LITERATURE CITED

1. V. A. Kaminskii, N. V. Kruglyakova, I. I. Mal'tsev, and M. N. Tilichenko, Khim. Geterotsikl. Soedin., No. 1, 95 (1981).
2. A. Sammour and H. H. Zoorob, Acta Chim. Acad. Sci. Hung., 86, 53 (1975).
3. L. M. Eremeeva, T. V. Moskovkina, Yu. V. Vasilenko, A. N. Saverchenko, V. A. Kaminskii, and M. N. Tilichenko, Khim. Geterotsikl. Soedin., No. 2, 240 (1979).
4. V. A. Kaminskii, A. N. Savarchenko, and M. N. Tilichenko, Zh. Org. Khim., 6, 404 (1970).
5. V. A. Kaminskii and M. N. Tilichenko, Khim. Geterotsikl. Soedin., No. 10, 1474 (1974).

RESEARCH ON UNSATURATED LACTONES.

49.* SYNTHESIS OF THIAZOLIDINES THAT CONTAIN AN α,β-UNSATURATED γ-LACTONE RING

A. N. Dzhandzhapanyan, A. A. Avetisyan, A. A. Oganesyan, and M. T. Dangyan

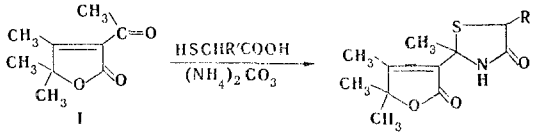
UDC 547.722.3'724.3'789.3

The corresponding thiazolidines containing a lactone ring and their hydrochlorides and N-benzoyl derivatives were obtained by the reaction of 2-acetyl-3,4,4-trimethyl-2-buten-4-olide with thioglycolic or mercaptosuccinic acids and ammonium carbonate.

It is known that many thiazolidine derivatives are biologically active substances; in particular, they have analgesic, antipyretic, and antibacterial activity [2, 3].

In order to synthesize new biologically active thiazolidine derivatives that contain an α,β-unsaturated γ-lactone ring we studied the reactions of 2-acetyl-3,4,4-trimethyl-2-buten-4-olide (I) with thioglycolic and mercaptosuccinic acids and ammonium carbonate.

2-Methyl-2-(3,4,4-trimethyl-2-buten-4-olid-2-yl)-4-oxothiazolidine (II) is formed in 20-32% yield from thioglycolic acid. The reaction with mercaptosuccinic acid proceeds more readily and gives a decarboxylated product, viz., 2,5-dimethyl-2-(3,4,4-trimethyl-2-buten-4-olid-2-yl)-4-oxothiazolidine (III), in 40% yield. Refluxing in xylene leads to considerable resinfication.



I

R' = H, CH_2COOH

II R = H; III R = CH_3

Absorption bands that are characteristic for lactone (1745-1750 cm^{-1}) and lactam (1695-1700 cm^{-1}) carbonyl groups, a double bond (1590-1620 cm^{-1}), and an NH group (3180-3200 cm^{-1}) are found in the IR spectra of the compounds obtained. The PMR spectrum of III contains, in addition to signals of protons of methyl groups in the 3 and 4 positions of the butenolide ring (2.08 and 1.53 ppm) and in the 2 position of the thiazolidine ring (1.18 ppm), of an NH group (13.09 ppm), and a proton in the 5 position of the thiazolidine ring (4.48 ppm), a signal of protons of a methyl group in the same position (2.18 ppm).

Hydrochlorides IV and V are formed from thiazolidines II and III in 30-40% yields. Reverse alkalization again gives the free thiazolidines.

Reactions with benzoyl chloride lead to the formation of N-benzoyl derivatives VI and VII in 45-50% yields. The IR spectra of VI and VII contain absorption bands at 1750-1755,

*See [1] for Communication 48.

Erevan State University, Erevan 375049. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 475-476, April, 1981. Original article submitted March 21, 1980.

 0009-3122/81/1704-0338$07.50 © 1981 Plenum Publishing Corporation

TABLE 1. Characteristics of the Synthesized Compounds

Compound	mp, °C	Found, %					Empirical formula	Calc., %					Yield, %
		C	H	Cl	N	S		C	H	Cl	N	S	
II	204—206 (alcohol)	55,2	6,2	—	5,3	12,8	$C_{11}H_{15}NO_3S$	54,8	6,2	—	5,3	13,3	32
III	158—160 (alcohol – ether)	56,7	6,2	—	5,9	12,2	$C_{12}H_{17}NO_3S$	56,3	6,7	—	5,5	12,6	40
IV	250—255 (acetone)	—	—	12,5	—	—	$C_{11}H_{16}ClNO_3S$	—	—	12,7	—	—	30
V	246—250 (acetone)	—	—	12,0	—	—	$C_{12}H_{18}ClNO_3S$	—	—	12,2	—	—	40
VI	210—212 (hexane)	62,8	5,4	—	3,9	9,1	$C_{18}H_{19}NO_4S$	62,6	5,5	—	4,1	9,3	45
VII	178—180 (benzene)	63,7	6,0	—	3,7	8,5	$C_{19}H_{21}NO_4S$	63,5	5,9	—	3,9	8,9	50

1685-1690, 1650-1660, and 1590-1600 cm^{-1}, which are characteristic for lactone and amide carbonyl groups, the C=C bond, and the benzene ring.

Biological tests showed that the synthesized thiazolidine derivatives are active substances. In particular, thiazolidine II has weak activity with respect to the herpes virus.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The PMR spectrum of a solution in CCl_4 was recorded with a Hitachi Perkin–Elmer R-20B spectrometer with hexamethyldisiloxane as the internal standard.

5-H- and 5-Methyl-Substituted 2-Methyl-2-(3,4,4-trimethyl-2-buten-4-olid-2-yl)-4-oxothiazolidines (II, III). A 3-g (0.031 mole) sample of ammonium carbonate was added with stirring to a solution of 4.2 g (0.025 mole) of butenolide I and 2.4 g (0.026 mole) of thioglycolic acid or 2.4 g (0.016 mole) of mercaptosuccinic acid in 30 ml of absolute xylene or benzene, respectively, and the mixture was refluxed for 15 h with a Dean–Stark trap. It was then cooled, and the precipitate that formed by the addition of ether or without it was removed by filtration, washed with ether, and recrystallized (Table 1).

Reaction of II and III with Hydrogen Chloride. Dry hydrogen chloride gas was passed through a solution of 0.005 mole of II or III in 10 ml of chloroform at room temperature for 8 h, and the resulting precipitate was removed by filtration and washed with chloroform to give water-soluble hydrochloride IV or V (Table 1).

Reaction of II and III with Benzoyl Chloride. A 0.7-g (0.005 mole) sample of benzoyl chloride was added with cooling to a solution containing 0.005 mole of II or III, 0.4 g (0.005 mole) of pyridine, and 5 ml of absolute benzene. After 1 h, the precipitate was removed by filtration and recrystallized to give VI and VII (Table 1).

LITERATURE CITED

1. A. A. Avetisyan, A. N. Dzhandzhapanyan, and M. T. Dangyan, Arm. Khim. Zh., 33, 805 (1980).
2. US Patent No. 4053471; Ref. Zh. Khim., 11098P (1978).
3. West German Patent Application No. 2614189; Ref. Zh. Khim., 130106P (1978).