STEREOCHEMISTRY OF THE METHYLATION OF THE (1¹S,4S) AND (1¹S,4R) DIASTEREOMERS OF 4-METHYL-1-(α-METHYLBENZYL)AZETIDIN-2-ONE

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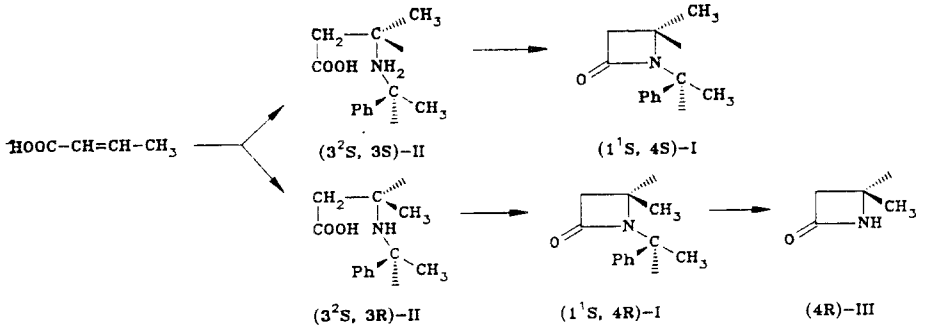
The methylation of the lithium derivatives of the (1¹S,4S) and (1¹S,4R) diastereomers of 4-methyl-1-(α-methylbenzyl)azetidin-2-one proceeds stereospecifically with the formation of only trans-(3S,4S)- and trans-(3R,4R)-dimethyl-1-[(S)-α-methylbenzyl]azetidin-2-one, respectively. The process is accompanied by epimerization at the asymmetric center of the N-α-methylbenzyl substituent.

In connection with the fact that the biological activity of all β-lactam antibiotics is intimately associated with the stereochemistry of the asymmetric centers of the azetidinone fragment, the development of approaches to the synthesis of monocyclic analogs of antibiotics of this class in the optically active form is extremely urgent.

The aim of the present research was to study the stereochemistry of the methylation of the (1¹S,4S) and (1¹S,4R) diastereomers of 4-methyl-1-(α-methylbenzyl)diastereomers2-one (I), which we obtained by cyclization of the individual (3²S,3S) and 3²S,3R) diastereomers of the corresponding N-substituted β-aminobutyric acid II under interphase-catalysis conditions. The individual stereoisomers of amino acid II, the diastereomeric purities of which were no less than 95% (according to PMR data), were obtained by the method in [1] by the addition of (S)-α-methylbenzylamine to crotonic acid.



All of the physicochemical characteristics and data from the ^1H and ^{13}C NMR spectra of the diasteromers of azetidinone I isolated by means of column chromatography are presented in Tables 1 and 2. The absence of strict correspondence between the literature data and the specific rotations and PMR spectral parameters that we obtained (Table 1) made it necessary to refine their stereochemistry. The N-debenzylation of the diastereomer of azetidinone I with a specific rotation of –22.1° by the action of sodium in liquid ammonia (without involvement of the $C_{(4)}$ asymmetric center [5]) led to the formation of one of the known [4] enantiomers of 4-methylazetidinone (III), the (R) configuration of which was established both on the basis of the sign of the specific rotation and on the basis of the character of the circular dichroism (CD) spectrum. Consequently, the starting diastereomer of azetidinone I also has an (R) configuration of the $C_{(4)}$ asymmetric center, while the second diastereomer has a (4S) configuration.

We have previously studied the stereochemistry of the asymmetric methylation of azetidinone IV with a single exocyclic chiral center at the nitrogen atom [6. 7] and showed that the (S)-α-methylbenzyl label dictates the predominant formation of a diastereomer of azetidinone V with an (S) configuration of the $C_{(3)}$ asymmetric center, despite the significant remoteness of the inducing center from the site of attack.

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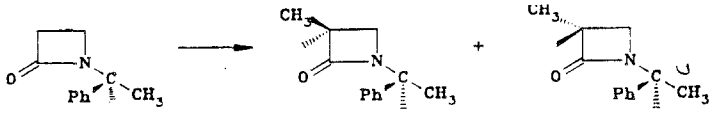
TABLE 1. Characteristics of the Stereoisomers of 4-Methyl-1-(α-methylbenzyl)-azetidin-2-one (I)

Compound	R_f*	$[\alpha]_D^{20}$, °, in CH_2Cl_2 (c)	PMR spectrum (CCl_4), δ, ppm				Yield, %	Literature cited
			4-CH_3	1'-H	1'-CH_3	4-H		
(1'S,4S)-I	0,54	−35,2 (2,44)	1,12	4,72	1,56	3,43	65	**
	—	−36,8	2,06	4,65	1,49	3,35	48	[2]
	—	−52***	1,28	4,82	1,75	3,52		[3]
		−40,6	—	—	—	—	—	[4]
(1'S,4R)-I	0,50	−22,1 (3,16)'	1,08	4,54	1,65	3,48	77	**
	—	—	1,12	4,58	1,70	4,25		[3]
	—	−22,2'	—	—	—	—	—	[4]

*Silufol, hexane–benzene–ethyl acetate (1:1:2).

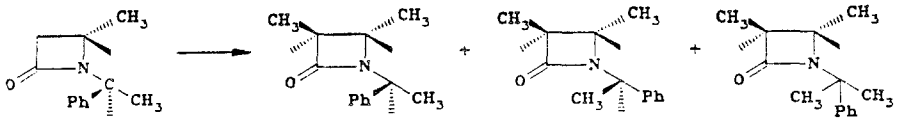
**Our data.

***The concentration and solvent were not indicated.



The presence of an additional chiral center at the $C_{(4)}$ atom in direct proximity to the site of attack made it possible to assume that methylation in the 3 position would prove to be more stereoselective. The known general tendency for trans substitution in reactions of metallated derivatives of 1,4-disubstituted azetidinones with electrophilic agents also constitutes evidence in favor of this [8, 9].

We studied the stereochemistry of the reactions of the lithium derivatives of the (4S) and (4R) diastereomers of azetidinone I with methyl iodide in tetrahydrofuran at −78°C. Like 1-[(S)-α-methylbenzyl]azetidinone (IV) [7], its (4S)-methyl analog I undergoes methylation with excess methyl iodide to give azetidinones VI and VII, respectively, as products of monomethylation (in the 3 position) and dimethylation (in the 1^1 and 3 positions).



As expected, azetidinones with a cis-3,4-configuration were not detected among the reaction products; the trans orientation of the methyl groups in the 3 and 4 positions of the β-lactam ring in VI and VII was established starting from the spin-spin coupling constants (SSCC) in the PMR spectra (J_{34} = 2.0-2.1 Hz), which are characteristics for trans-3,4-disubstituted 2-azetidinones [10]. These data, with allowance for the (4S) configuration of the starting stereoisomer of I, enabled us to conclude that the isolated stereoisomers of azetidinones VI and VII have a (3S,4S) configuration.

The formation of dimethylated azetidinone VII is not observed when one equivalent of methyl iodide is used in the reaction; monomethylated product VI was isolated and starting azetidinone I was regenerated by means of column chromatography. The PMR spectra of these azetidinones contain doubled sets of signal of all of the protons, which attests to their existence in the form of a mixture of two diastereomers (in the case of azetidinone VI in the individual state we were able to isolate only one of them chromatographically). The fact that the $C_{(4)}$ asymmetric center is not involved under the methylation conditions while the trans-3,4-configuration of azetidinones VI is apparent from the SSCC makes it possible to conclude that the reason for the diastereomerism of azetidinones I and IV is epimerization at the $C_{(1')}$ center of the N-α-methylbenzyl substituent under the influence of a strong base. In particular, the isolated mixture of stereoisomers of azetidinone I contains, in addition to the starting (1^1S,4S) diastereomer, its (1^1R,4S) epimer. The stereochemical lability of the N-α-methylbenzyl chiral center was also confirmed by the results obtained by treatment of the lithium derivative of the (1^1S,4S) diastereomer of azetidinone I with water: A mixture of the (1^1S,4S) and (1^1R,4S) epimers of azetidinone I in a ratio of 1:1 (according to PMR data) was isolated.

TABLE 2. ^{13}C NMR Spectra of the Stereoisomers of 2-Azetidinones I, VI, and VII in CCl_4

Stereoisomer	Chemical shifts, δ, ppm									
	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(1')}$	1'-CH_3	*i*-1'-Ph	*o*-1'-Ph	*m*-1'-Ph	*p*-1'-Ph	4-CH_3
(1'*S*,4*S*)-I	164,79	43,47	46,82	51,99	19,53	141,09	128,35	126,78	127,16	20,71
(1'*S*,4*S*)-I*	166,63	43,54	47,30	51,96	19,43	140,55	128,69	127,01	127,60	20,74
(1'*S*,4*R*)-I*	166,88	43,52	46,35	52,55	19,09	141,48	128,65	126,80	127,56	19,25
(1'*S*,3*S*,4*S*)-VI	164,61	43,62	46,82	52,09	19,57	141,20	128,39	126,86	127,19	20,81
(1'*R*,3*S*,4*S*)-VI	164,69	43,62	45,60	52,49	19,25	142,01	128,39	—	—	19,31
(3*S*,4*S*)-VII	—	50,37	54,98	57,94	27,74; 28,49	—	127,94	125,31	126,62	20,01

*In $CDCl_3$.

TABLE 3. Yields of the Products of Methylation of the Lithium Derivatives of the (1^1S,4S) and (1^1S,4R) Diastereomers of 2-Azetidinone I

Reaction product	Yield, %, based on the starting (1^1S,4S)-I stereomer		Reaction product	Yield, %, based on the starting (1^1S,4S)-I stereomer	
	4 equiv. CH_3I	1 equiv. CH_3I		4 equiv. CH_3I	1 equiv. CH_3I
(1^1S,3S,4S)-VI	3	10*	(1^1R,3R,4R)-VI	7*	5**
(1^1R,3S,4S)-VI	—	13*	(1^1S,3R,4R)-VI	10*	17**
(3S,4S)-VII	52	—	(3R,4R)-VII	20	11
(1^1S,4S)-I	—	21**	(1^1R,4R)-I	16**	—
(1^1R,4S)-I	—	15**	(1^1S,4R)-I		—

*The overall yield of the substance (isolated in individual form and in the form of a mixture of epimers).

**According to PMR data for a mixture of epimers.

TABLE 4. PMR Spectra of Stereoisomers of 4-Methyl-Substituted Azetidinones I and VI

Azetidinone	Stereoisomer	Chemical shifts, δ, ppm		
		4-CH_3	1^1-H	1^1-CH_3
I	(1^1S,4R) (1^1R,4S)*	1,06	4,54	1,65
	(1^1S,4S) (1^1R,4R)*	1,12	4,72	1,56
VI	(1^1S,3R,4R)* (1^1R,3S,4S)	1,06	4,44	1,69
	1^1S,3S,4S) (1^1R,3R,4R)*	1,18	4,77	1,60

*Isolated in the form of a mixture with the diastereomer that differs with respect to the configuration of $C_{(11)}$.

Qualitatively similar results were also obtained in the methylation of the (1^1S,4R) diastereomer of azetidinone I. Monomethylation (VI) and dimethylation (VII) products, which have a trans-(3R,4R) configuration, were also detected here. The starting azetidinone I and azetidinone VI isolated from the reaction mixture by means of column chromatography are a mixture of diastereomers formed as a result of epimerization. The quantitative differences in the results of the reactions carried out under identical conditions for two diastereomers of azetidinone I (Table 3) constituted evidence for the different reactivities of their lithium derivatives.

A detailed analysis of the PMR spectra of all four possible stereoisomers of azetidinone I (both the starting isomers and those formed as a result of epimerization) made it possible to uncover a number of principles that we used to establish the absolute configurations of the diastereomers of azetidinone VI.

An analysis of the relative positions of the signals of the protons of the $C_{(11)}$ and $C_{(4)}$ asymmetric centers in the PMR spectra proved to be diagnostically valuable. It follows from the data on the chemical shifts of these protons presented in Table 4 that in the case of diastereomers with the same configuration of the $C_{(11)}$ and $C_{(4)}$ centers [(1^1S,4S) or (1^1R,4R)] the signals of the 4-CH_3 and 1^1-H protons are located at weaker field and the 1^1-CH_3 protons are located at stronger field than for the diastereomers with different configurations of these centers [1^1S,4R) and (1^1R,4S)]; Δδ reaches 0.18 ppm. In the ^{13}C NMR spectra (Table 2) the signals of the $C_{(4)}$ and 4-CH_3 atoms for diastereomers with identical configurations of the $C_{(11)}$ and $C_{(4)}$ asymmetric centers lie at weaker field than for the diastereomers with different configurations of these centers (Δδ = 1.0-1.5 ppm). We used precisely these criteria to evaluate the absolute configurations of the exocyclic chiral center in the individual (–)-(1^1R,3S,4S) and (–)-(1^1S,3S,4S) epimers, as well as in the isolated (in the form of a mixture) (1^1R,3R,4R) and (1^1S,3R,4R) epimers of azetidinone VI (Table 4).

Thus we have shown that the combined action of the two inducing centers, $C_{(11)}$ and $C_{(4)}$, ensures complete trans-stereospecificity of methylation at the $C_{(3)}$ atom of the (1^1S,4S) and (1^1S,4R) diastereomers of azetidinone I; under the reaction conditions the exocyclic chiral center undergoes epimerization, while the asymmetric centers of the azetidinone ring are not involved.

EXPERIMENTAL

The IR spectra of suspensions of the solids in mineral oil and films of the liquids were recorded with IKS-22 and IR-20 spectrometers. The PMR spectra were measured with Varian T-60, XL-100, Tesla B-467, Bruker WM-250, and WM-400 spectrometers at room temperature with tetramethylsilane (TMS) as the internal standard. The ^{13}C NMR spectra were recorded with Varian FT-80A and Bruker WM-250 spectrometers. The mass spectra were recorded with a Varian MAT-111 spectrometer with introduction of the samples through a chromatograph and with an MKh-1303 spectrometer equipped with a system for direct introduction of the samples into the ion source at a vaporization temperature of 100-150°C and an ionizing-electron energy of 50-60 eV. The circular dichroism (CD) curves were recorded with a Jasco J-20 spectropolarimeter in cuvettes with lengths of 10, 1, and 0.1 mm.

Thin-layer chromatography (TLC) was carried out on Silufol UV-254 plates and on glass plates with a loose layer of Silpearl UV-254 silica gel with development in UV light. Column chromatography was carried out using L40/100 silica gel.

(3^2S,3S) and (3^2S,3R) Stereomers of N-(α-Methylbenzyl)-β-aminobutyric Acid (II). A mixture of 50 mmoles of freshly distilled crotonic acid in 14 ml of dry pyridine and 50 mmoles of (S)-α-methylbenzylamine with $[\alpha]_D^{20}$ –40° (without a solvent) was refluxed for 2 h, after which 200 ml of acetone was added to the cooled (to room temperature) reaction mixture, and the mixture was allowed to stand for 5 days at 20°C. Filtration gave 1.61 g (16%) of the less soluble (3^2S,3S) isomer with mp 174-176°C and $[\alpha]_D^{20}$ +17.9° (c = 2.8, H_2O). After two reprecipitations (by means of acetone) from a concentrated aqueous solution, 1.61 g of (3^2S,3S)-acid II yielded 1.13 g of a product with mp 181-182°C, R_f 0.35, and R_f" 0.25* [butanol–formic acid–water (16:1:3)], and $[\alpha]_D^{20}$ +21.3° (c = 2.7, H_2O). PMR spectrum: 1.50 (3H, d, 3-CH_3), 1.58 ppm (3H, d, 3^2-CH_3). According to the data in [4], $[\alpha]_D^{20}$ +19.4° (c = 1.5).

After 7 days, workup of the mother liquor and reprecipitation by means of acetone gave 1.34 g (13%) of isomeric (3^2S,3R)-acid II with mp 143-146°C, R_f 0.34 and R_f" 0.21 [butanol–formic acid–water (16:1:3)] and $[\alpha]_D^{20}$ –43.9° (c = 3.3, H_2O). PMR spectrum: 1.66 (3H, d, 3-CH_3), 1.99 ppm (3H, d, 3^2-CH_3). According to the data in [4], $[\alpha]_D^{20}$ –47° (c = 1.5).

(1^1S,4S) and (1^1S,4R) Diastereomers of 4-Methyl-1-(α-methylbenzyl)azetidin-2-one (I, $C_{12}H_{15}NO$). A solution of 2.96 g (26 mmoles) of methanesulfonyl chloride in 52 ml of chloroform was added to a solution of 13 mmoles of the (3^2S,3S) or (3^2S,3R) diastereomer of β-amino acid II, 5.2 g (52 mmoles) of $KHCO_3$, and 0.66 g (2 mmoles) of tetrabutylammonium hydrosulfate in 14 ml of water, and the resulting two-phase system was stirred with a magnetic stirrer for 24 h at room temperature. Water (50 ml) was then added, the aqueous mixture was extracted with ether (three 50-ml portions), and the extract was dried with magnesium sulfate. The ether was removed, and the residue was chromatographed with a column [benzene–ethyl acetate (2:1)].

The (1^1S,4S) diastereomer of I was obtained in 65% yield in the form of an oil with R_f 0.54 [hexane–benzene–ethyl acetate (1:1:2)] and $[\alpha]_D^{20}$ –35.2° (c = 2.44, CCl_4). IR spectrum: 1750 cm^{-1} (C=O). Data from the ^1H and ^{13}C NMR spectra are presented in Tables 1 and 2. Mass spectrum: M^+ 189.

The (1^1S,4R) diastereomer of I was obtained in 77% yield in the form of an oil with R_f 0.50 [benzene–hexane–ethyl acetate (1:1:2)] and $[\alpha]_D^{20}$ –22.1° (c = 4.16, CCl_4). IR spectrum: 1750 cm^{-1} (C=O). Data from the ^1H and ^{13}C NMR spectra are presented in Tables 1 and 2. Mass spectrum: M^+ 189.

(+)-(4R)-Methylazetidinone (III). A solution of 1.3 mmoles of the individual (1^1S,4R) stereoisomer of azetidinone I in 3 ml of absolute ether was added dropwise at –78°C to a solution of 50 mg (2 mmoles) of sodium metal in 10 ml of liquid ammonia, after which the mixture was stirred for 1.5 h. It was then decomposed by the addition of solid ammonium chloride, and the mixture was allowed to warm up to room temperature (until removal of the ammonia was complete). It was then extracted with absolute ether, the solvent was removed by distillation, and the residual yellow oil was purified with a column [benzene–acetone (1:1)] to give azetidinone III in 57% yield in the form of an oil with R_f 0.50 [benzene–acetone (1:1)] and $[\alpha]_D^{20}$ +2.1° (c = 1.16, CCl_4). PMR spectrum (CCl_4): 1.31 (3H, d, 4-CH_3), 2.33 (1H, m, 3-H), 2.92 (1H, m, 3-H), 3.64 (1H, m, 4-H), 7.56 ppm (1H, s, N–H). Mass spectrum: M^+ 85. According to the data in [4], $[\alpha]_D^{20}$ +3.6° (c = 1.47, CH_2Cl_2). According to the data in [2], the compound has the following PMR spectrum (CD_3COCD_3): 1.21 d, 2.33 2d, 2.92 q, 3.64 m (ppm).

*R_f" is the chromatographic mobility on the two-dimensional chromatogram.

Epimerization of (4S)-Methyl-1-[(S)-α-methylbenzyl]azetidinone (I). A solution of 76 mg (0.4 mmole) of (1^1S,4S)-azetidinone I, with $[\Theta]_{228\ nm}^{methanol}$ +3500°, in 2.5 ml of THF was added dropwise at –78°C in an argon atmosphere to 0.5 mmole of lithium diisopropylamide, obtained from 0.7 ml (0.5 mmole) of diisopropylamine in 2.5 ml of THF and 0.24 ml of a 2 N hexane solution of butyllithium. After 30 min, excess water in 2.5 ml of THF was added, and the mixture was stirred for 45 min. The reaction mixture was warmed up to room temperature and decomposed with a saturated solution of ammonium chloride, the aqueous mixture was extracted with ether, and the extract was dried over calcined magnesium sulfate. After removal of the ether, the residue was chromatographed with a column [benzene–ethyl acetate (3:1)] to give, in the form of several fractions, 26 mg (30%) of a mixture of the (1^1S,4S) and (1^1R,4S) epimers of I in a ratio of 1:1 (according to PMR data) with $[\Theta]_{225\ nm}^{methanol}$ +5031°.

Methylation of (4S)-Methyl-1-[(S)-α-methylbenzyl]azetidinone (I). A. A 2-mmole sample of (1^1S,4S)-azetidinone I, with $[\alpha]_D^{20}$ –47° (c = 8.3, CCl_4), in 5 ml of THF was added dropwise with stirring at –78°C in an argon atmosphere to 2 mmoles of lithium diisopropylamide, obtained from 2 mmoles of a solution of butyllithium. After 30 min, a solution of 2 mmoles of methyl iodide in 5 ml of THF was added dropwise, and the mixture was stirred for 45 min at –78°C. After warming to room temperature, the mixture was decomposed with a saturated solution of ammonium chloride, the aqueous mixture was extracted with ether, and the extract was dried with magnesium sulfate. After removal of the ether, the residue was applied to a column packed with silica gel and eluted with benzene–ethyl acetate (3:1). The chromatographically homogeneous fractions were combined, and the solvent was removed to give 51 mg (13.6%) of trans-(3S,4S)-dimethyl-1-[(R)-α-methylbenzyl)acetidinone (VI) and 40 mg (9.7%) of a mixture of the (1^1S,3S,4S) and (1^1R,3S,4S) epimers of azetidinone VI in a ratio of 1.3:1 (according to the PMR data). In addition, we isolated 134 mg (36%) of starting azetidinone I in the form of a mixture of the (1^1S,4S) and (1^1R,4S) epimers of I. (1^1R,3S,4S)-Azetidinone VI ($C_{13}H_{17}NO$) was obtained as an oil with R_f 0.37 [benzene–ethyl acetate (3:1)] and $[\alpha]_D^{20}$ –24.6° (c = 0.4, heptane). IR spectrum: 1750 cm^{-1} (C=O). Data from the ^{1}H and ^{13}C NMR spectra are presented in Tables 2 and 4. Mass spectrum: M^+ 203.

B. When we used a fourfold excess of methyl iodide, we obtained trans-(3S,4S)-dimethyl-1-(α,α-dimethylbenzyl)azetidinone (VII) in 56% yield and 8.5 mg (3%) of trans-(1^1S,3S,4S)-azetidinone VI. (3S,4S)-Azetidinone VII ($C_{14}H_{19}NO$) was obtained as an oil with R_f 0.40 [benzene–ethyl acetate (3:1)] and $[\alpha]_D^{20}$ +7.6° (c = 0.63, CCl_4). IR spectrum: 1750 cm^{-1}. PMR spectrum (CCl_4): 0.99 (3H, d, J = 6.1 Hz, 4-CH_3), 1.20 (3H, d, J = 7.2 Hz, 3-CH_3), 1.73 (6H, s, 1^1-2CH_3), 2.22 (1H, dq, J_1 = 7.2 Hz, J_2 = 2.1 Hz, 3-H), 3.03 ppm (1H, dq, J_1 = 6.1 Hz, J_2 = 2.1 Hz, 4-H). Mass spectrum: M^+ 217. (1^1S,3S,4S)-Azetidinone VI ($C_{13}H_{17}NO$) was obtained as an oil with R_f 0.37 [benzene–ethyl acetate (3:1)] and $[\alpha]_D^{20}$ –22.5° (c = 0.26, CCl_4). IR spectrum: 1750 cm^{-1} (C=O). Data from the ^{1}H and ^{13}C NMR spectra are presented in Tables 2 and 4. Mass spectrum: M^+ 203.

Methylation of (4R)-Methyl-1-[(S)-α-methylbenzyl)azetidinone (I). A. Under similar conditions of methylation of the lithium derivatives of the (1^1S,4R) stereomer of I (2 equivalents) using an equimolar amount of methyl iodide we obtained 50 mg (11%) of trans-(3R,4R)-dimethyl-1-(α,α-dimethylbenzyl)azetidinone (VII) and 90 mg (22%) of a mixture of the (1^1S,3R,4R) and (1^1R,3R,4R) epimers of VI in a ratio of 3:1 (according to the PMR spectral data) in the form of an oil with R_f 0.37 [benzene–ethyl acetate (3:1)] and $[\alpha]_D^{20}$ +42.8° (c = 1.2, CCl_4). IR spectrum: 1750 cm^{-1} (C=O). (3R,4R)-Azetidinone VII ($C_{14}H_{19}NO$) was obtained as an oil with R_f 0.40 [benzene–ethyl acetate (3:1)] and $[\alpha]_D^{20}$ –5.2° (c = 0.49, CCl_4). IR spectrum: 1750 cm^{-1} (C=O). Mass spectrum: M^+ 217.

B. When we used a fourfold excess of methyl iodide we obtained (3R,4R)-azetidinone VII (in 20% yield) and a mixture of the (1^1S,3R,4R) and (1^1R,3R,4R) epimers of VI (in 17% yield) and isolated the (1^1S,4R) and (1^1R,4R) epimers of starting azetidinone I (16%) from the reaction mixture.

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RECYCLIZATION OF ENAMINO KETONES THAT ARE IMIDAZOLIDINE DERIVATIVES TO 1-PYRROLIN-4-ONE 1-OXIDES

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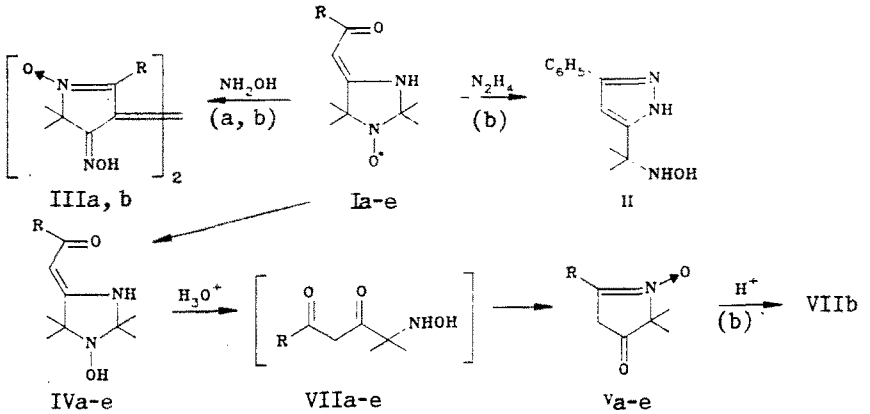
The recyclization in an acidic medium of enamino ketones that are imidazolidine derivatives leads to 1-pyrrolin-4-one 1-oxide derivatives, viz., cyclic β-oxo nitrones, which exist in the form of equilibrium mixtures of the ene hydroxyamino keto and oxo nitrone tautomeric forms, the ratio of which depends on the solvent and the character of the substituent.

Enamino ketones are capable of reacting with nucleophilic reagents at two reaction centers, viz., at the carbonyl group and at the enamine fragment [1]. We have shown that reduction of the nitroxyl group with the subsequent addition of hydrazine to the enamino keto fragment with opening of the imidazolidine heteroring and the formation of hydroxyaminopyrazole II occurs in the reaction of an enamino ketone, viz., imidazolidine 1-oxyl derivative Ib, with hydrazine (see [2]). In contrast to this, the reaction of enamino ketones Ia, b with hydroxylamine hydrochloride in pyridine leads to pyrroline derivatives IIIa, b (Table 1), i.e., in this case also recyclization with the participation of the hydroxyamino group of the imidazolidine occurs under the influence of the nucleophilic reagent. Similarly, maintenance of solutions of diamagnetic enamino ketones IV in 5-10% HCl solutions leads to their recyclization to 1-pyrrolin-4-one 1-oxide derivatives V [3]. It should be noted that when Vb is dissolved in concentrated HCl, the pyrroline ring is opened to give the hydrochloride of β-dioxohydroxylamine VIIb, which exists in the acyclic form only in acidic media. Starting pyrroline Vb is formed when attempts are made to neutralize it. The UV spectrum of VIIb in ethanol coincides completely with the spectrum of starting Vb. The structure of VIIb is confirmed by its ^{13}C NMR spectrum in 35% HCl–d_4-methanol (2:1); in this solution VIIb is evidently enolized at the carbonyl group bonded to the benzene ring (cf. [4]).



I, III—V, VII a R=CH_3, b R=C_6H_5, c R=CF_3, d R=$C(CH_3)_3$, e R= 2-pyridyl

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