Tetrahedron Vol. 47, No. 38, pp. 8145-8154, 1991
Printed in Great Britain

0040-4020/91 $3.00+.00
Pergamon Press plc

The TDE Sulfenyl Group as a Protective Group for Amines [1]

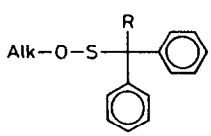
Thomas Netscher [2]* and Thomas Weller [3]

Chemisches Laboratorium der Universität Freiburg, Albertstr. 21, D-7800 Freiburg i. Br., FRG

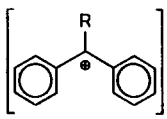
(*Received in Germany* 18 *July* 1991)

Abstract.- Various primary and secondary amines were transformed into their 2,2,2-trifluoro-1,1-diphenylethane- (TDE-) sulfenamides **5** in high yields. Efficient methods for cleavage and properties of these new derivatives are also described.

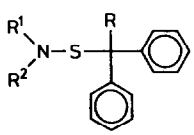
1. Introduction. In the course of a project, the aim of which was to synthesize sterically crowded sulfonate esters [4-7], we realized that 2,2,2-trifluoro-1,1-diphenylethane- (TDE-) sulfenic esters **1** are significantly more stable to acidic conditions than the corresponding trityl derivatives **2**, due to the drastically different formation tendencies of the destabilized carbocation **3** [8] and the triphenylmethyl (trityl) cation **4**.



1 R = CF_3
2 R = C_6H_5



3 R = CF_3
4 R = C_6H_5

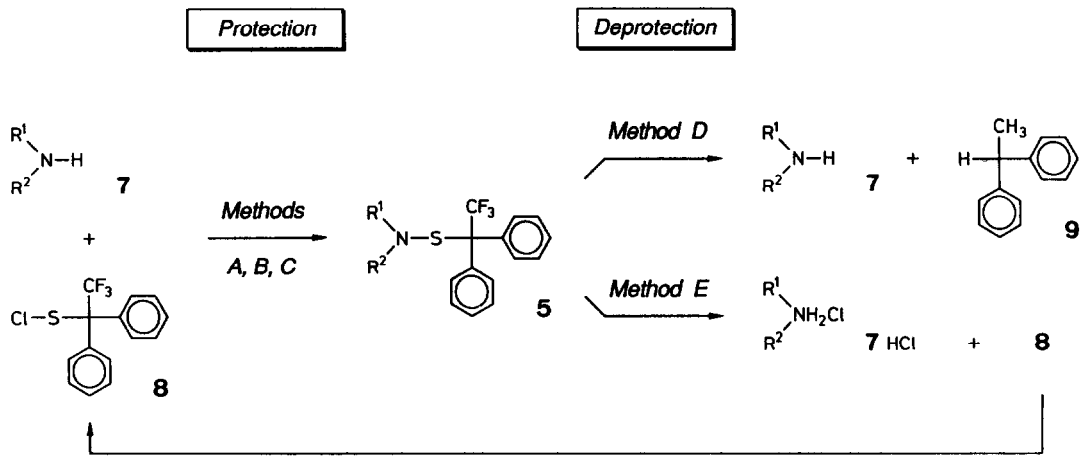


5 R = CF_3
6 R = C_6H_5

Since the tritylsulfenyl group is known to be useful protective group for primary and secondary amines [9], we investigated whether TDE sulfenamides **5** have also a stability different from tritylsulfenamides **6** which could offer the applicability of **5** to *N*-protection. Our results indicate that, in comparison to the great many other nitrogen protective groups [10], the TDE sulfenyl moiety possesses a set of properties which may provide a contribution to this synthetic arsenal.

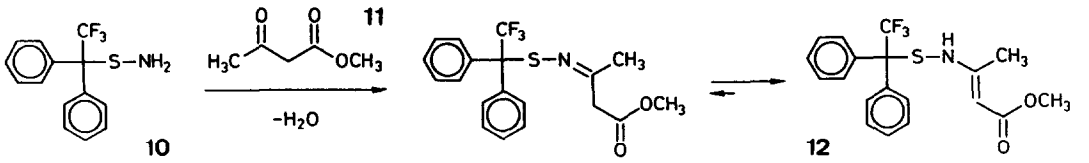
2. Protection. Different primary and secondary amines **7** [11] (*Scheme 1* and *Table 1*) were treated with TDE sulfenyl chloride **8** (which was synthesized from methyl trifluoroacetate in 75% overall yield [6]) at room temperature in the presence of triethylamine or sodium carbonate as a

base, in either a two-phase (*Method A*) or a homogeneous system (*Method B*). In the case of inexpensive reactants (**7g,h**), a twofold excess of the amine was used instead of the addition of an external base. Very rapid reaction (within seconds) accompanied by simultaneous decolourization of yellow **8** with **7** afforded the sulfenamides **5a-k** in yields of nearly 100% [4,12]. Because of the reduced basicity of the sulfenyl nitrogen, the products can be purified easily from an excess of amine(s) by an extractive workup with aqueous acid.



Scheme 1. *Method A*. Na_2CO_3, THF/ H_2O, r.t. - *Method B*. NEt_3, CH_2Cl_2, r.t. - *Method C*. Suspension of the amino acid in *N*-methylimidazole. - *Method D*. 20 equiv. Na, NH_3 (liq.), -78°C → r.t. - *Method E*. 4 equiv. HCl/ Et_2O, r.t.

Free amines, as well as amine hydrochlorides (e.g. *(+)*-3-aminomethylpinane hydrochloride, **7a**·HCl; 1-aminoadamantane hydrochloride, **7b**·HCl) can be used as starting materials. Because acid chloride **8** does not react with alcohols or water under the conditions employed, water-containing amines (**7k**) can be used, and compounds comprising hydroxyl groups (aminocyclohexanol, **7d**, R = H; *(-)*-ephedrine, **7k**) are derivatized only at the nitrogen atom. No precautions are necessary to exclude moisture from the reaction mixtures. In all instances of primary amines, only one N-H is sulfenylated. Compound **5h** derived from imidazole (**7h**) may be of interest with regard to the importance of substituted imidazoles in biological systems [13]. As shown with L-phenylalanine (**7m**), aminocarboxylic acids can also be *N*-protected in high yield, although a much longer reaction time is required for the formation of **5m** by stirring the suspension of the α-amino acid with **8** in *N*-methylimidazole (*Method C*). In contrast to these syntheses starting from the amines and the new protection reagent **8** presented, the vinylogous ester-sulfenamide **12** was prepared by the condensation reaction of methyl acetoacetate (**11**) with the sulfenamide **10** [6].



3. Deprotection. The TDE sulfenamides **5** are cleaved either under reducing or under acidic conditions (*Scheme 1* and *Table 1*). The amines **7** are liberated by the addition of the dissolved substrates to a solution of sodium in liquid ammonia at -78°C, followed by quenching with ammonium fluoride and warming up to room temperature (*Method D*). Where problems were encountered with the isolation of volatile (piperidine, **7g**) or water-soluble amines (imidazole, **7h**) by conventional extraction, no attempts were made to use special methods (e. g., formation of other derivatives, or extraction by ion-exchanged zeolithes under neutral conditions [14]). Total conversion of the starting materials was corroborated in all cases by the quantitative isolation of 1,1-diphenylethane (**9**) originating from the TDE sulfenyl moiety. Each S-N, C-S, and C-F bond consumes two gram equivalents of sodium.

Whereas TDE sulfenamides **5** are reasonably stable towards aqueous acid (see below), deprotection is also accomplished by anhydrous HCl in etheral solution upon standing for several hours at room temperature (*Method E*). The crystalline amine hydrochlorides (exception **7l**·HCl) and dihydrochlorides (**7f**·2 HCl), respectively, were isolated by simply filtering off in generally high yield. Crude sulfenyl chloride **8** is recovered from the filtrate quantitatively (87-91% after crystallization, not optimized).

4. Properties and Stability of TDE Sulfenamides 5. The air-stable, often crystalline sulfenamides **5** (*Table 1*) are highly soluble in apolar organic solvents due to their lipophilic TDE moiety, which also enables the TLC detection by UV-light and the use of ^{19}F-NMR spectroscopy. Our derivatives are stable to chromatography on silica gel and are able to withstand a variety of synthetically useful conditions (*Table 2*). Compared to the corresponding tritylsulfenamides **6** [9], TDE sulfenamides **5** show a higher resistance to aqueous acid (*entries 1, 2* [15]) and to anhydrous cupric salts at room temperature (*entry 18*). No detectable deprotection was found in strongly alkaline medium (*entry 4*). Exposure to diverse reducing agents (*entries 5-17*) results in evident decomposition only under forced conditions (*entries 11, 12, 15*). The decreased nucleophilicity of the *N*-atom protects them from acetylation (*entry 20*).

For example, the TDE sulfenyl group was applied by *Prinzbach and coworkers* during their studies of the total synthesis of aminoglycoside antibiotics [11,12,16] (*Scheme 2*). In the coupling reaction starting from glucal **13** by the NOCl method [17], aglycon **5e** showed some advantages over substrates containing either the NH-phenylethyl, NH-Cbz [18], NH-Fmoc [19], or Ox [20] group. The glycoside **14** was deblocked subsequently to **15**→**16** by selective reducing agents as illustrated in *Scheme 2* and *Table 2*.

Table 1. Formation and Cleavage of TDE Sulfenamides **5** According to *Scheme 1.*

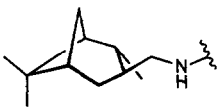
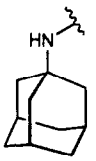
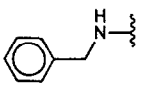
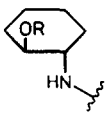
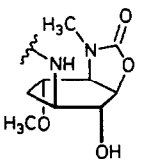
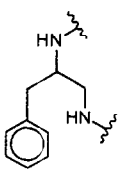
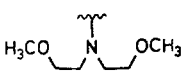
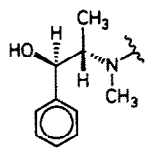
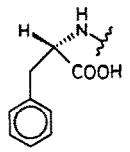
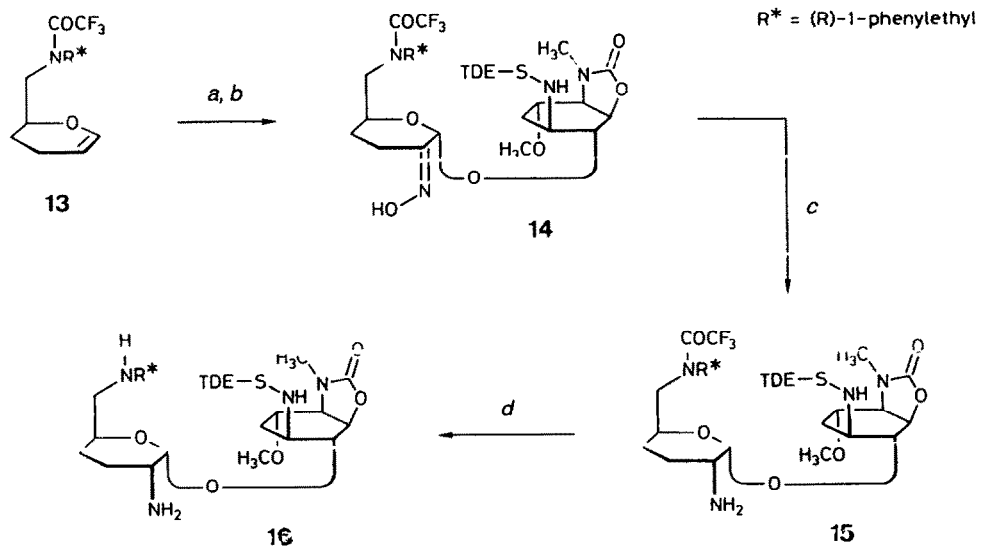
	7/5	7→5		m.p. 5	5→7	
		Method[a]	Yield (%)[b]	(°C)	Method[a]	Yield (%)[b]
a		A	96[c]	between 0 and -30°C	D	94
					E	95[d]
b		A	95[e]	101	D	67
					E	95[d]
c		A	95[c]	oil	D	---[f]
					E	93[d]
d	 R = H R = CH_2OCH_3	A	≈100[g]	oil	---	
					D	>90[h]
					E	80[d,h]
e[11]		A	≈100[g]	135	D	---[i,k]
					E	95[d]
f		B	87[c]	glass	E[m]	95[n]
g		B	94[e]	42	D	n.d.[i,p]
					E	86[d]
h		B	95[e]	96	D	n.d.[i,q]
					E	93[d]
i		B	96[e]	30-32	D	70
					E	95[r]

Table 1 (continued).

	7/5	7→5 Method[a]	7→5 Yield (%)[b]	m.p. 5 (°C)	5→7 Method[a]	5→7 Yield (%)[b]
k		B	96[c]	glass	E	98[d]
m		C	96[g]	glass	E	91[d]

[a] See *Scheme 1*. [b] Not optimized. [c] After chromatography. [d] Isolated as hydrochloride. [e] After crystallization. [f] Partial cleavage of the benzyl-CH_2-S bond. [g] Crude material. [h] Deacetalization of the MOM group by HCl during workup, alcohol isolated (R = H). [i] Not determined, complete deprotection based on isolated **9**. [k] Partial opening of the oxazolidinone ring. [m] 10 equiv. HCl used. [n] Bis-hydrochloride. [p] Highly volatile amine not isolated. [q] Water-soluble amine not isolated. [r] Oily hydrochloride isolated.



Scheme 2. *a)* NOCl. - *b)* **5e**. - *c)* $NaBH_4$/ MoO_3, MeOH, r.t., 3 h. - *d)* $NaBH_4$, EtOH, r.t.

Table 2. Reactivity of TDE Sulfenamides to Different Conditions.

Entry	Substrate	Reaction Conditions	Result
1	**5b**	1 N HCl (aq.)/ THF 3:1, room temp., 48 h	93% **5b** recovered
2	**5c**	1 N HCl (aq.)/ THF 3:1, room temp., 20 h [15]	92% **5c** recovered
3	**5c**	57% HI (aq., 2.2 equiv.)/ EtOH, room temp., 5 min	79% **7c**
4	**5b**	1 N NaOH (EtOH), room temp., 5 h	96% **5b** recovered
5	**15**	$NaBH_4$, EtOH, room temp.	84% **16** (overall from **14**, see below, and *Scheme 2*)
6	**14**	$NaBH_4$ / MoO_3, MeOH, room temp., 3 h [21]	**15** (see above)
7	**5e**	same conditions	no reaction
8	**5d**, R = MOM; **5e**	$NaBH_4$/ $NiCl_2$, Et_2O/ MeOH, room temp. [22]	no reaction
9	**5b**	$LiAlH_4$, Et_2O, 0°C, 1 h	no reaction
10	**5b**	$LiAlH_4$, Et_2O, room temp., 3 h	80% **5b** recovered; odour of H_2S
11	**5c**	$LiAlH_4$, THF, reflux, 5 h	>50% **5c** recovered
12	**5d**, R = H	$LiAlH_4$/ $TiCl_4$, THF, room temp. [23]	complex mixture
13	**5b**/ **5d**, R = H, MOM	n-Bu_3SnH (1.5 equiv.)/ AIBN, toluene, 90°C, 3 h	95% **5b**/ >90% **5d** recovered
14	**5d**, R = MOM	Raney-Ni (column), room temp. [24]	no reaction
15	**5d**, R = MOM	Raney-Ni, EtOH, reflux, 4 h	complete decomposition
16	**5e**	Pd/ C, H_2, H^+, MeOH, room temp. [11,25]	no reaction
17	**5e**	$Pd(OH)_2$, H_2, room temp. [26]	no reaction
18	**5d**, R = H	$CuCl_2$, THF/ EtOH, room temp., 48 h [9]	95% **5d** recovered
19	**5d**, R = H	$CuCl_2$, THF/ EtOH, reflux	decomposition
20	**5d**, R = H	Ac_2O/ pyridine, room temp, 24 h	88% **5d**, R = Ac; no N-Ac found

5. Conclusion. The TDE sulfenyl group applicable to the protection of amines has been shown to be introduced and removed under mild conditions by simple procedures. TDE sulfenyl chloride **8** can be recycled from this sequence thus satisfying the criterium of an ideal protecting reagent. The TDE sulfenamides **5** are stable and highly soluble compounds, possess a relatively nonbasic and non-nucleophilic *N*-atom, and are sufficiently robust to survive exposure to various reagents. In particular, they are significantly more stable to acidic conditions than the analogous trityl derivatives **6** [9].

6. Experimental

General. Elemental analyses: Analytische Abteilung des Chemischen Laboratoriums Freiburg i. Br.- Infrared Spectra: Perkin Elmer 457 Grating Infrared Spectrophotometer.- ^{1}H-NMR spectra: Bruker WM 250, Varian EM 390; internal standard tetramethylsilane; unless otherwise noted, 250 MHz data are given for $CDCl_3$ solutions.- MS (EI, 70 eV): Finnigan MAT 44 S.- Chromatography: TLC on thin layer plates silica gel 60 F_{254} (Merck); column chromatography on silica gel 60, particle size 0.063-0.2 mm (Macherey-Nagel).- Melting points: Monoskop IV from Bock, Frankfurt, and apparatus by Tottoli from Büchi, Flawil.

Method A (Protection of Amines by Using Na_2CO_3). A solution of 1.51 g (5.0 mmol, 1.0 equiv.) of TDE sulfenyl chloride **8** in 5 ml of THF is dropped to a stirred mixture of 5.0 mmol amine **7** in 20 ml of THF and 1.06 g (10.0 mmol) of Na_2CO_3 in 20 ml of H_2O [or multiple amounts, if amine hydrochlorides are used]. After stirring for 5 min, H_2O and Et_2O (30 ml each) are added. The org. layer is washed subsequently with 10% H_2SO_4, H_2O, and saturated $NaHCO_3$ solution, dried ($MgSO_4$), and evaporated to dryness *in vacuo*. The crude products **5** (ca. 100%) are purified by crystallization or chromatography.

Method B (Protection of Amines by Using NEt_3). A solution of 1.51 g (5.0 mmol, 1.0 equiv.) TDE sulfenyl chloride **8** in 5 ml of CH_2Cl_2 is dropped at 0°C into a solution of the amine **7** and 1.04 ml (7.5 mmol, 1.5 equiv.) of NEt_3 in 10 ml of CH_2Cl_2 [in the case of hydrochlorides/ polyamines, multiple equiv. of NEt_3; in the synthesis of **5g,h**, 15.0 mmol (3.0 equiv.) of the amine was used instead of the addition of NEt_3]. After completion of the addition (decolourization and recipitation of amine hydrochloride) and stirring for 5 min, the reaction mixture is diluted with 30 ml of CH_2Cl_2 [or more if necessary because of large amounts of salt], and the products are isolated as described above.

Method C (Protection of Aminocarboxylic Acids). To the suspension of 6.0 mmol of the aminocarboxylic acid in 20 ml of *N*-methylimidazole are added 1.82 g (6.0 mmol, 1.0 equiv.) of TDE sulfenyl chloride **8**. The mixture is stirred for 16 h at room temp., poured onto 300 ml of 4 N H_2SO_4, and extracted with CH_2Cl_2 (2x100 ml). Drying ($MgSO_4$) and evaporating the solvent yields 96-99% crude product.

Method D (Cleavage of Sulfenamides by Na/NH_3). (Feasible only for amines which are able to be extracted from water.) All glassware is dried at 120°C overnight under N_2. The solution of 0.5 mmol **5** in 2 ml THF (freshly distilled from Na/ benzophenone) is added by a syringe to the solution of 0.23 g (10.0 mmol, 20.0 mol equiv.) Na in 10-15 ml of NH_3 (dried over KOH and condensed at -78°C). The reaction mixture is stirred vigorously for 2 h, and the excess of Na is destroyed by quenching with NH_4F (NH_4Cl may also be used). After evaporation of NH_3 at room temp., the residue is taken up with a minimum of water and extracted with ethyl acetate or CH_2Cl_2. The crude amine **7** is obtained after drying ($MgSO_4$) and evaporating under reduced pressure.

Method E (Cleavage of Sulfenamides by dry HCl). 4.0 equiv. (**5f**: 10.0 equiv.) HCl (as a ca. 0.8 N etheral solution) are added to the solution of 0.5 mmol TDE sulfenamide **5** in 5-10 ml of Et_2O. After completion of the reaction (0.2-16 h; TLC), the amine hydrochloride **7**·HCl is isolated by suction filtration, washed with Et_2O and dried. The reagent **8** is recovered (≈ quant.) from the yellow filtrate by evaporating the solvent, and crystallized from petroleum ether (30-50°C) at -70°C (87-91%).

N-*[[(1S,2R,3R,5S)-2,6,6-Trimethylbicyclo[3.1.1]hept-3-yl]methyl]-2,2,2-trifluoro-1,1-diphenylethanesulfenamide* (**5a**). From *(+)*-3-aminomethylpinane hydrochloride (**7a**·HCl), *Method A*. TLC, petroleum ether 30-50°C: R_F(**7a**) 0.0, R_F(**8**) 0.70, R_F(**5a**) 0.63. After chromatography (silica gel 45/ 3 cm

for 5 mmol, same solvent) 96% colourless oil, m.p. between 0 and -30°C.- IR (film, NaCl): 3380, 2900, 1495, 1440, 1250, 1150, 690 cm^{-1}.-^{1}H-NMR: δ = 7.43-7.34 (m, 4 H, o-H_{arom}), 7.32-7.23 (m, 6 H, m-,p-H_{arom}), 2.55-2.42 (m, 2 H), 2.32 (mc, 1 H), 2.18 (mc, 1 H, J = 2.0 Hz), 1.84-1.74 (m, 2 H), 1.65 (mc, 1 H, J = 2.0 Hz), 1.59-1.42 (m, 1 H), 1.38-1.24 (m, 1 H, J = 2.0 Hz), 1.17-1.06 (m, 1 H), 1.14 (s, 1 CH_3), 0.91 (s, 1 CH_3), 0.88 (d, 1 CH_3, J = 7.5 Hz).- $C_{25}H_{30}F_3NS$ (433.6): Calc. C 69.26, H 6.97, N 3.23, S 7.40, Found C 69.22, H 6.98, N 3.14, S 7.59.

N-*(Tricyclo[3.1.1.13,7]dec-1-yl)-2,2,2-trifluoro-1,1-diphenylethanesulfenamide* (**5b**). From 1-aminoadamantane (**7b**), or its hydrochloride, *Method A*. TLC, petroleum ether 30-50°C/ ether (20:1): R_F(**7b**) 0.0, R_F(**8**) 0.74, R_F(**5b**) 0.75. After crystallization from petroleum ether 30-50°C (5 ml for 5 mmol) at -70°C 95% colourless crystals, m.p. 101°C.- IR (KBr): 2895, 1490, 1440, 1245, 1135, 685 cm^{-1}.-^{1}H-NMR: δ = 7.44-7.34 (m, 4 H, o-H_{arom}), 7.33-7.25 (m, 6 H, m-,p-H_{arom}), 2.58 (br.s, NH), 1.88 (mc, 3 H), 1.50 ("d", 3 H, J = 12.0 Hz), 1.40 ("d", 3 H, J = 12.0 Hz), 1.21 (d, 6 H, J = 3.0 Hz).- $C_{24}H_{26}F_3NS$ (417.5): Calc. C 69.04, H 6.28, N 3.35, S 7.68, Found C 69.27, H 6.22, N 3.32, S 7.68.

N-*Benzyl-2,2,2-trifluoro-1,1-diphenylethanesulfenamide* (**5c**). From benzylamine (**7c**), *Method A*. TLC, petroleum ether 30-50°C/ ether (20:1): R_F(**5c**) 0.55. After chromatography (silica gel 25/ 2.5 cm for 3 mmol, same solvent) 95% colourless oil.- IR (film, NaCl): 3370, 3055, 3020, 1490, 1440, 1250, 1150, 690 cm^{-1}.-^{1}H-NMR: δ = 7.46-7.35 (m, 4 H, TDE o-H_{arom}), 7.32-7.21 (m, 6 H, TDE m-,p-H_{arom}), 7.20-7.11 (m, benzyl. m-,p-H_{arom}), 6.95 (mc, benzyl o-H_{arom}), 3.54 (d, α-CH_2), 2.64 (t, NH); $J_{\alpha,NH}$ = 6.0 Hz.- $C_{21}H_{18}F_3NS$ (373.4): Calc. C 67.54, H 4.86, N 3.75, S 8.59, Found C 67.29, H 4.86, N 3.62, S 8.81.

(1α,2β)-2-(2,2,2-Trifluoro-1,1-diphenylethylsulfenyl)aminocyclohexan-1-ol (**5d**, *R = H*). From 1-aminocyclohexan-2-ol (**7d**, R = H), *Method A*. ≈100% yellowish oil, characterized as its acetate **5d**, R = Ac: after chromatographic purification (silica gel, ethyl acetate/ cyclohexane 2:1) colourless syrup.- IR (CCl_4): 3350, 2930, 1725, 1245, 1140, 1030, 905, 695 cm^{-1}.-^{1}H-NMR: δ = 7.49-7.22 (m, 10 H_{arom}), 4.28 (ddd, CH-O), 2.72 (d, NH), 2.24 (mc, CH-N), 1.94 (s, CH_3), 1.86-1.44 (m, 5-,6-H), 1.18-0.67 (m, 3-,4-H).- $C_{22}H_{24}F_3NO_2S$ (423.5): Calc. C 62.40, H 5.71, N 3.31, Found C 62.19, H 5.65, N 3.20.

D,L-*(1α,2β,3β,4α,6β)-2-O,3-N-Carbonyl-4-O-methyl-3-(methylamino)-6-(2,2,2-trifluoro-1,1-diphenylethylsulfenyl)aminocyclohexan-1,2,4-triol* (**5e**) From the racemic amine **7e**[11], *Method A*. Evaporation of the solvent afforded **5e** as a colourless oil (≈100%) which crystallized on trituration with a small amount of ether. After chromatography (silica gel, ethyl acetate/ cyclohexane 2:1) colourless crystals, m.p. 135°C.- IR (KBr): 3520, 3420, 3300, 2880, 1750, 1390, 1255, 1135, 1005, 715 cm^{-1}.-^{1}H-NMR: δ = 7.50-7.20 (m, 10 arom. H), 4.24 (t, 2-H), 3.60 (dd, 3-H), 3.48 (mc, 4-H), 3.33 (s, OCH_3), 3.22 (q, 1-H), 2.91 (d, NH), 2.78 (s, NCH_3), 2.61 (mc, 6-H), 2.47 (d, OH), 1.93 (mc, 5β-H), 1.26 (mc, 5α-H); $J_{1,2}$ = 7.5, $J_{1,6}$ = 7.0, $J_{2,3}$ = 7.5, $J_{3,4}$ = 3.0, $J_{3,5\alpha}$ = 1.2, $J_{4,5\alpha}$ = 10.0, $J_{5\alpha,5\beta}$ = 14.0, $J_{5\alpha,6}$ = 3.0, $J_{5\beta,6}$ = 10.0, $J_{6,NH}$ = 6.0 Hz.- $C_{23}H_{25}F_3N_2O_4S$ (482.5): Calc. C 57 25, H 5.22, N 5.81, Found C 57 17, H 5.44, N 5.72.

*1,2-Diamino-*N,N'*-bis(2,2,2-trifluoro-1,1-diphenylethylsulfenyl)-3-phenylpropane* (**5f**). From 1,2-diamino-3-phenylpropane (**7f**), *Method B*. TLC, hexane/ ethyl acetate (9:1): R_F(**7f**) 0.0, R_F(**8**) 0.48, R_F(**5f**) 0.26. After chromatography (silica gel, hexane/ ethyl acetate 97:3) 87% colourless oil, solidifying as a glass.- IR (KBr): 3375, 3050, 1495, 1255, 1155, 695 cm^{-1}.- ^{1}H-NMR (90 MHz): δ = 7.71-6.77 (m, 25 arom. H), 2.59-1.73 (m, 5 aliph. H, 2 NH).- MS: *m/e* = 591 (M^+ -C_7H_7, 1%), 447 (M^+ -TDE, 3), 386 (M^+ -$CH_2NHSTDE$, 14), 267 (12), 235 ($(C_6H_5)_2(CF_3)C^+$, 38), 215 (30), 183 (13), 166 (26), 165 (fluorenyl$^+$, 100), 91 ($C_7H_7^+$, 24) - $C_{37}H_{32}F_6N_2S_2$ (682.8): Calc. C 65.09, H 4.72, N 4.10, S 9.39, Found C 64.83, H 4.74, N 4.02, S 9.17.

N,N-*(Pentamethylene)-2,2,2-trifluoro-1,1-diphenylethanesulfenamide* (**5g**). From piperidine (**7g**), *Method B*. After crystallization from petroleum ether 30-50°C (5 ml for 5 mmol) at -70°C 94% yellowish crystals, m.p. 42°C.- IR (KBr): 2925, 2840, 1495, 1440, 1250, 1130, 695 cm^{-1}.- ^1H-NMR: δ = 7.45-7.34 (m, 4 o-H_{arom}), 7.33-7.25 (m, 6 m-,p-H_{arom}), 2.78-2.60 (m, 4 H, CH_2-N), 1.41-1.03 (m, 6 aliph. H.- $C_{19}H_{20}F_3NS$ (351.4): Calc. C 64.94, H 5.74, N 3.99, S 9.12, Found C 64.97, H 5.71, N 3.91, S 9.19.

S-*(1-Imidazolyl)-2,2,2-trifluoro-1,1-diphenylethanethiol* (**5h**). From imidazole (**7h**), *Method B*. TLC, cyclohexane/ ethyl acetate (10:3): R_F(**7h**) 0.0, R_F(**8**) 0.72, R_F(**5h**) 0.20. After recrystallization from ether/ petroleum ether 30-50°C 95% colourless crystals, m.p. 96°C.- IR (KBr): 1450, 1155, 1055, 745, 720 cm^{-1}.- ^1H-NMR: δ = 7.45-7.29 (m, 10 arom. H), 7.01 (mc, 1 H), 6.79 (mc, 1 H), 6.52 (mc, 1 H).- $C_{17}H_{13}F_3N_3S$ (334.4): Calc. C 61.07, H 3.92, N 8.38, S 9.59, Found C 61.14, H 3.88, N 8.32, S 9.39.

N,N-*Bis(2-methoxyethyl)-2,2,2-trifluoro-1,1-diphenylethanesulfenamide* (**5i**). From amine **7i**, *Method B*. TLC, hexane/ ethyl acetate (4:1): R_F(**8**) 0.54, R_F(**5i**) 0.29. The crude product (99% yellowish oil) is crystallized from 1 ml pentane (for 5 mmol) at -30°C: 96% colourless crystals, m.p. 30 -32°C.- IR (KBr): 2920, 1495, 1445, 1250, 1160, 1015, 930, 710 cm^{-1}.- ^1H-NMR: δ = 7.47-7.39 (m, 4 o-H_{arom}), 7.35-7.28 (m, 6 m-,p-H_{arom}), 3.24 (s, 2 OCH_3), 3.20 (mc, 4 H, OCH_2; J = 2 Hz), 3.07-2.92, 2.89-2.75 (2 m, 4 H, NCH_2).- MS: *m/e* = 399 (M^+, 6%), 354 (M^+ -C_2H_5O, 2), 235 (($(C_6H_5)_2(CF_3)C^+$, 100), 215 (55), 165 (fluorenyl$^+$, 100).- $C_{20}H_{24}F_3NO_2S$ (399.5): Calc. C 60.13, H 6.06, N 3.51, S 8.03, Found C 60.10, H 6.09, N 3 47, S 8.07.

N-*[(1S,2R)-(2-Hydroxy-1-methyl-2-phenyl)ethyl]*-N-*methyl-2,2,2-trifluoro-1,1-diphenylethanesulfenamide* (**5k**). From *(-)*-ephedrine (**7k**, containing 5% water), *Method B*. TLC, hexane/ ethyl acetate (9:1): R_F(**7k**) 0.0, R_F(**8**) 0.45, R_F(**5k**) 0.08. After chromatography (silica gel, same solvent) 96% colourless syrup, solidifying as a glass at room temp.- IR (film, NaCl): 3440, 3060, 2945, 1255, 1155, 1015, 700 cm^{-1}.- ^1H-NMR (CCl_4, 90 MHz): δ = 7.58-7.07 (m, 15 arom. H), 4.62 ("d", C<u>H</u>-OH; J = 4.0 Hz), 2.98 (mc, C<u>H</u>-CH_3; J = 4.0, 5.0 Hz), 2.55 (s, N-CH_3), 1.69 (br.s, OH), 0.68 ("d", C-CH_3; J = 5.0 Hz).- MS: *m/e* = 324 (M^+ -C_7H_7O, 31%), 267 (TDE-S^+, 16), 236 (9), 235 (($(C_6H_5)_2(CF_3)C^+$, 30), 215 (28), 165 (fluorenyl$^+$, 100), 107 ($C_7H_7O^+$, 13), 90 (51), 77 (22).- $C_{24}H_{24}F_3NOS$ (431.5): Calc. C 66.80, H 5.61, N 3.25, S 7.43, Found C 66.70, H 5.54, N 3.27, S 7.23.

(2S)-3-Phenyl-2-(2,2,2-trifluoro-1,1-diphenylethylsulfenyl)aminopropionic acid (**5m**). From L-phenylalanine (**7m**), *Method C*. TLC, hexane/ ethyl acetate (3:1) + 1% HOAc: R_F(**7m**) 0.0, R_F(**8**) 0.8, R_F(**5m**) 0.2. 96% slightly brownish glass.- IR (film, NaCl): 3360, 3030, 2635, 1715, 1495, 1155 cm^{-1}.- ^1H-NMR (90 MHz): δ = 10.0-8.5 (br.s, COOH), 7 61-7.19 (m, 13 arom. H), 7.07-6.90 (m, 2 arom. H), 3.42 (mc, C<u>H</u>-N; J = 5.0, 6 0 Hz), 2.94 (br.s, NH), 2.79 (<u>A</u>B, 1 H; J = 5.0, 14.0 Hz), 2.64 (A<u>B</u>, 1 H, J = 6.0, 14.0 Hz) - MS: *m/e* = 431 (M^+, 1%), 236 (($(C_6H_5)_2(CF_3)C^+$ +H, 13), 235 (($(C_6H_5)_2(CF_3)C^+$, 74), 215 (40), 166 (26), 165 (fluorenyl$^+$, 100), 91 ($C_7H_7^+$, 41).

*3-[*N-*(2,2,2-Trifluoro-1,1-diphenylethylsulfenyl)]aminobut-2-enoic methylester* (**12**). The solution of 850 mg (3.0 mmol) TDE sulfenamide **10**, 47 mg (0.15 mmol, 0.05 equiv.) pyridinium p-toluenesulfonate, and 0.355 ml (3.3 mmol) methyl acetoacetate (**11**) in 20 ml of CH_2Cl_2 is stirred vigorously under absolutely dry conditions with 1 81 g (15.0 mmol, 5.0 equiv.) $MgSO_4$. After ca. 2 h [TLC, petroleum ether 30-50°C/ ether (20:1): R_F(**10**) 0.38, R_F(**12**) 0.33], the reaction mixture is filtered through Celite, evaporated *in vacuo*, and filtered quickly through dry Al_2O_3 (Woelm, basic, Act. I, 15/ 2.5 cm; CH_2Cl_2): 0.99 g (87%) colourless oil.- IR (film, NaCl): 3230, 1665, 1610, 1250, 1155, 690 cm^{-1}. - ^1H-NMR (CCl_4, 90 MHz): δ = 9.12 (s, NH), 7.49-7.15 (10 arom. H), 4.53 (s, olef. H), 3.49 (s, OCH_3), 1.63 (s, CH_3).- $C_{19}H_{18}F_3NO_2S$ (381.4). Calc. C 59.83, H 4.76, N 3.67, S 8.41, Found C 60 10, H 4.63, N 3.63, S 8.65.

References and Notes

1) This paper is dedicated to *Professor Horst Prinzbach* on the occasion of his 60th birthday.

2) Present address: Department of Vitamin and Nutrition Research, F. Hoffmann-La Roche Ltd., CH-4002 Basel (Switzerland).

3) Present address: Hoechst Aktiengesellschaft, Forschung und Entwicklung GB-B, Technische Kunststoffe, D-6230 Frankfurt am Main 80 (FRG)

4) Th. Netscher, Dissertation, Universität Freiburg i. Br., 1986.

5) Th. Netscher, R. Schwesinger, B. Trupp, H. Prinzbach, *Tetrahedron Lett.* **1987**, *28*, 2115.

6) Th. Netscher, H. Prinzbach, *Synthesis* **1987**, 683.

7) Th. Netscher, *Tetrahedron Lett.* **1988**, *29*, 455.

8) G.A. Olah, Ch.U. Pittman Jr., *J. Am. Chem. Soc.* **1966**, *88*, 3310; K.-T. Liu, M.-Y. Kuo, *Tetrahedron Lett.* **1985**, *26*, 355; cf. cit. lit. in the review: Th.T. Tidwell, *Angew. Chem.* **1984**, *96*, 16; *ibid. Int. Ed. Engl.* **1984**, *23*, 20.

9) B.P. Branchaud, *J. Org. Chem.* **1983**, *48*, 3538; 3531.

10) Th.W. Greene, 'Protective Groups in Organic Synthesis', Wiley, New York, 1981.

11) Synthesis of **7e**: R. Kühlmeyer, B. Seitz, Th. Weller, H. Fritz, R. Schwesinger, H. Prinzbach, *Chem. Ber.* **1989**, *122*, 1729; R. Kühlmeyer, R. Schwesinger, H. Prinzbach, *Tetrahedron Lett.* **1984**, *25*, 3429.

12) Th. Weller, Dissertation, Universität Freiburg i. Br., 1988.

13) T.S. Manoharan, R.S. Brown, J. *Org. Chem.* **1988**, *53*, 1107, and cit. lit.

14) J.M. Widom, B. Ganem, *Tetrahedron Lett.* **1987**, *28*, 4389.

15) Under the conditions of entry 2, but after 5 h, *N*-benzyltritylsulfenamide shows at least three UV-active decomposition products, and is recovered in a 75% yield [9].

16) B. Seitz, R. Kühlmeyer, Th. Weller, W. Meier, Ch. Ludin, R. Schwesinger, L. Knothe, H. Prinzbach, *Chem. Ber.* **1989**, *122*, 1745.

17) B. Schwesinger, R. Schwesinger, H. Prinzbach, *Tetrahedron Lett.* **1984**, *25*, 1979.

18) M. Bergmann, L. Zervas, *Ber. Dtsch. Chem. Ges.* **1932**, *65*, 1192.

19) L.A. Carpino, G.Y. Han, *J. Org. Chem.* **1972**, *37*, 3404.

20) J.C. Sheehan, F.S. Guziec Jr., *J. Org. Chem.* **1973**, *38*, 3034.

21) J. Ipaktschi, *Chem. Ber.* **1984**, *117*, 856.

22) R. Annunziata, M. Cinquini, F. Cozzi, A. Gilardi, A. Restelli, *J. Chem. Soc., Perkin Trans. I*, **1985**, 2289; Y. Narita, Sh. Masuyoshi, T. Yamasaki, T. Naito, H. Kawaguchi, *J. Antibiot.* **1991**, *44*, 86.

23) T. Mukaiyama, M. Hayashi, K. Narasaka, *Chem. Lett.* **1973**, 291.

24) J. Meienhofer, *Nature* **1965**, *205*, 73.

25) R. Baltzly, P.B. Russell, *J. Am. Chem. Soc.* **1953**, *75*, 5598; A.W. Frahm, G. Knupp, *Tetrahedron Lett.* **1981**, *22*, 2633.

26) P.N. Rylander, 'Catalytic Hydrogenation over Platinum Metals', Academic Press, New York, 1967, p. 464.