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L-Cysteine, a Versatile Source of Sulfenic Acids. Synthesis of Enantiopure Alliin Analogues

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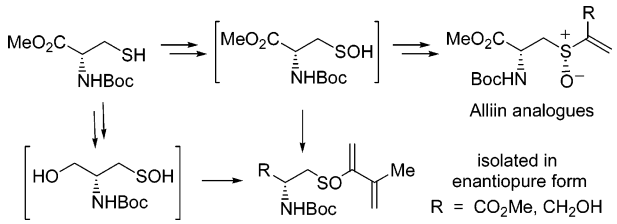

L-Cysteine is a stimulating starting product for the generation of transient sulfenic acids, such as **4**, **6**, **9**, and **15**, which add to suitable acceptors, allowing formation of sulfoxides showing a biologically active residue. These sulfoxides are easily isolated in enantiomerically pure form. For instance, *N*-(*tert*-butoxycarbonyl)-L-cysteine methyl ester (**1a**) furnished in few steps sulfenic acid **9a**, which was readily converted into (R,S_S)-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)ethene (**22**), the methyl ester of Boc-protected *nor*-alliin. Moreover, the addition of **9a** to 2-methyl-1-buten-3-yne has led to a sulfur epimeric and separable mixture of (*R*)-2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)-3-methyl-buta-1,3-dienes **10a** and **11a**, still possessing a "masked" sulfenic acid function, producible from their cysteine moieties once the dienes have been converted into the desired derivatives.

Introduction

The importance of sulfenic acids RSOH as transient intermediates in biological processes is widely recognized. Oxidation of thiol groups in living systems and much of the chemistry of the penicillin sulfoxides have been considered to involve sulfenic acid chemistry.[1] There is evidence for functional Cys-SOH in native proteins such as NADH peroxidase and oxidase. Cys-SOH forms of protein tyrosine phosphatases and glutathione reductase play key roles in important biological processes. In general, functional Cys-SOHs participate in diverse cellular processes, including signal transduction, oxidative stress response, and transcriptional regulation.[2] The recognized therapeutical properties of garlic, its typical flavor, and the disagreeable smell of breath and sweat after its ingestion or the lachrymatory factor of onion are tightly connected with reactions of self-condensation and rearrangement of sulfenic acids that originate from (S_S)-*S*-allyl-L-cysteine *S*-oxide (alliin) and (S_S,*E*)-*S*-(1-propenyl)-L-cysteine *S*-oxide (isoalliin) by the action of specific enzymes.[3]

In continuing our study on the *syn*-addition of enantiopure sulfenic acids to appropriate unsaturated molecules,[4] we envisaged that L-cysteine derivatives could represent convenient chiral starting products for the generation of various sulfenic acids and their involvement in stereocontrolled processes that allow the introduction of a cysteine *S*-oxide residue into a suitably chosen acceptor. Cysteine *S*-oxides are known for their cancero-protective and antioxidant potential,[5] L-cysteine is easily accessible in various protected forms and possesses functional groups that can be further transformed, but most of all, the L-cysteine *S*-oxide framework represents a kind of chiral auxiliary where the stereodifferentiating moiety is also a biologically active residue, so that it could be convenient to not remove the cysteine *S*-oxide group once it has played its auxiliary role. L-Cysteine deriva-

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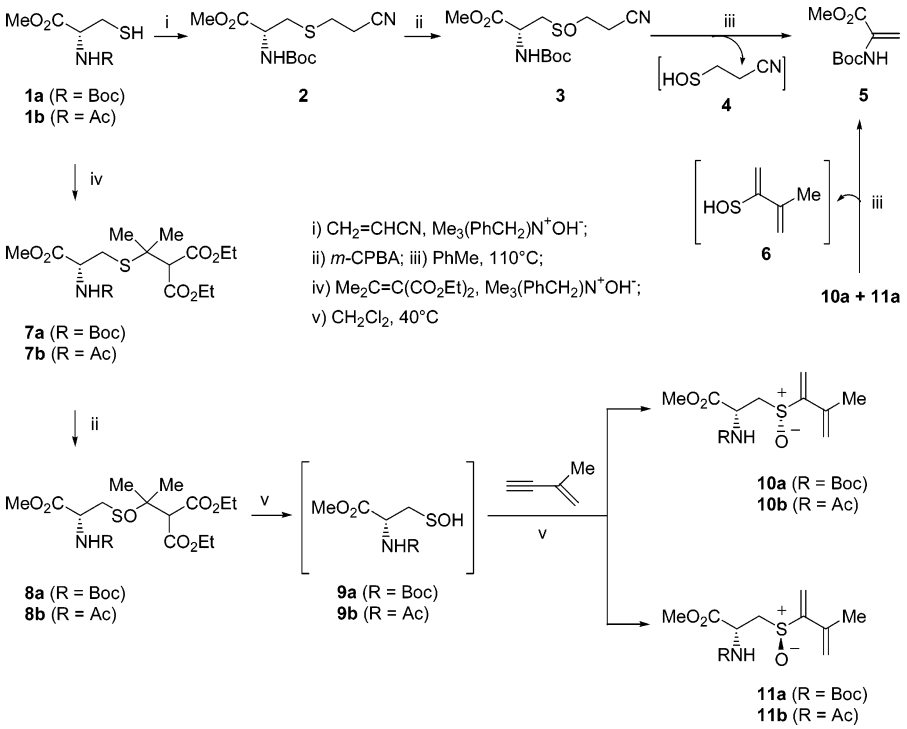
SCHEME 1



1a (R = Boc)
1b (R = Ac)
2
3
4
5
6
7a (R = Boc)
7b (R = Ac)
8a (R = Boc)
8b (R = Ac)
9a (R = Boc)
9b (R = Ac)
10a (R = Boc)
10b (R = Ac)
10a + 11a
11a (R = Boc)
11b (R = Ac)

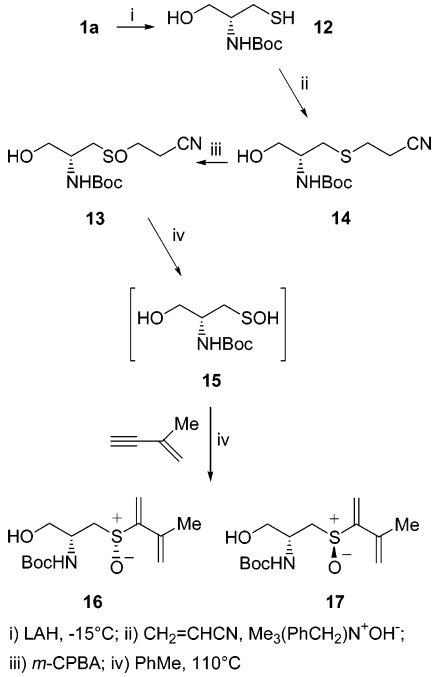
tives, obtained via sulfenic acids, can be therefore involved in asymmetric processes offering stimulating opportunities of synthetic applications.

In this paper we report the generation of enantiopure sulfenic acids from L-cysteine derivatives and the involvement of some of them in the stereoselective synthesis of enantiopure alliin analogues, such as (R,S_S)-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)ethene (**22**) and both sulfur epimers **21** and **23** of (*R*)-2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)propene.[6]

Results and Discussion

Commercial *N*-(*tert*-butoxycarbonyl)-L-cysteine methyl ester (**1a**) and *N*-acetyl-L-cysteine methyl ester (**1b**) were adopted as starting materials for preparing sulfoxides **3**, **8**, and **13** bearing alkyl residues with β-hydrogens to the sulfinyl group and electron-withdrawing substituents in suitable position to help the thermal *syn*-elimination of sulfenic acid (Schemes 1 and 2). Acetyl and *tert*-butoxycarbonyl are among the most popular protecting groups of the amine function in amino acid compounds. Therefore we found meaningful the comparison of synthetic

SCHEME 2



1a
12
13
14
15
16
17

results in the steps required for the preparation of sulfoxides **8a** and **8b**.

In a first instance, we chose 2-methyl-1-buten-3-yne as trapping agent of sulfenic acids **9a**, **9b**, and **15** because the completely chemo- and regioselective addition of sulfenic acid onto the triple bond of the enyne leads to enantiopure 2-sulfinylbuta-1,3-dienes, epimeric at sulfur atom (**10a** and **11a** from **8a**, **10b** and **11b** from **8b** in Scheme 1, **16** and **17** from **13** in Scheme 2). On the basis of our previous studies[4a,b,7] sulfinyl dienes **10**, **11**, **16**, and

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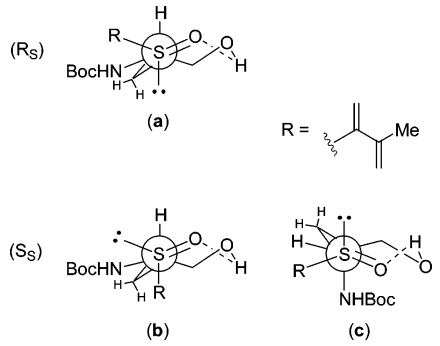
(6)) Authors decided to name the new compounds privileging the preservation in any case of the same indices for cysteine-like residues, instead of strictly applying IUPAC conventions.

17 are expected to be effective partners in asymmetric Diels−Alder cycloadditions.

The structural features of **1a** (Scheme 1) attracted our attention from the beginning because its conversion in sulfoxides **3** and **8a** occurs with maintenance, in the cysteine residue, of a β-proton to SO group whose mobility is guaranteed by the presence of both the ester and amine functions on the same carbon atom. These characteristics posed a problem of chemoselectivity in the elimination of sulfenic acid. Indeed, when we warmed sulfoxides **3**, in refluxing toluene and in the presence of 2-methyl-1-buten-3-yne, we obtained amino ester **5**,[8] as unique isolated product of the *syn*-elimination of sulfenic acid **4**. Rich and Tam had reported[8a] dehydrosulfenylation of Boc-protected 3-benzylsulfinyl amino acid derivatives, meaningfully influenced by intramolecular hydrogen bonding between the sulfoxide oxygen and the amide NH group. Epimeric sulfoxides **3** were prepared by treatment of cysteine derivative **1a** with acrylonitrile and benzyltrimethylammonium hydroxide (Triton B) and subsequent oxidation with *m*-CPBA of sulfide **2**,[9] which was obtained in 80% yield. *m*-CPBA oxidation of **2** to **3** was nearly quantitative, and sulfoxides **3** were obtained as a 1:1 mixture of epimers at sulfur atom.

LAH reduction of the ester moiety of the cysteine derivative **1a** to the hydroxymethyl function in **12** (Scheme 2) led to a significant modification of the initial structural features of **1a**, since the acidic character of the geminal hydrogen to NHBoc decreased in the cysteine-like residue, and a hydroxy function was introduced in the chiral auxiliary. It has been well demonstrated that the involvement of the sulfur-linked oxygen atom in intramolecular hydrogen bonding can prevent self-condensation of the sulfenic acid, enhance in some cases the stereoselectivity of the sulfenic acid addition, and facilitate the chromatographic separation of the obtained diastereoisomeric sulfoxides.[4a] Hydroxythiol **12**[10] was reacted with acrylonitrile and Triton B to give sulfide **14** in 95% yield. Oxidation of **14** with *m*-CPBA furnished the sulfur epimeric mixture **13** in 93% yield. Sulfoxides **13** underwent thermolysis in the presence of 2-methyl-1-buten-3-yne in refluxing toluene for 2.5 h, and the addition of sulfenic acid **15** to the triple bond of the enyne led to a mixture of sulfinyl dienes **16** and **17** in 70% total yield. The considerable difference in chromatographic mobility between the two epimeric dienes **16** and **17** confirmed the presence of an important intramolecular hydrogen bonding between the sulfoxide oxygen and the hydroxy group. Therefore, the absolute configuration at the sulfur atom in dienes **16** and **17** (Scheme 2) was assigned on the basis of intramolecular hydrogen bonding, related conformational preferences, and chromatographic mobility, as previously stated.[11] For this purpose we decided to represent Newman projections of **16** and **17** flattening the sulfur atom onto the carbon stereogenic center. The preferred hydrogen-bonded conformation was considered to be (**a**), which led to the assignment of the (R_S) configuration to the more mobile epimer **16**, whereas for the corresponding (S_S) isomer **17**, intramolecular hydrogen bonding should require the adoption of less favorable conformations (**b**) and/or (**c**) with four bulky substituents gauche to each other.



Thermolysis of sulfoxides to sulfenic acids is normally accelerated by increasing the acidity of β-hydrogens with the presence of electron-withdrawing and alkyl substituents β and α, respectively, to SO.[12] The introduction of a highly and suitably substituted alkyl group such as the 1,1-diethoxycarbonyl-2-methylprop-2-yl residue into the cysteine derivatives **1** enabled, finally, the generation of sulfenic acids **9**, which retain amine and carboxy function, typical of the cysteine (Scheme 1). Reaction of cysteine derivatives **1a** and **1b** with diethyl isopropylidenemalonate, in the presence of Triton B at −78 °C, furnished sulfides **7a** and **7b** in 85% and 80% yield, respectively. Sulfoxides **8a** and **8b** were obtained in 98% and 92% yield, respectively, by oxidation of sulfides **7** in the same conditions previously quoted for sulfides **2** and **14**. Two epimers at the sulfur atom were obtained in 1:1 ratio for sulfoxides **8a** and 1:2 ratio for sulfoxides **8b**. This low stereoselectivity was the only significant difference induced by the protective group Ac instead of Boc. Thermolysis of sulfoxides **8a** and **8b** in refluxing dichloromethane (40 °C) generated the transient species **9a** and **9b**, which added to the triple bond of 2-methyl-1-buten-3-yne giving sulfinyl dienes **10** and **11** in very good yields. Dienes **10a**, **11a**, **10b**, and **11b** were isolated in enantiomerically pure form by column chromatography. Noteworthy, compounds **10** and **11** still possess a "masked" sulfenic acid function that was expected to be producible

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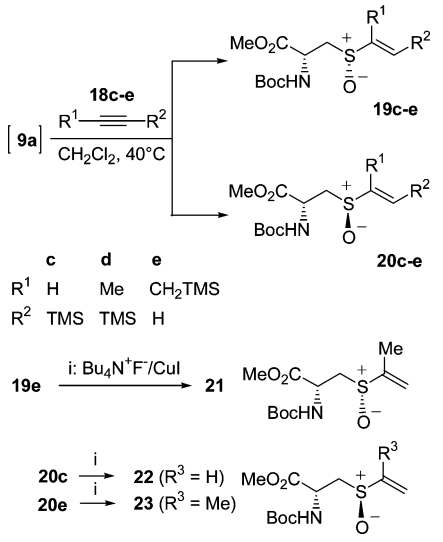
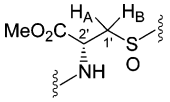
SCHEME 3



from the cysteine moieties by their heating at moderate temperature. Thermolysis of the mixture of sulfinyl dienes **10a** and **11a** in refluxing toluene (110 °C) led indeed to amino ester **5** (Scheme 1). The isolation of **5** represents indirect evidence of the elimination of sulfenic acid **6**, which self-condensates to volatile thiosulfinates whose structural features are greatly related to the alkenyl thiosulfinates, produced in *Allium* species by enzymic reaction when they are cut or ruptured, and characterizing the aroma profile of these vegetables.[3,13]

Sulfenic acid **9a**, generated in situ from sulfoxides **8a** (Scheme 1), was also added to the functionalized triple bond of (trimethylsilyl)acetylene (**18c**), 1-(trimethylsilyl)-1-propyne (**18d**), and 3-(trimethylsilyl)-1-propyne (**18e**), all of them commercially available (Scheme 3). The reactions were performed in dichloromethane and led to sulfoxides **19c**−**e** and **20c**−**e** in good yields. All the additions occurred with complete regioselectivity, and the mixtures of sulfoxides were separated by column chromatography, furnishing vinylsulfinyl L-cysteine derivatives **19** and **20** in enantiomerically pure form. Protodesilylation of compounds **20c**, **19e**, and **20e** with tetrabutylammonium fluoride (TBAF) and CuI[14] led to the formation of (*R*,S_S)-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)ethene (**22**) and (*R*,R_S)- and (*R*,S_S)-2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)propene (**21** and **23**, respectively) and represented the last step of an easy route of access to some alliin analogues.

We assigned the absolute configuration of sulfur atom in sulfoxides **10**, **11**, **19**, and **20** (Schemes 1 and 3) moving from the X-ray analysis of (*R*,*E*,S_S)-trimethyl-[2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)-vinyl]silane (**20c**), mp 134−135 °C, synthesized together with its sulfur epimer **19c** by thermolysis of **8a** in the presence of (trimethylsilyl)acetylene (**18c**). The diffractometry results unambiguously support the (*R*,S_S) configuration of sulfoxide **20c** and, as a consequence, the (*R*,R_S) configuration of **19c** and (*R*,S_S) configuration of **22**, this last obtained by protodesilylation of **20c**. Typical NMR parameters were compared for sulfur epimeric couples **10a** and **11a**, **19c**−**e** and **20c**−**e**, **21** and **23**, all characterized by the presence of (*R*)-2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl moiety, therefore showing analogous conformational preferences. We observed that, on going from a (R_S)-sulfoxide to its (S_S)-epimer, C-1′ resonance was shielded by 1 ppm and NH resonance deshielded by about 0.13 ppm. More significantly $J_{1'A,2'}$, $J_{1'B,2'}$, and $J_{2',NH}$ assumed almost the same values (6.6−4.8 Hz) for (R_S)-sulfoxides, while $J_{1'A,2'}$ was almost the same as $J_{2',NH}$ (8.0−7.4 Hz) and $J_{1'B,2'}$ clearly smaller (4.1−3.6 Hz) for (S_S)-sulfoxides. Analogous spectral trends allowed the assignment of configurations shown in Scheme 1 for epimeric sulfinyl dienes **10b** and **11b**, characterized by NHAc moiety.[15]



Conclusions

L-Cysteine represents a versatile source of sulfenic acids that can easily furnish several enantiopure sulfoxides. Both compounds **7a** and **7b** can act as convenient starting products for introducing L-cysteine *S*-oxide moiety into a suitable acceptor, via sulfenic acids **9a** and **9b**. Application of this strategy to the synthesis of alliin analogues **21**−**23** in enantiomerically pure form illustrates the versatility of this procedure. Moreover, the elimination of sulfenic acid **6** from the mixture **10a** + **11a** suggests that complex sulfoxides, such as **10** and **11**, obtained by addition of sulfenic acids **9** to unsaturated acceptors, can be stereoselectively derivatized and warmed again to eliminate an enamine such as **5** and simultaneously generate a new sulfenic acid moiety, useful in subsequent stereoselective transformations toward still more complex and enantiopure sulfoxides. This last application can be regarded as a further stimulating development of this chemistry.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$ solutions with TMS as internal standard; *J* values are given in Hz. The assignments are supported by Attached Proton Test (APT) and homodecoupling experiments. Protons and carbon nuclei marked with (′) pertain to the cysteine-like moieties. Mass spectra were measured by FAB (*m*-nitrobenzyl alcohol as matrix). All reactions were monitored by TLC on commercially available precoated plates (silica gel 60 F 254), and the products were visualized with acidic vanillin solution. Silica gel 60, 230−400 mesh, was used for column chromatography. Petrol refers to light petroleum, bp 30−40 °C.

***(R)*-2-*tert*-Butoxycarbonylamino-3-hydroxy-propane-1-thiol (12).**[10] A solution of *N*-(*tert*-butoxycarbonyl)-L-cysteine methyl ester (**1a**) (705 mg, 3.0 mmol) in anhydrous Et_2O (7

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(15) (*R*,R_S)-2-(2-Acetylamino-2-methoxycarbonyl-ethylsulfinyl)-3-methyl-buta-1,3-diene (**10b**): NH 6.80 ppm, C-1′ 55.0 ppm, $J_{1'A,2'}$ = $J_{2',NH}$ 5.7 Hz, $J_{1'B,2'}$ 5.5 Hz. (*R*,S_S)-2-(2-Acetylamino-2-methoxycarbonyl-ethylsulfinyl)-3-methyl-buta-1,3-diene (**11b**): NH 7.04 ppm, C-1′ 54.0 ppm, $J_{1'A,2'}$ 6.9 Hz, $J_{2',NH}$ 7.3 Hz, $J_{1'B,2'}$ 3.9 Hz.

mL) was added dropwise to a LAH suspension (171 mg, 4.5 mmol) in anhydrous Et_2O (10 mL) at −15 °C. After 15 min the reaction appeared complete by TLC and LAH in excess was carefully quenched by adding wet Et_2O and H_2O. The organic phase was filtered, dried (Na_2SO_4), and concentrated under reduced pressure to give the hydroxythiol **12** as an oil, which did not need purification (560 mg, 2.7 mmol, 90% yield): ^{1}H NMR δ 5.03 (br d, NH), 3.8−3.7 (m, H-2, H_2-3), 2.76 (m, H_2-1), 1.50 (m, SH), 1.46 (s, CMe_3); ^{13}C NMR δ 156.0 (NHCO), 80.0 (*C*Me_3), 62.8 (C-3), 53.5 (C-2), 28.2 (C*Me*$_3$), 25.7 (C-1). Anal. Calcd for $C_8H_{17}NO_3S$: C 46.35, H 8.27, N 6.76. Found: C 46.38, H 7.95, N 6.84.

2-Cyanoethyl Sulfides 2 and 14. General Procedure. Acrylonitrile (80 μL, 1.2 mmol) was added slowly to a solution of thiol **1a** or **12** (1.0 mmol) and Triton B (50 μL, 0.12 mmol, 40 wt % solution in MeOH) in anhydrous THF (4 mL) at −78 °C. When the reaction appeared complete by TLC, water was added. The crude product was extracted with Et_2O (3 × 15 mL) and dried (Na_2SO_4).

***(R)*-3-(2-*tert*-Butoxycarbonylamino-2-methoxycarbonyl-ethylthio)propionitrile (2).**[9] The conversion of **1a** to **2** was complete after allowing the solution to spontaneously reach −20 °C and remain at this temperature for 30 min. Evaporation of the solvent gave an oily residue that was purified by column chromatography. Elution with petrol/EtOAc 90:10 afforded compound **2** (80% yield) as an oil: ^{1}H NMR δ 5.36 (br d, $J_{2',NH}$ 6.4, NH), 4.55 (m, H-2′), 3.79 (s, OMe), 3.09 (AB dd, $J_{1'A,1'B}$ 14.0, $J_{1'A,2'}$ 5.1, H_A-1′), 3.01 (AB dd, $J_{1'B,2'}$ 5.3, H_B-1′), 2.82 (split t, J_{vic} 7.1, H_2-3), 2.64 (split t, H_2-2), 1.46 (s, CMe_3); ^{13}C NMR δ 171.0 (*C*O_2Me), 155.0 (NHCO), 117.9 (C-1), 80.3 (*C*Me_3), 53.3 (C-2′), 52.7 (OMe), 34.5 (C-1′), 28.2 (C*Me*$_3$), 28.1 (C-3), 18.6 (C-2); MS *m/z* (%) 289 (M + 1, 10), 233 (63), 189 (58), 172 (20), 95 (50), 81 (55), 69 (74), 57 (100). Anal. Calcd for $C_{12}H_{20}N_2O_4S$: C 49.98, H 6.99, N 9.71. Found: C 50.17, H 6.83, N 9.64.

***(R)*-3-(2-*tert*-Butoxycarbonylamino-3-hydroxy-propylthio)propionitrile (14).** The conversion of **12** to **14** was complete after 15 min at −78 °C. Evaporation of the solvent gave compound **14** as an oil not needing any purification (95% yield): ^{1}H NMR δ 5.07 (br d, NH), 3.8−3.7 (m, H-2′, H_2-3′), 2.9−2.7 (m, H_2-1′,2,3), 1.45 (s, CMe_3); ^{13}C NMR δ 155.8 (NHCO), 118.3 (C-1), 80.0 (*C*Me_3), 62.9 (C-3′), 51.6 (C-2′), 33.1 (C-1′), 28.3 (C*Me*$_3$), 27.8 (C-3), 18.8 (C-2); MS *m/z* (%) 261 (M + 1, 8), 205 (19), 81 (55), 95 (54), 69 (78), 57 (97), 55 (100). Anal. Calcd for $C_{11}H_{20}N_2O_3S$: C 50.75, H 7.74, N 10.76. Found: C 50.87, H 7.57, N 10.86.

(*R*)-2-[1-(2-*tert*-Butoxycarbonylamino-2-methoxycarbonyl-ethylthio)-1-methyl-ethyl]malonic Acid Diethyl Ester (7a). Diethyl isopropylidenemalonate (0.61 mL, 3.0 mmol) was added to a stirred solution of *N*-(*tert*-butoxycarbonyl)-L-cysteine methyl ester (**1a**) (235 mg, 1.0 mmol), and Triton B (38 μL, 0.09 mmol, 40 wt % solution in MeOH) in anhydrous THF (2.5 mL) at −78 °C. The reaction was slowly brought to room temperature, and when it appeared complete by TLC, after 2 h, water was added. The crude product was extracted with Et_2O (3 × 15 mL). The combined organic layers were washed with saturated NaCl solution (3 × 15 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the residue was purified by column chromatography (petrol/EtOAc 95:5 up to 50:50) to afford compound **7a** as an oil (370 mg, 0.85 mmol, 85% yield): $[\alpha]^{25}_D$ +12.2 (*c* 4.82, $CHCl_3$); ^{1}H NMR δ 5.37 (br d, $J_{2',NH}$ 7.6, NH), 4.54 (br dt, $J_{1',2'}$ 5.0, H-2′), 4.21 and 4.20 (two q, J_{vic} 7.1, 2 x OCH_2), 3.76 (s, OMe), 3.58 (s, H-2), 3.04 (d, H_2-1′), 1.54 (s, $SCMe_2$), 1.44 (s, CMe_3), 1.28 (two t, 2 × CH_2*Me*); ^{13}C NMR δ 171.2 (*C*O_2Me), 166.9 (C-1,3), 155.1 (NHCO), 80.1 (*C*Me_3), 61.4 (OCH_2), 60.3 (C-2), 52.9 (C-2′), 52.5 (OMe), 45.8 (S*C*Me_2), 30.8 (C-1′), 28.2 (C*Me*$_3$), 26.53 and 26.48 (SC*Me*$_2$), 14.0 (CH_2*Me*); MS *m/z* (%) 436 (M + 1, 6), 380 (13), 336 (100), 318 (32), 247 (18), 220 (15), 201 (75), 176 (51), 155 (48), 127(15), 99 (33), 57 (39). Anal. Calcd for $C_{19}H_{33}NO_8S$: C 52.40, H 7.64, N 3.22. Found: C 52.18, H 7.61, N 3.40.

(*R*)-2-[1-(2-Acetylamino-2-methoxycarbonyl-ethylthio)-1-methyl-ethyl]malonic Acid Diethyl Ester (7b). Diethyl isopropylidenemalonate (0.81 mL, 4.0 mmol), *N*-acetyl-L-cysteine methyl ester (**1b**) (177 mg, 1.0 mmol), and Triton B (25 μL, 0.06 mmol, 40 wt % solution in MeOH) were reacted as previously described for compound **7a**. The crude residue was purified by column chromatography (petrol/EtOAc 90:10 up to 20:80) to afford compound **7b** as an oil (302 mg, 0.80 mmol 80% yield): $[\alpha]^{25}_D$ +26.4 (*c* 4.70, $CHCl_3$); ^{1}H NMR δ 6.56 (br d, $J_{2',NH}$ 7.4, NH), 4.79 (dt, $J_{1'A,2'}$ 5.1, $J_{1'B,2'}$ 4.9, H-2′), 4.19 (two q) and 4.18 (two q) (J_{vic} 7.0, 2 × OCH_2), 3.74 (s, OMe), 3.56 (s, H-2), 3.06 (AB dd, $J_{1'A,1'B}$ 12.6, H_A-1′), 3.03 (AB dd, H_B-1′), 2.04 (s, MeCO), 1.52 (s, $SCMe_2$), 1.26 (two t, 2 × CH_2*Me*); ^{13}C NMR δ 171.0 (*C*O_2Me), 167.1, 167.05, and 167.03 (C-1,3, NHCO), 61.42 and 61.36 (OCH_2), 60.4 (C-2), 52.6 (C-2′), 51.6 (OMe), 45.6 (S*C*Me_2), 30.1 (C-1′), 26.5 and 26.3 (SC*Me*$_2$), 22.7 (*Me*CO), 13.9 and 13.8 (CH_2*Me*); MS *m/z* (%) 378 (M + 1, 100), 318 (26), 218 (58), 201 (39), 178 (36), 176 (25), 155 (39), 144 (29), 99 (32). Anal. Calcd for $C_{19}H_{33}NO_8S$: C 52.40, H 7.64, N 3.22. Found: C 52.22, H 7.69, N 3.34.

***m*-CPBA Oxidation of Sulfides 2, 7, and 14 to Sulfoxides 3, 8, and 13, Respectively. General Procedure.** *m*-CPBA (0.17 g 80%, 0.8 mmol) was dissolved in CH_2Cl_2 (6 mL) and added dropwise to a solution of the sulfide (0.8 mmol) in CH_2Cl_2 (5 mL) at −50 °C. When the reaction appeared complete by TLC, a 10% solution of $Na_2S_2O_3$ was added (10 mL), and the organic layer was extracted and washed with a saturated solution of $NaHCO_3$ (2 × 10 mL) and water (2 × 10 mL).

***(R)*-3-(2-*tert*-Butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)propionitriles 3.** The conversion of **2** into **3** was complete after 20 min. Evaporation of the solvent under reduced pressure gave sulfoxides **3** (95% yield, sulfur epimeric ratio 1:1) as an oil usable for the next step without purification: ^{1}H NMR δ 5.65 (br m, NH), 4.66 (m, H-2′), 3.81 (s, OMe), 3.5−2.8 (m, H_2-1,1′,2), 1.46 (s, CMe_3); ^{13}C NMR δ 170.5 and 170.1 (*C*O_2Me), 155.3 (NHCO), 117.2 (C-1), 80.8 (*C*Me_3), 54.3, 53.7, and 53.0 (C-2′, OMe), 49.5 and 49.3 (C-1′), 47.0 and 46.6 (C-3), 28.1 (C*Me*$_3$), 11.1 and 10.9 (C-2). Anal. Calcd for $C_{12}H_{20}N_2O_5S$: C 47.35, H 6.62, N 9.20. Found: C 47.00, H 6.62, N 9.10.

(*R*)-2-[1-(2-*tert*-Butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)-1-methyl-ethyl]malonic Acids Diethyl Esters 8a. The conversion of **7a** into **8a** was complete after 5 min. Evaporation of the solvent under reduced pressure gave sulfoxides **8a** (98% yield, sulfur epimeric ratio 1:1) as an oil usable for the next step without purification: ^{1}H NMR δ 5.73 (br d, $J_{2',NH}$ 9.0) and 5.69 (br d, $J_{2',NH}$ 6.3) (NH), 4.74 (m, H-2′), 4.3−4.2 (m, 2 × OCH_2), 3.80 and 3.79 (two s, OMe), 3.72 (s, H-2), 3.3−3.0 (m, H_2-1′), 1.48 and 1.46 (s, $SCMe_2$), 1.45 and 1.44 (s, CMe_3), 1.28 (m, 2 × CH_2*Me*); ^{13}C NMR δ 170.4 (*C*O_2Me), 166.50, 166.46, 166.15, and 166.12 (C-1,3), 155.2 and 155.1 (NHCO), 80.4 (*C*Me_3), 61.9, 61.82, 61.76, and 61.73 (OCH_2), 58.1 (C-1′), 55.1 (C-2), 52.8 and 52.7 (C-2′), 50.3 and 50.2 (OMe), 47.3 and 46.5 (S*C*Me_2), 28.2 (C*Me*$_3$), 13.9 (CH_2*Me*); MS *m/z* (%) 452 (M + 1, 11), 396 (15), 368 (43), 329 (9), 201 (64), 155 (52), 81 (35), 69 (53), 57 (100). Anal. Calcd for $C_{19}H_{33}NO_9S$: C 50.54, H 7.37, N 3.10. Found: C 50.83, H 7.40, N 3.16.

(*R*)-2-[1-(2-Acetylamino-2-methoxycarbonyl-ethylsulfinyl)-1-methyl-ethyl]malonic Acids Diethyl Esters 8b. The conversion of **7b** into **8b** was complete after 20 min. Evaporation of the solvent under reduced pressure gave sulfoxides **8b** (92% yield, sulfur epimeric ratio 1:2) as an oil usable for the next step without purification: ^{1}H NMR δ 7.17 (br d, $J_{2',NH}$ 8.1, NH of minor epimer), 6.87 (br d, $J_{2',NH}$ 5.9, NH of major epimer), 5.0−4.9 (m, H-2′), 4.23 (m, 2 × OCH_2), 3.76 (s, OMe), 3.68 (s, H-2 of minor epimer), 3.67 (s, H-2 of major epimer), 3.29 (AB dd, $J_{1'A,1'B}$ 12.9, $J_{1'A,2'}$ 5.5, H_A-1′ of major epimer), 3.26 (AB dd, $J_{1'A,1'B}$ 13.0, $J_{1'A,2'}$ 7.2, H_A-1′ of minor epimer), 3.15 (AB dd, $J_{1'B,2'}$ 4.5, H_B-1′ of major epimer), 3.00 (AB dd, $J_{1'B,2'}$ 3.9, H_B-1′ of minor epimer), 2.05 (s, MeCO

of minor epimer), 2.04 (s, MeCO of major epimer), 1.44, 1.40, 1.29, and 1.28 (four s, $SCMe_2$), 1.3−1.2 (m, 2 × CH_2Me); ^{13}C NMR δ 170.5 and 170.4 (CO_2Me), 166.6, 166.5, 166.23, 166.16, and 165.8 (C-1,3, NHCO), 61.95, 61.90, 61.84, 61.79, 60.7, and 58.1 (C-1′, OCH_2), 55.1 and 55.0 (C-2), 52.9 and 52.8 (C-2′), 49.3, 49.2, 49.1, and 49.0 (OMe, $SCMe_2$), 23.0 and 22.9 ($MeCO$), 17.8, 17.4, 17.2, and 17.1 ($SCMe_2$), 14.0, 13.9, 13.8, and 13.7 (CH_2Me); MS *m/z* (%) 394 (M + 1, 100), 201 (49), 194 (16), 176 (92), 155 (50), 144 (22), 99 (26). Anal. Calcd for $C_{16}H_{27}NO_8S$: C 48.84, H 6.92, N 3.56. Found: C 48.45, H 7.13, N 3.43.

***(R)*-3-(2-*tert*-Butoxycarbonylamino-3-hydroxy-propylsulfinyl)propionitriles 13.** The conversion of **14** into **13** was complete after 20 min. Evaporation of the solvent under reduced pressure gave sulfoxides **14** (93% yield, sulfur epimeric ratio 1:1) as an oil usable for the next steps without purification: ^1H NMR δ 5.46 and 5.43 (two br d, NH), 4.1−3.7 (m, H-2′, H_2-3′), 3.2−2.9 (m, H_2-1′,2,3), 1.45 (s, CMe_3); ^{13}C NMR δ 155.7 (NHCO), 117.2 (C-1), 80.5 (CMe_3), 63.9 and 63.5 (C-3′), 56.1 and 53.7 (C-1′), 49.1 and 48.9 (C-2′), 46.9 and 46.2 (C-3), 28.2 (CMe_3), 11.0 (C-2); MS *m/z* (%) 277 (M + 1, 15), 221 (49), 177 (42), 95 (38), 81 (44), 69 (61), 57 (100). Anal. Calcd for $C_{11}H_{20}N_2O_4S$: C 47.81, H 7.29, N 10.14. Found: C 47.42, H 7.14, N 9.95.

Thermolysis of Sulfoxides 3, 8, and 13 in the Presence of 2-Methyl-1-buten-3-yne. General Procedure. A solution of the sulfoxides (0.72 mmol) and 2-methyl-1-buten-3-yne (1 mL, 10.4 mmol) in toluene (110 °C, 15 mL) or CH_2Cl_2 (40 °C, 15 mL) was maintained at reflux temperature. When the reaction appeared complete by TLC (disappearance of starting sulfoxides), the solvent was removed under reduced pressure.

Thermolysis of *(R)*-3-(2-*tert*-Butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)propionitriles 3 in the Presence of 2-Methyl-1-buten-3-yne. The reaction occurred in toluene and afforded in 1 h methyl 2-(*tert*-butoxycarbonyl)-aminoacrylate (**5**) as unique isolated product.[8]

Thermolysis of (*R*)-2-[1-(2-*tert*-Butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)-1-methyl-ethyl]malonic Acids Diethyl Esters 8a in the Presence of 2-Methyl-1-buten-3-yne. The reaction, performed in CH_2Cl_2, was complete after 20 h. The crude mixture of sulfoxides **10a** and **11a** (60% yield, sulfur epimeric ratio 1:1) was purified by column chromatography (petrol/EtOAc 80:20): MS *m/z* (%) 318 (M + 1, 22), 262 (88), 218 (59), 102 (70), 57 (100). First eluted was (*R,R*$_S$)-2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)-3-methyl-buta-1,3-diene (**10a**) as an oil: $[\alpha]^{26}_D$ +42.5 (*c* 0.46, $CHCl_3$); ^1H NMR δ 6.02 (s, H_A-1, *cis* to SO), 5.86 (s, H_B-1, *trans* to SO), 5.67 (br d, $J_{2',NH}$ 6.1, NH), 5.15 (br s, H_A-4, *trans* to 3-Me), 5.08 (br s, H_B-4, *cis* to 3-Me), 4.65 (br ddd, H-2′), 3.79 (s, OMe), 3.63 (AB dd, $J_{1'A,1'B}$ 13.5, $J_{1'A,2'}$ 5.6, H_A-1′), 2.97 (AB dd, $J_{1'B,2'}$ 4.8, H_B-1′), 2.01 (t, $J_{4,Me}$ 0.7, 3-Me), 1.45 (s, CMe_3); ^{13}C NMR δ 170.6 (CO_2Me), 154.9 (NHCO), 151.8 (C-3), 137.5 (C-2), 115.8 and 115.1 (C-1,4), 80.4 (CMe_3), 55.7 (C-1′), 52.8 (C-2′), 49.7 (OMe), 28.2 (CMe_3), 21.8 (3-Me). Anal. Calcd for $C_{14}H_{23}NO_5S$: C 52.98, H 7.30, N 4.41. Found: C 52.62, H 7.43, N 4.30. Then (*R,S*$_S$)-2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)-3-methyl-buta-1,3-diene (**11a**) was eluted as an oil: $[\alpha]^{26}_D$ −15.5 (*c* 0.20, $CHCl_3$); ^1H NMR δ 6.06 (s, H_A-1, *cis* to SO), 5.89 (s, H_B-1, *trans* to SO), 5.74 (br d, NH), 5.16 (br s, H_A-4, *trans* to 3-Me), 5.07 (br s, H_B-4, *cis* to 3-Me), 4.67 (br ddd, H-2′), 3.79 (s, OMe), 3.56 (br AB dd, $J_{1'A,1'B}$ 13.5, $J_{1'A,2'}$ 7.4, H_A-1′), 2.90 (AB dd, $J_{1'B,2'}$ 3.7, H_B-1′), 2.01 (br s, 3-Me), 1.45 (s, CMe_3); ^{13}C NMR δ 170.7 (CO_2-Me), 155.2 (NHCO), 151.9 (C-3), 137.4 (C-2), 115.7 and 115.1 (C-1,4), 80.3 (CMe_3), 55.2 (C-1′), 52.7 (C-2′), 50.5 (OMe), 28.1 (CMe_3), 21.7 (3-Me). Anal. Calcd for $C_{14}H_{23}NO_5S$: C 52.98, H 7.30, N 4.41. Found: C 52.79, H 7.16, N 4.07.

Thermolysis of (*R*)-2-[1-(2-Acetylamino-2-methoxycarbonyl-ethylsulfinyl)-1-methyl-ethyl]malonic Acids Diethyl Esters 8b in the Presence of 2-Methyl-1-buten-3-yne. The reaction, performed in CH_2Cl_2, was complete after 20 h. The crude mixture of sulfoxides **10b** and **11b** (67% yield, sulfur epimeric ratio 1:1) was purified by column chromatography (petrol/EtOAc 60:40): MS *m/z* (%) 260 (M + 1, 43), 144 (86), 95 (29), 69 (69), 55 (100), 41 (90). First eluted was (*R,R*$_S$)-2-(2-acetylamino-2-methoxycarbonyl-ethylsulfinyl)-3-methyl-buta-1,3-diene (**10b**) as an oil: $[\alpha]^{25}_D$ + 46.5 (*c* 3.06, $CHCl_3$); ^1H NMR δ 6.80 (br d, $J_{1'A,2'} = J_{2',NH}$ 5.7, NH), 6.01 (s, H_A-1, *cis* to SO), 5.87 (s, H_B-1, *trans* to SO), 5.17 (br s, H_A-4, *trans* to 3-Me), 5.05 (s, H_B-4, *cis* to 3-Me), 4.90 (dt, $J_{1'B,2'}$ 5.5, H-2′), 3.79 (s, OMe), 3.65 (AB dd, $J_{1'A,1'B}$ 13.7, H_A-1′), 3.01 (AB dd, H_B-1′), 2.09 (s, MeCO), 2.01 (d, $J_{4A,Me}$ 0.5, 3-Me); ^{13}C NMR δ 170.3 and 170.2 (CO_2Me, NHCO), 151.7 (C-3), 137.2 (C-2), 115.7 and 115.3 (C-1,4), 55.0 (C-1′), 52.8 (C-2′), 49.2 (OMe), 22.8 ($MeCO$), 21.7 (3-Me). Calcd for $C_{11}H_{17}NO_4S$: C 50.95, H 6.61, N 5.40. Found: C 50.76, H 6.61, N 5.41. Then (*R,S*$_S$)-2-(2-acetylamino-2-methoxycarbonyl-ethylsulfinyl)-3-methyl-buta-1,3-diene (**11b**) was eluted as an oil: ^1H NMR δ 7.04 (br d, $J_{2',NH}$ 7.3, NH), 6.03 (s, H_A-1, *cis* to SO), 5.91 (s, H_B-1, *trans* to SO), 5.19 (br s, H_A-4, *trans* to 3-Me), 5.06 (s, H_B-4, *cis* to 3-Me), 4.97 (ddd, $J_{1'A,2'}$ 6.9, $J_{1'B,2'}$ 3.9, H-2′), 3.80 (s, OMe), 3.57 (AB dd, $J_{1'A,1'B}$ 13.6, H_A-1′), 2.90 (AB dd, H_B-1′), 2.05 (s, MeCO), 2.02 (br s, 3-Me); ^{13}C NMR δ 170.3 and 170.2 (CO_2Me, NHCO), 151.7 (C-3), 137.3 (C-2), 115.9 and 115.4 (C-1,4), 54.0 (C-1′), 52.8 (C-2′), 49.8 (OMe), 22.9 ($MeCO$), 21.8 (3-Me). Anal. Calcd for $C_{11}H_{17}NO_4S$: C 50.95, H 6.61, N 5.40. Found: C 50.60, H 6.87, N 5.48.

Thermolysis of *(R)*-3-(2-*tert*-Butoxycarbonylamino-3-hydroxy-propylsulfinyl)propionitriles 13 in the Presence of 2-Methyl-1-buten-3-yne. The reaction, performed in toluene, was complete after 2.5 h. The crude mixture of sulfoxides **16** and **17** (70% yield, sulfur epimeric ratio 1:1) was purified by column chromatography (petrol/EtOAc 60:40). First eluted was (*R,R*$_S$)-2-(2-*tert*-butoxycarbonylamino-3-hydroxy-propylsulfinyl)-3-methyl-buta-1,3-diene (**16**) as an oil: $[\alpha]^{24}_D$ +62.3 (*c* 0.82, $CHCl_3$); ^1H NMR δ 6.06 (s, H_A-1, *cis* to SO), 5.90 (s, H_B-1, *trans* to SO), 5.54 (br d, NH), 5.17 (m, $J_{4,Me}$ 0.9, H_A-4, *trans* to 3-Me), 5.07 (br s, H_B-4, *cis* to 3-Me), 4.1−3.7 (m, H-2′, H_2-3′), 3.69 (AB dd, $J_{1'A,1'B}$ 13.8, $J_{1'A,2'}$ 6.0, H_A-1′), 2.63 (AB dd, $J_{1'B,2'}$ 2.7, H_B-1′), 2.01 (m, 3-Me), 1.45 (s, CMe_3); ^{13}C NMR δ 155.3 (NHCO), 150.8 (C-3), 137.5 (C-2), 116.0 and 115.5 (C-1,4), 79.9 (CMe_3), 63.7 (C-3′), 58.6 (C-1′), 49.5 (C-2′), 28.3 (CMe_3), 21.8 (3-Me). Anal. Calcd for $C_{13}H_{23}NO_4S$: C 53.95, H 8.01, N 4.84. Found: C 54.31, H 7.97, N 4.91. Then (*R,S*$_S$)-2-(2-*tert*-butoxycarbonylamino-3-hydroxy-propylsulfinyl)-3-methyl-buta-1,3-diene (**17**) was eluted as an oil: $[\alpha]^{26}_D$ −4.3 (*c* 0.89, $CHCl_3$); ^1H NMR δ 6.03 (s, H_A-1, *cis* to SO), 5.88 (s, H_B-1, *trans* to SO), 5.53 (br d, NH), 5.18 (m, H_A-4, *trans* to 3-Me), 5.12 (br s, H_B-4, *cis* to 3-Me), 4.1−3.3 (m, H_A-1′, H-2′, H_2-3′), 2.72 (AB dd, $J_{1'A,1'B}$ 13.7, $J_{1'B,2'}$ 5.3, H_B-1′), 2.02 (t, $J_{4,Me}$ 0.6, 3-Me), 1.44 (s, CMe_3); ^{13}C NMR δ 155.8 (NHCO), 151.6 (C-3), 137.5 (C-2), 115.7 and 115.4 (C-1,4), 80.1 (CMe_3), 64.3 (C-3′), 55.5 (C-1′), 49.9 (C-2′), 28.3 (CMe_3), 21.9 (3-Me). Anal. Calcd for $C_{13}H_{23}NO_4S$: C 53.95, H 8.01, N 4.84. Found: C 53.80, H 8.36, N 4.99.

Thermolysis of (*R*)-2-[1-(2-*tert*-Butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)-1-methyl-ethyl]malonic Acids Diethyl Esters 8a in the Presence of Alkynes 18. General Procedure. A solution of sulfoxides **8a** (402 mg, 0.89 mmol) and alkynes **18** (13.3 mmol) in CH_2Cl_2 (10 mL) was maintained at reflux temperature. After 20 h the reaction appeared complete by TLC (disappearance of sulfoxides **8a**), and the solvent was removed under reduced pressure.

Thermolysis of 8a in the Presence of (Trimethylsilyl)-acetylene (18c). The column chromatography of the crude product mixture, eluted with hexane/EtOAc 80:20, afforded sulfoxides **19c** and **20c** (65% yield, sulfur epimeric ratio 1:1). First eluted was (*R,E,S*$_S$)-trimethyl-[2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)vinyl]silane (**20c**), mp 134−135 °C: $[\alpha]^{22}_D$ +58.2 (*c* 3.80, $CHCl_3$); ^1H NMR δ 6.91 (AB d, $J_{1,2}$ 17.7, H-2), 6.69 (AB d, H-1), 5.78 (br d, $J_{2',NH}$ 7.7, NH), 4.63 (m, H-2′), 3.76 (s, OMe), 3.30 (AB dd, $J_{1'A,1'B}$ 13.3, $J_{1'A,2'}$ 7.6, H_A-1′), 3.00 (AB dd, $J_{1'B,2'}$ 3.9, H_B-1′), 1.42 (s, CMe_3), 0.14 (s, $SiMe_3$); ^{13}C NMR δ 170.8 (CO_2Me), 155.2 (NHCO), 144.5 (C-1), 138.8 (C-2), 80.4 (CMe_3), 54.3 (C-1′), 52.8 (C-2′), 50.1

(OMe), 28.2 (C*Me*$_3$), −1.7 (SiMe$_3$); MS *m/z* (%) 350 (M + 1, 23), 294 (78), 250 (46), 77 (76), 73 (61), 57 (100). Anal. Calcd for $C_{14}H_{27}NO_5SSi$: C 48.11, H 7.79, N 4.01. Found: C 47.76, H 8.04, N 3.74. Then (*R,E,R*$_S$)-trimethyl-[2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)vinyl]silane (**19c**) was eluted as an oil: ^{1}H NMR δ 6.92 (AB d, $J_{1,2}$ 17.8, H-2), 6.75 (AB d, H-1), 5.62 (br d, $J_{2',NH}$ 6.6, NH), 4.67 (m, H-2′), 3.80 (s, OMe), 3.37 (AB dd, $J_{1'A,1'B}$ 13.5, $J_{1'A,2'}$ 5.1, H$_A$-1′), 3.09 (AB dd, $J_{1'B,2'}$ 5.9, H$_B$-1′), 1.46 (s, CMe$_3$), 0.17 (s, SiMe$_3$); ^{13}C NMR δ 170.4 (*C*O$_2$Me), 155.0 (NHCO), 144.6 (C-1), 138.9 (C-2), 80.5 (*C*Me$_3$), 55.2 (C-1′), 52.9 (C-2′), 49.7 (OMe), 28.2 (C*Me*$_3$), −1.7 (SiMe$_3$); MS *m/z* (%) 350 (M + 1, 14), 294 (49), 250 (43), 77 (66), 73 (81), 57 (100). Anal. Calcd for $C_{14}H_{27}NO_5SSi$: C 48.11, H 7.79, N 4.01. Found: C 47.72, H 7.63, N 3.92.

Thermolysis of 8a in the Presence of 1-(Trimethylsilyl)-1-propyne (18d). The column chromatography of the crude product mixture, eluted with hexane/EtOAc 80:20, afforded sulfoxides **19d** and **20d** (60% yield, sulfur epimeric ratio 1:1): MS *m/z* (%) 364 (M + 1, 23), 308 (53), 264 (14), 250 (18), 178 (64), 146 (9), 113 (23), 73 (100), 57 (33). First eluted as an oil was (*R,E,S*$_S$)-trimethyl-[2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)prop-1-enyl]silane (**20d**): ^{1}H NMR δ 6.49 (br s, H-1), 5.80 (br d, $J_{2',NH}$ 7.7, NH), 4.63 (m, H-2′), 3.79 (s, OMe), 3.32 (AB dd, $J_{1'A,1'B}$ 13.3, $J_{1'A,2'}$ 8.0, H$_A$-1′), 2.88 (AB dd, $J_{1'B,2'}$ 3.7, H$_B$-1′), 1.99 (d, $J_{1,3}$ 1.0, H$_3$-3), 1.45 (s, CMe$_3$), 0.21 (s, SiMe$_3$); ^{13}C NMR δ 170.9 (*C*O$_2$Me), 155.3 (NHCO), 152.3 (C-2), 130.5 (C-1), 80.3 (*C*Me$_3$), 52.7 (C-2′), 52.4 (C-1′), 50.3 (OMe), 28.2 (C*Me*$_3$), 14.4 (C-3), − 0.6 (SiMe$_3$). Anal. Calcd for $C_{15}H_{29}NO_5SSi$: C 49.56, H 8.04, N 3.85. Found: C 49.60, H 7.99, N 3.87. Then (*R,E,R*$_S$)-trimethyl-[2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)prop-1-enyl]silane (**19d**) was eluted as an oil: ^{1}H NMR δ 6.45 (br s, H-1), 5.60 (br d, $J_{2',NH}$ 6.4, NH), 4.61 (m, H-2′), 3.79 (s, OMe), 3.40 (AB dd, $J_{1'A,1'B}$ 13.3, $J_{1'A,2'}$ 4.8, H$_A$-1′), 2.97 (AB dd, $J_{1'B,2'}$ 5.4, H$_B$-1′), 1.98 (d, $J_{1,3}$ 1.0, H$_3$-3), 1.45 (s, CMe$_3$), 0.21 (s, SiMe$_3$); ^{13}C NMR δ 170.6 (*C*O$_2$Me), 155.1 (NHCO), 152.7 (C-2), 130.9 (C-1), 80.5 (*C*Me$_3$), 53.0 (C-1′), 52.9 (C-2′), 49.7 (OMe), 28.2 (C*Me*$_3$), 14.1 (C-3), −0.6 (SiMe$_3$). Anal. Calcd for $C_{15}H_{29}NO_5SSi$: C 49.56, H 8.04, N 3.85. Found: C 49.58, H 8.06, N 3.84.

Thermolysis of 8a in the Presence of 3-(Trimethylsilyl)-1-propyne (18e). The column chromatography of the crude product mixture, eluted with hexane/EtOAc 80:20, afforded sulfoxides **19e** and **20e** (60% yield, sulfur epimeric ratio 1:1). First eluted was (*R,R*$_S$)-trimethyl-[2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)prop-2-enyl]-silane (**19e**) as an oil: ^{1}H NMR δ 5.73 (s, H$_A$-3, *cis* to SO), 5.70 (br d, $J_{1'A,2'} = J_{1'B,2'} = J_{2',NH}$ 5.5, NH), 5.46 (br s, H$_B$-3, *trans* to SO), 4.63 (q, H-2′), 3.79 (s, OMe), 3.45 (AB dd, $J_{1'A,1'B}$ 13.4, H$_A$-1′), 3.02 (AB dd, H$_B$-1′), 1.88 (AB d, $J_{1A,1B}$ 14.9, H$_A$-1), 1.45 (s, CMe$_3$), 1.39 (AB dd, $J_{1B,3B}$ 0.9, H$_B$-1), 0.09 (s, SiMe$_3$); ^{13}C NMR δ 170.6 (*C*O$_2$Me), 155.1 (NHCO), 150.3 (C-2), 113.8 (C-3), 80.4 (*C*Me$_3$), 53.6 (C-1′), 52.8 (C-2′), 49.9 (OMe), 28.2 (C*Me*$_3$), 18.4 (C-1), −1.5 (SiMe$_3$); MS *m/z* (%) 364 (M + 1, 46), 308 (96), 264 (46), 178 (20), 73 (100), 57 (40). Anal. Calcd for $C_{15}H_{29}NO_5SSi$: C 49.56, H 8.04, N 3.85. Found: C 49.62, H 8.23, N 4.04. Then (*R,S*$_S$)-trimethyl-[2-(2-*tert*-butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)prop-2-enyl]silane (**20e**)-was eluted as an oil: ^{1}H NMR δ 5.79 (br d, NH), 5.76 (s, H$_A$-3, *cis* to SO), 5.48 (br s, H$_B$-3, *trans* to SO), 4.63 (m, H-2′), 3.80 (s, OMe), 3.38 (AB dd, $J_{1'A,1'B}$ 13.4, $J_{1'A,2'}$ 7.8, H$_A$-1′), 2.97 (AB dd, $J_{1'B,2'}$ 3.6, H$_B$-1′), 1.90 (AB d, $J_{1A,1B}$ 14.6, H$_A$-1), 1.46 (s, CMe$_3$), 1.39 (AB d, H$_B$-1), 0.09 (s, SiMe$_3$); ^{13}C NMR δ 170.8 (*C*O$_2$Me), 155.3 (NHCO), 150.2 (C-2), 113.6 (C-3), 80.3 (*C*Me$_3$), 53.2 (C-1′), 52.7 (C-2′), 50.5 (OMe), 28.2 (C*Me*$_3$), 18.5 (C-1), −1.5 (SiMe$_3$); MS *m/z* (%) 364 (M + 1, 41), 436 (12), 308 (100), 264 (55), 178 (25), 73 (93), 57 (32). Anal. Calcd for $C_{15}H_{29}NO_5SSi$: C 49.56, H 8.04, N 3.85. Found: C 49.68, H 8.20, N 3.65.

Protodesilylation of Sulfoxides 19e, 20e and 20c. General Procedure. A freshly prepared 1 M solution of TBAF·3H$_2$O in THF (3 mL, 3.0 mmol) was added to a solution of sulfoxide **19e**, **20e**, or **20c** (1.0 mmol) and CuI (286 mg, 1.5 mmol) in THF (7 mL).[14] The reaction appeared complete after 5 min for sulfoxides **19e** or **20e**, whereas in the case of **20c** the reaction was stopped after 24 h despite being unfinished. The crude mixture was filtered through SiO$_2$, and the solid residue was washed with CH$_2$Cl$_2$ (20 mL). The solvent was evaporated under reduced pressure.

(*R,R*$_S$)-2-(2-*tert*-Butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)propene (21). The oily residue obtained from **19e** was purified by column chromatography eluting with petrol/EtOAc 60:40 to give compound **21** as an oil (85% yield): ^{1}H NMR δ 5.82 (br s, H$_A$-1, *cis* to SO), 5.68 (br d, $J_{1'A,2'} = J_{1'B,2'} = J_{2',NH}$ 5.5, NH), 5.65 (br s, H$_B$-1, *trans* to SO), 4.64 (q, H-2′), 3.79 (s, OMe), 3.39 (AB dd, $J_{1'A,1'B}$ 13.4, H$_A$-1′), 3.12 (AB dd, H$_B$-1′), 1.99 (dd, $J_{1,3}$ 1.5 and 1.0, H$_3$-3), 1.45 (s, CMe$_3$); ^{13}C NMR δ 170.5 (*C*O$_2$Me), 155.1 (NHCO), 147.8 (C-2), 118.5 (C-1), 80.5 (*C*Me$_3$), 52.8 (C-2′), 52.7 (C-1′), 49.7 (OMe), 28.2 (C*Me*$_3$), 14.0 (C-3). Anal. Calcd for $C_{12}H_{21}NO_5S$: C 49.47, H 7.26, N 4.81. Found: C 49.35, H 7.38, N 4.80.

(*R,S*$_S$)-2-(2-*tert*-Butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)propene (23). The oily residue obtained from **20e** was purified by column chromatography eluting with petrol/EtOAc 60:40 to give compound **23** as an oil (87% yield): ^{1}H NMR δ 5.82 (br s, H$_A$-1, *cis* to SO), 5.80 (br d, NH), 5.65 (br s, H$_B$-1, *trans* to SO), 4.65 (dt, $J_{1'A,2'} = J_{2',NH}$ 7.8, H-2′), 3.79 (s, OMe), 3.29 (AB dd, $J_{1'A,1'B}$ 13.4, H$_A$-1′), 3.07 (AB dd, $J_{1'B,2'}$ 3.9, H$_B$-1′), 1.99 (dd, $J_{1,3}$ 1.5 and 1.0, H$_3$-3), 1.44 (s, CMe$_3$); ^{13}C NMR δ 170.8 (*C*O$_2$Me), 155.2 (NHCO), 147.8 (C-2), 118.1 (C-1), 80.3 (*C*Me$_3$), 52.8 (C-2′), 52.3 (C-1′), 50.2 (OMe), 28.2 (C*Me*$_3$), 14.2 (C-3). Anal. Calcd for $C_{12}H_{21}NO_5S$: C 49.47, H 7.26, N 4.81. Found: C 49.43, H 7.35, N 4.44.

(*R,S*$_S$)-(2-*tert*-Butoxycarbonylamino-2-methoxycarbonyl-ethylsulfinyl)ethene (22). The oily residue obtained from **20c** was purified by column chromatography. Elution with hexane/EtOAc 70:30 gave as first eluted the amino ester **5** (15% yield), followed by unreacted sulfoxide **20c** (50% yield). Finally, elution with hexane/EtOAc 50:50 led to the isolation of compound **22** (30% yield) as an oil: ^{1}H NMR δ 6.68 (dd, $J_{1,2A}$ 16.5, $J_{1,2B}$ 9.8, H-1), 6.16 (d, H$_A$-2, *cis* to SO), 6.02 (d, H$_B$-2, *trans* to SO), 5.69 (br d, $J_{1'A,2'} = J_{2',NH}$ 7.4, NH), 4.68 (dt, $J_{1'B,2'}$ 4.1, H-2′), 3.80 (s, OMe), 3.32 (AB dd, $J_{1'A,1'B}$ 13.4, H$_A$-1′), 3.13 (AB dd, H$_B$-1′), 1.45 (s, CMe$_3$); ^{13}C NMR δ 170.7 (*C*O$_2$-Me), 155.2 (NHCO), 140.4 (C-1), 122.6 (C-2), 80.6 (*C*Me$_3$), 54.6 (C-1′), 52.9 (C-2′), 50.1 (OMe), 28.2 (C*Me*$_3$). Anal. Calcd for $C_{11}H_{19}NO_5S$: C 47.64, H 6.91, N 5.05. Found: C 47.72, H 6.82, N 5.05.

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Supporting Information Available: X-ray crystallographic data of **20c** (details of data collection, structure refinement, crystal and unit-cell parameters, ORTEP view, tables of atomic coordinates and thermal parameters, bond lengths, bond angles, torsion angles, anisotropic displacement parameters) in PDF and CIF files (CCDC deposition number 245984). This material is available free of charge via the Internet at http://pubs.acs.org.

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