3] Although the reactivity of β-thiolactones has been relatively little explored, it was known that one of the simplest, 3-methylthietan-2-one (**1**), on reaction with benzylamine undergoes apparent exclusive ring opening by an attack at the carbonyl position.[4] In contrast, the close all-oxygen analogue, 4-methyloxetan-2-one (**2**), displays both modes of reactivity despite the more highly substituted nature of its 4-position (Scheme 1).[5]

SCHEME 1. Differing Modes of Reactivity for β-Thiolactones and β-Lactones toward Benzylamine



In spite of this observation, we reasoned that softer nucleophiles than amines, to wit, thiols, might still allow us to access the S_N2-ring opening mode of the β-thiolactones. As we describe herein, this supposition has been reduced to practice and provides a novel entry to thioacids and three-component coupling sequences.

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(1) (a) Pommier, A.; Pons, J.-M. *Synthesis* **1993**, 441–459. (b) Pommier, A.; Pons, J.-M. *Synthesis* **1995**, 729–744. (c) Lowe, C.; Vederas, J. C. *Org. Prep. Proced. Int.* **1995**, *27*, 305–346. (d) Wang, Y.; Tennyson, R. L.; Romo, D. *Heterocycles* **2004**, *64*, 605–658. (e) Yang, H. W.; Romo, D. *Tetrahedron* **1999**, *55*, 6403–6434.

(2) (a) Arnold, L. D.; Kalantar, T. H.; Vederas, J. C. *J. Am. Chem. Soc.* **1985**, 7105–7109. (b) Arnold, L. D.; Drover, J. C. G.; Vederas, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 4649–4659. (c) Ratemi, E. S.; Vederas, J. C. *Tetrahedron Lett.* **1994**, *35*, 7605–7608.

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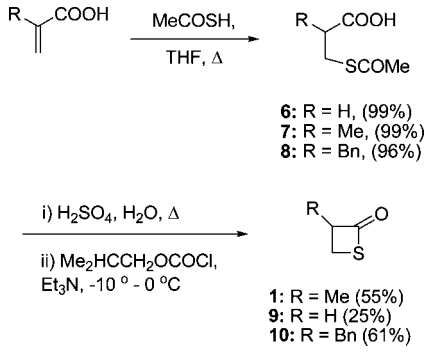
Results and Discussion

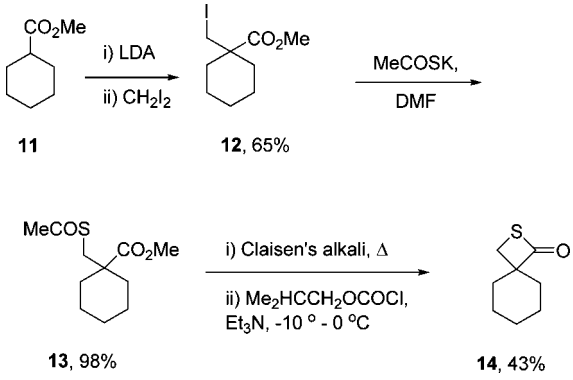
Substrate Preparation. Simple β-thiolactones were readily accessed by conjugate addition of thioacetic acid to acrylic acid derivatives branched at the 2-position, followed by acidolysis and then ring closure with isobutyl chloroformate (Scheme 2).[4] The moderate yield reported for the parent substance is mainly due to the volatility of this substance.

SCHEME 2. Preparation of Simple β-Thiolactones



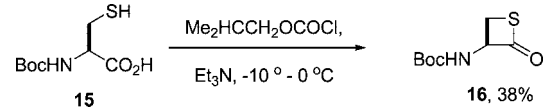
A spirocyclic version, 2-thiaspiro[3.5]nonan-1-one (**14**), was prepared from methyl 1-(acetylthiomethyl)cyclohexanecarboxylate (**13**), which was obtained from methyl cyclohexanecarboxylate (**11**) by the literature procedure (Scheme 3).[6]

SCHEME 3. Synthesis of 2-Thiaspiro[3.5]nonan-1-one



The carbamoyl derivative **16** was prepared from *N*-Boc-L-cysteine by cyclization with isobutyl chloroformate in the usual manner (Scheme 4). No loss of stereochemical integrity was

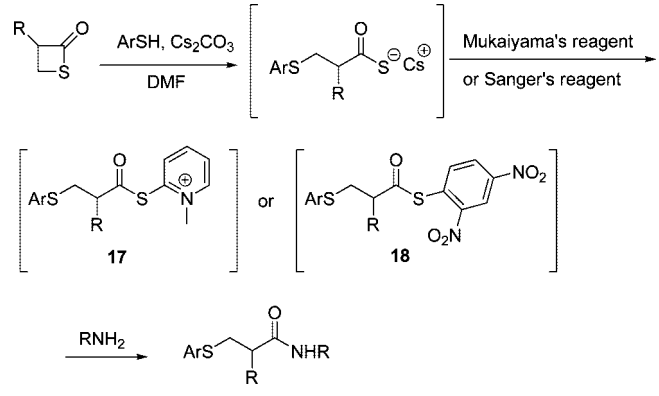
SCHEME 4. Synthesis of an Amino Acid Synthon



observed in the formation of **16** as determined with the aid of chiral shift reagents.

With these β-thiolactones in hand, we investigated a reaction sequence involving reaction with an aromatic thiolate followed by trapping of the intended thiocarboxylate by nucleophilic aromatic substitution with Mukaiyama's reagent (2-chloro-*N*-methylpyridinium iodide)[7] to give a highly active thioester (**17**).[31] The thioester was then subjected to reaction with an amine, resulting overall in a one-pot, three-component coupling process (Scheme 5). A directly analogous protocol employed Sanger's reagent (2,4-dinitrofluorobenzene)[8] in the place of Mukaiyama's reagent and involved the alternative intermediate thioester **18** (Scheme 5).[31] In a third series of experiments the thiocarboxylate intermediate was intercepted by a set of 2,4-dinitrobenzenesulfonamides in a process that involves nucleophilic aromatic substitution leading to the formation of active ester **18** and concomitant liberation of the latent amine in the sulfonamide for the final amide bond forming step.[3h,i,k] A final protocol relied on trapping of the intermediate thiocarboxylate with a sulfonyl azide,[3a−e] again resulting in the formation of the amide bond.

SCHEME 5. Three-Component Coupling Processes



With a series of aromatic thiols as nucleophiles in the presence of cesium carbonate as a base, the reaction followed the anticipated course, resulting, after addition of Mukaiyama's reagent or Sanger's reagent and an amine, in the formation of a range of 3-arylthiocarboxamides (Table 1).

As is clear from Table 1, entries 1−11, the general protocol of a reaction of an aromatic cesium thiolate with β-thiolactone itself or with analogues monosubstituted in the 3-position followed by capture by an electron-deficient arene and ultimate introduction of an amine follows the anticipated route. This sequence of reactions enables the one-pot formation of both secondary and tertiary 3-arylmercaptocarboxamides in a straightforward manner and proceeds effectively with either Mukaiyama's or Sanger's reagent as the electron-deficient arene.

The examples employing the cysteine derived β-thiolactone **16** (Table 1, entries 12−17) are particularly interesting. The

(3) (a) Shangguan, N.; Katukojvala, S.; Greenberg, R.; Williams, L. J. *J. Am. Chem. Soc.* **2003**, *125*, 7754–7755. (b) Merkx, R.; Brouwer, A. J.; Rijkers, D. T. S.; Liskamp, R. M. J. *Org. Lett.* **2005**, *7*, 1125–1128. (c) Barlett, K. N.; Kolakowski, R. V.; Katukojvala, S.; Williams, L. J. *Org. Lett.* **2006**, *8*, 823–826. (d) Kolakowski, R. V.; Shangguan, N.; Sauers, R. R.; Williams, L. J. *J. Am. Chem. Soc.* **2006**, *128*, 5695–5702. (e) Merkx, R.; Van Haren, M. J.; Rijkers, D. T. S.; Liskamp, R. M. J. *J. Org. Chem.* **2007**, *72*, 4574–4577. (f) Gulevich, A. V.; Balenkova, E. S.; Nenajdenko, V. G. *J. Org. Chem.* **2007**, *72*, 7878–7885. (g) Dawson, P. E.; Muir, T. W.; Clark-Lewis, I.; Kent, S. B. H. *Science* **1994**, *266*, 776–779. (h) Messeri, T.; Sternbach, D. D.; Tomkinson, N. C. O. *Tetrahedron Lett.* **1998**, *39*, 1673–1676. (i) Messeri, T.; Sternbach, D. D.; Tomkinson, N. C. O. *Tetrahedron Lett.* **1998**, *39*, 1669–1672. (j) Crich, D.; Bowers, A. A. *Org. Lett.* **2007**, *9*, 5323–5325. (k) Crich, D.; Sana, K.; Guo, S. *Org. Lett.* **2007**, *9*, 4423–4426. (l) Crich, D.; Sharma, I. *Angew. Chem., Int. Ed.* **2009**, *48*, 2355–2358.

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(7) Bald, E.; Saigo, K.; Mukaiyama, T. *Chem. Lett.* **1975**, 1163–1166.

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TABLE 1. β-Thiolactone-Based, Three-Component Coupling Process

Entry	Thiolactone	Nucleophile	Reagents for Amide Bond Formation	Product (yield)
1	**9**	PhSH	$PhCH_2CH_2NH_2$,	**19** (66%)
2	**9**	4-ClC_6H_4SH	$PhCH_2CH_2NH_2$,	**20** (67%)
3	**9**		$PhCH_2CH_2NH_2$,	**21** (56%)
4	**9**	4-ClC_6H_4SH	Piperidine,	**22** (59%)
5	**9**	PhSH	L-PheOMe.HCl,	**23** (61%)
6	**1**	4-ClC_6H_4SH	$PhCH_2CH_2NH_2$,	**24** (67%)
7	**1**	4-ClC_6H_4SH	Piperidine,	**25** (58%)
8	**10**	PhSH	$PhCH_2CH_2NH_2$,	**26** (64%)
9	**10**	4-ClC_6H_4SH	$PhCH_2CH_2NH_2$,	**27** (68%)
10	**10**	4-ClC_6H_4SH	Piperidine,	**28** (59%)
11	**10**		Piperidine,	**29** (57%)
12	**16**	4-ClC_6H_4SH	$PhCH_2CH_2NH_2$,	**30** (64%)
13[a]	**16**	4-ClC_6H_4SH	**31**	**30** (70%)
14[a]	**16**		**31**	**32** (61%)
15[a]	**16**	PhSH	**33**	**34** (57%)
16[a]	**16**	4-ClC_6H_4SH	**35**	**36** (62%)
17	**16**	4-ClC_6H_4SH	**37**	**38** (68%)
18	**14**	4-ClC_6H_4SH	$PhCH_2CH_2NH_2$,	**39** (80%)
19	**10**	morpholine	-	**40** (67%)

[a] Ar = 2,4-dinitrophenyl.

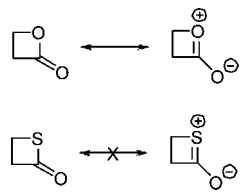
products are obtained in highly enantiomerically enriched form, thereby distinguishing the chemistry presented here from the more classical point of entry to such derivatives involving conjugate addition to dehydroalanine derivatives followed by standard amide bond forming protocols.[9] An especially noteworthy example is that involving the cysteine β-thiolactone **16** with capture by the dinitrobenzenesulfonamide of the methyl L-phenylalaninate that couples the nucleophilic ring opening of the thiolactone with a peptide bond forming step (Table 1, entry 16). In the case of the spirocyclic β-thiolactone **14** (Table 1, entry 18) the highly sterically hindered neopentyl-like nature of the 4-position effectively prevents the S_N2 mode of ring opening, paving the way for the ultimate attack of the amine on the carbonyl carbon with subsequent ring opening. The thiolate generated in the course of this process is then captured by the intended coupling reagent, Sanger's reagent, to afford a product differing only by the subsitutents on the arylthio moiety from the one intended, albeit by a completely different route. The attempted use of alkanethiols and/or thiolates as nucleophiles in this chemistry was unproductive under a variety of conditions and resulted only in the formation of complex reaction mixtures.

Finally, we investigated briefly the possibility of replacing the thiolate nucleophile by an amine (Table 1, entry 19) but were unable to divert the chemistry away from an attack at the β-thiolactone carbonyl carbon as had been described previously in the literature for this class of nucleophile (Scheme 1).

We suggest that the differing reactivity between the β-thiolactones and their all-oxygen counterparts, apparent from the literature (Scheme 1) and highlighted by the contrast among entries 1−17, 18, and 19 of Table 1, is likely due to the much-reduced resonance of the ring heteroatom with the carbonyl group in the case of the thiolactones. The reduced resonance may be attributed to the weakness of the carbon−sulfur double

(9) For example, see: (a) Zhu, Y.; van der Donk, W. A. *Org. Lett.* **2001**, *3*, 1189–1192. (b) Bernardes, G. J. L.; Chalker, J. M.; Errey, J. C.; Davis, B. G. *J. Am. Chem. Soc.* **2008**, *130*, 5052–5053.

SCHEME 6. Reduced Resonance Delocalization in the Thiolactones



bond[10] and has the effect of making the 4-position softer and less reactive toward hard nucleophiles (Scheme 6).

Experimental Section

2-Thiaspiro[3.5]nonan-1-one (14): Methyl 1-acetylsulfanylmethylcyclohexane carboxylate[6] (3.92 g, 17 mmol) was dissolved in 22 mL of Claisen's alkali (6.25 mol/L KOH in a mixture of CH_3OH and H_2O (v/v: 3/1)), heated to reflux for 3 h, and then cooled to 0 °C. The reaction mixture was acidified with 1 N HCl to pH = 1, and dichloromethane was added; the organic layer was extracted, washed with water and brine, and dried. Evaporation of the solvent afforded crude 1-(mercaptomethyl)cyclohexane carboxylic acid, which was taken forward for cyclization without purification.

To a stirred solution of the crude 1-(mercaptomethyl)cyclohexane carboxylic acid (2.8 g, 16.1 mmol) and triethylamine (2.6 mL, 17.6 mmol) in dichloromethane (70 mL) at −10 °C was added dropwise *iso*-butyl chloroformate (2.4 mL, 17.6 mmol). After the addition was complete, the reaction mixture was allowed to come to 0 °C over a period of 45 min. The resulting mixture was neutralized at 0 °C, with 1 N HCl at pH ∼ 4, and the organic layer was extracted, dried, and concentrated. Chromatographic purification using 2% ethyl acetate in hexane afforded **14** (1.08 g, 43%). Colorless liquid. IR ($CHCl_3$): 2931, 2854, 1771, 1745 cm^{-1}. ^1H NMR (500 MHz) δ: 2.81 (s, 2H), 1.88−1.79 (m, 4H), 1.74−1.70 (m, 2H), 1.52−1.50 (m, 1H), 1.41−1.30 (m, 1H). ^{13}C NMR (125 MHz) δ: 199.2, 77.1, 32.9, 29.5, 25.0, 22.2. EI-HRMS: calcd for $C_8H_{12}OS$ $[M]^+$, 156.0609; found, 156.0615.

(*S*)-*O*-(*tert*-Butyl) *N*-(Thietan-2-on-3-yl) Carbamate (16): Following the same procedure as for the preparation of 2-thiaspiro-[3.5]nonan-1-one, using *N*-*tert*-butoxycarbonyl-L-cysteine as substrate and eluting with 20% ethyl acetate in hexane, **16** was obtained in 38% yield. White solid, crystallized from ethyl acetate/hexane, mp: 140.5−141.5 °C. $[\alpha]^{22}_D$ −40.3 (*c* 1.2). IR ($CHCl_3$): 3352, 2927, 1747, 1716, 1682 cm^{-1}. ^1H NMR (500 MHz) δ: 5.44 (s, 1H), 5.35 (bs, 1H), 3.44−3.41 (t, *J* = 7.5 Hz, 1H), 3.34−3.31 (t, *J* = 7.5 Hz), 1.46 (s, 9H). ^{13}C NMR (125 MHz) δ: 193.7, 154.4, 81.4, 72.5, 28.4. ESI-HRMS: calcd for $C_8H_{13}NO_3S$ $[M + Na]^+$, 226.0514; found, 226.0502.

General Procedure (A) for Multicomponent Coupling Reactions Using 3-Methylthietan-2-one (1), Thietan-2-one (9), 3-Benzylthietan-2-one (10), and Mukaiyama's Reagent. To a stirred solution of 3-substituted-thietan-2-one (**1**, **9**, or **10**; 1.0 equiv) in DMF (0.15−0.2 M) were added aromatic thiol (1.5 equiv) and Cs_2CO_3 (1.0 equiv) at room temperature. The reaction mixture was allowed to stir for 2 h, after which time the reaction mixture had turned a faint yellow color. Then 2-chloro-1-methylpyridinium iodide (1.5 equiv) was added, followed immediately by 0.9 equiv of amine. Upon addition of the 2-chloro-1-methylpyridinium iodide and amine, the reaction mixture became a dark yellow color and further deepened in color as the reaction continued. The reaction mixture was allowed to stir for 5 h, after which the DMF was removed under high vacuum, and the crude mixture was dissolved in EtOAc, washed with water and brine, and dried. Evaporation of the solvent followed by column chromatography provided the products as described below.

General Procedure (B) for Multicomponent Coupling Reactions Using 3-Methylthietan-2-one (1), Thietan-2-one (9), 3-Benzylthietan-2-one (10), and Sanger's Reagent. To a stirred solution of 3-substituted-thietan-2-one (**1**, **9**, or **10**; 1.0 equiv) in DMF (0.15−0.2 M) were added thiol (1.5 equiv) and Cs_2CO_3 (1.0 equiv) at room temperature. The reaction mixture was allowed to stir for 2 h, after which time the reaction mixture had turned a faint yellow color. Then 1-fluoro-2,4-dinitrobenzene (1.5 equiv) was added, followed immediately by 0.9 equiv of amine. Upon addition of the 2,4-dinitrofluorobenzene and amine, the reaction mixture turned dark red in color and further deepened in color as the reaction continued. The reaction mixture was allowed to stir for 2 h, after which the DMF was removed under high vacuum, and the crude mixture was dissolved in EtOAc, washed with water and brine, and dried. Evaporation of solvent followed by column chromatography provided the coupled products as described below.

***N*-Phenethyl-3-(phenylthio)propanamide (19):** Following the general procedure A, using thietan-2-one and eluting with 30% ethyl acetate in hexane, **19** was obtained in 66% yield. White solid, crystallized from chloroform/hexane, mp: 74.5−75.0 °C. ^1H NMR (300 MHz) δ: 7.34−7.16 (m, 10H), 5.63 (s, 1H), 3.54−3.48 (q, *J* = 6.6 Hz, 2H), 3.21−3.16 (t, *J* = 7.5 Hz, 2H), 2.83−2.78 (t, *J* = 6.6, 2H), 2.43−2.39 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (75 MHz) δ: 171.0, 139.0, 135.6, 129.8, 129.3, 129.0, 128.9, 126.8, 126.6, 40.9, 36.4, 35.8, 29.6. ESI-HRMS: calcd for $C_{17}H_{19}NOS$ $[M + Na]^+$, 308.1085; found, 308.1078.

3-(4-Chlorophenylthio)-2-methyl-*N*-phenethylpropanamide (24): Following general procedure B, using 3-methylthietan-2-one and eluting with 25% ethyl acetate in hexane, **24** was obtained in 67% yield. White solid, crystallized from chloroform/hexane, mp: 93.0−94.0 °C. ^1H NMR (500 MHz) δ: 7.33−7.30 (t, *J* = 7.5 Hz, 2H), 7.27−7.19 (m, 7H), 5.47 (s, 1H), 3.58−3.48 (m, 2H), 3.23−3.18 (dd, *J* = 8.0, 13.5 Hz, 1H), 2.92−2.88 (dd, *J* = 6.5, 13.5 Hz, 1H), 2.84−2.81 (t, *J* = 6.5 Hz, 2H), 2.33−2.26 (m, 1H), 1.22−1.20 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz) δ: 174.4, 139.0, 134.8, 132.4, 130.9, 129.4, 129.1, 128.9, 126.8, 41.5, 40.7, 37.8, 35.8, 17.9. ESI-HRMS: calcd for $C_{18}H_{20}NOSCl$ $[M + Na]^+$, 356.0852; found, 356.0859.

General Procedure (C) for Multicomponent Coupling Reactions Using (*S*)-*O*-(*tert*-Butyl) *N*-(Thietan-2-on-3-yl) Carbamate (16): To a stirred solution of **16** (1.0 equiv) in DMF (0.15−0.2 M) were added aromatic thiol (1.2 equiv) and Cs_2CO_3 (1.0 equiv) at room temperature. The reaction mixture was allowed to stir for 6 h, after which time the reaction mixture had turned a faint yellow color. Then 2,4-dinitrobenbenzene sulfonamide (1.2 equiv) was added to the reaction mixture. Upon addition of the sulfonamide the reaction mixture became a dark red color and further deepened in color as the reaction continued. The reaction mixture was allowed to stir for 1 h, after which the DMF was removed under high vacuum, and the crude mixture was dissolved in EtOAc, washed with water and brine, and dried. Evaporation of solvent followed by column chromatography provided the coupled products as described below.

(*R*)-*O*-(*tert*-Butyl) *N*-(3-(4-Chlorophenylthio)-1-(phenethylaminocarbonyl)propan-2-yl) Carbamate (30): Following general procedure C, eluting with 30% ethyl acetate in hexane, **30** was obtained in 70% yield. White solid, crystallized from ethyl acetate/hexane, mp: 116.5−117.5 °C. $[\alpha]^{22}_D$ −6.0 (*c* 1.2). ^1H NMR (500 MHz) δ: 7.32−7.22 (m, 7H), 7.19−7.17 (d, *J* = 7.0 Hz, 2H), 6.25 (s, 1H), 5.25 (s, 1H), 4.20 (bs, 1H), 3.55−3.40 (m, 2H), 3.26−3.21 (m, 2H), 2.80−2.77 (t, *J* = 7.0 Hz, 2H), 1.43 (s, 9H). ^{13}C NMR (125 MHz) δ: 170.2, 155.5, 138.7, 133.5, 133.0, 131.4, 129.5, 129.0, 128.9, 126.9, 80.7, 54.1, 41.0, 36.5, 35.7, 28.5. ESI-HRMS: calcd for $C_{22}H_{27}N_2O_3SCl$ $[M + Na]^+$, 457.1329; found, 457.1313.

Methyl *N*-*tert*-Butoxycarbonyl-(4-chlorophenylsulfanyl)-L-alaninyl-L-phenylalaninate (36): Following general procedure C, eluting with 25% ethyl acetate in hexane, **36** was obtained in 62% yield.

(10) Hadad, C. M.; Rablen, P. R.; Wiberg, K. B. *J. Org. Chem.* **1998**, *63*, 8668–8681.

Colorless syrup. $[\alpha]^{22}_D$ +15.6 (*c* 1.1). ^{1}H NMR (500 MHz) δ: 7.33−7.25 (m, 7H), 7.10−7.08 (d, *J* = 7.0 Hz, 2H), 6.67−6.65 (d, *J* = 7.5 Hz, 1H), 5.18 (s, 1H), 4.79−4.76 (q, *J* = 6.0 Hz, 1H), 4.21 (s, 1H), 3.73 (s, 3H), 3.24 (bs, 2H), 3.16−3.12 (dd, *J* = 6.0, 13.8 Hz, 1H), 3.10−3.06 (dd, *J* = 5.5, 13.5 Hz, 1H), 1.44 (s, 1H). ^{13}C NMR (125 MHz) δ: 171.6, 169.9, 155.4, 135.8, 133.4, 133.2, 131.8, 129.5, 128.8, 127.4, 80.8, 54.0, 53.6, 52.6, 38.1, 36.6, 28.5. ESI-HRMS: calcd for $C_{24}H_{29}N_2O_5SCl$ [M + Na]$^+$, 515.1383; found, 515.1371.

(*R*)-*O*-(*tert*-Butyl) *N*-3-(4-Chlorophenylthio)-1-(4-acetamidophenylsulfonamido)propan-2-yl) Carbamate (38): To a stirred solution of **16** (40 mg, 0.2 mmol) in DMF (1 mL) were added 4-chlorothiophenol (34 mg, 0.24 mmol) and Cs_2CO_3 (64 mg, 0.2 mmol) at room temperature. The reaction mixture was allowed to stir for 6 h, after which time the reaction mixture had turned a faint yellow color. 4-Acetamidobenzenesulfonyl azide (38 mg, 0.16 mmol) was added to the reaction mixture. The reaction mixture was allowed to stir for 1 h, after which the DMF was removed under high vacuum, and the crude mixture was purified by column chromatography using 5% methanol in dichloromethane to give **38** (57 mg, 68%). White solid, crystallized from ethyl acetate/hexane, mp: 169.0−170.0 °C. $[\alpha]^{22}_D$ −13.1 (*c* 0.1, MeOH). ^{1}H NMR (500 MHz, MeOH-d_4) δ: 7.92−7.90 (d, *J* = 8.5 Hz, 2H), 7.74−7.73 (d, *J* = 8.0 Hz, 2H), 7.31−7.26 (m, 4H), 4.15 (bs, 1H), 3.23−3.19 (dd, *J* = 5.5, 13.5 Hz, 1H), 3.09−3.05 (dd, *J* = 7.5, 13.0 Hz, 1H), 2.16 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (125 MHz, MeOH-d_4) δ: 170.9, 156.1, 143.7, 134.3, 133.9, 132.5, 132.0, 131.5, 129.2, 129.1, 129.0, 118.8, 79.8, 54.8, 35.5, 27.5, 22.9. ESI-HRMS: calcd for $C_{22}H_{26}N_3O_6S_2Cl$ [M + Na]$^+$, 550.0849; found, 550.0826.

Supporting Information Available: Full experimental details and copies of ^{1}H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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