RECYCLIZATION REACTIONS OF SMALL RINGS. 8.* SYNTHESIS OF 5-SUBSTITUTED 2-OXAZOLIDONES FROM THIAZOLIDINE-2,4-DIONE AND OXIRANES

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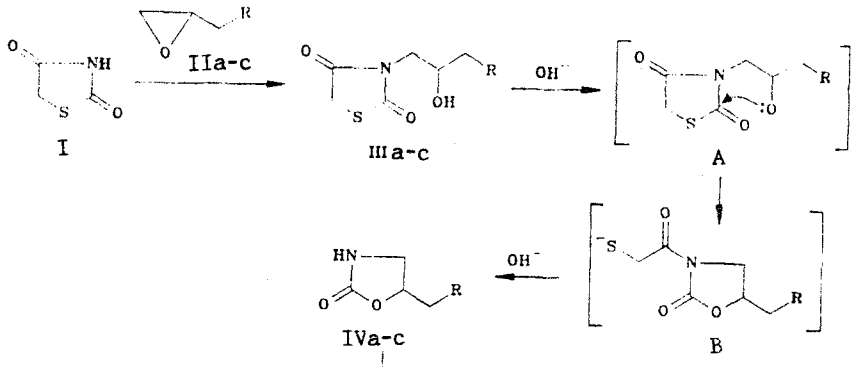
Treatment of oxiranes with thiazolidine-2,4-dione gives N-(2-hydroxypropyl)-thiazolidine-2,4-diones which can recyclize to 5-substituted 2-oxazolidones in basic medium.

It has been shown [2] that thiazolidine-2,4-diones which contain N-acylmethyl fragments can recyclize under the influence of nucleophiles to different azacyclic systems. The reaction involves both the exocyclic fragment and the meso position of the heterocycle.

In this work we have shown that thiazolidine-2,4-dione (I) reacts with oxiranes IIa-c to give N-(2-hydroxy-3-R-propyl)-thiazolidine-2,4-diones IIIa-c which recyclize in the presence of base to give 5-substituted 2-oxazolidones IVa-c (Table 1).



II—IV a R=Cl, b R=OC_6H_5, c R=$OC_{10}H_7$-α

The potassium salt of thiazolidine-2,4-dione reacts in the presence of base similarly but in a single stage. The yields of the condensation products IIIa-c are 85-99% and of the oxazolidones IVa-c 43-75%.

Compound IIIa forms the benzylidene (V) and benzoyl (VI) derivatives which confirm its structure.

The IR spectra of thiazolidinediones IIIa-c, V, and VI show absorption bands typical of this five-membered ring for C=O at 1665-1685 and 1710-1745 and for OH at 3355-3500 cm^{-1}. The oxazolidones IVa, b show bands for C=O at 1725-1735 and NH at 3150-3320 cm^{-1}. The PMR spectra of IIIa-c, V, and VI show signals for the protons of the CH_2 of the thiazolidine ring (3.8-4.2) and the CH_2 (3.6-4.1), CH (3.7-5.5, and OH (3.2-5.5 ppm) of the hydroxypropyl fragment. The spectra of IVa, b show signals for the CH_2 (3.3-3.7), CH (4.7-5.0), and NH protons (6.9-7.7 ppm) of the oxazolidine ring and the CH_2 protons of the exocyclic RCH_2 fragment at 3.8-4.3 ppm (Table 1).

Conversion of the thiazolidinediones IIIa-c to oxazolidones IVa-c occurs via the intermediate compound of type A which recyclizes to anion B through intramolecular exchange of the cyclic sulfur atom for oxygen. In basic

*For Communication 7 see [1].

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TABLE 1. Constants for the Thiazolidinediones IIIa-c, V, and VI and Oxazolidones IVa-c

Compound	Empirical formula	mp, °C*[1]	R_f	IR spectrum, cm^{-1}			PMR spectrum, δ, ppm (spin coupling, J, Hz)*[2]					Yield, %
				C=O	X–H*[3]	CH–S	CH_2–R	CH_2–N	CH_{aliph}	CH_{arom}	X–H*[3]	
IIIa	$C_6H_8ClNO_3S$	64...65	0,55	1682 s., 1745 s.	3355 m.	4,00s.	3,80d (4,0)	3,60 d (4,0)	3,7*[4]	—	3,20 d (6,0)	99
IIIb	$C_{12}H_{13}NO_4S$	134...135	0,64	1665 s., 1720 m,	3395 m.	4,19s.	3,93d (4,2)	3,66 d (6,0)	3,8*[4]	6,99 m; 7,36 m	5,39 d (5,4)	90
IIIc	$C_{16}H_{15}NO_4S$	105...106	0,54	1665 s., 1725 m,	3370 w.	3,83s.	4,08m*[4]	3,87 d (1,0)	4,08*[4]	6,70 m; 7,47 m; 7,77 m; 8,27 m	3,00s	85
IVa	$C_4H_6ClNO_2$	98...100	0,45	1725 s.	3150 m, 3225 m.	—	3,79d (4,8)	3,33 d (12,0); 3,43 d	—	4,76	7,51 s	43
IVb	$C_{10}H_{11}NO_3$	114...115	0,55	1735 s.	3160 w., 3320 s.	—	4,16d (4,4)	3,43 d (18,0); 3,56 d	4,93	7,03 m; 7,36 m	7,73 s	52
IVc	$C_{14}H_{13}NO_3$	127...128	0,47	1725 s.	3180 w., 3225 w., 3380 w.	—	4,25d (3,8)	3,68 m	5,03	7,50 m; 7,82 m; 8,27 m	6,87 d (5,6)	75
V	$C_{17}H_{12}ClNO_3S$	154...155	0,75	1670 s, 1735 s.	3500 m.	—	3,69d	3,69 d	3,96*[4]	7,93 s; 7,54 m	5,54 d (5,6)	73
VI	$C_{13}H_{12}ClNO_4S$	94...96	0,81	1685 s, 1710 s., 1745 s.	—	3,87	3,73d (4,0)	4,00 m	5,47	7,45 m; 8,07 m	—	85

*[1]Compound IVa was recrystallized from $CHCl_3$, VI from diethyl ether, the rest from isopropanol.

*[2]PMR spectra of IIIa-c and VI recorded in $CDCl_3$, IVa-c and V in DMSO-D_6.

*[3]For compounds IIIa-c and V, X = O; for IVa-c, X = N.

*[4]Approximate values because of the superimposing of the CH, CH_2N, and CH_2Cl signals. The top of the latter peaks is clearly seen and the CH signal is included on the basis of the integrated area of the whole signal.

medium, separation of thioglycolate occurs to give oxazolidones IVa-c.

The conversion (I → III → IV) resembles the reaction of phenylglycidyl ether with cyanuric acid [3] to give the phenoxymethyloxazolidone IVb. It differs significantly from the latter in the reaction mechanism which is a nucleophilic recyclization of the thiazolidine and oxirange rings. By contrast, the synthesis of the oxazolidone by [3] includes an acid catalyzed fission of the triazine ring and cyclization of the intermediate 2-hydroxypropylisocyanates. Notably, the new reaction occurs more readily, in milder condition, in higher yield of final products, and through formation of stable crystalline intermediates.

It was stated in [4] that reaction of the potassium salt of thiazolidine-2,4-dione I with epichlorohydrin gives a polymer of N-glycidyl-thiazolidine-2,4-dione. However, we found no appreciable amount of oligomer formed under the reported conditions and conclude that their report [4] is in error.

EXPERIMENTAL

IR spectra were recorded on a UR-20 instrument in Nujol medium with slit program 4 and scan speed 160 cm^{-1}. PMR spectra were taken on a Tesla BS-467C (60 MHz) spectrometer using TMS or HMDS as internal standard. Thin-layer chromatography was carried out on Silufol silica gel using chloroform—methanol (10:1) as eluent and iodine vapor visualization.

Satisfactory elemental analytical data for C, H, N (S, Cl) was obtained for all new compounds.

3-(2-Hydroxy-3-R-propyl)-thiazolidine-2,4-diones (IIIa-c). A. A mixture of thiazolidine-2,4-dione I (1.17 g, 10 mmoles), the corresponding oxirane IIa, b (11 mmoles), and tetraethylammonium chloride (0.03 g, 0.2 mmole) was stirred at 80°C for 2 h. TLC showed that the thiazolidinedione had reacted fully, in the case of synthesis of IIIb the reaction product precipitates.

Compounds IIIa, b were separated by dilution of the reaction mixture with ether and, in the case of IIIb, the reaction product was filtered off, dried, and recrystallized from the corresponding solvent. Compound IIIa crystallized slowly at 0°C and was filtered off and purified by recrystallization.

B. A solution of thiazolidine-2,4-dione (5.85 g, 0.05 mole) in epichlorohydrin (40 ml, ≈0.5 mole) was stirred at 70°C for 12 h. The solution was evaporated in vacuo and the residue was triturated with ether and allowed to crystallize at −10°C. Separation was by method **A.**

5-R-Methyl-2-oxazolidones (IVa-c). A. A solution of 2-hydroxy-3-chloropropyl-thiazolidine-2,4-dione (IIIa, 0.5 g, 2.4 mmoles) in epichlorohydrin (8 ml) and isopropanol (1 ml) was heated to 50°C and granular sodium hydroxide (0.2 g, 5 mmoles) added at this temperature over 30 min. Stirring was continued under these conditions for 4.5 h. The precipitate was filtered and the mother liquor evaporated to dryness in vacuo. The residue was triturated with diethyl ether, the solution decanted, chloroform (0.5 ml) added to the oily residue, and the product was stirred and left at −10°C until the product (IVa) crystallized. The precipitate was filtered, washed with chloroform and ether, and recrystallized

B. A solution of the 2-hydroxy-3-aryloxypropyl-thiazolidine-2,4-diones (IIIb, c, 12.4 mmoles) was dissolved in a methanolic solution (10 ml) of KOH (2 g, 36 mmoles) and refluxed for 4 min. The product was diluted with water (100 ml) and the precipitate filtered thoroughly, washed with water, and recrystallized

3-(2-Hydroxy-3-chloropropyl)-5-benzylidene-thiazolidine-2,4-dione (V). Benzaldehyde (0.32, 3 mmoles) and N-methylmorpholine (0.3 g, 3 mmoles) were added to a solution of 3-(2-hydroxy-3-chloropropyl)-thiazolidine-2,4-dione (IIIa, 0.58 g, 2.77 mmoles) and heated at 100°C for 2 h. The product was cooled and the white precipitate was washed with ether and recrystallized.

3-(2-Benzoyloxy-3-chloropropyl)-thiazolidine-2,4-dione (VI). Benzoyl chloride (0.42 g, 3 mmoles) was added dropwise over 30 min to a solution of 3-(2-hydroxy-3-chloropropyl)-thiazolidine-2,4-dione (IIIa, 0.57 g, 2.72 mmoles) in dry pyridine (5 ml). Pyridine hydrochloride precipitated after heating the solution at 70°C for 1 h and the mixture was cooled and poured into water (50 ml). Over several hours the oily product crystallized. It was filtered, dried, and recrystallized from diethyl ether.

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