HETEROATOMIC DERIVATIVES OF AZIRIDINE.

9.* N-(α-ORGANYL-β-ACYLVINYL)AZIRIDINES AND THEIR REACTION WITH MERCAPTO ACIDS

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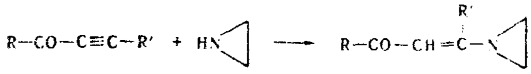
Mixtures of N-(α-organyl-β-acylvinyl)aziridines with preponderance of the cis adducts were obtained by the addition of aziridine to acetylenic ketones. The synthesized products react with mercaptosuccinic and thioglycolic acids with opening of the aziridine ring; depending on the reaction conditions, either aminoethylthio derivatives or, as a result of hydrolytic cleavage of the aziridine ring, 3-oxo-1,4-perhydrothiazine are formed. The IR and PMR spectra of the compounds obtained are discussed.

From a pharmacological point of view, N-(α-organyl-β-acylvinyl)aziridines are potential antitumorigenic substances. In addition, they are extremely reactive and may find application for the preparation of new forms of polymers and as valuable intermediates in organic synthesis [2].

The first information regarding N-(α-organyl-β-acylvinyl)aziridines appeared relatively recently. The reaction of β-halovinyl ketones with aziridine, which leads to the formation of N-(α-organyl-β-acylvinyl)aziridines and β,β-bis(aziridinyl)ethyl ketones, has been described [3]. The addition of aziridine to phenylbenzoylacetylene has been studied [4]. One of us has previously accomplished the synthesis of some N-(α-organyl-β-acylvinyl)aziridines by the addition of aziridine to thienylacetylenic ketones [5].

In a continuation of our study of the latter reaction we obtained N-(α-organyl-β-acylvinyl)aziridines via the scheme



I-VI

I R=C_4H_3S†, R′=C_4H_9; II R=C_4H_3S, R′=C_6H_5; III R=R′=C_4H_3S; IV R=C_4H_3S, R′=α-Br—C_4H_2O‡; V R=α-Cl—C_4H_2S**, R′=C_6H_5; VI R=R′=C_6H_5

Aziridine adds to acetylenic ketones in methanol when the mixture is heated to 50°C. The reaction product is a mixture of cis and trans adducts, the ratio of which was established by PMR spectroscopy (Table 1).

Analysis of the chemical shifts of the protons by an additive scheme with allowance for the contribution of the substituents makes it possible to assign the signals at weak field to the cis isomer [6]. The singlet signal of the aziridine protons in the spectra of each isomer constitutes evidence for rapid (on the PMR scale) inversion of the nitrogen atom in the aziridine ring.

We studied the reactions of some N-(α-organyl-β-acylvinyl)aziridines with thioglycolic and mercaptosuccinic acids. N-(α-Phenylbenzoylvinyl)aziridine (VI) reacts with mercapto-

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*See [1] for communication 8.
†The formula C_4H_3S stands for 2-thienyl.
‡The formula α-Br—C_4H_2O stands for 5-bromo-2-furyl.
**The formula α—Cl—C_4H_2S stands for 5-chloro-2-thienyl.

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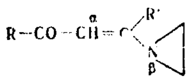
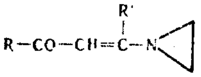
TABLE 1. Parameters of the PMR Spectra (δ, ppm) of



R	R'	cis Isomer		trans Isomer		Isomer ratio, %	
		H_α	H_{azir}	H_α	H_{azir}	cis	trans
C_4H_3S	C_4H_9	6,04 (s)	2,15 (s)	5,99 (s)	2,02 (s)	70	30
C_4H_3S	C_4H_3S	6,56 (s)	2,32 (s)	6,20 (s)	2,13 (s)	90	10
α-Cl—C_4H_2S	C_6H_5	6,35 (s)	2,21 (s)	6,10 (s)	2,02 (s)	90	10
C_6H_5	C_6H_5	6,54 (s)	2,19 (s)	6,48 (s)	2,12 (s)	60	40

TABLE 2. N-(α-Organyl-β-acylvinyl)aziridines



Compound	R	R'	bp, °C (mm)	mp, °C	Found, %				Empirical formula	Calc., %				Yield, %
					C	H	N	S		C	H	N	S	
I	C_4H_3S	C_4H_9	186—188 (5)	—	66,3	7,3	5.5	13.9	$C_{13}H_{17}NOS$	66,4	7,3	5,9	13,6	80
II	C_4H_3S	C_6H_5	238—240 (2)	—	—	—	5,2	—	$C_{15}H_{13}NOS$	70,6	5,1	5,5	12,5	78
III	C_4H_3S	C_4H_3S	—	100—101	59,8	4,3	—	24.5	$C_{13}H_{11}NOS_2$	59,8	4,2	5,3	24,5	82
IV	C_4H_3S	α-Br—C_4H_2C	—	117—118	—	—	—	9,7	$C_{13}H_{10}BrNO_2S$*	—	—	—	9,9	83
V	α-Cl—C_4H_2S	C_6H_5	—	97—98	—	—	5,3	10,6	$C_{15}H_{12}ClNOS$†	—	—	4,9	11,1	79
VI	C_6H_5	C_6H_5	—	75—76	81,7	5,9	5,3	—	$C_{17}H_{15}NO$	81,9	6,0	5,6	—	85

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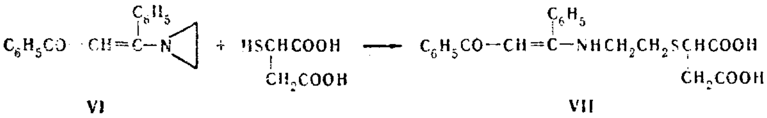
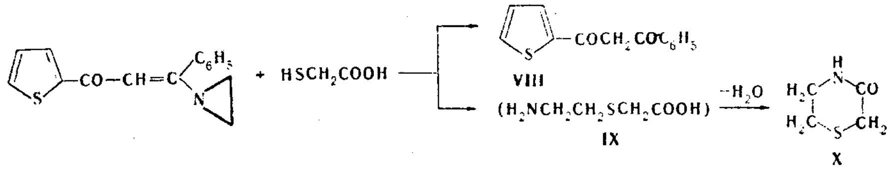
*Found: Br 25.3%. Calculated: Br 24.7%.
†Found: Cl 11.6%. Calculated: Cl 12.1%.

succinic acid with opening of the aziridine ring to give [N-(α-phenyl-β-benzoylvinyl)-β-aminoethylthio]succinic acid (VII) in 83% yield.



The reaction of N-(α-phenyl-β-thenoylvinyl)aziridine (II) with thioglycolic acid in ethanol is accompanied by hydrolytic cleavage of the aziridine ring and leads to the formation of 1-(2-thienyl)-3-phenyl-1,3-propanedione (VIII) and an oily substance (IX), which underwent dehydration when it was vacuum distilled to give crystalline 3-oxo-1,4-perhydrothiazine (X).



Absorption bands of a conjugated carbonyl group and a conjugated double bond at 1630-1640 and 1610-1620 cm^{-1} are present in the IR spectra of I-VI, whereas these bands are observed at 1610 and 1595-1600 cm^{-1}, respectively, in the spectrum of VII. The decrease in the frequencies of the vibrations of the C=O and C=C bonds in the spectrum of VII is due to the existence of an intramolecular hydrogen bond [7]. The absorption band of an associated N-H bond lies at 3120-3200 cm^{-1}. The absorption bands of a carboxy group are found at 1730 and 2500-2700 cm^{-1}. The spectrum of X contains frequencies of the vibrations of an amide group at 1647 and 3260-3290 cm^{-1}.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were obtained with a UR-20 spectrometer. The PMR spectra of solutions of the compounds in CCl_4 (I, III, V, and VI) and CF_3COOH (X) were recorded with a Tesla BS-487-C spectrometer (80 MHz); the chemical shifts are presented on the δ scale with respect to tetramethylsilane.

N-(α-n-Butyl-β-thenoylvinyl)aziridine (I). A mixture of 1.74 g (9.0 mmole) of 1-(2-thienyl)hept-1-ynone, 0.39 g (9.0 mmole) of aziridine, and 20 ml of methanol was heated at 50°C for 4 h, after which the solvent was removed by distillation at reduced pressure, and the residue was vacuum distilled to give 1.7 g (80%) of a product with bp 186-188°C (5 mm). Compounds II-VI were similarly obtained (Table 2).

[N-(α-Phenyl-β-benzoylvinyl)aminoethylthio]succinic Acid (VII). A 1.24-g sample of N-(α-phenyl-β-benzoylvinyl)aziridine (VI) was added to a solution of 0.75 g (5.0 mmole) of mercaptosuccinic acid in 30 ml of methanol, and the mixture was stirred at room temperature for 6 h. Ether was then added, and the liberated oil was separated and dried in vacuo to give 1.65 g (83%) of VII. Found: C 63.1; H 6.0; N 3.3%. $C_{21}H_{21}NO_5S$. Calculated: C 63.2; H 5.3; N 3.5%.

Reaction of N-(α-Phenyl-β-thenoylvinyl)aziridine with Thioglycolic Acid. A solution of 2.41 g (0.01 mole) of N-(α-phenyl-β-thenoylvinyl)aziridine in 10 ml of ethanol was added to a solution of 0.92 g (0.01 mole) of 80% thioglycolic acid in 20 ml of ethanol, and the mixture was stirred at 60°C for 6 h. At the end of the reaction the precipitate was removed by filtration and recrystallized from 80% ethanol to give 1.6 g (70%) of 1-(2-thienyl)-3-phenyl-1,3-propanedione (VIII) with mp 78°C. Found: C 68.0; H 4.6; S 13.7%. $C_{13}H_{10}O_2S$. Calculated: C 67.8; H 4.3; S 13.9%. According to the data in [8], this compound has mp 78-78.5°C.

The filtrate was evaporated, and the residual oil was vacuum distilled to give 0.6 g (80%) of 3-oxo-1,4-perhydrothiazine (X) with bp 145°C (5 mm) and mp 87-88°C. The PMR spectrum contains the following signals: 2.56 (2H, m), SCH_2C, 3.44 (3H, m), CH_2NH, and 3.75 ppm (2H, s) $SCH_2C{=}O$. Found: C 41.0; H 5.9; N 12.0; S 27.4%. C_4H_7NOS. Calculated: C 41.0; H 6.0; N 12.0; S 27.3%. According to the data in [9], this compound has bp 185°C (18 mm) and mp 87-89°C.

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