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SELECTIVE SYNTHESIS OF SULFONYLUREAS AND CARBOXYSULFAMIDES A NOVEL ROUTE TO OXAZOLIDINONES.

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Summary. Starting with chlorosulfonylisocyanate (CSI) two new series of 2-haloethyl carboxysulfamides 5 and 2-haloethyl oxosulfonylureas 6 have been prepared. The haloethyl carboxylate 5 underwent a novel cyclisation in the presence of Et_3N to furnish quantitative yields of N-substituted oxazolidin-2-ones. This procedure constitutes a new route to these heterocycles.

In connection with our previous work on nitrosoureas[2], we were interested in preparing new agents which might eventually release under physiological conditions the bioactive effector, i.e., the chloroethyl cation. We explored the use of chlorosulfonylisocyanate (CSI,1)[3] for this purpose as this reagent could be converted to two new series of compounds containing the chloroethyl functionality which *via* decomposition could lead to the desired cation. CSI has two reactive sites (labeled a and b in scheme 1) which can undergo reaction and in preparing the title compounds we took advantage of both centers.

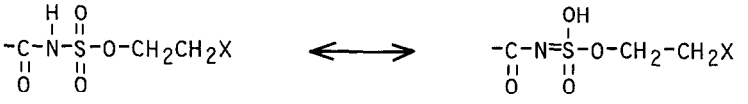
When equimolar quantities of 1 and either bromo or chloroethanol were stirred at room temperature in methylene chloride, reaction occured at site a to furnish the 2-haloethylcarboxysulfamyl chlorides 3 in excellent yield. Subsequent treatment of 3 with various amines then provided the 2-haloethylcarboxylsulfamides 5.

On the other hand, if 1 was first converted to the active ester derivatives 2, reaction with the haloethanols was directed at site b to afford the (O-aryl carbamyl)haloethyl sulfonates 4. Unlike 3, the (O-aryl carbamyl)haloethyl sulfonates 4 were somewhat unstable and necessited immediate conversion with the desired amine to the N-substituted haloethyl oxosulfonylureas 6. Table 1 illustrates the variety of amines used in obtaining the desired title compounds 5 and 6.

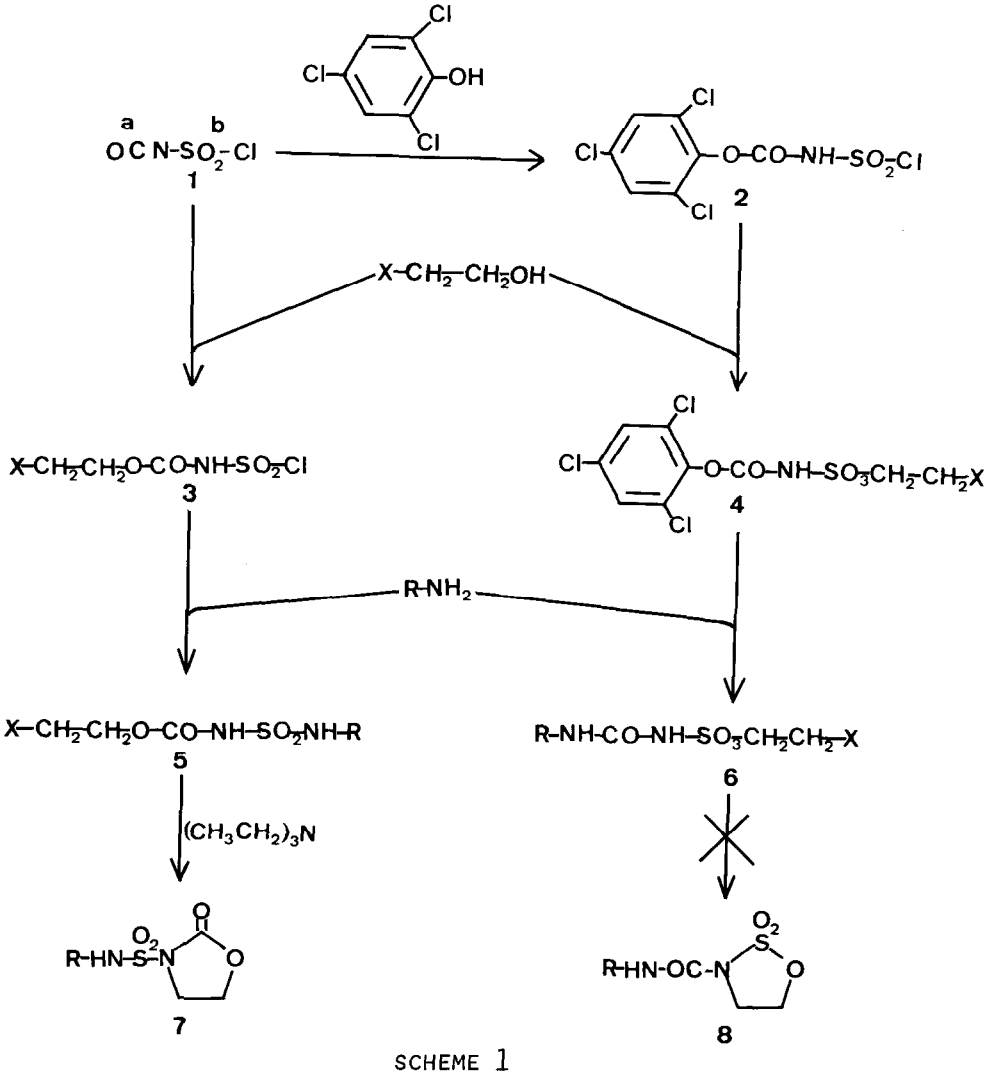
Initially, there existed the possibility of transposing the structures of 5 and 6 due to the reported rearrangement of certain sulfochlorides 3 to their haloethyl sulfonylisocyanates[4]. The chemical shifts of the O-methylene protons of both 5 and 6, were quite similar (4.4 and 4.6 p.p.m., respectively) and an assignment based only on this data would, be equivocal.

However, the compounds of type 5 could be cyclised quantitatively in the presence of triethylamine to the N-sulfamyl oxazolidin-2-ones 7 (Table 2). The structure of 7 (R=phenyl) was confirmed by a X-ray crystallographic analyses[5].

Compounds 6 under a variety of experimental conditions resisted cyclisation to 8 possibly due to the tautomerism depicted below.



This phenomenon may account for the NH signal ($-C-\underset{H}{N}-S-O-$) being barely visible above the base line in the ^1H NMR spectra of compounds 6.



SCHEME 1

TABLE 1. PHYSICOCHEMICAL DATA AND PREPARATION OF CARBOXYLSULFAMIDES 5 AND OXOSULFONYLUREAS 6[6]

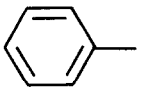
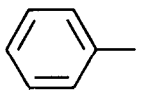
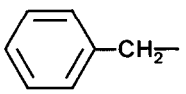
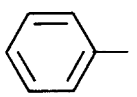
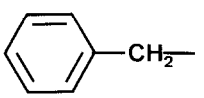
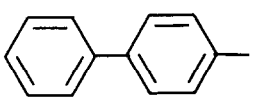
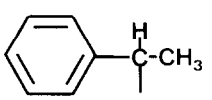
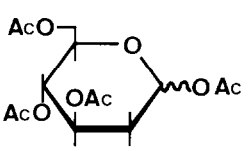
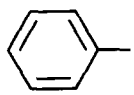
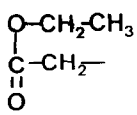
ENTRY	R	X	YIELDS	M.P.[6]
5A		Cl	72	146-148
5B		Br	68	143-145
5C		Cl	77	148-150
5D	$(CH_3CH_2)_2$	Cl	64	Liq.
5E		Cl	72	152-154
5F	$CH_3(CH_2)_4$—	Cl	65	130-131
6A		Cl	65	150-153
6B		Cl	78	160-161
6C		Cl	58	178-180
6D		Cl	75	165-167
6E	$CH_3(CH_2)_4$—	Cl	70	101-103
6F		Cl	52	158-160

TABLE 2. PHYSICOCHEMICAL DATA ON SELECTED N-SULFAMYL OXAZOLIDINONES 7[6].

ENTRY	R	M.P.[6]	^{1}H NMR[6] C_4H_2	C_5H_2
7A		140-142	3.85 (M)	4.26 (M)
7B	$(CH_3CH_2)_2$	54-56	4.07 (M)	4.52 (M)
7C		147-149	3.95 (M)	4.40 (M)

In conclusion we have prepared from CSI two new series of compounds (5 and 6) which possess the chloroethyl functionality. Compounds 5, in the presence of triethylamine, undergo cyclization to the oxazolidinones 7. This procedure represents a new synthetic approach to this heterocyclic ring system.

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References and footnotes

1. New address: Laboratoire de Chimie Bio-Organique, U.S.T.L., Place E -Bataillon, 34060 Montpellier Cedex, France.

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4. Lattrell, R., Lohaus, G. ; Chem. Ber., 1972, 105, 2800. Appel, R., Montenarh, M. ; Chem. Ber. 1974, 107, 706.

5. Viani, R., Montero, J-L., Dewynter, G. ; Acta Crystall., in press.

6. Satisfactory (C,H,N) analysis were obtained on all compounds listed. Melting points are uncorrected. The ^{1}H nmr spectra were determined on a Varian A-60 MHz spectrometer using $CDCl_3$ as solvent. Chemical shifts are expressed in δ values with respect to TMS.

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