Simple And Efficient Cleavage Reaction of The Boc Group in Heterocyclic Compounds

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Dedicated to the memory of Pr. Ladjama Daif

A series of chiral *cyclosulfamides* have been synthesized by alkaline cyclisation starting from N-benzoyl-amino acids (Ala, Val, Leu, Phe) derivatives and chlorosulfonyl isocyanate. A simplified and regioselective deprotection of the cyclic compounds *(cyclosulfamides*) containing the *tert*-butyloxycarbonyl group (Boc) has been achieved in good yield by fusion under reduced pressure.

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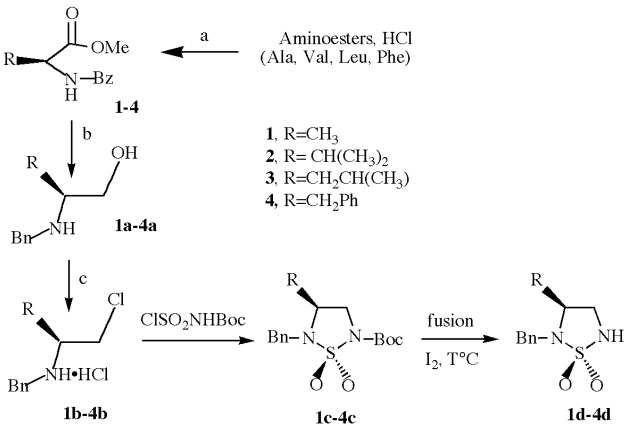
The selection of the protective group is an important step in synthetic methodology, and reports of new protective groups appear regularly. When a chemical reaction is to be carried out selectively at one reactive site in a multifunctional compound, other reactive sites must be temporarily blocked. A protective group must fulfil a number of requirements. It must react selectively in good yield to give a protected substrate that is stable to the projected reactions. The protective group must be selectively removed in good yield by readily available, preferably nontoxic reagents that do not attack the regenerated functional group. Among the large array of protecting groups, the *tert*-butyloxycarbonyl (Boc) substituent is considered to be one of the most useful. The Boc group is used extensively in peptide synthesis for amine protection [1]. This utility is clearly due to the ease of introducing and removing Boc and to the fact that it can be perfectly orthogonally associated with many other protecting groups.

The Boc group is not hydrolysed under basic conditions and is inert to many nucleophilic reagents [2-3]. The Boc derivatives are commonly prepared in 75-95% yield by treating the amine with $(Boc)_2O$ H_2O at 25 °C [4].

In literature, many methods for Boc cleavage have been reported [5-10]. The Boc group can be cleaved in HCl or trifluoroacetic acid, removed thermally, either neat (185 °C, 20-30 min) or in 10% H_2SO_4 in dioxane. Recently, we have reported the synthesis of new chiral N^2-Boc, N^5-Bn, 1,2,5-thiadiazolidines 1,1-dioxides that are natural amino acid derivatives [11-13]. These Chiral *cyclosulfamides* **1c-4c** (sulfa-analogues of cyclic ureas) have been synthesized in four steps starting from aminoesters (Ala, Val, Leu, Phe). We describe here the convenient, simple and efficient cleavage reaction of the Boc group from the N^2 position of a series of five membered cylosulfamides **1c-4c** by a new and rapid fusion method that proceeds under reduced pressure.

The preparation of chiral cyclosulfamides **1c-4c** has been performed starting from N-substituted Ala, Val, Leu, Phe.

Scheme



(a) BzCl, K_2CO_3, CH_3Cl ; (b) $LiAlH_4$, THF; (c) $SOCl_2$, CH_2Cl_2 .

Preparation of heterocyclic compounds and deprotection.

Benzoylation of the amino acids, followed by reduction using $LiAlH_4$, and chlorination using thionyl chloride gave the chiral 1-substituted N-benzyl 2-chloroethylamine hydrochlorides (substituted mustards) **1b-4b**. Under alkaline conditions the sulfonylation by *N*-Boc sulfamoyl chloride (using an excess of triethylamine in dichloromethane), spontaneously cyclized to give chiral N^5-Boc, N^2-Bn thiadiazolidine 1,1-dioxides **1c-4c**. The cyclosulfamides **1c-4c** with orthogonal protecting group can be independently remove under the appropriate conditions. The fusion method was used for Boc cleavage to give the deprotected chiral cyclosulfamides N^2-Bn thiadiazolidines **1d-4d** in 90-95% yield (see Scheme). The fusion method consisted of stirring the solution containing the cyclosulfamides **1c-4c** (0.3 mmol) in the presence of a catalytic quantity of iodine under reduced pressure. The structures of all compounds were unambiguously confirmed by ir, ^1H nmr and mass spectrometry. Cyclosulfamides **1c-4c** were characterized by ir --

spectroscopy based on the presence of characteristic bands at 1110-1170 cm^{-1} and 1340-1370 cm^{-1} for the sulfonyl group and by intense absorption at 1700-1710 cm^{-1} characteristic of the carbamate group. As expected, this latter signal was not present in the spectrum after cleavage. Deprotection was also verified by ^1H nmr based on the disappearance of signal corresponding to the *tert*-butyl protons.

Conclusion.

In this work, we have established the strategy described herein as an effective method for the selective deprotection and efficient cleavage reaction of the Boc group in heterocyclic cyclosulfamides. This method has the advantage that it requires a short length of time (5 min). The reaction proceeds without racemisation. These compounds are currently being evaluated for biological activity and for their use as tools in asymmetric synthesis and their incorporation in biomolecules. This method will be extended to acyclic compounds containing the Boc group and the results of those investigations will be reported in due course.

EXPERIMENTAL

All commercial chemicals and solvents were used as received. Meting points were determined in open tubes on a Büchi apparatus and are uncorrected. IR spectra were recorded on Pekin-Elmer spectrophotometer. Microanalysis were performed in ENSCM (Montpellier). Proton Nuclear Magnetic Resonance was determined with an AC 250 MHz Brüker spectrometer. Chemical shifts are recorded in ppm (δ) and coupling constants in hertz, relative to tetrametylsilane as internal standard. Multiplicity is indicated as s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet), and combination of these signals. Fast-atom bombardment mass spectra (FAB) were recorded in positive or negative mode on a JEOL DX 300 spectrometer with G, GT, or NOBA as matrix. Optical rotations, for solution in $CHCl_3$ were measured using a digital polarimeter POLAX model 2L. All reactions were monitored by Thin-Layer Chromatography (TLC) on silica gel Merck 60-F_{254} precoated aluminium plates and were developed by spraying with ninhydrine solution. Column chromatography was performed using Merck silica gel 60 (230-400 mesh) as stationary phase.

N-Benzoyl-aminoesters (**1-4**).

To a solution of aminoester hydrochloride (10 mmol) in $CHCl_3$ and an aqueous solution of K_2CO_3 2 *N* (25 mmol) in $CHCl_3$ (200 mL) was added dropwise benzoyl chloride (1.40 g, 10 mmol). The reaction medium was stirred vigorously and heated at reflux for 3 h. The reaction was quenched with water and the mixture was extracted twice with $CHCl_3$ (2x100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo* to afford *N*-benzoylaminoesters as white powder in quantitative yields.

N-Benzoyl-alanine Methyl Ester (**1**).

This compound was obtained in 98% yield; R_f=0.54 (CH_2Cl_2-MeOH, 95-5); Mp= 61-63 °C; $[\alpha]_D$=+25 (c=1, $CHCl_3$); ir (potassium bromide):ν cm^{-1}: 3225 (NH); 1745 and 1705 (C=O); ^1H nmr (deuteriochloroform): δ 7.76 (m, 5H), 5.50 (d, J=6.2 Hz, 1H), 4.10 (m, 1H), 3.80 (s, 3H), 1.25 (d, J=6.9 Hz, 3H); ms (NOBA, FAB>0): 208 [M+H]+, (M=207).

Anal. Calcd. for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.28; N, 6.76. Found: C, 63.71; H, 6.23; N, 6.72.

N-Benzoyl-valine Methyl Ester (**2**).

This compound was obtained in 97% yield; R_f=0,56 (CH_2Cl_2-MeOH, 95-5); Mp=95-97 °C, $[\alpha]_D$=-46 (c=1, $CHCl_3$); ir (potassium bromide): ν cm^{-1}: 3209 (NH); 1750 and 1710 (C=O); ^1H nmr (deuteriochloroform): δ 7.70 (m, 5H), 6.80 (d, J=8.5 Hz, 1H), 4.70 (m, 1H), 3.75 (s, 3H), 2.10 (m, 1H), 1.05 (2d, J=6.1 Hz, 6H); ms (NOBA, FAB>0): 236 [M+H]+, (M=235).

Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.38; H, 7.23; N, 5.95. Found: C, 66.40; H, 7.26; N, 5.92.

N-Benzoyl-leucine Methyl Ester (**3**).

This compound was obtained in 99% yield; R_f=0,60 (CH_2Cl_2-MeOH, 95-5); Mp= 80-82 °C; $[\alpha]_D$=+38 (c=1, $CHCl_3$); ir (potassium bromide): ν cm^{-1}: 3205 (NH); 1750 and 1710 (C=O); ^1H nmr (deuteriochloroform): δ 7.80 (m, 5H), 6.10 (d, J=8.2 Hz, 1H), 4.80 (m, 1H), 3.75 (s, 3H), 1.50 (m, 2H); 1.35 (m, 1H); 0.90 (d, 6H, J=6.1 Hz); ms (NOBA, FAB>0): 250 [M+H]+, (M=249).

Anal. Calcd. for $C_{14}H_{19}O_3N$: C, 67.46; H, 7.63; N, 5.62. Found: C, 67.43; H, 7.61; N, 5.61.

N-Benzoyl-phenylalanine Methyl Ester (**4**).

This compound was obtained in 99% yield; Rf=0,69 (CH_2Cl_2-MeOH, 95-5); Mp=81-83 °C; $[\alpha]_D$=+25 (c=1, $CHCl_3$); ir (potassium bromide): ν cm^{-1}: 3215 (NH); 1752 and 1712 (C=O); ^1H nmr (deuteriochloroform): δ 7.74-7.10 (m, 10H), 6.60 (d, J=6.2 Hz, 1H), 4.00 (m, 1H), 3.80 (s, 3H), 3.20-3.50 (2dd, J= 6.4, 6.1, 16.3 Hz, 2H); ms (NOBA, FAB>0): 284 [M+H]+, (M=283).

Anal. Calcd. for $C_{17}H_{17}NO_3$: C, 72.08; H, 6.00; N, 4.94. Found: C, 72.10; H, 6.05; N, 4.91.

N-Benzylaminoalcoohols (**1a-4a**).

A solution of *N*-benzoylaminoester (20 mmol) in anhydrous THF (20 mL) was added slowly to a mixture of lithium aluminium hydride (1.15 g, 30 mmol) in the same solvent (60 mL) and the medium was refluxed with stirring for 3 h. The reaction mixture was cooled on ice and the lithium aluminium complex was decomposed by the slow addition of THF-water (4:1, 20 mL). The resulting mixture was stirred for 1 h and then filtered through Celite®. The organic layer was dried (Na_2SO_4) and evaporated *in vacuo*. The residue was purified by flash chromatography eluted with dichloromethane.

N-Benzyl-alaninol (**1a**).

This compound was obtained in 87% yield; R_f=0,25 (CH_2Cl_2-MeOH, 95-5); oil; $[\alpha]_D$=-17 (c=1, $CHCl_3$); ir (film, CCl_4): ν cm^{-1}: 3320 (NH) and 3412 (OH); ^1H nmr (deuteriochloroform): δ 7.26 (m, 5H), 6.10 (m, 1H), 4.05 (d, J=6.15 Hz, 2H), 3.90-3.50 (2dd, J=3.9, 6.8 Hz, 2H), 2.70 (m, 1H), 2.00 (s, 1H), 1.25 (d, J=6.9 Hz, 3H); ms (NOBA, FAB>0): 166 [M+H]+, 91, (M=165).

Anal. Calcd. for $C_{10}H_{15}NO$: C, 72.72; H, 9.09; N, 8.48. Found: C, 72.74; H, 9.13; N, 8.51.

N-Benzyl-valinol (**2a**).

This compound was obtained in 88% yield; R_f=0,30 (CH_2Cl_2-MeOH, 95-5); oil; $[\alpha]_D$=+56 (c=1, $CHCl_3$); ir (film, CCl_4): ν cm^{-1}

3325 (NH) and 3430 (OH); ^{1}H nmr (deuteriochloroform): δ 7.34 (m, 5H), 5.80 (m, 1H), 4.00 (d, J=6.2 Hz, 2H), 3.80-3.30 (2dd, J= 3.8, 6.7 Hz), 2.80 (m, 1H), 2.30 (s, 1H), 2.10 (m, 1H), 0.95 (2d, J=6.7 Hz, 6H); ms (NOBA, FAB>0): 194 [M+H]+, 91, (M=193).

Anal. Calcd. for $C_{13}H_{21}NO$: C, 74.61; H, 9.84; N, 7.25. Found: C, 74.65; H, 9.87; N, 7.21.

N-Benzyl-leucinol (**3a**).

This compound was obtained in 84% yield; R_f=0.32 (CH_2Cl_2-MeOH, 95-5); oil; $[\alpha]_D$=+105 (c=1, $CHCl_3$); ir (film, CCl_4): ν cm^{-1}: 3320 (NH) and 3400 (OH); ^{1}H nmr (deuteriochloroform): δ 7.64 (m, 5H), 5.70 (m, 1H), 3.90 (d, J=6.2 Hz, 2H), 3.70-3.20 (2dd, J= 3.9, 6.7 Hz, 2H), 2.00 (s, 1H), 1.50 (m, 2H), 1.35 (m, 1H); 0.90 (d, J=6.1 Hz, 6H); ms (NOBA, FAB>0): 208 [M+H]+, 91, (M=207).

Anal. Calcd. for $C_{13}H_{21}NO$: C, 75.36; H, 10.14; N, 6.76. Found: C, 75.39; H, 10.16; N, 6.71.

N-Benzyl-phenylalaninol (**4a**).

This compound was obtained in 80% yield; R_f=0,28 (CH_2Cl_2-MeOH, 95-5); Mp =67-69°; $[\alpha]_D$=+55 (c=1, $CHCl_3$); ir (potassium bromide): ν cm^{-1}: 3315 (NH) and 3390 (OH); ^{1}H nmr (deuteriochloroform): δ 7.20 (m, 10H), 5.80 (m, 1H), 4.10 (d, J=6.2 Hz, 2H), 3.80-3.30 (2dd, J= 3.9, 6.7 Hz, 2H), 3.20-3.50 (ddd, J=6.4, 6.1, 16.3 Hz, 2H), 2.20 (s, 1H); ms (NOBA, FAB>0): 242 [M+H]+, 91, (M=241).

Anal. Calcd. for $C_{16}H_{19}NO$: C, 79.66; H,7.88; N, 5.80. Found: C, 79.69; H, 7.90; N, 5.75.

Substituted Mustards (**1b-4b**).

To a refluxing solution of *N*-benzylaminoalcohol (14.60 mmol) in $CHCl_3$ (50 mL) was slowly added a solution of thionyl chloride (60 mL, 126 mmol) in 30 mL of $CHCl_3$. When the addition was completed, the reflux was continued for 2 h. The reaction mixture was concentrated *in vacuo* to give the crude product as white powder in good yields.

N-Benzyl-*N*-(2-chloro-1-methylethyl)aminechlorhydrate (**1b**).

This compound was obtained in 60% yield; Mp =145-146 °C; $[\alpha]_D$=-17 (c=1, $CHCl_3$); ir (potassium bromide): ν cm-^{1}: 3275 (NH); ^{1}H nmr (deuteriochloroform): δ 7.26 (m, 5H), 6.10 (m, 1H), 4.10 (d, J=6.15 Hz, 2H), 3.70-3.50 (2dd, J=3.9, 6.8 Hz, 2H), 2.70 (m, 1H), 1.25 (d, J=6.9 Hz, 3H); ms (NOBA, FAB>0): 221 [M+H]+, 91, (M=220-222).

Anal. Calcd. for $C_{10}H_{15}Cl_2N$: C, 54.54; H, 6.81; N, 6.36. Found: C, 54.59; H, 6.85; N, 6.30.

N-Benzyl-*N*-(2-chloro-1-*iso*propylethyl)aminechlorhydrate (**2b**).

This compound was obtained in 58% yield; Mp=126-128 °C; $[\alpha]_D$=-27, (c=1, $CHCl_3$); ir (potassium bromide): ν cm-^{1}:3265 (NH); ^{1}H nmr (deuteriochloroform): δ 7.65 (m, 5H), 6.10 (m, 1H), 4.05 (d, J=6.15 Hz, 2H), 3.60-3.40 (2dd, J=3.9, 6.8 Hz, 2H), 2.65 (m, 1H), 2.10 (m, 1H), 0.95 (2d, J=6.7 Hz, 6H); ms (NOBA, FAB>0): 249 [M+H]+, 91, (M=248-250).

Anal. Calcd. for $C_{12}H_{19}Cl_2N$: C, 58.06; H, 7.66; N, 5.64. Found: C, 58.10; H, 7.71; N, 5.59.

N-Benzyl-*N*-(2-chloro-1-*iso*butylethyl)aminechlorhydrate (**3b**).

This compound was obtained in 58% yield; Mp =132-134 °C; $[\alpha]_D$=-142 (c=1, $CHCl_3$); ir (potassium bromide):ν cm-^{1}: 3274 (NH); ^{1}H nmr (deuteriochloroform): δ 7.45 (m, 5H), 5.80 (m, 1H), 3.90 (d, J=6.3 Hz, 2H), 3.50-3.30 (2dd, J=3.9, 6.8 Hz, 2H), 2.55 (m, 1H), 1.50 (m, 2H); 1.35 (m, 1H); 0.90 (d, 6H, J=6.1 Hz); ms (NOBA, FAB>0): 263 [M+H]+, 91, (M=262-264).

Anal. Calcd. for $C_{13}H_{21}Cl_2N$: C, 59.54; H, 8.01; N, 5.34. Found: C, 59.57; H, 8.03; N, 5.31.

N-Benzyl-*N*-(2-chloro-1-benzylethyl)aminechlorhydrate (**4b**).

This compound was obtained in 58% yield; Mp =145-147 °C; $[\alpha]_D$=-65 (c=1, $CHCl_3$); ir (potassium bromide): ν cm-^{1}: 3234 (NH); ^{1}H nmr (deuteriochloroform): δ 7.45 (m, 10H), 5.50 (m, 1H), 4.32 (d, J=6.3 Hz, 2H), 3.68-3.26 (2dd, J=3.9, 6.8 Hz, 2H), 2.55 (m, 1H), 3.20-3.50 (2dd, J=6.4, 6.1, 16.3 Hz, 2H), 2.95 (m, 1H); ms (NOBA, FAB>0): 297 [M+H]+, 91, (M=296-298).

Anal. Calcd. for $C_{16}H_{19}Cl_2N$: C, 64.86; H, 6.42; N, 4.73. Found: C, 64.90; H, 6.45; N, 4.68.

General Procedure for Preparation of N^2-Boc-N^5-benzyl-4-substituted-1,2,5-thiadiazolidine 1,1-Dioxides (**1c-4c**).

To a strirred solution of (5 mL, 8.15 g, 57.4 mmol) of chlorosulfonyl isocyanate (CSI) in 100 mL of anhydrous dichloromethane at 0 °C were added (4.24 g, 57.4 mmol) of absolute *tert*-butylalcohol in the same solvent. After being strirred for 30 min, the resulting solution of Boc-sulfamoyl chloride and 24 mL of triethylamine (17.40 g, 171.8 mmol) in 100 mL of dichloromethane was added drop wise to a 57.4 mmol solution of *N*-benzyl-4-chloroalkylamine hydrochlorides in 125 mL of dichloromethane. The reaction temperature did not rise above 5°C. The resulting solution was allowed to warm up to rt over 2 h. The reaction mixture was diluted with 100 mL of dichloromethane, washed with HCl 0.1 *N* solution and brine. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*, the residue was purified by flash chromatography. Elution with CH_2Cl_2/MeOH (95:5) gave cyclic sulfamides in 75-80% yield as colorless solids.

N^2-Boc-4-methyl-N^5-benzyl-1,2,5-thiadiazolidine 1,1-Dioxide (**1c**).

This compound was obtained in 77% yield; R_f=0,72 (CH_2Cl_2-MeOH, 95-5); Mp= 95-97°C; $[\alpha]_D$=+25 (c=1, $CHCl_3$); ir (potassium bromide): ν cm-^{1}:1708 (C=O); 1330 and 1150 (SO_2); ^{1}H nmr (deuteriochloroform): δ 7.40 (m, 5H), 4.30 (2d, J=15.2 Hz, 1H), 3.88 and 3.50 (2dd, J= 2.7, 5.6 Hz, 2H), 3.50 (m, 1H), 1.58 (s, 9 H), 1.25 (d, J=6.9 Hz, 3H); ms (NOBA, FAB>0): 327 [M+H]+, 226, 91, (M=326).

Anal. Calcd. for $C_{15}H_{22}N_2O_4S$: C, 55.21; H, 6.75; N, 8.59. Found: C, 55.30; H, 6.73; N, 8.51.

N^2-Boc-4-isopropyl-N^5-benzyl-1,2,5-thiadiazolidine 1,1-Dioxide (**2c**).

This compound was obtained in 75% yield; R_f=0,72 (CH_2Cl_2-MeOH, 95-5); Mp =82-84°C; $[\alpha]_D$=+5 (c=1, $CHCl_3$); ir (potassium bromide): ν cm-^{1} 1710 (C=O); 1340 et 1160 (SO_2) ^{1}H nmr (deuteriochloroform): δ 7.40 (m, 5H), 4.30 (dd, J=14.6 Hz), 3.90–35.50 (2dd, J= 3.2, 6.7 Hz, 1H), 3.50 (m, 1H), 1.58 (s+m, 10 H), 0.97-1.05 (2d, J= 6.9 Hz, 6H); ms (NOBA, FAB>0): 355 [M+H]+, 91, 254, (M=354).

Anal. Calcd. for $C_{17}H_{26}N_2O_4S$: C, 57.62; H,7.34; N, 7.91. Found: C, 57.55; H, 7.41; N, 7.85.

N^2-Boc-4-*iso*butyl-N^5-benzyl-1,2,5-thiadiazolidine 1,1-dioxide (**3c**).

This compound was obtained in 78% yield; R_f=0,69 (CH_2Cl_2-MeOH, 95-5); Mp = 87-89 °C; $[\alpha]_D$=-3 (c=1, EtOH); ir (potassium

bromide): ν cm1: 1708 (C=O); 1345 and 1165 (SO_2); ^{1}H nmr (deuteriochloroform): δ 7.35 (m, 5H, ArH); 4.30 (dd, 2H, J=15.2 Hz); 3.80 (m, 1H); 3.50 (m, 2H), 1.60 (m, 2H), 1.50 (m, 2H), 1.35 (m, 1H), 0.90 (2d, J=6.1Hz, 6H); ms (NOBA, FAB>0): 369 [M+H]+, 91, 268, (M=368).

Anal. Calcd. for $C_{18}H_{28}N_2O_4S$: C, 58.69; H, 7.61; N, 7.61; Found: C, 58.67; H, 7.52; N, 7.55.

*N*2-Boc-*N*5-4-dibenzyl-1,2,5-thiadiazolidine 1,1-Dioxide (**4c**).

This compound was obtained in 77% yield; R_f-0.72 (CH_2Cl_2-MeOH, 95-5); Mp=103-105 °C; $[\alpha]_D$=-30 (c=1, $CHCl_3$); ir (potassium bromide): ν cm-1: 1710 (C=O); 1335 and 1150 (SO_2); ^{1}H nmr: (deuteriochloroform): δ 7.30 (m, 10H), 4.25 (2d, J=15.2 Hz, 2H), 3.65 (dd, J=7.5, 6.7 Hz, 1H), 3.50 (m, 1H), 3.20-3.50 (2dd, J= 6.4, 6.1, 16.3 Hz, 2H), 1.58 (s, 9 H); ms (NOBA, FAB>0): 403 M+H]$^+$, 302, 91, (M=402).

Anal. Calcd. for $C_{21}H_{26}N_2O_4S$: C, 62.68; H, 6.47; N, 6.96. Found: C, 62.61; H, 6.41; N, 6.93.

Deprotection.

General Procedure for the Synthesis of Cyclosulfamides (**1d-4d**).

Compounds **1c-4c** were heated in fusion with 0.4% iodine *in vacuo* (20 mmHg) for 10 min. The resulting residue was purified by column chromatography (eluent: dichloromethane) to give **1d-4d** in good yields.

*N*2-Benzyl-3-methyl-1,2,5-thiadiazolidine 1,1- Dioxide (**1d**).

This compound was obtained in 95% yield; R_f= 0.62 (CH_2Cl_2-MeOH, 95-5); Mp = 100-102 °C; $[\alpha]_D$ = -18 (c=1, $CHCl_3$; ir (potassium bromide): ν cm^{-1} : 3267 (NH); 1332 and 1153 (SO_2); ^{1}H nmr**:** (deuteriochloroform): δ 7.40 (m, 5H), 4.75 (t, J= 9.6 Hz,1H); 4.30 (dd, J= 15.2 Hz), 3.62 (m, 2H), 3.50 (m, 1H), 1.25 (d, J=6.9 Hz, 3H); ms (NOBA, FAB>0): 227 [M+H]$^+$, 91, (M=226).

Anal. Calcd. for $C_{10}H_{14}N_2O_2S$: C, 53.09; H, 6.19; N, 12.39. Found: C, 53.00; H, 7.41; N, 12.31.

*N*2-Benzyl-3-*iso*propyl-1,2,5-thiadiazolidine 1,1-Dioxide (**2d**).

This compound was obtained in 96% yield; R_f = 0.62 (CH_2-MeOH 95-5); Mp = 104-106 °C; $[\alpha]_D$= +23° (c=1, $CHCl_3$); ir (potassium bromide): ν cm^{-1}: 3252 (NH); 1345 and 1165 (SO_2); ^{1}H nmr (deuteriochloroform): δ 7.40 (m, 5H), 4.85 (t, J=9.6 Hz, 1H), 4.40 (m, 1H); 3.60 (ddd, J=6.2, 5.9, 6.3 Hz, 1H); 3.35 (2d, J=15 Hz, 2H), 3.20 (ddd, J=6.2, 5.9, 6.3 Hz, 1H), 2.25 (m,1H), 0.95 (2d, J= 6.9 Hz, 6H); ms: (FAB>0, NOBA): 255 [M+H]$^+$, 91, (M=254).

Anal. Calcd. for $C_{12}H_{18}N_2O_2S$: C, 56.69; H, 7.08; N, 11.02; Found: C, 56.47; H,7.14; N, 10.95.

*N*2-Benzyl-3-*iso*butyl-1,2,5-thiadiazolidine 1,1-Dioxide (**3d**).

This compound was obtained in 92% yield; R_f=0,60 (CH_2Cl_2-MeOH 95-5); Mp=117-119 °C; $[\alpha]_D$= +3° (c=1, $CHCl_3$); ir (potassium bromide): ν cm^{-1} : 3245 (NH); 1345 and 1165 (SO_2) cm^{-1}. ms (NOBA,FAB>0): 269 [M+H]$^+$, 91; ^{1}H nmr **:** (deuteriochloroform): δ 7.35 (m, 5H), 4.75 (t, J= 9.6 Hz,1H), 3.60 (m, 2H); 3.50 (m, 1H); 3.45 (m, 2H), 1.50 (m, 2H), 1.35 (m, 1H), 0.90 (d, 6H, J=6.2 Hz).

ms: (NOBA, FAB>0): 269 [M+H]$^+$, 91, (M=268).

Anal. Calcd. for $C_{13}H_{20}N_2O_2S$: C, 58.21; H,7.46; N, 10.45; Found: C, 58.31; H, 7.53; N, 10.41.

N^2,3-Dibenzyl-1,2,5-thiadiazolidine 1,1 dioxide (**4d**).

This compound was obtained in 93% yield; R_f=0,52 (CH_2-Cl_2); Mp = 97-98°C; $[\alpha]_D$= -23° (c=1, $CHCl_3$); ir (potassium bromide): ν cm^{-1} :3264 (NH); 1345 and 1165 (SO_2); ^{1}H nmr (deuteriochloroform): δ 7.40 (m, 10H), 4.85 (t, J= 9.6 Hz, 1H), 4.40 (m, 1H), 3.60 (m, 2H), 4.35 (dd, J=15.2 Hz, 2H), 3.15 (ddd, J=6.2, 5.9, 16.3 Hz, 1H); ms: (NOBA, FAB>0): 303 [M+H]$^+$, 91, (M=302).

Anal. Calcd. for $C_{16}H_{18}N_2O_2S$: C, 63.36; H, 5.96; N, 09.27; Found: C, 63.41; H, 5.92; N, 9.29.

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