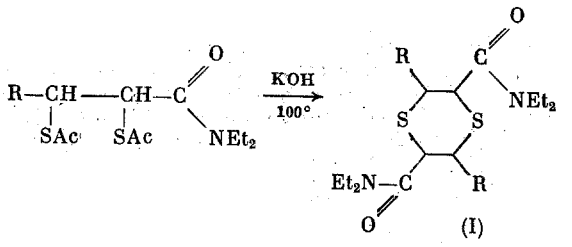
1,4-DITHANE-2,5-DICARBOXYLIC ACID

N. M. Karimova, L. P. Kuzina,
and O. V. Kil'disheva

UDC 542.91:547.842

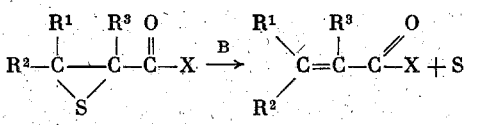
Thiiranes dimerize in several cases to give dithianes by the action of alkali [1]. In the present work, we studied the possibility of achieving such a dimerization for thioglycidic acids and the behavior of these acids in the presence of bases.

1,4-Dithiane-2,5- and 2,6-dicarboxylic acids were initially obtained by the addition of SCl_2 to acrylic acid and the subsequent action of Na_2S. The structure of these products was studied in detail by Gundermann and Burba [2]. Analogous compounds were subsequently isolated in an attempt to synthesize the diethylamides of thioglycidic acids by the action of alkali on the diethylamides of 1,2-(diacetylthio)alkanecarboxylic acids [3]:



R = H, Me.

The formation of dithianes is attributed to the dimerization of the intermediate thioglycidic acid derivatives. We have studied the reaction of a series of thioglycidic acids and their derivatives with nucleophilic reagents, but dimerization to give dithianecarboxylic acids was not observed. Elimination of sulfur with the formation of α,β-unsaturated acids occurs in almost all cases:



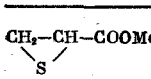
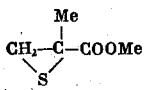
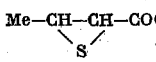
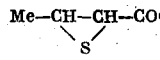
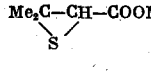
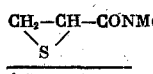
$R^1 = R^2 = R^3 = H$; $R^1 = R^2 = H$, $R^3 = Me$; $R^1 = R^3 = H$, $R^2 = Me$; $R^1 = R^2 = Me$, $R^3 = H$, X = OH, OR, NR_2; B = NaOH, NaOEt, R_2N, Ph_3P

The facile desulfurization is apparently a consequence of the destabilizing effect of the carboxyl group on the thiirane ring. In the case of esters (II)-(VI), we studied the effect of the thioglycidic acid structure on the tendency to undergo desulfurization upon the action of various bases (Table 1). The effect of substitution in the carboxyl group was shown by comparison of ester (II) and dimethylamide (VII). The facility of desulfurization was evaluated relative to the amount of sulfur released or Ph_3PS in the case of triphenylphosphine. The unreacted starting compounds and the α,β-unsaturated acid derivatives formed were determined in the mother liquor by gas–liquid chromatography. As expected, the amides are more stable than the esters relative to sulfur elimination due to the electron-donor effect of the amide group [compare (II) and (VII)]. The thiirane ring is also strengthened upon the introduction of a methyl group, especially in the α position. Desulfurization occurs more readily when it results in the formation of the thermodynamically more stable unsaturated compound [compare (IV) and (V), (IV) and (VI)].

A. N. Nesmeyanov Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 11, pp. 2630-2633, November, 1985. Original article submitted January 28, 1985.

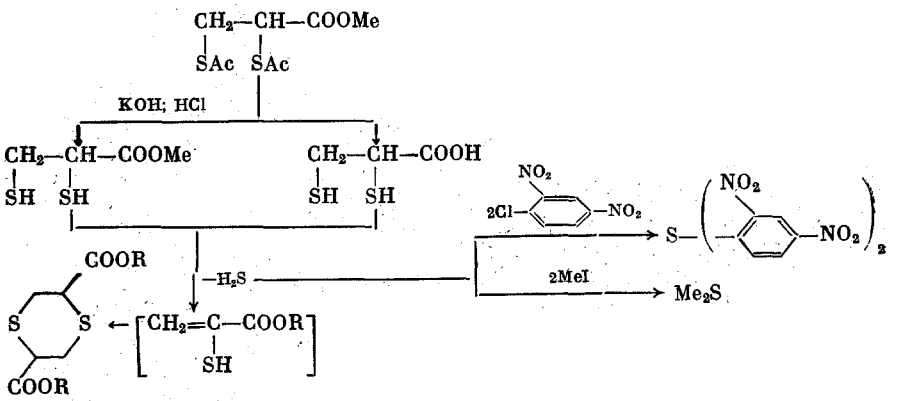
0568-5230/85/3411-2437$09.50

TABLE 1. Reactions of Thioglycidic Acid Derivatives* with Bases

Compound		0,7 *N* NaOH in EtOH		$(CH_2)_5NH$		Me_2NH		Ph_3P	
		time, h	sulfur yield, %	time, h	sulfur yield, %	time, h	sulfur yield, %	time, h	sulfur yield, %
	(II)	0,25	89	0,5	97	0,5	86	1	84
	(III)	24	63	15	56	24	15	1	52,7
	(IV) trans	24	77	17	78	24	30	1	70
	(V) cis	–	–	–	–	–	–	1	55
	(VI)	5	81	3	85	24	67	1	76
	(VII)	24	88	24	94	48	90	1	80

*Syntheses reported in our previous work [3].

We have found that thioglycidic acids and their derivatives do not dimerize upon the action of nucleophiles but rather lose sulfur. Thus, in order to explain the formation of dithianes (I), we studied the transformations of 1,2-(diacetylthio)- and 1,2-dimercaptopropionic acids in the presence of alkali. Thus, heating the methyl ester of 1,2-(diacetylthio)propionic acid in KOH solution at reflux (the conditions of Tang and Speziale [3]) gives trans-1,4-dithiane-2,5-dicarboxylic acid (VIII) along with 1,2-dimercaptopropionic acid, its methyl ester and K_2S. The formation of K_2S was indicated by the release of H_2S upon acidification of the reaction mass.



R = H (VIII), Me (IX).

Treatment of the methyl ester of 1,2-dimercaptopropionic acid by a solution of KOH in aqueous methanol at 20°C leads to the formation of dimethyl ester (IX). The formation of K_2S in this case was indicated by the addition of 2,4-dinitrochlorobenzene to the reaction mass after acidification and formation of the corresponding sulfide; Me_2S was released upon treatment with MeI.

β-Substituted propionic acids tend to undergo β-elimination [4, 5]. On the basis of these results, namely, the release of H_2S, we may propose the following scheme for the formation of dithianedicarboxylic acids from 1,2-(diacetylthio)- and 1,2-dimercaptopropionic acids. The action of alkali leads to β elimination with the release of H_2S, and the α-mercaptoacrylic acid formed dimerizes to give a symmetrical dithianedicarboxylic acid.

Thus, we have shown that the scheme for the formation of amides of dithianedicarboxylic acids (I) from amides of 1,2-(diacetylthio)propionic acids through intermediate thiiranes as proposed by Tang and Speziale [3] is incorrect since thioglycidic acids and their derivatives are not formed under these conditions.

EXPERIMENTAL

The gas–liquid chromatographic analysis was carried out on a Tsvet 4-67 chromatograph with a thermal conductivity detector on a column packed with polyethylene glycol on Chromosorb W and helium as the carrier gas.

Trans-1,4-Dithiane-2,5-dicarboxylic Acid (VIII). A solution of 23.6 g (0.1 mole) methyl 1,2-(diacetylthio)propionate [6] in 0.5 N aq. KOH was heated at reflux for 0.5, cooled to 20°C, and acidified with conc. HCl to pH 3 with the observation of H_2S release. Water was removed in vacuum, and the solid residue was dissolved in 30 ml dioxane. Insoluble KCl was separated, and dioxane was removed in vacuum until the onset of crystallization. A total of 1.36 g (13%) (VIII) was obtained, mp 246°C [2]. The dioxane filtrate was diluted with benzene, and the precipitated oil was separated and fractionated to yield 7.3 g (48%) methyl 1,2-dimercaptopropionate, bp 75°C (2 mm), n_D^{20} 1.5246 [6] and 2.3 g (16.7%) 1,2-dimercaptopropionic acid, bp 55°C (0.02 mm), mp 72°C (from $CHCl_3$) [6].

Dimethyl Ester of trans-1,4-Dithiane-2,5-dicarboxylic Acid (IX). a) A sample of 0.84 g (15 mmoles) KOH in 20 ml 50% aqueous methanol was added with stirring to a solution of 1.52 g (10 mmoles) methyl 1,2-dimercaptopropionate [6] in 3 ml methanol, and the mixture was maintained for 24 h at 20°C. The precipitate formed was washed with benzene and ether and reprecipitated from acetone by the addition of ethanol to yield 295 mg (25%) (IX), mp 122°C [2]. Found: C 40.76; H 5.06; S 27.27%. Calculated for $C_8H_{12}O_4S_2$: C 40.79; H 5.06; S 27.11%. A sample of 2.03 g (10 mmoles) 2,4-dinitrochlorobenzene was added to one half of the filtrate, and the mixture was heated at reflux for 10 min. The precipitate that formed upon cooling was filtered off to give 2.5 g (68%) dimethyl sulfide, bp 37-38°C [8].

b) A sample of 0.21 g (1 mmole) (VIII) was treated at 20°C with an ethereal solution of diazomethane until no further nitrogen was released. The ether was removed to give 0.23 g (97.5%) (IX), mp 121-122°C. The melting point of a mixed probe with a sample of the ester described above was not depressed.

General Method for the Reactions of Thioglycidic Acids (II)-(VII) with Bases. A catalytic amount (5-10 drops) of base was added to a 5% solution of 10 mmoles of the thioglycidic acid in ether or benzene. Triphenylphosphine was taken in an equimolar amount in 25 ml 3:2 ether–benzene. The mixture was maintained at 20°C, and after some time, the sulfur or Ph_3PS that separated was filtered off (yields are given in Table 1). The unreacted starting compounds and unsaturated products in the mother liquor were identified by gas–liquid chromatography.

LITERATURE CITED

1. J. Gierer and L. A. Smedman, Acta Chem. Scand., 20, 1769 (1966).
2. K. D. Gundermann and C. Burba, Chem. Ber., 94, 2157 (1961).
3. C. C. Tang and A. J. Speziale, J. Org. Chem., 29, 1577 (1964).
4. P. F. Butskus and G. I. Denis, Usp. Khim., 35, 1999 (1966).
5. K. D. Gundermann, Angew. Chem., 75, 1194 (1963).
6. W. A. Lazier, A. A. Pavlic, and W. J. Peppel, US Patent No. 2,422,246; Chem. Abstr., 41, 6277h (1947).
7. Beilsteins Handbuch der Organischen Chemie, E116, p. 315.
8. Encyclopedic Chemical Dictionary [in Russian], Moscow (1983), p. 171.
9. N. M. Karimova, M. G. Lin'kova, O. V. Kil'disheva, and I. L. Knunyants, Izv. Akad. Nauk. SSSR, Ser. Khim., 212 (1973); 1788 (1973); 229 (1978).
10. M. G. Lin'kova, L. P. Parshina, O. V. Kil'disheva, and I. L. Knunyants, Izv. Akad. Nauk. SSSR, Ser. Khim., 2413 (1968).