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DERIVATIVES OF HETEROCYCLIC α-IMINOCARBOXYLIC ACIDS.

4.* REDUCTION OF N-ALKOXYCARBONYL DERIVATIVES OF α-IMINOCARBOXYLIC ACIDS

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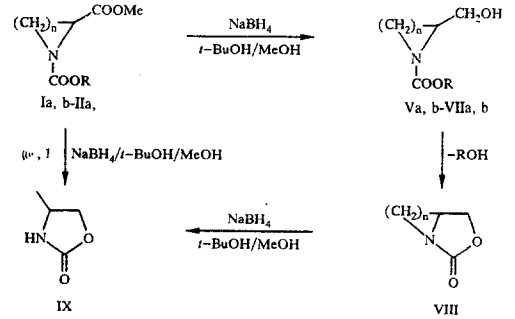
When N-methoxycarbonyl and N-benzoxycarbonyl derivatives of methyl esters of aziridine-2-carboxylic acid, L-proline, L-thioproline, and pipecolic acid interact with $NaBH_4$ in tert-butanol/methanol, the products of reduction of the C-methoxycarbonyl group of the original compounds are accompanied by bicyclic urethanes and oxazolidines. Reduction of N-maleates and N-fumarates of heterocyclic α-iminocarboxylic acids leads to the formation of α-hydroxymethyl-N-[4-(2-oxo-2,5-dihydrofuryl)] derivatives of pyrrolidine, piperidine, 1,3-thiazolidine, and 1,4-thiazan. In the latter case, 1-aza-2-hydroxymethyl-4-oxo-5-oxa-9-thiabicyclo [5.4.0]undecene-2 is also obtained. The N-maleates and fumarates of aziridine-2-carboxylic acid are reduced anomalously by sodium borohydride, forming 2-hydroxymethyl-2-(β-hydroxyethyl)-3-oxa-1-azabicyclo[3.1.0]hexanes.

Heterocyclic N-alkoxycarbonyl-α-iminocarbinols can be used as synthons for the construction of condensed heterocyclic systems [1]. A convenient path for the synthesis of the original α-iminocarbinols is the reduction of the readily accessible N-alkoxycarbonyl derivatives of α-iminocarboxylic acids [1, 2]. It is known that the reduction of esters of N-alkyl- and N-aryl-substituted derivatives of aziridine-2-carboxylic acids, at room temperature or elevated temperatures, proceeds with the formation of N-substituted aziridine-2-carbinols [3, 4]. By the reduction of esters of L-proline, L-thioproline, tetrahydro-1,4-thiazine-3-carboxylic acid, and pipecolic acid, the corresponding amino alcohols have also been obtained [1, 5-8]. Lithium aluminum hydride is commonly used as the reducing agent. It was shown subsequently that sodium borohydride in solution in tert-butanol/methanol readily reduces the C-methoxycarbonyl group on the heterocycle of α-iminocarboxylic acids [1, 7]. In this reaction, cyclization of the carbinol product to a bicyclic urethane is sometimes observed [1].

Continuing these studies, we investigated the possibility of using sodium borohydride in methanol/tert-butanol solution for the reduction of N-carboxy derivatives of esters of aziridine-2-carboxylic acid (I), L-proline (II), pipecolic acid (III), and L-thioproline (IV). Compounds I-III are readily reduced at the C-carboxyl group under these conditions.



Ia VIIa n = 1, R = CH_3; Ib, VIIb n = 1, R = $C_6H_5CH_2$; IIa, Va n = 3, R = CH_3; IIb, Vb n = 3, R = $C_6H_5CH_2$; IIIa, VIa n = 4, R = CH_3; IIIb, VIb n = 4, R = $C_6H_5CH_2$

*For Communication 3 see [2].

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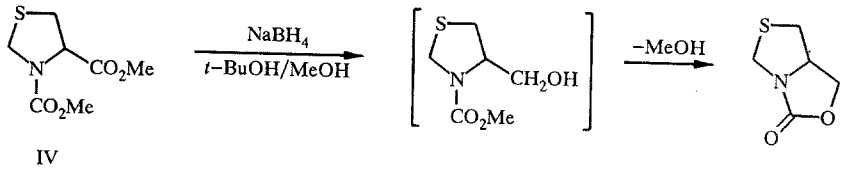
The bicyclic lactam VIII is evidently formed as an intermediate. Chromatography/mass spectrometry has detected a product in the mixture with the corresponding mass ($M^{+\cdot}$ = 99 and $M^+ - CO = 71$), but we were unable to isolate this compound.

It was characteristic that even by refluxing for an extended period, increasing the quantity of sodium boro-hydride, or introducing a stronger base (sodium methylate), we were not successful in "cross-cyclizing" the carbinols IIb-IIIb, which contain a benzyl group that leaves readily. From the ester I, in contrast, by extending the reaction time to 3-6 h, we obtained a 57% yield of the oxazolidine IX. The structure of IX was confirmed by spectrometry (^1H and ^{13}C NMR, chromatography/mass spectrometry) and by elemental analyses. The product yield could be increased to 80% and the reaction time cut to 1 h by the application of ultrasonic irradiation.

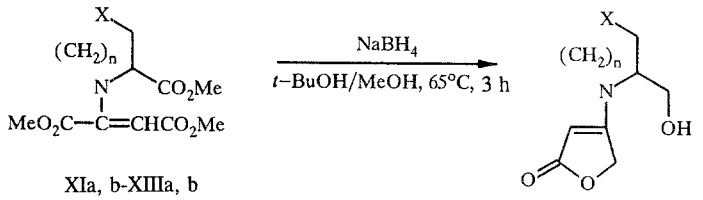
Sodium borohydride in tert-butanol/methanol is also a convenient reagent for the reduction of sulfur-containing α-iminocarboxylic acids [1]. For the diester IV, the process concludes with the formation of bicyclic urethane X:



IV X

A similar cyclization is characteristic for tetrahydro-1,3-thiazandicarboxylic acids.

It had been shown previously that the products from the addition of propiolates or acrylates to heterocyclic α-iminocarboxylic acids can be reduced by sodium borohydride to carbinols or diols [1, 7]. We found that the products from the addition of derivatives of α-iminocarboxylic acids to the dimethyl ester of acetylenedicarboxylic acid XIa,b-XIIIa,b, under the same conditions, form the lactones XIV-XVI:



XIa, b-XIIIa, b XIV – XVI

XIa,b XIV n = 1, X = CH_2; XIIa,b, XV n = 1, X = S; XIIIa,b, XVI n = 2, X = CH_2

A mixture of Z and E isomers was introduced into the reaction. The results indicate that both the ring and enamine ester groups enter into the reaction.

In the case of the thiazan derivative XVIIa,b, reduction of a mixture of Z and E isomers led to the formation of two compounds in a 95:5 ratio (as determined by HPLC). The main reaction product was isolated by crystallization. Analysis of ^1H and ^{13}C NMR spectra of this compound, along with its IR and mass spectra, provided grounds for assigning the structure 2-hydroxymethyl-4-oxo-5-oxa-9-thia-1-azabicyclo[5.1.0]undecene-2 (XVIII).

By fractional crystallization, we recovered from the reaction mixture, along with the bicyclic compound XVIII, the lactone XIX, the structure of which was proven by x-ray diffraction analysis. The isomeric product XVIII gives absorption bands in the IR spectrum that are characteristic for an unsaturated lactone ($\nu_{C=C}$ 1594 cm^{-1} and $\nu_{C=O}$ 1687 cm^{-1}), and also a band of stretching vibrations of the OH group at 3310^{-1}. In the PMR spectrum of the bicyclic compound XVIII, in addition to the signals of the protons of the tetrahydro-1,4-thiazan ring in the 2.53-4.72 ppm region, there is a broad singlet of the OH group proton at 3.66 ppm. The protons of the OCH_2 group of the ring resonate in the form of a doublet of doublets at 4.72 ppm ($J_{H6a,6e}$ = 14.0 Hz and J_{H6e7e} = 13.8 Hz); signals of protons of the exocyclic CH_2OH are present in the form of a doublet of doublets at 4.90 ppm; for the proton of the vinyl fragment C=CH—, a singlet is observed at 5.15 ppm. The conclusions regarding the structure of the bicyclic compound XVIII are further confirmed by the ^{13}C NMR spectrum (Fig. 1).

Since the lactone XVIII can be formed only from the Z-isomer (XVIIa), whereas its isomeric product XIX can be formed from the E-isomer (XVIIIb), and since an excess of the E-form (9:1) is observed in the original mixture, we can conclude tentatively that under the conditions of the reaction, E—Z isomerization takes place. And indeed, when the original mixture of E,Z-isomers XVIIa,b is heated at 80°C in a tert-butanol/methanol mixture, even when no sodium borohydride is

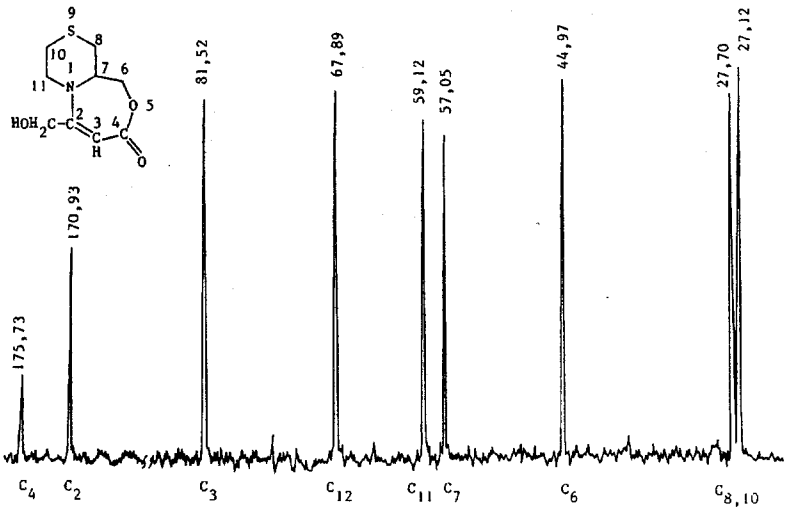


Fig. 1. ^{13}C NMR spectrum of 2-hydroxymethyl-4-oxo-5-oxa-9-thiabicyclo[5.4.0]undecene-2 in DMSO.

present, the Z—E isomer ratio XVIIa:XVIIb changes during 3 h from 1:9 to 4:6. Thus we can assume that in the process of reduction, in view of the basicity of the medium, E—Z isomerization is the reason for the predominant formation of the bicyclic compound XVIII.

When the adducts of esters of acetylenedicarboxylic acid to 2-methoxycarbonylaziridine (XXa,b) were reduced under analogous conditions, the products were greatly different in spectral characteristics from the lactones XIV-XVI and also from the bicyclic compound XVIII.

In the IR spectra of the product, we found a broad maximum at 3240-3300 cm^{-1}, characteristic for stretching vibrations of the OH group. There were no signals that could be attributed to absorption of a carbonyl group or a C=C double bond. The PMR spectrum of this compound consisted of complex multiplets in the 1.45-4.08 ppm region, among which we did not find any signals of vinyl-fragment C=CH protons or signals of $COOCH_3$ group protons. On the basis of the ^1H and ^{13}C NMR spectra, the product that we recovered in the reduction of the esters XXa,b can be assigned the structure of a mixture of isomers XXIa,b in a 2:1 ratio.

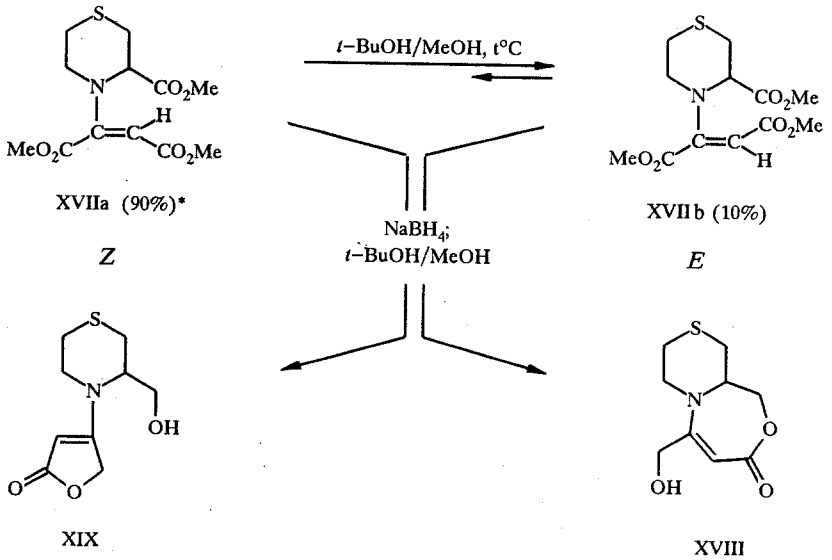


TABLE 1. ^{13}C NMR Spectra of Compounds XIV-XVI and XIX

Compound	C=O	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	CH_2O	CH	CH_2N	Other C	Solvent
XIV	166,69	79,98	174,66	66,68	61,52	61,52	48,18	27,37(CH_2CH) 22,54(CH_2CH_2CH)	$CDCl_3$
XV	166,66	82,00	174,46	67,09	60,37	63,60	49,90	31,85(SCH_2CH)	$CDCl_3$
XVI	169,88	79,01	175,01	66,86	58,85	56,33	43,03	26,40($CHCH_2$) 24,64(NCH_2CH_2) 18,44(CH_2CH_2CH)	DMSO
XIX	169,77	80,37	174,58	66,73	58,03	55,89	43,81	26,54($CHCH_2S$) 25,98(CH_2CH_2S)	DMSO

The diol product XXIa,b is an extremely hygroscopic substance that does not give a molecular ion in the mass spectrum. The presence of two hydroxyl groups was confirmed by silylation with hexamethyldisilazane. In the chromatogram/mass spectrum of the silylated product XXIIa,b, along with the signal from the molecular ion (m/z = 303) there are signals with m/z = 200 [M − CH_2OSiMe_3] and m/z = 83 [200 − $CH_2CH_2OSiMe_3$], confirming the presence of exocyclic hydroxymethyl and hydroxyethyl groups in the molecule of XXIa,b.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were obtained in Bruker WH-90/OS (90 MHz) and Bruker WH-360 (360 MHz) instruments; internal standards TMS and hexamethyldisilazane (PMR), cyclohexane and $CDCl_3$ (^{13}C NMR). The mass spectra were taken in an MS-50 AEI spectrometer (ionizing voltage 70 eV). The chromatogram/mass spectra were obtained a Kratos MS-25 instrument (ionizing voltage 70 eV).

The IR spectra were taken in UR-20 and Perkin—Elmer 580-B spectrometers, in mineral oil or on the pure substance. Analytical chromatography was performed in a Chrom 5 instrument in columns with SE-30 stationary phase.

Analytical and preparative high-performance liquid chromatography was performed in a Du Pont 830 Prep instrument with a UV detector (λ = 229, 254, and 334 nm); analytical column Zorbax-Sil (250 × 4.6 mm), preparative column Zorbax-Sil (250 × 22.4 mm). For the column chromatography, a 250 × 30 mm column with L 40/100 silica gel was used. The course of the reaction and the purity of the products were monitored by means of TLC on Silufol UV-254 plates with detection in UV light at 254 nm, and also by spot development in iodine vapor.

General Procedure for Obtaining N-alkoxycarbonyl Esters of Cyclic α-Iminocarboxylic Acids (IIa,b, IIIa,b, and IV). A solution of 50 mmoles of the methyl ester of L-proline, pipecolic acid, or L-thioproline, plus 8.4 ml (60 mmoles) of triethylamine, in 50 ml of dry THF, was chilled to 0°C, and a solution of 5.7 g (60 mmoles) of methyl chloroformate in 10 ml of dry THF was added dropwise with stirring. The mixture was warmed to room temperature and stirred for an additional 1 h. The precipitated triethylamine salt was filtered off, the filtrate was evaporated to dryness, and the residue was vacuum-distilled.

1,2-Bis(methoxycarbonyl)pyrrolidine (IIa), bp 100-104°C (0.1 mm Hg). PMR spectrum ($CDCl_3$): 1.2-2.2 (4H, m, β-CH_2, γ-CH_2), 3.3-3.5 (2H, m, δ-CH_2), 3.71 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 4.0 ppm (1H, t, α-CH).

1-Benzoxycarbonyl-2-methoxycarbonylpyrrolidine (IIb), bp 178-183°C (0.1 mm Hg). PMR spectrum ($CDCl_3$): 1.08-2.23 (4H, m, β-CH_2, γ-CH_2), 3.28 (2H, d, NCH_2Ph), 3.34-3.55 (2H, m, δ-CH_2), 4.01 (1H, t, α-CH), 7.1-7.6 ppm (5H, m, C_6H_5).

1,2-Bis(methoxycarbonyl)piperidine (IIIa), bp 116-121°C (0.1 mm Hg). PMR spectrum ($CDCl_3$): 1.2-4.2 (9H, m, ring protons, 3.76 (3H, s, OCH_3), 3.81 ppm (3H, s, OCH_3).

1-Benzoxycarbonyl-2-methoxycarbonylpiperidine (IIIb). Viscous oil, decomposing upon distillation at 152-160°C (0.01 mm Hg). PMR spectrum ($CDCl_3$): 1.21-4.8 (9H, m, ring protons), 3.60 (2H, d, NCH_2Ph), 3.80 (3H, s, OCH_3), 7.1-7.5 ppm (5H, m, C_6H_5).

3,4-Bis(methoxycarbonyl)-1,3-thiazolidine (IV), bp 110-112°C (0.1 mm Hg). PMR spectrum ($CDCl_3$): 3.21 (2H, dd, S—CH_2), 3.71 (3H, s, $COOCH_3$), 3.80 (3H, s, $COOCH_3$), 4.33 (2H, d, SCH_2N), 4.50 ppm (1H, t, α-CHCO).

General Procedure for Obtaining 1-Alkoxycarbonyl-2-hydroxymethylpyrrolidines Va,VIa, Piperidines Vb,VIb, and Aziridines VIIa,b. To a solution of 0.1 mole of the ester I-IIIa,b and 9.5 g (0.25 mole) of $NaBH_4$ in 400 ml of tert-butanol, 100 ml of methanol was added over the course of 2 h, and the mixture was refluxed until the reduction was completed, requiring 1-4 h (completion determined by TLC monitoring for content of the original ester). The reaction mixture was cooled, the sodium borohydride residue was decomposed with water, and the mixture was extracted with chloroform. The extract was dried with anhydrous Na_2SO_4, filtered, and evaporated. A waxlike substance was obtained, decomposing at 200°C (0.01 mm Hg). With the use of ultrasonic irradiation, the reaction was completed in 0.5 h, with very nearly quantitative formation of the carbinols Va,b and VIa,b.

1-Methoxycarbonyl-2-hydroxymethylpyrrolidine (Va). IR spectrum: 1740 (CO), 3310-3260 cm^{-1} (OH). PMR spectrum ($CDCl_3$): 1.48-2.20 (5H, m, β-CH_2, γ-CH_2, OH), 3.72 (3H, s, $COOCH_3$), 3.24-4.1 (2H, m, γ-CH_2OH), 4.21 (2H, m, δ-CH_2), 4.53 ppm (1H, q, α-CH).

1-Methoxycarbonyl-2-hydroxymethylpiperidine (Vb). IR spectrum: 1760 (CO), 3300-3208 cm^{-1} (OH). PMR spectrum ($CDCl_3$): 1.3-4.2 (12H, m, CH_2OH and ring protons), 3.78 ppm (3H, s, $COOCH_3$).

1-Benzoxycarbonyl-2-hydroxymethylpyrrolidine (VIa). IR spectrum: 1738 (CO), 3300-3210 cm^{-1} (OH). PMR spectrum ($CDCl_3$): 1.18-2.3 (5H, m, β-CH_2, OH), 3.38 (2H, d, OCH_2Ph), 3.20-4.10 (4H, m, δ-CH_2OH), 4.35 (1H, q, α-CH), 7.2-7.5 ppm (5H, m, C_6H_5).

1-Benzoxycarbonyl-2-hydroxymethylpiperidine (VIb). IR spectrum: 1738 (CO), 3280-3176 cm^{-1} (OH). PMR spectrum ($CDCl_3$): 1.2-4.7 (12H, m, CH_2OH and ring protons), 3.78 (2H, d, OCH_2Ph), 7.1-7.6 ppm (5H, m, C_6H_5).

2-Hydroxymethylene-N-methoxycarbonylaziridine (VIIa), 2-Hydroxymethylene-N-benzyloxycarbonylaziridine (VIIb), 2-Oxo-3-oxa-1-azabicyclo[3.2.0]hexane (VIII), and 2-Oxo-4-methyl-1,3-oxazolidine (IX). By means of the general procedure, a mixture of products was obtained: VIIa (57%), VIII (5%), and IX (20%), and also VIIb (51%), VIII (7%) and IX (26%) (the mixture compositions were determined by chromatography/mass spectrometry using as standards VIIa,b and IX). When the reaction time was extended to 6 h, the content of the product IX increased to 50% and 57%; and with ultrasonic irradiation, the amount of compound IX in the mixture was 76% and 80%, respectively. Vacuum distillation at 185-191°C (0.1 mm Hg) gave the oxazolidine IX with a 67% yield. Mass spectrum: 101 (31) $[M^+]$, 86 (100) $[M-CH_3]^+$, 73 (13), 42 (60). PMR spectrum ($CDCl_3$): 0.66 (3H, d, CH_3), 3.21 (2H, m, CH_2), 3.67 (1H, q, CH), 7.1 ppm (1H, br.s, CONH).

8-Oxo-7-oxa-3-thia-1-azabicyclo[3.3.0]octane (X). Obtained by reduction of diester IV with $NaBH_4$ in tert-butanol/methanol solution, following the procedure described above. Yield 83%, mp 60-62°C (from ether). PMR spectrum ($CDCl_3$): 2.67 (1H, dd, 4-H_a, J_{4a4e} = 11.0, J_{4a5a} = 8.6 Hz), 3.16 (1H, dd, 4-H_e, J_{4e4a} = 11.0, J_{4e5a} = 7.2 Hz), 4.18 (2H, m, 6-CH_2), 4.27 (1H, d, 2-H_a, J = 11.8 Hz), 4.50 (1H, dd, 5-H_a, J_{5a4a} = 8.6, J_{5a4e} = 7.2 Hz), 4.91 ppm (1H, d, 2-H_e, J_{2e2a} = 11.8 Hz). IR spectrum: 1738 cm^{-1} (CO).

2-Hydroxymethyl-1-[4-(2-oxo-2,5-dihydrofuryl)]pyrrolidine (XIV). Obtained by reduction procedure described above, from mixture of E- and Z-isomers (XIa,b), with a 65% yield (see preceding communication); mp 109-111°C (ethanol—ether). IR spectrum: 1600 (C=C), 1686 (C=O), 3296 cm^{-1} (OH). PMR spectrum ($CDCl_3$): 1.15-2.04 (4H, m, β-CH_2, γ-CH_2), 2.20-3.36 (5H, m, δ-CH_2, CH_2OH), 4.10 (1H, q, α-CH), 4.82 (1H, s, C=CH), 4.70 ppm (2H, m, CCH_2O). See Table 1 for ^{13}C NMR spectrum.

4-Hydroxymethyl-1-[4-(2-oxo-2,5-dihydrofuryl)]-1,3-thiazoline (XV). Obtained by the reduction procedure described above, from a mixture of E- and Z-isomers XIIa,b, with a 48% yield (see preceding communication); mp 105-106°C (methanol). IR spectrum: 1600 (C=C), 1680 (C=O), 3310 cm^{-1} (OH). PMR spectrum ($CDCl_3$): 3.20 (2H, dd, 5-CH_2), 3.68 (1H, br.s, OH), 4.48 (2H, dd, 2-CH_2, J = 7.2 Hz), 4.75 (2H, s, OCH_2), 4.90 (2H, dd, CH_2OH), 5.05 (1H, m, CHN), 5.15 ppm (1H, s, C=CH). See Table 1 for ^{13}C NMR spectrum.

2-Hydroxymethyl-1-[4-(2-oxo-2,5-dihydrofuryl)]piperidine (XVI). Obtained as described above, from a mixture of Z- and E-isomers XIIIa,b, with a 67% yield (see preceding communication); mp 126-128°C (ethanol—ether). IR spectrum: 1602 (C=C), 1740 (C=O), 3260 cm^{-1} (OH). PMR spectrum ($CDCl_3$): 1.1-3.8 (12H, m, ring protons and CH_2OH), 4.76 (2H, m, $=CCH_2O$), 4.76 (2H, m, $=CCH_2O$), 4.80 ppm (1H, C=CH). See Table 1 for ^{13}C NMR spectrum.

1-Aza-2-hydroxymethyl-4-oxo-5-oxa-9-thiabicyclo[5.4.0]undecene-2 (XVIII). A solution of 1.51 g (5 mmoles) of a mixture of Z- and E-isomers of the thiazine XVIIa,b was reduced under the conditions described above, obtaining 0.92 g (85.6%) of colorless crystals of XVIII, mp 146-147°C (from chloroform). IR spectrum: 1594 (C=C), 1687 (C=O), 3310 cm^{-1} (OH). ^{13}C NMR spectrum (22.63 MHz, DMSO): 27.12 $C_{(10)}$, 27.70 $C_{(8)}$, 46.97 $C_{(11)}$, 57.05 $C_{(7)}$, 59.12 $C_{(12)}$, 67.89 $C_{(6)}$, 81.52 $C_{(3)}$, 170.93 $C_{(2)}$, 175.73 ppm $C_{(4)}$. PMR spectrum (360 MHz, $CDCl_3$): 2.53 (1H, m, 10-He, J_{10e10a} = 13.2, J_{10e11a} = 2.8, J_{10e11e} = 1.8 Hz), 2.68 (1H, m, 8-He, J_{8e8a} = 14.0, J_{8e7e} = 1.7 Hz), 2.76 (1H, m, 10-Ha, J_{10a11e} = 13.2,

J_{10a11a} = 10.5, J_{10a11e} = 4.8 Hz), 3.04 (1H, m, dd, 8Ha, J_{8a7e} = 3.9 Hz), 3.50 (1H, m, 11-Ha, J_{11a11e} = 13.8, J_{11a10a} = 10.5, J_{11a10e} = 2.6 Hz), 3.66 (1H, br.s, OH), 3.97 (1H, m, 11He, J_{11e11a} = 13.8, J_{11e10a} = 4.8, J_{11e10e} = 1.8 Hz), 4.21 (1H, m, 7-He, J_{7e8a} = 3.9, J_{7e8e} = 1.7, J_{7e6a} = 13.8 Hz), 4.72 (2H, dd, 6-CH_2, J_{6a6e} = 14.0, J_{6a7e} = 13.8 Hz), 4.90 (2H, dd, CH_2OH), 5.15 ppm (1H, s, C=CH). Mass spectrum: 215(16) $[M]^+$, 184(100) $[M-CH_2OH]^+$, 156(8) $[M-CH_2OH-CO]^+$, 142(13), 124(11), 115(11), 102(11).

3-Hydroxymethyl-4-[4-(2-oxo-2,5-dihydrofuryl)]tetrahydro-1,4-thiazine (XIX). After recovering the bicyclic compound XXVIII, HPLC of the same mother solution (eluent hexane/2-propanol, 3:1 ratio) gave the thiazine XIX, mp 152-153°C. IR spectrum: 1602 (C=C), 1683 (C=O), 3320 cm^{-1} (OH). PMR spectrum (360 MHz, $CDCl_3$): 2.51 (1H, dd, 6-He, J_{6e6a} = 13.5, J_{6e5a} = 2.5, J_{6e5e} = 2.0 Hz), 2.66 (1H, m, 2-H_a, J_{2a2e} = 14.0 Hz), 2.82 (1H, m, 6-H_a, J_{6a6e} = 13.5, J_{6a5a} = 12.0, J_{6a5e} = 4.0 Hz), 3.00 (1H, dd, 2-H_e, J_{2e2a} = 14.0 Hz), 3.45 (1H, m, 5-H_a, J_{5a5e} = 12.0, J_{5a6a} = 12.0, J_{5a6e} = 2.5 Hz), 3.75 (2H, m, 3-H_a, J_{3a2e} = 4.0 Hz), 3.75 (2H, m, 5-H_e, J_{5e5a} = 12.0, J_{5e6e} = 2.0, J_{5e6a} = 4.0 Hz), 4.68 (1H, br.s, OH), 4.80 (1H, s, C=CH), 4.78 ppm (2H, m, CCH_2O). Mass spectrum: 215(22), 184(100), 159(12), 158(4), 157(20), 156(24), 142(10), 140(6), 138(11), 124(11), 115(10), 110(13), 102(8), 101(8), 100(8), 99(11), 98(9), 84(17).

2-Hydroxymethyl-2-(β-hydroxyethyl)-3-oxa-1-azabicyclo[3.1.0]hexane (XXIa,b). Obtained by reduction of esters XXIIa,b with $NaBH_4$ as described above, yield 80%. Recovered from reaction mixture by column chromatography on silica gel, eluent ethanol/ethyl acetate (10-40% ethanol). The diol XXIa,b was recovered in the form of an oily mixture of isomers in a 2:1 ratio, arbitrarily designated A and B, differing in absolute configuration of the asymmetric $C_{(2)}$ atom. IR spectrum: 1240, 3038, 3075 (CH of aziridine ring), 3200-3300 cm^{-1} (OH). PMR spectrum ($CDCl_3$): isomer A 1.45, 1.63 (2H, d, CH_2), 1.85 (2H, m, CCH_2), 2.58 (1H, m, NCH), 3.5-3.95 (6H, m, OCH_2), 4.08 ppm (2H, br.s, OH); isomer B 1.58, 1.59, (2H, d, NCH_2), 1.85 (2H, m, C—CH_2), 2.58 (1H, m, NCH), 3.5-3.95 (6H, m, OCH_2), 4.08 ppm (2H, br.s, OH). ^{13}C NMR spectrum ($CDCl_3$): isomer A 24.58 (t, CCH_2), 35.52 (t, NCH_2), 37.60 (d, NCH), 58.29, 63.66, 65.09 (t, OCH_2), 99.19 ppm (s, OCN); isomer B 24.85 (t, CCH_2), 35.84 (t, NCH_2), 36.72 (d, NCH)< 57.91, 63.39, 64.74 (t, OCH_2), 99.27 ppm (s, OCN).

2-Trimethylsilyloxymethyl-2-(β-trimethylsilyloxyethyl)3-oxa-1-azabicyclo[3.1.0]hexane (XXIIa,b). To a solution of 318 mg (2 mmoles) of the diol XXIa,b in 1 ml of absolute chloroform, 5 ml of hexamethyldisilazane was added, and the mixture was held for 6 h at 50°C. The solvent was removed under an inert atmosphere. The oily product was vacuum-dried; bp 186-191°C (0.01 mm Hg). PMR spectrum ($CDCl_3$): 0.05 (18H, $Si(CH_3)_3$), 1.40, 1.61, (2H, d, NCH_2) 1.85 (2H, m, CCH_2), 2.60 (1H, m, NCH), 3.52-3.97 ppm (6H, m, OCH_2 and OCH_2CH_2). Mass spectrum: 303(8) [M]+, 288(10) $[M-CH_3]^+$, 200(90) $[M-CH_2OSi(CH_3)_3]^+$, 186(7) $[M-CH_2CH_2OSi(CH_3)_3]^+$, 73(100).

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