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Synthesis of N-sulfamoyloxazolidinones and -perhydrooxazinones Reactivity and Use as Donors in the *Transsulfamoylation* Reaction; Application to the Preparation of 2-Chloroethylnitrososulfamides. IV.

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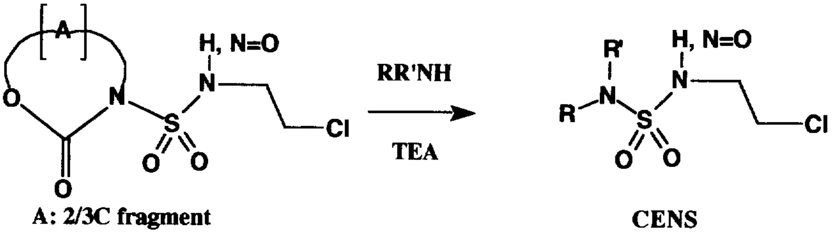
Abstract
Starting from chlorosulfonyl isocyanate, successive addition of selected 1,2 and 1,3 haloalcohols, sulfamoylation with the nitrogen mustard and cyclization in alkaline conditions give title compounds in good yields. These sulfamoyloxazolidinones and sulfamoylperhydrooxazinones were revealed as efficient 2-chloroethylsulfamoyl donors in the 2-chloroethylnitrososulfamides synthesis; five new CENS *(derivated from heterocyclic amines and amino acids) were thus synthezised. According to the experimental conditions, N-sulfamoylcyclocarbamates can be reopened by nucleophiles giving addition products by transcarbamoylation.* Copyright © 1996 Elsevier Science Ltd

Introduction

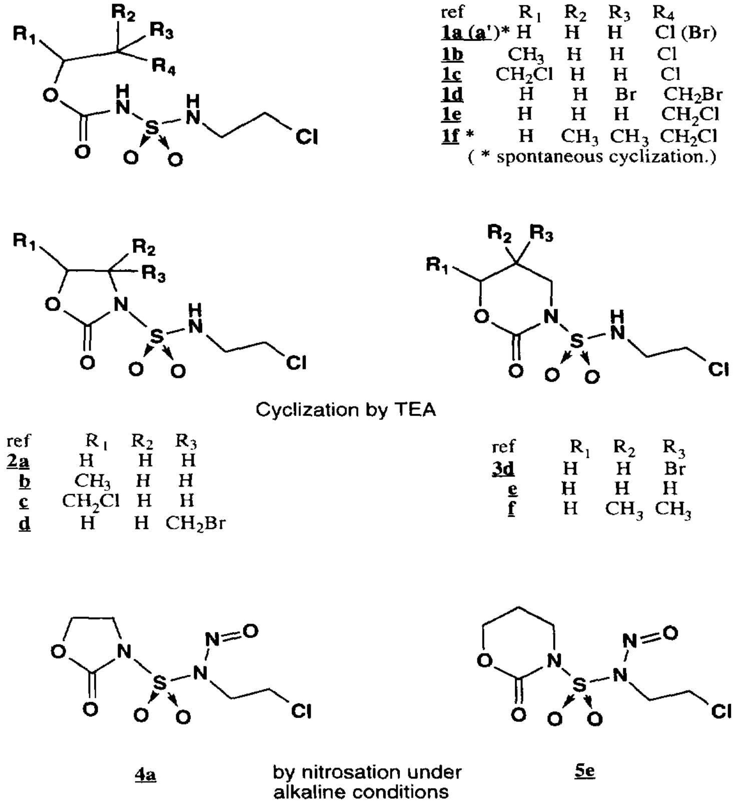
In a previous reports [1-3] we have reported the syntheses and the promising oncostatic properties of the 2-chloroethylnitrososulfamides (CENS). The four-step approach for the preparation of CENS, described as an *insertion of sulfamoyl group* [4] was carried out in a 40-60 % overall yield starting from chlorosulfonyl isocyanate (CSI) and primary or secondary amines. In the perspective of the synthesis of a larger series, necessary for the pharmacomodulation studies and to establish QSAR, we have developed a *transsulfamoylation* alternative route, which would allow the direct access to the expected sulfamides through a shortened procedure (scheme 1). This reaction evolves from a nucleophilic exchange of a 5 or 6-membered heterocyclic leaving group by the required primary or secondary amine. The approach by the displacement of this activated group is commonly used in acyl transfer reactions [5-12], but no example was found in the sulfamoylated derivatives chemistry.



Scheme 1

Preparation of N-sulfamoyl-2-oxazolidinones and -1,3-perhydrooxazin-2-ones

The synthesis of the N-carboxylsulfamides 1a-f was carried out starting from chlorosulfonyl isocyanate, 1-2 or 1-3 haloalcohols, nitrogen mustard and triethylamine through a previously described [1] one-pot procedure in a 65-95 % yield. Haloalcohols used are chloro- and bromoethanol (**a**, **a'**), 1-chloro-2-propanol (**b**), 1,3-dichloro-2-propanol (**c**), 2,3-dibromo-1-propanol (**d**), 3-chloro-1-propanol (**e**), and 2,2-dimethyl-3-chloro-1-propanol (**f**).



ref	R_1	R_2	R_3	R_4
1a (a')*	H	H	H	Cl (Br)
1b	CH_3	H	H	Cl
1c	CH_2Cl	H	H	Cl
1d	H	H	Br	CH_2Br
1e	H	H	H	CH_2Cl
1f *	H	CH_3	CH_3	CH_2Cl

(* spontaneous cyclization.)

Cyclization by TEA

ref	R_1	R_2	R_3
2a	H	H	H
b	CH_3	H	H
c	CH_2Cl	H	H
d	H	H	CH_2Br

ref	R_1	R_2	R_3
3d	H	H	Br
e	H	H	H
f	H	CH_3	CH_3

4a

by nitrosation under alkaline conditions

5e

Fig 1

The cyclization of carboxylsulfamides (Fig 1; top) is achieved by triethylamine addition in quantitative yield [13-15]. Compounds 1a-c give N-sulfamoyl-2-oxazolidinones 2a-c and compounds 1e-f give homologous perhydrooxazinones 3e-f (Fig1; middle). Compounds 1a-a' and 1f can be spontaneously cyclized during the first step (relating to the excellent leaving group character of Br for 1a', and *gem*dimethyl effect for 1f). The alkaline treatment of dibromopropylcarbamate 1d affords both the 5 and 6-membered ring derivatives 2d and 3d in a 3:5 ratio. In this case, the structural determination was established by ^{1}H-DEPT and ^{13}C-NMR (experimental section). No cyclization is observed relating to the sulfamide mustard moiety, this is probably in relation to the level of the rotational barrier around the sulfamido group. Selected physicochemical and spectroscopic data concerning the obtained series 1, 2 and 3 are reported in the following Table.

The synthesis of N-nitrosated compounds starting from the mustard sulfamides 2a-d and 3d-f (scheme 2, bottom) can be only achieved by addition of nitrosyl chloride, or nitrosyl tetrafluoroborate in aqueous solution of LiOH. In other conditions (sodium nitrite in formic acid, NOCl, $NOHSO_3$, $NOBF_4$ in triethylamine) an equilibrium of nitrosation-denitrosation was observed in the reaction medium. The resulting derivatives 4a-d and 5d-f were unstable and kept under argon atmosphere at -20°C. Only device compounds (Fig 1; bottom) **4a** and **5e** could be characterized.

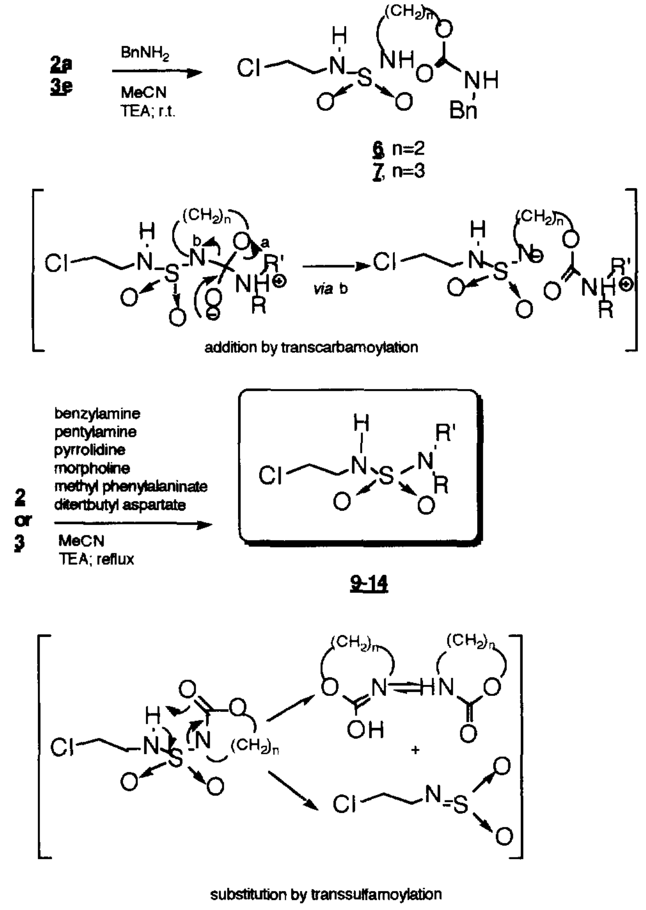
-**Table 1**-

ref	**mp**	**Yield**	**rf**	**IR** (KBr,ν cm^{-1})			**^1H NMR** (δ ppm)
	°C	**%**		NH	C=O	SO_2	
1b	136-137	65	0.41 (a)	3275	1745	1355 1165	(c) 6.32 (t, 1H, $NHCH_2$), 5.18 (m, 1H, C*H), 3.65 (m, 4H, CH_2Cl), 3.40 (q, 2H, CH_2NH), 1.35 (d, 3H, CH_3).
1c	134-137	83	0.81 (a)	3300	1725	1350 1150	(d) 8.20 (t, 1H, NHCO), 5.15 (m, 1H, C*H), 3.90 (m, 4H, CH_2ClC), 3.65 (t, 2H, CH_2Cl), 3.25 (q, 2H, CH_2N).
1d	129-131	94	0.44 (a)	3300 3200	1710	1350 1160	(d) 11.50 (t, 1H, NHCO), 8.16 (t, 1H, $NHCH_2$), 4.62 (m, 1H, CHBr), 4.43 (s, 2H, CH_2O), 3.87 (t, 2H, CH_2Cl), 3.62 (q, 2H, CH_2NH), 3.25 (d, 2H, CH_2Br)
1e	135-136	70	0.40 (a)	3225	1725	1345 1150	(d) 8.15 (t, 1H, $NHCH_2$), 4.20 (t, 2H, CH_2O), 3.75 (t, 2H, CH_2Cl), 3.65 (t, 2H, CH_2Cl), 3.25 (q, 2H, CH_2NH), 2.05 (m, 2H, CH_2).
2a	84-86	71	0.76 (a)	3300	1750	1360 1140	(c) 6.23 (t, 1H, NH), 4.49 (t, 2H, CH_2O), 4.12 (t, 2H, CH_2N), 3.72 (t, 2H, CH_2Cl), 3.58 (q, 2H, CH_2NH).
2b	69-70	60	0.36 (a)	3275	1745	1355 1160	(c) 5.97 (s, 1H, NH), 4.73 (m, 1H, C*H), 4.08 (t, 2H, CH_2N), 3.62 (t, 2H, CH_2Cl) , 3.47 (q, 2H, CH_2NH).
2c	60-63	58	0.75 (a)	3300	1755	1350 1160	(c) 6.08 (s, 1H, NH), 4.94 (m, 1H, C*H), 4.15 (m, 2H, CH_2N het), 3.82 (m, 2H, CH_2Cl het), 3.71 (t, 2H, CH_2Cl), 3.54 (q, 2H, CH_2NH).
2d	85-86	32	0.55 (b)	3300	1740	1350 1160	(d) 8.40 (t, 1H, NH), 4.55 (m, 1H, CHN), 3.95 (d, 2H, CH_2O), 3.52 (t, 2H, CH_2Cl), 3.35 (q, 2H, CH_2NH), 3.15 (d, 2H, CH_2Br)
3d	110-112	51	0.40 (b)	3230	1700	1350 1150	(d) 8.55 (t, 1H, NH), 5.02 (m, 1H, CHBr), 4.46 (2d, 2H, CH_2N), 3.70 (2d, 2H, CH_2O) 3.62 (t, 2H, CH_2Cl), 3.37 (q, 2H, CH_2N).
3e	81-82	65	0.54 (b)	3225	1690	1355 1160	(d) 6.20 (s, 1H, NH), 4.31 (t, 2H, CH_2O), 3.80 (t, 2H, CH_2N), 3.60 (t, 2H, CH_2Cl), 3.37 (q, 2H, CH_2NH), 2.11 (m, 2H, CH_2).
3f	108-110	83	0.53 (a)	3250	1695	1340 1160	(c) 5.72 (t, 1H, NH), 4.07 (s, 2H, CH_2O), 3.67 (t, 2H, CH_2Cl), 3.47 (q, 2H, CH_2NH) 3.41 (s, 2H, CH_2N), 1.04 (s, 6H, 2 CH_3).

(a): dichloromethane:methanol 95:5 (b): dichloromethane (c): DMSOd_6 (d): $CDCl_3$

Transsulfamoylation

The assays of the direct transsulfamoylation starting from N-nitrosated derivatives **4** and **5** are however disappointing, giving decomposition products due to the excessive lability of these series of compounds. In contrast, the treatment of sulfamoyloxazolidinone by amines gave, in accordance with the experimental conditions reported in the scheme 2, two series resulting from both *addition by transcarbamoylation* (top) or *substitution by transsulfamoylation* (bottom) reactions:



Scheme 2

Two different mechanisms would be in fact involved. At r.t., the reaction proceeds through the nucleophilic attack on the carbonyl site giving the tetrahedral intermediate and the subsequent formation (route b) of the sulfonamide anion (more stable in this case than the oxanion in route a). Thus the resulting product of this addition by N to N'-acyl transfer is the sulfamide-carbamate. The structure of the obtained products **6** and **7**, starting from benzylamine and sulfamoyloxazolidinone **2a** or sulfamoyloxazinone **3e** respectively, is clearly established with NMR, IR and MS data, versus the hypothetical isomer N-(2-hydroxyethyl)carbamoylsulfamide resulting to the route a. By prior heating with triethylamine in acetonitrile, the initial step would be the intermediary formation, through a concerted six-membered rearrangement, of the very reactive sulfonimide [16-18]. The subsequent addition of amine gives the expected chloroethylsulfamides. An excess of amine can be reacted with the remaining oxazolidinone by addition-opening and gives a substituted 2-hydroxyethylurea such as **8** (with benzylamine). Thus the experimental conditions can easily directed the selective formation of the desired series. By the transsulfamoylation procedure with selected amines such as benzylamine, pentylamine, pyrrolidine, morpholine, methyl phenylalaninate and ditertbutyl aspartate, the chloroethylsulfamides **9-14** are respectively recovered in variable yields according to the nature of heterocyclic leaving group (see experimental section).

Satisfactory results are obtained with compounds **2a**, **2b**, **3e** and **3f** as sulfamoylating agent and the best yields are observed with the primary amines derivatives. Using others donors (**2c**, **2d-3d**) the experimental conditions were more tedious and by-products accompanied the waited compounds. CENS **15-20** were then respectively afforded from precursors **9-14** by the previously described method [1,2]. Relating to the pharmacomodulation described in the nitrosoureas series, the association of the pharmacophore CENS with the amino acids (**19** and **20**) is potentially interesting for an eventual vectorization [19-22]. By comparison with our previous works, the overall yield (starting from the utilized amine) is increased in a range 25-40%. In conclusion the N-sulfamoyl*cyclocarbamates* are efficient donors of sulfamoyl group in the two-step synthesis of CENS. Moreover in controlled experimental conditions, these key-compounds give opened carbamates-sulfamides; hence further studies are in progress.

Experimental

Melting points were determined in open capillary tubes on a Thermotechnal apparatus and are uncorrected. Proton and ^{13}C nuclear magnetic resonance were determined with a AC 250 Bruker spectrometer. Fast-atom bombardment mass spectra (FAB-MS) were recorded in the positive or negative ion mode on a JEOL DX 300 mass spectrometer and the matrix was glycerol (G), a mixture of glycerol and thioglycerol (50/50 v/v) (GT) or metanitrobenzyl alcohol (NBA). Thin layer chromatography (TLC) was performed on precoated aluminium sheets of silica gel 60 F_{254}.

Typical procedures

1. Carbamoylation-sulfamoylation-cyclisation.

A solution of 0.05 mol of N-(chlorosulfonyl)haloalkylcarbamate was prepared by addition of haloalcohol (0.05 mol in 25 mL of dried dichloromethane) into a solution of CSI (7.1 g in the same solvent). This reagent was slowly added at 0° C into a solution containing a primary (or secondary) amine (0.05 mol in 100 mL dichloromethane) and 1.1 equiv of triethylamine. The reaction was achieved in 45 minutes. The medium was diluted with 100 mL dichloromethane, washed with two fractions of HCl 0.1 N, dried and concentrated *in vacuo*. The crude residue of N-(haloalkoxy carbonyl) sulfamides was then purified by column chromatography (yield 80-95 %).

To a solution of N-(haloalkoxycarbonyl) sulfamide (0.03 mol) in dichloromethane (25 mL) pure triethylamine (1.5 equiv) was added dropwise. The reaction was monitored by TLC. After 30 min of stirring, the medium was diluted with dichloromethane, washed with fractions of HCl 0.1 N, dried and concentrated *in vacuo*. The residue affords the crude heterocyclized compounds **2a-e** and **3e-g**, then purified by column chromatography (eluent: dichloromethane).

2. **Transsulfamoylation; transcarbamoylation.** To a refluxing solution of sulfamoyl oxazolidinone or perhydrooxazinone (1 equiv) and 1 equiv of triethylamine in acetonitrile was added 1.1 equiv of selected amine. The reaction was stirred for 15 to 120 min to give the 2-chloroethylsulfamides **9-14** and free oxazolidinone (or superior homologue), separated by water washing. The transcarbamoylation giving **6** and **7** was carried out at r.t. by the same mixture of reactants and solvent.

3. Nitrosation.

To a stirred solution of 0.01 mol of sulfamoyloxazolidinone (or homologue) in CH_2Cl_2 (25 mL) and 2 equiv of lithium hydroxide in 5 mL of water, 2.5 equiv of nitrosyl chloride in the same solvent was added under stirring at 0°C. The reaction medium was then separated and the organic phase was washed by HCl 0.1 N, dried and evaporated under reduced pressure.

The sulfamides **9-14** were nitrosated following a work-up previously described [19]: Dried sodium nitrite (2 equiv) was added to a stirred solution of N-(2-chloroethyl)sulfamide (0.01 mol) in 25 mL of dichloromethane and 1 mL of concentrated hydrochloric acid at 0° C during a period of 30 min. After filtering the suspension, the solution was washed, dried and evaporated under reduced pressure.

N-[(N-2-chloroethyl)sulfamoyl]-4-(bromomethyl)-2-oxazolidinone 2d
Rd: 32%
^{13}C NMR (DMSOd_6): 152.24 (C=O), 68.08 (C-O), 54.94 (C-N), 51.73 (C-NH), 48.50 (C-Cl), 42.02 (C-Br).

N-[(N-2-chloroethyl)-sulfamoyl]-5-bromoperhydro-1,3-oxazin-2-one 3d
Rd: 51%
^{13}C NMR (DMSOd_6): 147.33 (C=O), 71.59 (C-O), 53.73 (C-N), 44.93 (C-NH), 42.59 (C-Cl), 41.28 (C-Br).
Surprisingly, the favourized cyclization affords the 6-membered derivative, relating to the preponderant influence of the steric *vs* electronic factors.

N-[(N-2-chloroethyl, N-nitroso)-sulfamoyl]-2-oxazolidinone 4a
Yield: 70%. Rf: 0.89 (CH_2Cl_2/MeOH: 95/5).
^{1}H NMR ($CDCl_3$): 4.58 (t, 2H, CH_2NNO), 4.45 (t, 2H, CH_2O), 4.30 (t, 2H, CH_2Cl), 4.08 (t,2H, CH_2N).

N-[(N-2-chloroethyl, N-nitroso)sulfamoyl]-perhydro-1,3-oxazin-2-one 5e
Yield: 65%. Rf: 0.70 (CH_2Cl_2/MeOH: 95/5).
^{1}H NMR, $CDCl_3$): 4.40 (t, 2H, CH_2NNO), 4.25 (s, 2H, CH_2O), 4.10 (t, 2H, CH_2Cl), 3.78 (t, 2H, CH_2N), 2.10 (m, 2H, C^5H_2).

N-(2-O-benzylaminocarboxylethyl)-N'(2-chloroethyl)sulfamide 6
Starting from N-(N-2-chloroethylsulfamoyl)-2-oxazolidinone (1 equiv), benzylamine (1.2 equiv) in acetonitrile-triethylamine, at r.t. during 60 min.
Yield 73%. mp: 99-100°C. Rf: 0.55 (diethylether).
IR (KBr, νcm^{-1}): 3300, 3200 (NH), 1745 (C=O), 1350, 1150 (SO_2).
^{1}H NMR ($CDCl_3$): 7.35 (m, 5H, ArH), 5.20 (s, 1H, NHCO), 4.87, 4.79 (2t, 2H, 2NH), 4.40 (d, 2H, CH_2Ph), 4.30 (t, 2H, CH_2O), 3.70 (t, 2H, CH_2Cl), 3.35 (m, 4H, $2CH_2NH$).
MS (FAB>0; thioglycerol): 336 (M+H]$^+$), 300 (M-Cl]$^+$), 203 (carbamoyl cleavage), 106 ($PhCH_2NH$]$^+$).

N-(3-O-benzylaminocarboxypropyl)-N'(2-chloroethyl)sulfamide 7
Starting from N-[(N-2-chloroethyl)sulfamoyl)]-1,3,2-perhydrooxazinone (1 equiv), benzylamine (1.3 equiv) in acetonitrile-triethylamine, at r.T. during 60 min..
Yield 73%. mp: 98°C. Rf: 0.50 (CH_2Cl_2/MeOH: 95/5).
^{1}H NMR (DMSOd_6): 7.68 (t, 1H, NHCO), 7.40-7.20 (m, 6H, ArH+NH), 7.00 (t, 1H, NH), 4.19 (d, 2H, CH_2Ph), 4.00 (t, 2H, CH_2O), 3.62 (t, 2H, CH_2Cl), 3.16, 2.90 (2q, 4H, $2\mathbf{CH_2}NH$), 1.75 (m, 2H, CH_2 prop.).
MS (FAB<0; GT): 348 (M-H]$^-$), 312 (M-Cl]$^-$), 201 (carbamoyl cleavage), 106 ($PhCH_2NH$]$^-$).

N-(2-hydroxyethyl)-N'-benzylurea 8
Foam. Rf: 0.67 (diethylether).
IR (neat; νcm^{-1}): 3450-3550 (OH), 3300, 3250 (NH), 1750 (C=O).
^{1}H NMR ($CDCl_3$): 7.30 (m, 5H, ArH), 4.75 (s, 1H, OH), 4.60 (t, 2H, 2NH), 4.20 (s, 2H, CH_2Ph), 3.45 (q, 2H, $\mathbf{CH_2}NH$), 3.25 (t, 2H, CH_2OH).

N-(2-chloroethyl)-N'-benzylsulfamide 9 [1,3]
Yields and reaction times; starting from **2a**: 95% (15 min); **2b**: 90% (30 min); **2c**: 65% (120 min); **2-3d** mixt: 50% (120 min); **3e**: 92% (45 min); **3f**: 86% (60 min).

N-(2-chloroethyl)-N'-pentylsulfamide 10
Starting from **2a**: 97% (25 min); **2b**: 92% (45 min); **3f**: 86% (60 min).
mp: 97 °C. Rf: 0.82 (CH_2Cl_2/MeOH: 95/5)
IR (KBr, νcm^{-1}): 3300 (NH), 1365, 1135 (SO_2).
^{1}H NMR ($CDCl_3$): 4.45 (t, 1H, N^3H), 4.25 (t, 1H, N^1H), 4.00 (t, 2H, CH_2Cl), 3.48 (q, 2H, CH_2NH), 3.00 (q, 2H, N^3CH_2), 1.62 (m, 2H, $N^3CH_2\mathbf{CH_2}$), 1.20 (m, 4H, CH_2 pent.), 0.85 (t, 3H, CH_3).

N-[(N-2-chloroethyl)sulfamoyl]pyrrolidine 11
starting from **2a**: 85% (20 min); **2-3d** mixt: 55% (100 min).
Foam. Rf: 0.82 (CH_2Cl_2/MeOH: 95/5)
IR (neat, vcm^{-1}): 3300 (NH), 1365, 1150 (SO_2).
^{1}H NMR ($CDCl_3$): 4.45 (t, 1H, NH), 3.59 (t, 2H, CH_2Cl), 3.33 (q, 2H, CH_2NH), 3.23 (m, 4H, NCH_2 pyrr.), 1.85 (m, 4H, CH_2CH_2).

N-[(N-2-chloroethyl)sulfamoyl]morpholine 12
starting from **2a**: 80% (15 min); **2c**: 58% (60 min).
Foam. Rf: 0.70 (CH_2Cl_2/MeOH: 95/5)
^{1}H NMR, ($CDCl_3$): 6.48 (t, 1H, NH), 3.70 (t, 4H, CH_2O), 3.61 (t, 2H, CH_2Cl), 3.37 (q, 2H, CH_2NH), 3.15 (t, 4H, CH_2N).

Methyl N-[(N-2-chloroethyl)sulfamoyl]phenylalaninate 13
Starting from **2a**: 92% (25 min); **3e**: 76% (60 min).
mp: 100-102 °C. Rf: 0.88 (CH_2Cl_2/MeOH: 95/5)
IR (KBr, vcm^{-1}): 3300, 3250 (NH), 1750 (C=O), 1355, 1140 (SO_2).
^{1}H NMR ($CDCl_3$): 7.25 (m, 5H, ArH), 4.90 (d, 1H, NHC*), 4.55 (t, 1H, $NHCH_2$), 4.25 (m, 1H, C*H), 3.52 (s, 3H, OCH_3), 3.45 (t, 2H, CH_2Cl), 3.10 (q, 2H, CH_2NH), 2.95 (m, 2H, CH_2Ph).

Di *tert* butyl N-[(N-2-chloroethyl)sulfamoyl]aspartate 14
Starting from **2a**: 84% (40 min); **3e**: 65% (60 min).
Foam. Rf: 0.91 (CH_2Cl_2/MeOH: 98/2).
^{1}H NMR ($CDCl_3$): 5.45 (d, 1H, NHC*), 4.95 (t, 1H, CH_2NH), 4.05 (m, 1H, C*H), 3.65 (t, 2H, CH_2Cl), 3.38 (q, 2H, CH_2NH), 2.78 (ddd, 2H, CH_2C*), 1.48, 1.42 (2s, 18H, 2 *t* Bu).

N-nitroso, N-(2-chloroethyl)-N'-benzylsulfamide 15
Physicochemical and spectral data are previously reported [1,3].

N-nitroso, N (2-chloroethyl)-N'-pentylsulfamide 16
Yield: 70%. Foam. Rf: 0.86 (CH_2Cl_2).
^{1}H NMR ($CDCl_3$): 4.50 (t, 1H, N^3H), 4.01 (t, 2H, CH_2NNO), 3.55 (t, 2H, CH_2Cl), 3.05 (q, 2H, CH_2NH), 1.65 (m, 2H, $N^3CH_2CH_2$), 1.18 (m, 4H, CH_2 pent.), 0.88 (t, 3H, CH_3).

N-[(N-nitroso, N-2-chloroethyl)sulfamoyl]pyrrolidine 17
Yield: 95%. mp<50°C. Rf: 0.80 (CH_2Cl_2)
^{1}H NMR ($CDCl_3$): 4.08 (t, 2H, CH_2NNO), 3.56-3.44 (m, 6H, CH_2Cl+NCH_2 pyrr.), 1.94 (m, 4H, CH_2CH_2).

N-[(N-2-chloroethyl)sulfamoyl]morpholine 18
Yield: 95%. mp<50°C. Rf: 0.76 (CH_2Cl_2)
^{1}H NMR ($CDCl_3$): 4.12 (t, 2H, CH_2NNO), 3.80 (t, 4H, CH_2O), 3.53 (t, 2H, CH_2Cl), 3.45 (t, 4H, CH_2N).

Methyl N-[(N-nitroso, N-2-chloroethyl)sulfamoyl]phenylalaninate 19
Yield: 65%. Foam. Rf: 0.81 (CH_2Cl_2)
^{1}H NMR ($CDCl_3$): 7.20 (m, 5H, ArH), 5.05 (d, 1H, NHC*), 4.50 (m, 1H, C*H), 3.80 (t, 2H, CH_2NNO), 3.52 (s, 3H, OCH_3), 3.34 (t, 2H, CH_2Cl), 2.90 (m, 2H, CH_2Ph).

N-[(N-nitroso, N-2-chloroethyl)sulfamoyl]aspartic acid 20
Yield: 55%. mp: 75-85°C (dec).
^{1}H NMR ($DMSOd_6$): 9.3-8.5 (m broad, 2 COOH), 6.80 (d, 1H, NHC*), 4.45 (m, 1H, C*H), 3.88 (t, 2H, CH_2NNO), 3.55 (t, 2H, CH_2Cl), 2.90-2.75 (ddd, 2H, CH_2C*).

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