STEREOSPECIFIC SYNTHESIS OF THIAZOLIDINE-2-THIONES

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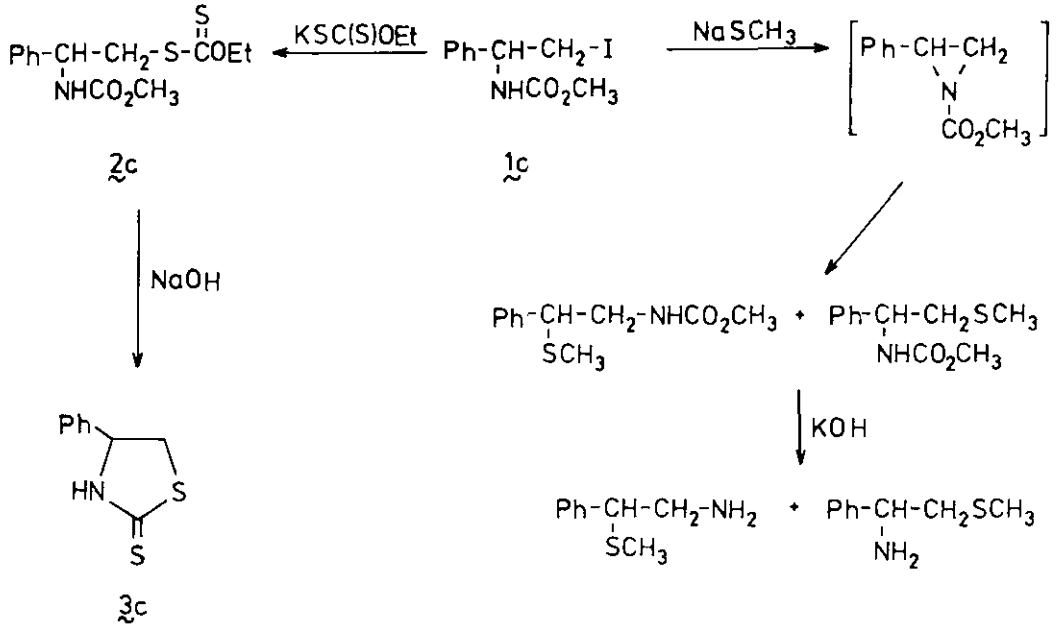
Abstract - The synthesis of thiazolidine-2-thiones from vic-iodoalkanecarbamates, stereospecifically obtained from cis and trans-butene, is reported. Reaction of the iodo-derivatives with potassium ethylxanthate and sodium hydroxide, allowed the stereospecific formation of thiazolidine-2-thiones. The stereochemistry of the latter reaction could be controlled by the experimental conditions. 4-Phenylthiazolidine-2-thione was obtained from the vic-iodoalkanecarbamate generated from styrene. A separable mixture of thiazolidin-2-ones (major component) and thiazolidine-2-thiones was obtained by reduction with $NaBH_4$ from the substitution product of vic-iodoalkanecarbamates with potasium ethylxanthate.

INTRODUCTION

The well known addition of iodoisocyanate to olefins, followed by reaction with an alcohol[1], allowed the stereospecific formation of vic-iodoalkanecarbamates[1,2] with an excellent overall yield. These compounds have been proved to be useful intermediates in the synthesis of heterocyclic compounds[3,4], and β-funtionalized amines[1,5]. The application of these intermediates to obtain 2-methyltio-1-phenylethylamine (Scheme 1) was not feasible because of the formation of regioisomeric mixtures that could not be separated.

These results could be explained on the basis of the strong basicity of the sodium methylsulfide which could abstract the proton from the carbamate function[6] generating an aziridine intermediate by internal substitution. The alternative route to the vic-methythioalkylamine was the reaction of 1c with potassium ethylxanthate (KEX, less basic than NaSMe). The only product obtained in this way was the desired regioisomer 2c. The formation of the vic-mercaptoalkylamine derivative from 2c by simultaneous reduction or hydrolysis of the xanthate and carbamate groups was not

possible.



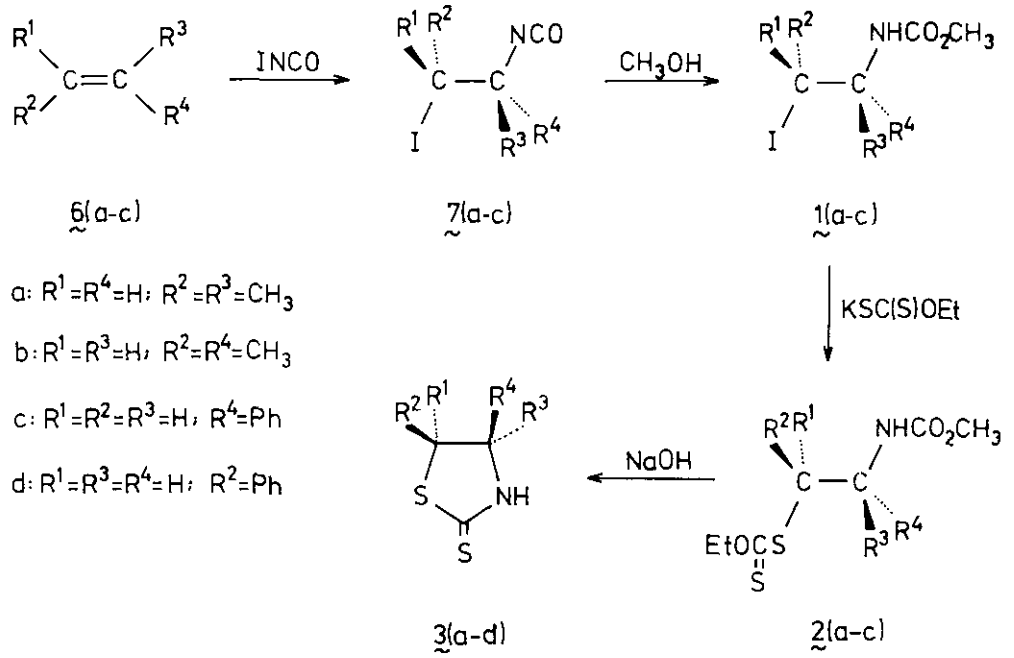
Scheme 1

The isolated products were the thiazolidine-2-thiones and thiazolidin-2-ones. These results exhibite the synthetic potentiality of the compounds with xanthate and carbamate groups on vicinal carbons (easily obtained from olefins) which could be used as precursors in the stereospecific synthesis of 4,5-substituted thiazolidine-2-thiones (and 2-ones). In the present paper we report the results on the study of the stereo and regiochemical course of the cyclization of vic-iodoalkanecarbamates and vic-carbamate alkylxanthates generated from olefins (styrene, cis and trans-butene) by the above mentioned reactions.

RESULTS AND DISCUSSION

The model compounds chosen were the vic-iodoalkanecarbamates 1(a-c) generated by addition of iodoisocyanate to the corresponding olefins (6a: trans-butene, 6b: cis-butene and 6c: styrene) and further reaction with methanol. The addition of INCO to 6a and 6b allowed the formation of a single stereoisomer (7a or 7b respectively) as was expected on the basis of the trans-stereospecific character of these reactions previously described by Hassner and co-workers[2,7]. The methanol addition did not affect the stereochemistry of the substrates and afforded compounds 1a(erythro-

configuration) and 1b (threo-configuration). The use of base catalysts for methanol addition gave a mixture of stereoisomers. Thus, in the presence of NaOMe, we obtained similar mixtures of 1a and 1b by reaction of 7a or 7b respectively with methanol. The addition of INCO and MeOH to styrene gave high yields of 1c.



Scheme 2

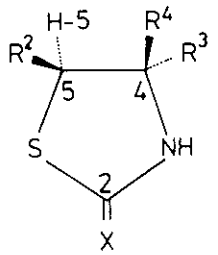
The stereospecific substitution of the halogen in the vic-iodoalkanecarbamates 1(a, b) with potasium ethylxanthate took place in quantitative yields to give 2(a, b). The small differences observed on the ^{1}H and ^{13}C NMR spectra of compounds 2a and 2b (see experimental part) made it impossible for these parameters to serve as a basis for the configurational assignment. The observed stereospecificity could be the result of the inversion of the configuration in the chiral center, (S_N2 process) or the retention of the configuration (double inversion), if the process took place with anchimeric assistance of the N via the intermediate aziridine. A study was undertaken to determine this question. The reaction of 1c with KEX afforded exclusively the regioisomer 2c in quantitative yield. The comparison of this result with the reaction of 1c with NaSMe (see Scheme 1), allowed us to stablish that, in this

case, the formation of the intermediate aziridine was not possible. This fact indicated that the S_N2 process took place with an inversion of the configuration at the reaction center. In this way, 2a would be the threo and 2b the erythro-compound with the opposite configuration of the vic-iodoalkanecarbamates 1a and 1b (Scheme 2).

The treatment of compounds 2(a-c) with sodium hydroxide under reflux gave the thiazolidine-2-thiones 3(a-c). The relative stereochemistry of the methyl groups in compounds 3a and 3b could be established from their spectroscopic data. The vicinal coupling constants between protons on C-4 and C-5 were very similar for 3a and 3b and the configuration assignment could not be made on this basis. The chemical shifts of the two methyl groups for 3b were coincident with those found in the literature for cis-4,5-dimethylthiazolidine-2-thione[8]. On the other hand, the chemical shifts of the protons on C-4 and C-5 in 3a were smaller (~0.3-0.4 ppm) than in 3b. This fact was compatible with a trans stereochemistry for 3a because of the effect of the methyl groups on C-4 and C-5 over the chemical shifts of the protons on the same carbons. The ^{13}C chemical shift of C-4, C-5 and methyl groups at C-4 and C-5 positions in 3a were larger (~4 ppm) than those observed for the cis-isomer 3b. This could be expected from the spatial interaction of the methyl groups in 3b, which was not possible in 3a with a trans disposition between them. In addition, on the basis of the additivity rules, the observed parameteres for C-4 and C-5 in 3a were coincident with the calculated values from the substituents effect in these heterocyclic compounds[9]. Furthermore, the melting points of 3a and 3b were similar to those previously described for trans and cis-4,5-dimethylthiazolidine-2-thiones[10] respectively. The reaction of 2c with NaOH afforded 3c with the same physical characteristics as the 4-phenylthiazolidine-2-thione previously described in the bibliography[10,11]. The spectroscopic data (NMR in Table 1) of 3c were in accordance with this structure.

The formation of these heterocyclic compounds could be explained through the sequence represented in Scheme 3, that began with the abstraction by the base[6] of the proton from the $-NHCO_2Me$ group. In this step, the configuration of the chiral carbons in 2a and 2b was preserved. In the following step, the nitrogen attacked the thiocarbonyl group of the xanthate, and the carbamate hydrolysis completed the process.

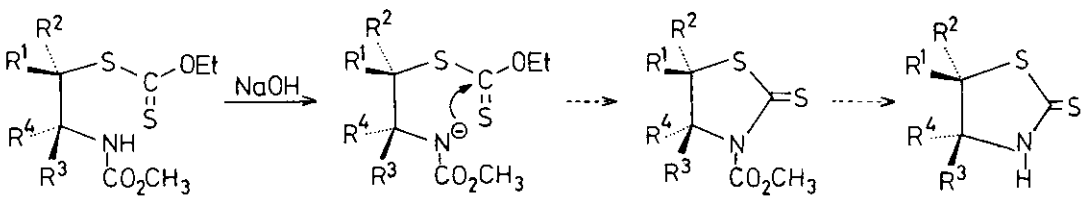
Table 1. ^{1}H and ^{13}C NMR parameters of compounds 3 and 4.



	3a	3b	3c*	3d**	4a	4b	4c***
X	S	S	S	S	O	O	O
R^2	CH_3	CH_3	H	Ph	CH_3	CH_3	H
R^3	CH_3	H	H	H	CH_3	H	H
R^4	H	CH_3	Ph	H	H	CH_3	Ph
H-5	3.67	3.94	3.52	5.20	3.54	3.90	3.32
R^2	1.46	1.37	3.86	7.4	1.46	1.37	3.65
R^3	1.40	4.34	5.32	4.02	1.31	3.97	4.97
R^4	3.92	1.32	7.41	4.29	3.54	1.24	7.40
$^{3}J_{5,R^3}$		6.7	8.2	7.93		6.5	8.3
$^{3}J_{5,R^4}$	6.6			7.87			
C-2	199.7	200.6	199.2	201.5	174.9	175.2	175.1
C-4	66.5	62.2	65.4	58.3	58.6	55.4	59.1
C-5	51.9	48.5	40.8	54.2	48.3	45.0	37.8
R^2	19.0	15.2			19.8	16.0	
R^3	18.4		19.2				
R^4		14.0				15.0	

* J_{gem}= 11.2 Hz; $^{3}J_{R^2,R^3}$ = 8.1 Hz; ** J_{gem} = 11.2 Hz; *** J_{gem}= 11.1 Hz; J_{R^2,R^3} = 7.4 Hz

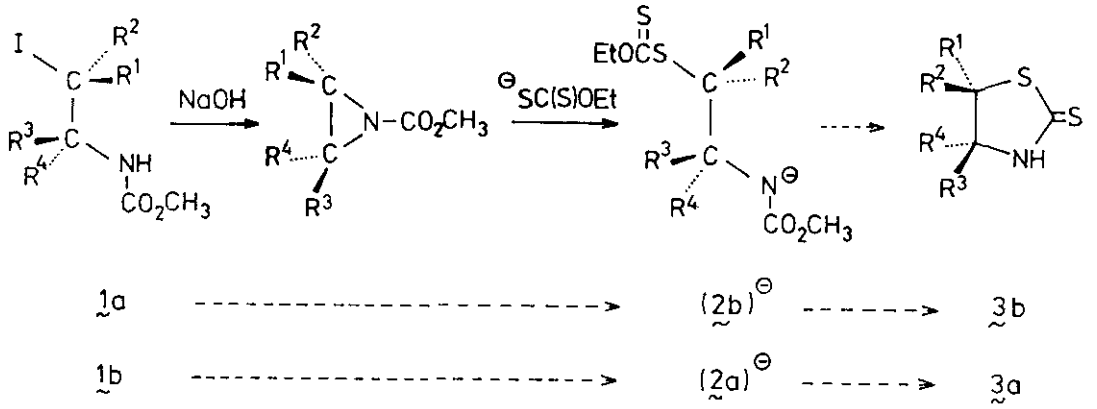
The heterocyclic compound 3b with the cis-disposition of the methyl groups was correlated with the erythro-derivative 2b, and the trans isomer 3a proceeded from the threo-derivative 2a. This correlation supports the above proposed assignment for the vic-carbamatealkanexanthates 2a and 2b.



2 3

Scheme 3

When the reaction of vic-iodoalkanecarbamates was carried out with a mixture of KEX and NaOH, the thiazolidine-2-thiones were also stereospecifically obtained. The stereochemical course of the reaction, however, was the opposite. From 1a (erythro) the final product was cis-4,5-dimethylthiazolidine-2-thione 3b and the product obtained from 1b (threo) was the trans-isomer 3a. Taking into account that the vic-iodoalkanecarbamates are transformed into aziridines[3] in basic media, the sterochemical result could be explained from the attack of KEX to the aziridinic intermediate. In this way, the configuration of C-4 and C-5 in the resulting thiazolidine-2-thiones was the same as the vic-iodoalkanecarbamates 1a and 1b.



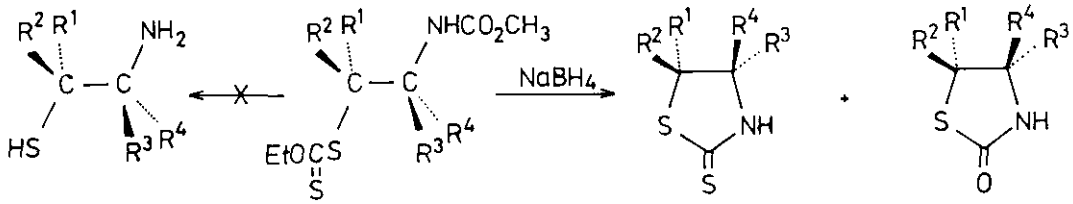
Scheme 4

The reaction of 1c in these conditions (simultaneous treatment with KEX and NaOH) provided a complex mixture of compounds. Between them, it was possible to identify (by ^{1}H NMR) the regioisomers 4- and 5-phenylthiazolidine-2-thione. From the mixture it was only possible to isolate by crystallization, the 5-phenylthiazolidine-2-thione[10,12] 3d, regioisomer of 3c. The isolation of the regioisomer 3d was a solid support to the indicated mechanism because the only route to the formation of 3d was via the aziridine intermediate. On the other hand, this result also confirmed the route proposed in Scheme 2, because the exclusive obtention of the regioisomer 3c, prevented the formation of the aziridine.

The possibility of other mechanisms that involved decomposition of KEX in the presence of sodium hydroxide and further reaction of the CS_2 generated[13,14] with aminic nitrogens, could be excluded in our case because of the stereo and regiochemi-

cal results.

Finally, we carried out the reduction of the vic-carbamatealkanexanthates in the presence of $NaBH_4$. The reaction of 2(a-c) with $NaBH_4$ afforded a mixture of two main compounds, the chromatographic separation of which allowed the isolation of the thiazolidine-2-thiones 3(a-c) [with the same stereochemistry as the products obtained from 2(a-c) with $NaOH^-$ and thiazolidin-2-ones 4(a-c) as major component (4:3 = 2:1). The structure of compounds 4 was assigned on the basis of their spectroscopic data.



2(a-c) 3(a-c) 4(a-c)

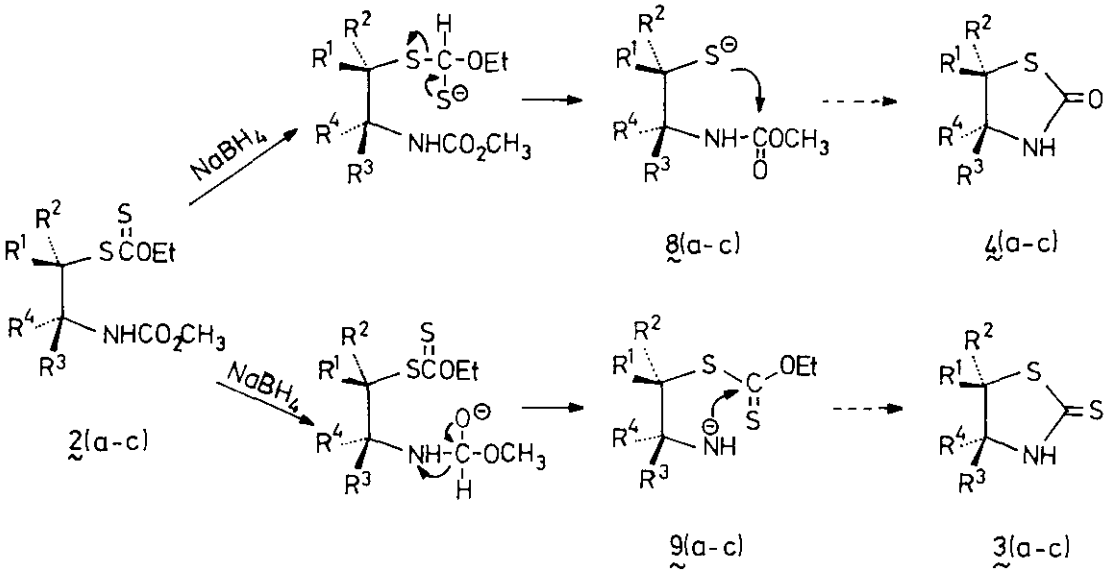
Scheme 5

The ^1H NMR spectra of 4b and 4c showed a coupling constant J_{CH-NH}= (~0.9Hz) which allowed the characterization of the proton bearing C-4. Compound 4a did not show this coupling because the signals of the two methinic protons appeared in the same chemical shift. The chemical shifts in ^1H and ^{13}C NMR spectra made possible the assignment of the relative stereochemistry of the methyl groups in 4a and 4b. From Table 1 it can be seen that the $\Delta\delta$ values between the protons of 4a and 4b are similar to those observed in the comparison of 3a and 3b. Similarly, the ^{13}C chemical shifts of C-4, C-5 and the methyl groups on these carbons in 4b (cis) are smaller (~3-4 ppm) than those observed in the trans-stereoisomer 4a. This situation was similar in the case of 3a and 3b.

For thiazolidine-2-thiones, these differences in ^1H and ^{13}C NMR chemical shifts were attributed to the effects of the relative stereochemistry of the methyl groups. These effects should be very similar despite the nature of the heteroatom on C-2 (S or O). Therefore, it was possible to assign the trans-stereochemistry for 4a (similar to 3a) and the cis-disposition of the methyl groups for 4b (similar

to 3b).

The reduction of 2 produced a mixture of 3 and 4 maintaining the configuration of the chiral centers from the initial substrate. This fact suggested the mechanism for this reaction indicated in the following Scheme.



Scheme 6

The competition between the xanthate and the carbamate groups to react with the hydride reductor, suggested the formation of 8(R-S⁻) and 9(R-N⁻). The intramolecular evolution of these intermediates took place more rapidly than the second group reduction.

At the present we are investigating the last of these reactions in order to find the reduction reagents and experimental conditions that produced an almost exclusive generation of thiazolidine-2-ones.

EXPERIMENTAL

All melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in the FT mode transforming 8K data points on a Brucker WM-200 SY instrument, or on a Varian XL 100. Me_4Si was used as internal standard and $CDCl_3$ was employed as solvent in all cases. Analyses of the ^{1}H NMR spectra were carried out by a Panic program on the Aspec 2000 computer of the Brucker spectrometer. We esti-

mated the reliability of all values to be ± 0.1 Hz and the root mean square deviations for the calculated and the experimental lines were always better than 0.05 Hz. Infrarred spectra (IR) were determined on a Pye Unicam SP 1100 spectrophotometer. Mass spectra (MS) were obtained on a Hewlett-Packard 5985 instrument at electron impact (EI) and/or chemical ionization (CI, CH_4 as reagent gas) ionizing modes. Silica gel Merck - G (layer thickness 0.25 mm) was used for analytical t.l.c., and Merck F-254 (layer thickness 2 mm) for preparative t.l.c.

vic-Iodoalkanecarbamates 1 were prepared following the procedure of Foglia and Swern[4] from the corresponding vic-iodoalkaneisocyanates 7 obtained by addition of iodoisocyanate to the adequated olefins .

Reaction of methyl N-(1-phenyl-2-iodoethyl) carbamate 1c with sodium methyl sulfide. A solution of 15% of sodium methylsulfide (1.68 g, 24 mmol) in methanol was added to a solution of 5g (16 mmol) of methyl N-(1-phenyl-2-iodoethyl) carbamate 1c in 50 ml. of methanol. The mixture was stirred for 12 hours at room temperature and concentrated to a half of its volume. To the concentrated mixture were added 100 ml of water . The extraction of the aqueous layer with methylene chloride afforded, after evaporation to dryness, 3.4 g (95% yield) of a yellow oil that was identified as a 2.6:1 mixture of methyl N-(1-phenyl-2-methylthioehtyl) carbamate and N-(2-phenyl-2 -methylthioethyl) carbamate. The separation of the regioisomers could not be possible in our hands,and the ratio of them have to be stablish by integration of the signals of the methylsulfenyl groups that appeared at different field in the ^1H NMR spectrum of the mixture. IR (film) 3360, 1730, 1550, 1270, 780, 745 and 710 cm^{-1}. ^1H NMR 7.80(m, 1H, NH); 7.40(m, 5H, C_6H_5); 4.75 and 3.98(2m, 1H, CHN and CHS); 3.61 and 3.57 (s,3H, CH_3O); 3.44 and 2.84 (m, 2H, CH_2N and CH_2S); 2.12 and 1.96(s, 3H, CH_3S); mass spectrum (EI) m/z: 225$(M)^+$ (1.1), 178 (1.2), 177 (6.4), 165 (10.3), 164 (97.1), 150 (44.5), 137 (100), 121 (27.9), 104 (16.8).

1 (and 2) Phenyl-2-methylthioethylamine. A mixture of 3.4g (15 mmol) of methyl N- 1(and 2) phenyl -2-methylthioethyl carbamate, 3g (48 mmol) of potasium hydroxide and 50 ml of ethanol was dissolved in water and refluxed for 10 hours. After this time, the resulting solution was diluted with water, carefully neutralized with hydrochloric acid (20%) and extracted with chloroform. The aqueous

layer was neutralized with sodium hydroxide (20%), extracted with chloroform and concentrated to dryness. The resulting yellow oil was identified as a 2.5:1 mixture of 1-phenyl-2-methylthioethylamine and 2-phenyl-2-methylthioethylamine that could not be separated. The ratio could be stablished by integration of the signals of the methylsulfenyl groups of both regioisomers in the ^{1}H NMR spectrum of the mixture. ^{1}H NMR 7.35 (m, 5H, C_6H_5); 4.12 and 3.72 (2m, 1H, CHN and CHS); 3.07 and 2.73 (2m, 2H, CH_2N and CH_2S); 2.08 and 1.92 (2S, 3H, CH_3S).
The unequivocal assignment of the structures of these regioisomers was carried out by comparison of spectroscopic data of the regioisomers mixture with that of authentic samples obtained by an independent way[15].

Reactions of vic-iodoalkanecarbamates with potasium ethylxanthate (KEX). General procedure A. A solution of KEX (40 mmol) in 50 ml of dry acetone was added to an ice-cold solution of vic-iodoalkanecarbamate 2 (20mmol) in 200 ml of acetone. The mixture was stirred for 2 hours and allowed to warm to room temperature. The white precipitate that appeared was filtered and the solution was concentrated under reduced pressure to a half of its volume. After hydrolisis the mixture was extracted with ethyl acetate. The extracts were dried over Na_2SO_4 and the pale yellow oil obtained, after removal the solvent, was used without further purification. For characterization , a small fraction of the vic-carbamatealkanexanthate was purified by preparative t.l.c. (eluent : chloroform/petroleum ether/ ethyl acetate: 2/7/1).

Ethyl S-threo-3 (methoxycarbamoil) 2-butylxanthate 2a. Was prepared from methyl N-erythro-3-iodo-2-butylcarbamate 7a in quantitative yield as a pale yellow oil. IR (film) 3360, 1720, 1550, 1460, 1240, 1120 and 1055 cm^{-1}; ^{1}H NMR 4.84 (bs, 1H, $NHCO_2CH_3$); 4.66 (c, 2H, J=7.1 Hz, OCH_2CH_3); 3.40 (s, 3H, OCH_3); 4.00 (m, 2H, SCHCHN); 1.44 (t, 3H, J= 7.1. Hz, CH_3CH_2O); 1.38 (d, 3H, J= 7.1 Hz, CH_3CHS); and 1.23 (d, 3H, J=6.6 Hz, CH_3CHN); ^{13}C NMR 213.67 (C=S); 156.39 (C=O); 70.00 (CH_2O); 52.02 (CH_3O); 50.90 and 50.79 (2CH); 18.73 and 17.21 (2 CH_3CH); and 13.66 (CH_3CH_2O); mass spectrum (CI) m/z 292 $(M + 41)^+$ (7.3), 280 $(M + 29)^+$ (17.6) and 252 $(M + 1)^+$ (100). Anal. calc. for $C_9H_{17}NO_3S_2$: C,43.03; H, 6.77; N, 5.57; S, 25.5. Found: C, 43.49; H, 6.94; N, 5.57; S, 25.88.

Ethyl S-erythro-3 (methoxycarbamoil) 2-butylxanthate 2b. Was prepared from methyl N-threo-3-iodo-2-butylcarbamate 7b in 98% yield as a pale yellow oil. IR (film) 3360, 1730, 1540, 1465, 1260, 1125 and 1060 cm^{-1}. ^1H NMR 4.90 (bs, 1H, $NHCO_2CH_3$); 4.62 (m, 2H, OCH_2CH_3); 4.07 (m, 2H, SCHCHN); 3.66 (s, 3H, OCH_3); 1.42 (t, 3H, J= 6.7 Hz, CH_3CH_2O); 1.38 (d, 3H, J= 7 Hz, CH_3CHS); and 1.18 (d, 3H, J= 6.8 Hz, CH_3CHN); ^{13}C NMR 213.42 (C=S); 156.14 (C=O); 69.83 (CH_2O); 51.89 (CH_3O); 50.95 and 50.45 (2 CH); 17.34 and 17.18 ($2CH_3CH$); and 13.57 (CH_3CH_2O); mass spectrum (CI) m/z 292 $(M+41)^+$ (8.4), 280 $(M+29)^+$ (22.5) and 252 $(M+1)^+$ (100).

Ethyl S-(2-phenyl-2-methoxycarbamoil) ethylxanthate 2c. Was prepared from methyl N-1-phenyl-2-iodoethylcarbamate 7c in 99% yield as a white solid. Recrystallized from methanol; m.p. 120-122º. IR (nujol) 3340, 1690, 1525, 1265, 1120, 1055, 1040 735 and 700 cm^{-1}. ^1H NMR 7.34 (m, 5H, C_6H_5); 5.44 (bs, 1H, $NHCO_2CH_3$); 5.05 (m, 1H, CHN); 4.68 (q, 2H, J= 7 Hz, CH_3CH_2O); 3.67 (s, 3H, CH_3O); 3.60 (m, 2H, CH_2S); 1.44 (t, 3H, J= 7 Hz, CH_3CH_2O); mass spectrum (EI) m/z 299 $(M)^+$(0.23), 225 (1.04), 208 (0.84), 191 (0.62), 177 (100), 164 (98.2), 135 (19.6), 121 (34.4), 104 (16.2), 91 (22.9), 77 (16.0). Anal. calc. for $C_{13}H_{17}O_3NS_2$: C, 52.2; H, 5.7; N, 4.7; S, 21.4. Found: C, 52.4; H, 5.9; N, 4.8; S, 21.2.

Reactions of vic-carbamatealkanexanthates with aqueous NaOH . General procedure B. A mixture of vic-carbamatealkanexanthate 5 (4 mmol), sodium hydroxide (8 mmol) and 50 ml of water, was stirred and refluxed for 1 hour. The solution was allowed to cool to room temperature, neutralized with HCl (20%) and extracted with ethyl acetate. The extracts were dried over Na_2SO_4 and concentrated to dryness at reduced pressure. The white solid obtained was purified by recrystalization.

Reactions of vic-iodoalkanecarbamates with KEX and sodium hydroxide. General procedure C. A mixture of vic-iodoalkanecarbamate 7 (2 mmol), KEX (4 mmol), sodium hydroxide (1 mmol) and 50 ml of water was stirred and refluxed for 3 hours. The final solution was allowed to reach room temperature, neutralized with HCl (20%) and extracted with ethyl acetate. The extracts were dried over Na_2SO_4 and concentrated to dryness at reduced pressure. The yellow oil obtained was purified by t.l.c. (eluent: toluene/ethyl acetate: 1.5/0.5) or by recrystallization.

trans-4,5 -Dimethylthiazolidine-2-thione 3a. Was prepared by general procedure B from ethyl S-threo-3-methoxycarbamoil-2-butylxanthate 2a in quantitative yield. Recrystallized from hexane , m.p. 100-101º (lit.[10] 100.5-101.5º). IR (nujol) 3165, 1470, 1385, 1300, 1280 1110 and 1015 cm^{-1}. ^1H NMR 8.36 (bs, $NHCO_2CH_3$), 3.92 (d quintet, 1H, $J_{H,NH}$= 1.2 Hz, $J_{H,CH}$= J_{H,CH_3}= 6.6 Hz, CH_3CHNH); 3.67 (quintet, 1H, $J_{H,CH}$= J_{H,CH_3}= 6.6 Hz, CH_3CHS); 1.46 (d, 3H, J= 6.7 Hz, CH_3CHS); 1.40(d, 3H, J= 6.6 Hz, CH_3CHN); ^{13}C NMR 199.7 (C=S); 66.5 (CHN); 51.9 (CHS); 19.0 (CH_3CHS); 18.4 (CH_3CHN); mass spectrum (EI) m/z 149 (27), 147 $(M)^+$ (100), 86 (24), 61 (33), 55 (29). 3a was also obtained by general procedure C from methyl N-threo-3-iodo--2-butylcarbamate 7b in 74% yield as a pale yellow oil which crystallized on standing.

cis-4,5-Dimethylthiazolidine-2-thione 3b. Was prepared by general procedure B from ethyl S-erythro-3-methoxycarbamoil-2-butylxanthate 2b in 61% yield as a white solid. Recrystallized from hexane, m.p. 117-119º (lit[14] 119.2-120.1º). IR (nujol) 3160, 1470, 1295, 1060, 1010 cm^{-1}. ^1H NMR 8.64 (bs, $NHCO_2CH_3$); 4.34 (d quintet, 1H, $J_{H,NH}$= 1.0 Hz, $J_{H,CH}$= J_{H,CH_3}= 6.7 Hz, CH_3CHN); 3.94 (quintet, 1H, $J_{H,CH}$= = J_{H,CH_3}= 6.7 Hz, CH_3CHS); 1.37 (d, 3H, J= 6.7 Hz, CH_3CHS); 1.32 (d, 3H, J=6,7 Hz, CH_3CHN); ^{13}C NMR 200.6 (C=S); 62.2 (CHN); 48.5 (CHS); 15.2 (CH_3CHS); and 14.0 (CH_3CHN); mass spectrum (EI) m/z 149 (9), 147 $(M)^+$ (100), 86 (24.5), 61 (50.4), 55 (39.5); (CI) m/z 188 $(M+41)^+$ (5.0), 178 (3.3), 176 $(M+29)^+$ (23.6), 150 (8.9), 148 $(M+1)^+$ (100). 3b was also prepared by general procedure C from methyl N--erythro-3-iodo-2-butylcarbamate 7a in 64% yield as a pale yellow oil which was purified by t.l.c.

4-Phenylthiazolidine-2-thione 3c. Was prepared by general procedure B from ehtyl S (2-phenyl-2-methoxycarbamoil) ethylxanthate 2c in 51% yield as a white solid. Recrystallized from ethanol-water, m.p. 187-189 (lit[12] 191º). IR (nujol) 3140, 1495, 1255, 1052, 1040, 940, 755 and 690 cm^{-1}. ^1H NMR 7.60-7.30 (m, 6H, $NHCO_2CH_3$ and C_6H_5), 5.32 (m, 1H, ^3J= 8.2 Hz, ^3J=8.1 Hz, CHN); 3.86 (m, 1H, J_{gem}= = 11.2 Hz , ^3J= 8.2 Hz, CH_2S); 3.52 (m, 1H, J_{gem}= 11.2 Hz, ^3J= 8.1 Hz, CH_2S); ^{13}C NMR (DMSO) 199.2 (C=S); aromatic ring; 139.8 (C-ipso); 128.7 (C-ortho); 128.2 (C-meta); 126.2 (C-para); 66.4 (C-4) and 40.6 (C-5); mass spectrum m/z 197 (7.1), 196 (10.5), 195 $(M)^+$ (73.3), 148 (37.8), 135 (100), 104 (27.7), 91

(48.6) and 77 (26.7). Anal. calc. for $C_9H_9NS_2$: C, 55.4; H, 4.6; N, 7.2; S, 32.8. Found: C, 55.6; H, 4.7; N, 7.6; S, 32.6.

5-Phenylthiazolidine-2-thione 3d. *Was prepared by general procedure C from methyl* N-1-phenyl-2-iodoethylcarbamate 7c. The crude yellow oil obtained was solved in CCl_4 and the white precipitate that appeared was filtered, recrystallized (CH_2Cl_2) and characterized as 3d, m.p. 167-168º (lit[11] 169-170º) (31% yield). IR (nujol) 3160, 1520, 1475, 1300, 1050, 995, 775 and 710 cm^{-1}. ^1H NMR 7.51 (bs, 1H, $NHCO_2CH_3$); 7.47-7.28 (m, 5H, C_6H_5); 5.20 (m, 1H, ^3J=7.87 Hz, ^3J= 7.93 Hz, CHS); 4.29 (m, 1H, $J_{H,NH}$= 0.9 Hz, J_{gem}= 11.2 Hz, ^3J= 7.87 Hz, CH_2N); 4.02 (m, 1H, $J_{H,NH}$= = 1 Hz, J_{gem}= 11.2 Hz, ^3J= 7.93 Hz, CH_2N); ^{13}C NMR 201.5 (C=S); *aromatic ring:* 137.8 (C-ipso); 129.2 (C-ortho); 128.8 (C-meta); 127.3 (C-para); 58.3 (C-4) and 54.2 (C-5); mass spectrum (EI) m/z 197(16.1), 195 $(M)^+$(100), 135 (67.7), 104 (58.1), 91 (67.5) and 77 (58.1). (CI) m/z 229 $(M+29)^+$ (20), 196 $(M+1)^+$ (100).

Reduction of vic-carbamatealkanexanthates with $NaBH_4$. General procedure D. A solution of vic-carbamatealkanexanthate 2 (8 mmol) in 30 ml of dry THF was added *dropwise over a suspension of* $NaBH_4$ *(16 mmol) in 20 ml of* THF. The mixture was stirred and refluxed for 2 hours. The resulting suspension was hydrolized carefully with HCl (20%), neutralized with CO_3K_2 (20%) and extracted with chloroform. The extracts were dried over Na_2SO_4 and concentrated. The yellow oil obtained has two main components that were separated by t.l.c. (eluent : toluene/ethyl acetate: 1.5/0.5).

Reduction of ethyl S-threo-3 (methoxycarbamoil) 2-butylxanthate 2a. The general procedure D allowed the isolation of trans-4,5-dimethylthiazolidine-2-thione 3a in a 12% yield and trans-4,5-dimethylthiazolidine-2-one 4a in a 17% yield. The product 4a was obtained as a colorless oil.

trans-4,5-dimethylthiazolidin 2-one 4a. IR (film) 3320, 1680 cm^{-1}. ^1H NMR 6.69 (bs, 1H, $NHCO_2CH_3$); 3.54 (m, 2H, NCHCHS); 1.46 (d, 3H, J=5.9 Hz, CH_3CHS); 1.31 (d, 3H, J= 5.5 Hz, CH_3CHN); ^{13}C NMR 174.9 (C=O); 58.6 (CHN); 48.3 (CHS); 19.8 (CH_3CHS) and 19.2 (CH_3CHN). mass spectrum (EI) m/z 133 (4.0), 132 (5.4), 131 $(M)^+$ (85.5), 116 (48.5), 88 (30.8), 61 (100) and 55 (32.2).

Reduction of ethyl S-erythro -3 (methoxycarbamoil)-2-butylxanthate 2b. The general procedure D allowed the isolation of cis-4,5-dimethylthiazolidine-2-thione 3b in 18% yield and cis-4,5-dimethylthiazolidine-2-one 7b in 25% yield. Compound 4b was obtained as a white solid. Recrystallized from petroleum ether, m.p. 66-68º.

cis-4,5-Dimethylthiazolidin 2-one 4b. IR (nujol) 3265, 1690 cm^{-1}. ^1H NMR 5.57 (bs, 1H, $NHCO_2CH_3$); 3.97 (d quintet, 1H, $J_{H,NH}$= 0.8 Hz, $J_{H,CH}$= 6.6 Hz, J_{H,CH_3}=6.6 Hz, CH_3CHN); 3.90 (quintet, 1H, $J_{H,CH}$= J_{H,CH_3}= 6.5 Hz, CH_3CHS); 1.37 (d, 3H, J_{H,CH_3}= = 6.5 Hz, CH_3CHS); 1.24 (d, 3H, J_{H,CH_3}= 6.6 Hz, CH_3CHN); ^{13}C NMR 175.2 (C=O); 55.4 (CHNH); 45.0 (CHS); 16.0 (CH_3CHS); and 15.0 (CH_3CHN). mass spectrum (EI) m/z 133 (5.6), 132 (13.8), 131 $(M)^+$ (100), 116 (65.6), 88 (24.4) and 61 (34.2). Anal. calc. for C_5H_9NSO: C, 45.80; H, 6.87; N, 10.68; S, 24.42. Found: C, 45.6; H, 6.88; N, 11.00; S, 24.56.

Reduction of ethyl S-(2-phenyl-2-methoxycarbamoil) ethylxanthate 2c. The general procedure D allowed the isolation of 4-phenylthiazolidine-2-thione 3c in 30% yield and 4-phenylthiazolidine-2-one 4c in 50% yield. Compound 4c recrystallized from CCl_4, m.p. 135-138º (lit[16] 139-140.5º).

4-Phenylthiazolidin 2-one 4c . IR (nujol) 3360, 1720, 1700, 1050, 770 and 615 cm^{-1}. ^1H NMR 7.40-7.30 (m, 5H, C_6H_5); 6.20 (bs, 1H, NH); 4.97 (m, 1H, $J_{H,NH}$= 0.9 Hz, ^3J=8.3 Hz, ^3J= 7.4 Hz, CHNH); 3.65 (m, 1H, J_{gem}= 11.1 Hz, ^3J= 7.4 Hz, CH_2S); 3.32 (m, 1H, J_{gem}= 11.1 Hz, ^3J= 8.3 Hz, CH_2S); ^{13}C NMR 175.1 (C=O); aromatic ring: 139.8 (C-ipso); 129.1 (C-ortho); 128.7 (C-meta); 126.0 (C-para); 59.0 (C-4) and 52.2 (C-5).mass spectrum (EI) m/z 181 (2.6), 180 (6.2), 179 $(M)^+$ (43.3), 135 (100), 105 (27.3), 104 (35.6), 91 (60.8) and 77 (44.8).

Dedicatory. We would like to dedicate this paper to the memory of the late Prof. Dr. Juan Borges del Castillo.

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