HETEROATOMIC DERIVATIVES OF AZIRIDINE. 14.* REACTIONS OF 1-(CARBOMETHOXYETHYL)-, 1-[1,2-BIS(CARBETHOXY)ETHYL]-, AND 1-[1,2-BIS(CARBOMETHOXY)VINYL]AZIRIDINE WITH THIOLS, 1,2-ETHANEDITHIOL, AND THIOLCARBOXYLIC ACIDS

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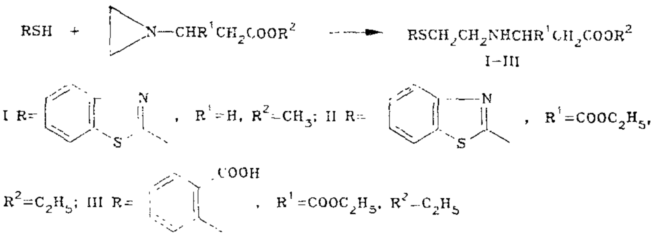
UDC 547.717'898

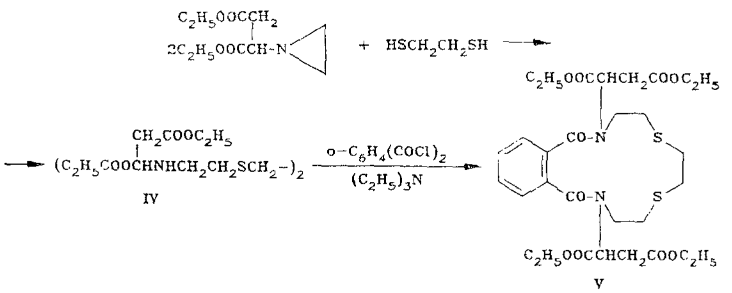
The reactions of 1-(carbomethoxyethyl)-, 1-[1,2-bis(carbethoxy)-ethyl]-, and 1-[1,2-bis(carbomethoxy)vinyl]aziridine with thiols and thiolcarboxylic acids produce the corresponding sulfides and esters of S-substituted N-(2-mercaptoethyl)amino acids. The reaction of 1-[1,2-bis(carbethoxy)ethyl]aziridine with 1,2-ethane-dithiol results in the formation of {1,8-bis[1,2-bis(carbethoxy)-ethyl]amino}-3,6-dithiaoctane. Cyclization of the latter by condensation with phthaloyl chloride gives 9,10-benzo-8,11-dioxo-1,4-dithia-7,12-bis[1,2-bis(carbethoxy)ethyl]-7,12-diazacyclotetradec-9-ene.

Derivatives of 2-aminoethanethiol are presently employed as chelating agents [2-4], antiradiation agents, and antidotes [5-7]. They have antibacterial, fungicidal, and herbicidal properties [5-7]. For the purpose of obtaining new open-chain and macroheterocyclic chelating agents in this series, as well as potentially biologically active compounds, we studied the reactions of N-substituted aziridines with thiols, 1,3-ethanedithiol, and thiolcarboxylic acids.

1-(Carbomethoxyethyl)- and 1-[1,2-bis(carbethoxy)ethyl]aziridines react with 2-mercaptobenzothiazole to form sulfides I and II, and the latter reacts with o-mercaptobenzoic acid to form compound III.



1,2-Ethanedithiol reacts with 1-[1,2-bis(carbethoxy)ethyl]-aziridine in a 1:2 mole ratio and is thereby converted into {1,8-bis[1,2-bis(carbethoxy)ethyl]amino}-3,6-dithiaoctane (IV).



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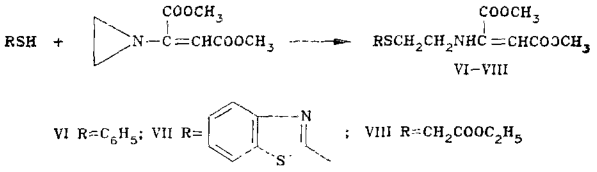
*For report 13 see [1].

Irkutsk Institute of Organic Chemistry, Academy of Sciences of the USSR, Siberian Branch, Irkutsk 664033. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1340-1342, October, 1984. Original article submitted April 11, 1983; revision submitted April 23, 1984.

0009-3122/84/2010-1099$08.50

For the purpose of converting diamine IV into macroheterocycle V, it was cyclized with phthaloyl chloride.

The reaction of 1-[1,2-bis(carbomethoxy)vinyl]aziridine with thiophenol, 2-mercaptobenzothiazole, and ethyl thioglycolate take place with the opening of the aziridine ring and the formation of the corresponding sulfides (VI-VIII).



The IR spectra of compounds I, II, IV, and VI-VIII contain absorption bands of esteric and amino groups at 1735-1750 and 3300-3330 cm^{-1}, respectively. Compound III should be assigned a betaine structure, since its spectrum contains absorption bands for NH_2^+ at 3070, 1645, and 1560 cm^{-1}. The ionized carboxyl group absorbs at 1590 and 1375 cm^{-1}. The absorption frequency of the esteric group in compound III is found at 1730 cm^{-1}. In the spectrum of macroheterocycle V there are absorption bands for amide and esteric groups at 1640 and 1735 cm^{-1}, respectively. Compounds I, II, and VII contain absorption bands at 1640-1670 cm^{-1}, which corresponds to a C=N group. The vibrational frequencies of the sulfide group in compounds I-VIII are found in the 715-760-cm^{-1} range.

EXPERIMENTAL

The IR spectra were obtained on a UR-20 instrument. The PMR spectra were recorded on a Tesla BS-487 spectrometer (80 MHz). The solvent for IV and V was $CDCl_3$, and the solvent for III was CF_3COOH. Thin-layer chromatography (TLC) was carried out on Silufol with a 5:1 benzene–methanol mixture as the solvent. The molecular weight of macroheterocycle V was determined cryoscopically in benzene.

Methyl N-[2-(Benzothiazolylthio)ethyl]-3-aminopropionate (I). A mixture of 6.45 g (50 mmole) of 1-(2-carbomethoxyethyl)aziridine and 8.35 g (50 mmole) of 2-mercaptobenzothiazole in 100 ml of ethanol is heated for 6 h at 80°C. The ethanol is distilled off, and the residue is dissolved in chloroform and precipitated by petroleum ether in the cold. The yield is 10.36 g (70%) of an oil. IR spectrum, cm^{-1}: 715 m, 1030 s, 1085 s, 1180 m, 1260 s, 1320 m, 1360 m, 1640 m, 1735 s, 2850 m, 2950 m, 2980 m, 3300 m. Found: C, 52.6; H, 5.05; N, 9.2; S, 21.3%. Calculated for $C_{13}H_{16}N_2O_2S_2$: C, 52.7; H, 5.4; N, 9.5; S, 21.6%.

Diethyl [N-(Benzothiazolylthio)-2-aminoethyl]succinate (II). This compound is obtained in analogy to I from 10.75 g (50 mmole) of 1-[1,2-bis(carbethoxy)ethyl]aziridine and 8.35 g (50 mmole) of 2-mercaptobenzothiazole. The yield is 13 g (68%) of an oil. IR spectrum, cm^{-1}: 760 m, 1030 s, 1090 s, 1180 s, 1260 s, 1320 m, 1360 m, 1640 m, 1735 s, 2840 m, 2950 m, 2980 m, 3070 m, 3300 m. Found: C, 53.2; H, 5.51 N, 7.1, S, 16.2%. Calculated for $C_{17}H_{22}N_2O_4S_2$: C, 53.4; H, 5.8; N, 7.3; S, 16.7%.

O-{N-[1,2-Bis(carbethoxy)ethyl]-2-aminoethylthio}benzoic Acid (III). A solution of 7.7 g (50 mmole) of o-mercaptobenzoic acid in 100 ml of methanol is slowly given an addition of a solution of 10.75 g (50 mmole) of 1-[1,2-bis(carbethoxy)ethyl]aziridine in 30 ml of methanol at room temperature. The mixture is stirred for 2 h and precipitated by ethyl ether in the cold. The precipitate formed is recrystallized from ethanol. The yield is 14.8 g (80%), and the mp 109-110°C. IR spectrum, cm^{-1}: 750 m, 1030 s, 1100 s, 1160 s, 1180 s, 1375 m, 1470 m, 1560 m, 1590 m, 1645 m, 1735 s, 2860 m, 2980 m, 3070 m. PMR spectrum, ppm: 1.28 (6H, t, CH_3), 2.80 (4H, m, NCH_2, SCH_2), 3.60 (4H, q, OCH_2), 7.25-7.60 (4H, m, C_6H_4), 7.80 (2H, m, NH_2^+). Found: C, 55.1; H, 5.9; N, 4.0; S, 8.4%. Calculated for $C_{17}H_{23}NO_6S$: C, 55.3; H, 6.2; N, 3.8; S, 8.7%.

{1,8-Bis[1,2-bis(carbethoxy)ethyl]amino}-3,6-dithiaoctane (IV). A mixture of 10.75 g (50 mmole) of 1-[1,2-bis(carbethoxy)ethyl]aziridine and 2.35 g (25 mmole) of 1,2-ethanedithiol in 100 ml of methanol is heated for 6 h at 60°C. The methanol is driven off, and the residue is dissolved in chloroform and precipitated by petroleum ether in the cold. The yield is 9.8 (75%) of an oil. IR spectrum, cm^{-1}: 760 w, 1010 m, 1170 m, 1205 m, 1260 m, 1360 w, 1440 m, 1735 s, 2860 m, 2965 m, 3320 w. PMR spectrum, ppm: 1.25 (12H, t, CH_3), 2.66-2.80

(12H, m, NCH_2, SCH_2), 3.60 (8H, q, OCH_2). Found: C, 50.1; H, 7.3; N, 5.2; S, 11.8%. Calculated for $C_{22}H_{40}N_2O_8S_2$: C, 50.4; H, 7.6; N, 5.3; S, 12.2%.

9,10-Benzo-8,11-dioxo-1,4-dithia-7,12-bis[1,2-bis(carbethoxy)ethyl]-7,12-diazacyclotetradec-9-ene (V). A mixture of 13.1 g (25 mmole) of diamine IV, 5.05 g (50 mmole) of triethylmaine in 500 ml of dry benzene, and 5.15 h (25 mmole) of phthaloyl chloride in 500 ml of dry benzene is added separately over the course of 6 h at room temperature with intense stirring to 1 liter of dry benzene. The precipitate formed is filtered out, and the solvent is distilled off at reduced pressure. The residue is purified chromatographically on aluminum oxide with a 5:1 benzene–methanol solvent mixture as the eluent. The solvent is driven off, and the residue is dissolved in chloroform and precipitated by petroleum ether in the cold. The yield is 11.45 g (70%) of an oil. R_f 0.36. IR spectrum, cm^{-1}: 760 m, 780 m, 1080 m, 1140 m, 1200 m, 1290 s, 1360 w, 1440 m, 1595 m, 1640 m, 1735 s, 2860 m, 3010 m. PMR spectrum, ppm: 1.30 (12H, t, CH_3), 2.88 (12H, m, NCH_2, SCH_2), 3.60 (8H, q, OCH_2), 7.50-8.16 (4H, m, C_6H_4). Found: C, 55.2; H, 6.1; N, 4.0; S, 10.2%; M 625. Calculated for $C_{30}H_{42}N_2O_{10}S_2$: C, 55.1; H, 6.4; N, 4.3; S, 9.8%; M 654.

Dimethyl [N-(Phenylthio)-2-aminoethyl]maleate (VI). A mixture of 2.8 g (15 mmole) of 1-[1,2-bis(carbomethoxy)vinyl]aziridine and 1.7 g (15 mmole) of thiophenol in 50 ml of ethanol is heated at 80°C for 6 h. The ethanol is distilled off, and the residue is dissolved in chloroform and precipitated by petroleum ether in the cold. The yield is 2.25 g (50%) of an oil. IR spectrum, cm^{-1}: 715 m, 750 m, 1010 m, 1030 m, 1110 m, 1160 s, 1240 s, 1360 m, 1440 s, 1580 m, 1610 m, 1660 m, 1680 m, 1735 s, 2860 m, 2960 s, 3010 m, 3330 m. Found: N, 4.3%. Calculated for $C_{14}H_{17}NO_4S$: N, 4.7%.

Dimethyl [N-(Benzothiazolylthio)-2-aminoethylthio]maleate (VII) is obtained in a similar manner from 0.65 g (3.5 mmole) of 2-mercaptobenzothiazole. The yield is 0.9 g (71%) of an oil. IR spectrum, cm^{-1}: 760 s, 785 m, 940 w, 1000 s, 1040 m, 1085 m, 1160 s, 1180 s, 1240 s, 1275 s, 1430 s, 1460 s, 1610 s, 1670 s, 1735 s, 2850 w, 2960 m, 3300 m. Found: C, 51.5; H, 4.6; N, 8.01 S, 18.4%. Calculated for $C_{15}H_{15}N_2O_4S_2$: C, 51.2; H, 4.5; N, 8.0; S, 18.2%.

Ethyl {N-[1,2-Bis(carbethoxy)vinyl]-2-aminoethylthio}acetate (VIII) is obtained in a similar manner from 1.53 g (10 mmole) of 1-[1,2-bis(carbomethoxy)vinyl]aziridine and 1.2 g (10 mmole) of ethyl thioglycolate. The yield is 1.6 g (60%) of an oil. IR spectrum, cm^{-1}: 740 m, 780 m, 950 w, 1010 m, 1040 m, 1160 s, 1240 s, 1280 s, 1440 s, 1660 m, 1735 s, 2860 w, 2960 m, 3300 m. Found: C, 47.0; H, 6.3; N, 4.2; S, 10.3%. Calculated for $C_{12}H_{19}NO_6S$: C, 47.2; H, 6.2; N, 4.6; S, 10.5%.

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