Chemistry of Heterocyclic Compounds, Vol. 40, No. 5, 2004

OXIDATIVE REACTIONS OF AZINES. 11*. THE INFLUENCE OF MANGANESE DIOXIDE ON THE REACTION OF TETRAHYDROPYRIDINES WITH FORMALDEHYDE: SYNTHESIS AND MOLECULAR STRUCTURES OF 3-OXA-7-AZABICYCLO[3.3.1]- AND 6-OXA-2-AZABICYCLO[3.2.1]OCTANES

A. T. Soldatenkov[1], K. B. Polyanskii[1], A. V. Temesgen[1], N. D. Sergeeva[1], V. V. Vysotskaya[1], B. B. Averkiev[2], M. Yu. Antipin[2], and N. N. Lobanov[1]

New derivatives of piperidino[4,5-d]dioxane and 3-oxa-7-bicyclo[3.3.1]nonane were obtained by the oxidatively catalysed condensation of 4-aryl-1,2,3,6-tetrahydropyridines with formaldehyde. The direction of this reaction is sharply altered in the presence of manganese dioxide to give 6-oxa-2-azabicylo[3.2.1]octan-4-one – the product of the oxidative condensation of a new type.

Keywords: manganese dioxide, oxabicycloalkanes, tetrahydropyridines, formaldehyde, Prins reaction.

As the result of oxidatively catalysed condensation of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (**1a**) with formaldehyde (the Prins reaction) with a small excess of the latter 3-hydroxymethyl-1-methyl-6-phenyltetrahydropyridine is formed [2], while with a ten-fold excess the product is a substituted piperidino[4,5-*d*]dioxane **2** [3].

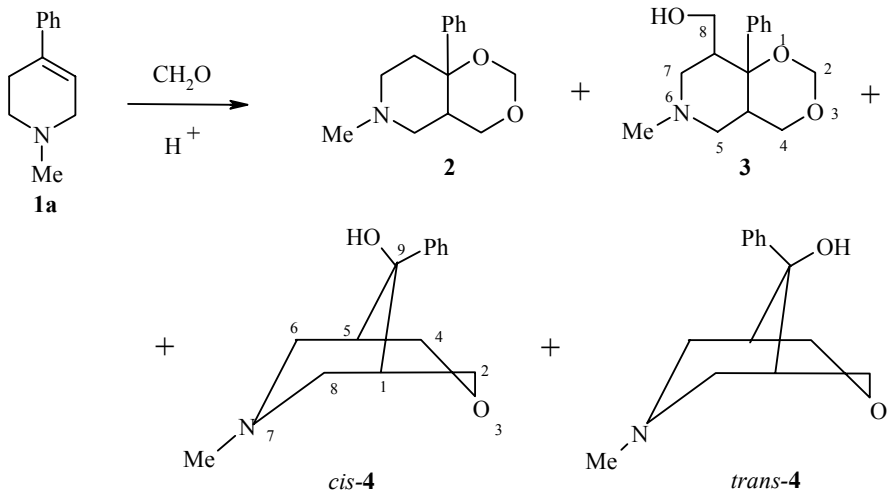
There have been no reports so far on the influence of oxidants on the Prins reaction. In a continuation of our studies to discover new reactions of hydropyridines initiated by manganese compounds with different oxidation states [4-6] we have studied in this work the condensation of 4-aryl-substituted 1-methyl-1,2,3,6-tetrahydropyridines **1a,b** with formaldehyde under conditions of the modified Prins reaction (in the presence of manganese dioxide.

In the first place, to study the composition of the reaction mixture formed in the classical Prins reaction in greater detail, we carried out the condensation of tetrahydropyridine **1** with a four-fold excess of formaldehyde which has been described previously [3]. By the use of crystallization and chromatography we succeeded in isolating from the reaction mixture not only the known 1,3-dioxane **3**, but also a series of new condensation products: 8-hydroxymethyl derivatives of the piperidinodioxane **3** and also *cis*- and *trans*-9-hydroxy-7-methyl-9-phenyl-3-oxa-7-azabicyclo[3.3.1]nonanes (**4**), which are isomers with respect to the

* Paper 10, see [1].

[1] Russian People's Friendship University, Moscow 117198; e-mail: asoldatenkov@sci.pfu.edu.ru. [2] A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Moscow 117813. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 755-764, May 2004. Original article submitted April 13, 2001.

position of the 9-hydroxy groups relative to the nitrogen atom. In the ^{1}H NMR spectra of compounds **2** and **3** the protons in position 4 take the form of a broad doublet (at 3.5-3.6 ppm) with geminal coupling of 1.5 Hz and a doublet of doublets (at 3.6-3.8 ppm) with a vicinal coupling of 2.5-2. Hz which indicates the stereoselectivity of the *cis*-coupling of the heterocyclic fragments [3].



The individual isomers were isolated by crystallization from the mixture of *cis*- and *trans*-bicyclononanes **4** (2:1 according to the ^{1}H NMR spectrum). They were identified on the basis of the magneto-anisotropic influence of the phenyl substituent on the chemical shifts of the protons of the methylene group. Thus in the *cis* isomer of **4** the protons on the $C_{(2)}$ and $C_{(4)}$ atoms of the tetrahydropyran ring fall within the region of shielding and their signals occur at 3.64 and 2.75 ppm. In the *trans* isomer of **4** the analogous signals appear at weaker field – at 4.02 and 4.54 ppm respectively. Similarly the protons in *trans*-**4** at positions 6 and 8 (the piperidine ring) are screened and their signals occur at 2.42 and 3.0 ppm, whereas the analogous signals for *cis*-**4** occur at 2.84 and 3.25 ppm. In $CDCl_3$ solution, according to the ^{1}H NMR spectrum, the piperidine ring of *cis*-**4** has the *boat* conformation, fixed by an intramolecular hydrogen bond. In order to refine the spatial structure of the isomers under discussion the X-ray structure of the *cis* isomer of **4** was determined. The overall structure of the molecule is shown in Fig. 1, the atomic coordinates are given in Tables 1 and 2, and the bond lengths and bond angles in Table 3.

The basic geometric parameters of the molecule are normal [7]. The piperidine and tetrahydropyran rings have the *chair* conformation. The hydroxy group forms an intermolecular hydrogen bond O–H···N with the nitrogen atom of neighboring molecules, forming a chain along the *c* axis (Fig. 2). The parameters of the hydrogen bond are O(11)···N(1) 2.869(1), H(11)···N(1) 2.06(2) A, and the angle O(11)–H(11)–N(1) 150(1)°.

The hydroxy group is positioned axially to the piperidine ring, while the phenyl group is equatorial (the deviation of atoms O(11) and C(12) from the mean squared plane of the ring is 1.731(1) and 0.057(1) Å respectively). The situation is reversed with respect to the tetrahydropyran ring: the OH group takes an equatorial position , while the phenyl group is axial (the respective deviations of O(11) and C(12) are -0.221(2) and 1.830(2) Å). The angle of rotation of the phenyl ring relative to the piperidine ring is 13.55(7)° and relative to the tetrahydropyran ring is 81.83(5)°, while the torsion angle C(4)–C(5)–C(12)–C(13) is 45.1(1)°.

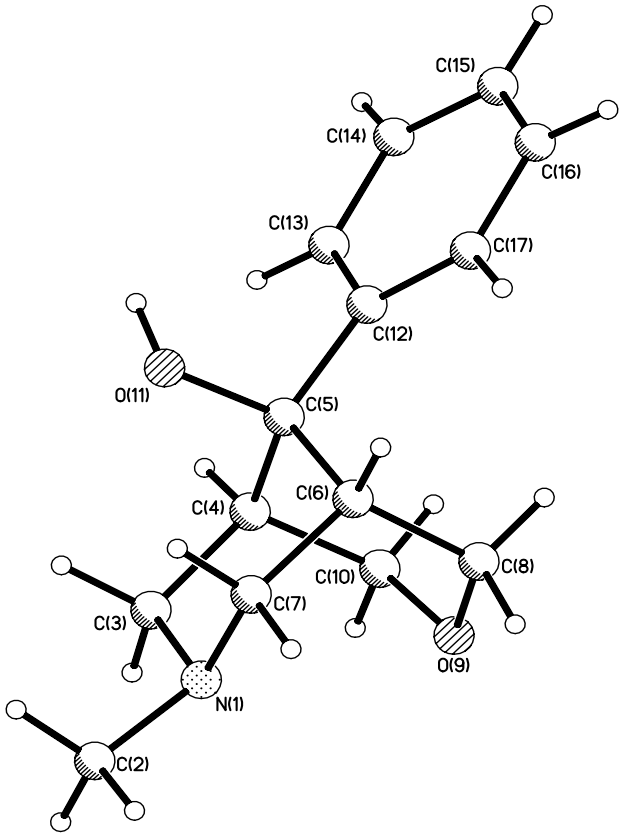


Fig. 1. General view of the molecule of the *cis* isomer of **4**.

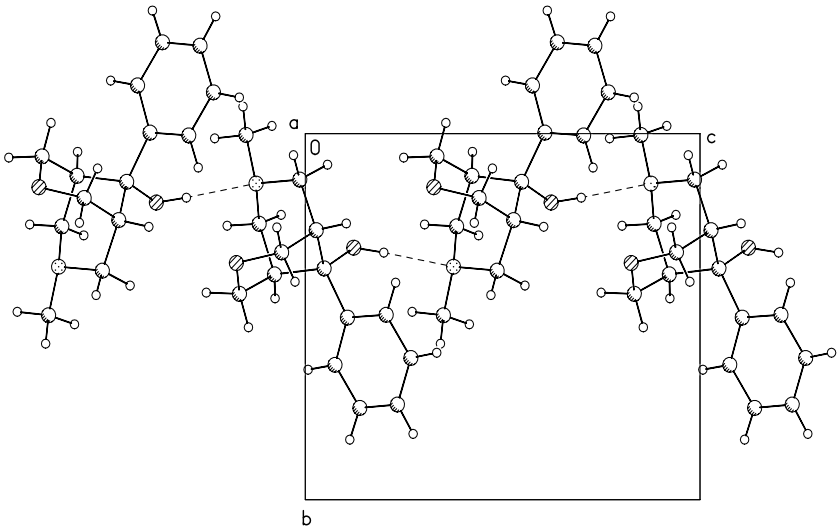


Fig. 2. Formation of a chain of molecules of the *cis* isomer of **4** in the crystal.

TABLE 1. Coordinates of the Non-hydrogen Atoms ($\times 10^4$) and Equivalent Isotropic Thermal Parameters U_{eq} ($\times 10^3$) in the Structure of the *cis* Isomer of **4**

Atom	*x*	*y*	*z*	U_{eq}, Å^2
N(1)	6633(1)	3638(1)	3753(1)	36(1)
C(2)	6035(1)	4963(1)	3499(1)	53(1)
C(3)	7526(1)	3743(1)	4861(1)	41(1)
C(4)	8099(1)	2362(1)	5277(1)	37(1)
C(5)	7154(1)	1316(1)	5478(1)	32(1)
C(6)	6384(1)	1154(1)	4220(1)	35(1)
C(7)	5787(1)	2536(1)	3833(1)	38(1)
C(8)	7123(1)	621(1)	3333(1)	45(1)
O(9)	8111(1)	1464(1)	3255(1)	48(1)
C(10)	8810(1)	1758(2)	4401(1)	48(1)
O(11)	6413(1)	1883(1)	6227(1)	40(1)
C(12)	7677(1)	-27(1)	6068(1)	39(1)
C(13)	8612(1)	49(2)	7049(1)	51(1)
C(14)	9053(1)	-1129(2)	7674(2)	69(1)
C(15)	8579(2)	-2401(2)	7335(2)	76(1)
C(16)	7648(2)	-2495(2)	6383(2)	74(1)
C(17)	7196(1)	-1317(1)	5753(1)	55(1)

When the condensation of the tetrahydropyridines **1a,b** with formaldehyde analogous to that described above but in the presence of manganese dioxide was carried out quite different products were obtained the structures of which did not correspond to any of the possible products of the classical Prins reaction (see [2, 3,

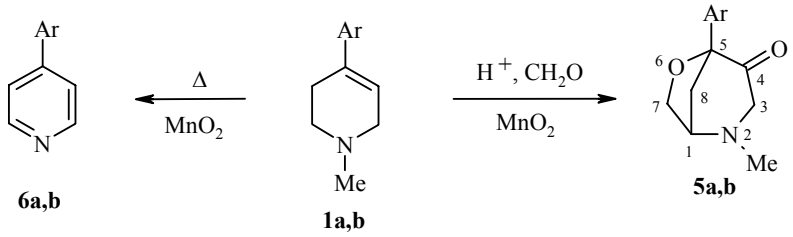
TABLE 2. Coordinates of the Hydrogen Atoms ($\times 10^4$) and Equivalent Isotropic Thermal Parameters U_{eq} ($\times 10^3$) in the Structure of the *cis* Isomer of **4**

Atom	*x*	*y*	*z*	U_{eq} Å^2
H(2C)	5457(14)	4870(17)	2706(16)	66(5)
H(2B)	6609(16)	5740(20)	3424(16)	78(5)
H(2A)	5604(14)	5211(17)	4155(16)	72(5)
H(3B)	8126(13)	4412(16)	4702(13)	53(4)
H(3A)	7190(11)	4151(15)	5562(12)	44(3)
H(4)	8634(11)	2545(14)	6038(12)	44(3)
H(6)	5737(11)	499(14)	4234(11)	40(3)
H(7B)	5262(11)	2780(13)	4389(11)	40(3)
H(7A)	5253(12)	2484(13)	3022(12)	44(3)
H(8B)	7391(12)	-292(17)	3560(13)	52(4)
H(8A)	6636(12)	656(16)	2492(14)	55(4)
H(10B)	9368(14)	2437(17)	4280(14)	60(4)
H(10A)	9207(12)	953(16)	4741(12)	49(4)
H(11)	6752(13)	1750(17)	6988(14)	60(4)
H(13)	8948(13)	928(18)	7287(14)	62(4)
H(14)	9673(18)	-988(21)	8329(20)	94(6)
H(15)	8855(17)	-3203(22)	7729(18)	92(6)
H(16)	7326(16)	-3361(24)	6128(17)	91(6)
H(17)	6550(15)	-1450(18)	5071(16)	72(5)

TABLE 3. Bond Lengths (*d*) in The Compound *cis*-**4**

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
N(1)–C(2)	1.460(2)	C(5)–C(12)	1.532(2)	C(12)–C(13)	1.397(2)
N(1)–C(7)	1.464(2)	C(5)–C(6)	1.536(1)	C(13)–C(14)	1.386(2)
N(1)–C(3)	1.468(1)	C(6)–C(8)	1.531(2)	C(14)–C(15)	1.373(3)
C(3)–C(4)	1.526(2)	C(6)–C(7)	1.531(2)	C(15)–C(16)	1.374(3)
C(4)–C(10)	1.524(2)	C(8)–O(9)	1.424(2)	C(16)–C(17)	1.393(2)
C(4)–C(5)	1.542(2)	O(9)–C(10)	1.421(2)		
C(5)–O(11)	1.429(1)	C(12)–C(17)	1.387(2)		

8] and this paper). For example, after standard treatment of the reaction mixture by chromatography compounds **5a,b** were isolated which, according to ^{1}H and ^{13}C NMR, had the structure of 6-oxa-2-azabicyclo[3.2.1]octan-4-ones, which indicates the unexpected addition of formaldehyde to one of the α-positions of the piperidine ring (for a preliminary report see [9]).



6a,b **1a,b** **5a,b**

a Ar = Ph; **b** Ar = *p*- MeC_6H_4

The structures of compounds **5a** and **5b** were established on the basis of the complete assignment of the signals in the ^{1}H and ^{13}C NMR spectra using H,H COSY, C,H COSY and ^{13}C DEPT. In the ^{1}H NMR spectra of both compounds signals of two methylene groups attached to heteroatoms appear at weak field (protons at position 3 at 4.10-4.42 ppm and at position 7 at 3.73-4.23 ppm). The signals of protons at $C_{(8)}$, bonded only to carbon are found at stronger field (2.98-3.16 ppm). The chemical shift of the methyne proton (at 4.00-4.07 ppm)

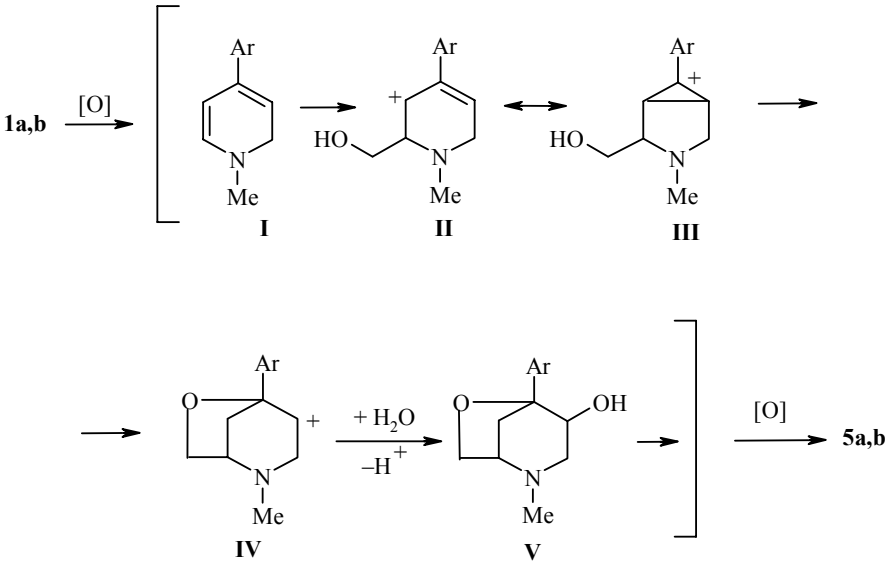
TABLE 4. Bond Angles (ω) in Compound *cis*-**4**

Angle	ω, deg.	Angle	ω, deg.
C(2)–N(1)–C(7)	110.76(10)	C(8)–C(6)–C(5)	110.22(9)
C(2)–N(1)–C(3)	109.65(10)	C(7)–C(6)–C(5)	108.99(9)
C(7)–N(1)–C(3)	111.56(8)	N(1)–C(7)–C(6)	112.53(9)
N(1)–C(3)–C(4)	113.33(9)	O(9)–C(8)–C(6)	114.06(10)
C(10)–C(4)–C(3)	113.16(10)	C(10)–O(9)–C(8)	112.39(9)
C(10)–C(4)–C(5)	109.51(10)	O(9)–C(10)–C(4)	112.82(9)
C(3)–C(4)–C(5)	109.95(9)	C(17)–C(12)–C(13)	117.64(12)
O(11)–C(5)–C(12)	107.47(8)	C(17)–C(12)–C(5)	123.13(11)
O(11)–C(5)–C(6)	106.40(8)	C(13)–C(12)–C(5)	118.92(11)
C(12)–C(5)–C(6)	115.32(9)	C(14)–C(13)–C(12)	121.05(15)
O(11)–C(5)–C(4)	111.24(9)	C(15)–C(14)–C(13)	120.5(2)
C(12)–C(5)–C(4)	112.87(9)	C(14)–C(15)–C(16)	119.34(14)
C(6)–C(5)–C(4)	103.40(8)	C(15)–C(16)–C(17)	120.6(2)
C(8)–C(6)–C(7)	112.70(9)	C(12)–C(17)–C(16)	120.9(2)

indicates that the CH group is bonded to a nitrogen atom. The presence of similar groups bonded in the O–CH_2–CH–CH_2 system is also confirmed by the ^{13}C NMR spectrum of compound **5b** (see experimental section). In this spectrum there are also signals assigned to the C=O group (at 200.0 ppm) and of a quaternary aliphatic carbon atom, the chemical shift of which (at 129.7 ppm) confirms the presence of the grouping O–C_{quat}–C=O. These results indicate the addition of one molecule of formaldehyde at the α-position of the piperidine ring with subsequent cyclization of the hydroxymethyl group at the γ-position (with formation of the tetrahydrofuran unit) and oxidation to structures **5a,b**.

Analysis of the parameters of the ^1H and ^{13}C NMR spectra, Dreiding models, and calculation of the energies of the conformers by molecular mechanics methods, showed that there is some preference for a compressed *boat* conformation for the piperidine, *cis*-1,3-diaxially coupled to the tetrahydropyran ring, which has a firmly fixed envelope conformation.

The key stage in the probable route to the formation of compounds **5a,b** is evidently the oxidative dehydrogenation of the initial tetrahydropyridines, the products of which can then be attacked by formaldehyde. An indirect confirmation of such a dehydration was obtained by separate experiments on the aromatization of substrates **1a,b** by boiling their solutions in toluene in the presence of manganese dioxide. Evidently the arylpyridines **6a,b** (isolated in 42-45% yield) should be formed via dihydropyridine intermediates. The results discussed permit the suggestion of the following sequence for the formation of the bicyclooctanes **5a,b** in the oxidative condensation of tetrahydropyridines with formaldehyde:



The dihydropyridines **I**, formed in the initial (oxidative) stage, add a protonated formaldehyde at the α-position, which leads to the carbocation **II**, stabilized by form **III**. An intramolecular cycloaddition then follows to give the bicyclic cation **IV** which is hydroxylated to the alcohol **V** by the addition of a molecule of water. The final stage is the oxidation of the alcohols **V** to the ketones **5a,b** (the conversion of alcohols to ketones is well documented [10]).

Thus it is established using piperidines as an example that the direction of the Prins reaction can be controlled by manganese dioxide to give the unusual oxidative condensation of tetrahydropyridines with formaldehyde with "one-step" formation of a new group of 6-oxa-2-azabicyclo[3.2.1]octan-4-ones. We note that the structure of the end products in the method we have developed differs principally from the structure of the products of the Prins reaction in the formation of a tetrahydrofuan ring and a β-piperidine unit.

EXPERIMENTAL

IR spectra were recorded on a UR-20 instrument. Mass spectra were obtained with an MX-1303 machine. NMR spectra of $CDCl_3$ solutions with TMS as internal standard were recorded with Bruker W-80, Bruker WM-250, and DPX-500 spectrometers (80, 250, and 500 MHz respectively). The course of reactions and the purity of individual compounds were monitored by TLC on Silufol UV-254 strips with development by iodine vapor. Separation and purification of compounds was carried out by column chromatography on silicagel L-60 (40/100).

X-ray Crystallographic Analysis of Compound *cis*-4. Crystals of the bicyclononane *cis*-**4**, with composition $C_{14}H_{19}NO_2$, grown from ether, were monoclinic and had the following crystallographic parameters: $P2_1/c$, $a = 11.599(3)$, $b = 9.681(3)$, $c = 11.324(3)$ Å; $\beta = 101.18(2)°$; $V = 1248.4(6)$ Å^3; $Z = 4$; $d_{calc} = 1.241$ g/cm^3; M = 233.3. The parameters of the unit cell and the intensities of 2869 reflexions were measured on a Siemens P3/PC automatic four-circle diffractometer (T = 20°C, λMoK_α radiation, graphite monochromator, $\theta/2\theta$ scanning, $\theta_{max} = 27°$). The structure was solved by direct methods and refined by full matrix least squares analysis in the anisotropic approximation for non-hydrogen atoms. The hydrogen atoms were localized in difference Fourier maps and refined isotropically. The final residual factors were $R_1 = 0.0402$ from 2217 independent reflexions with $I > 2\sigma$ and $wR_2 = 0.1262$ with all 2731 reflexions. All calculations were carried out using the SHELXTL PLUS (PC version 5.0) family of programs [11].The numbering of the atoms is shown in Fig. 1.

Condensation of 4-Phenyltetrahydropyridine 1a with Formaldehyde (the Prins Peaction). A mixture of tetrahydropyridine **1a** (3 g, 17.3 mmol) and formaldehyde (as paraformaldehyde) (2 g, 67 mmol) in 60% sulfuric acid (10.5 ml) was boiled for 7 h and then stood at room temperature for 18 h. The reaction mixture was diluted with water (10 ml), 20% potassium hydroxide solution was added to a pH of 10, and the mixture was then extracted with benzene (3 × 20 ml). The extract was washed with water and dried over magnesium sulfate. The solvent was removed in vacuum and the reside was dissolved in ether. The precipitate which separated on cooling the ether solution was washed with ether and dried to give **9-hydroxy-7-methyl-9-phenyl-3-oxa-7-azabicyclo[3.3.1]nonane (4)** (0.85 g, 21%) (as a 2:1 mixture of the *cis*- and *trans*-isomers according to the NMR spectrum) as a coarse white powder (mp ~160°C), containing some clear monocrystals of the *cis*-isomer, mp 176°C (from crystallographic data and the NMR spectrum). The *cis*-isomer was also isolated by crystallization from methylene chloride in a yield of 8% (0.32 g). R_f 0.40 (acetone). IR spectrum (KBr), ν, cm^{-1}: 3220, 3100 br. (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.38 (3H, s, CH_3); 2.68 (2H, m, H-1 and H-5); 2.84 (2H, dd, $^2J = 11.1$, $^3J = 2.5$, H-6 and H-8); 3.25 (2H, dd, $^2J = 11.1$, $^3J = 7.3$, H-6 and H-8); 3.64 (2H, d, $^2J = 11.4$, H-2 and H-4); 3.75 (2H, d, $^2J = 11.4$, H-2 and H-4); 7.30-7.50 (5H, m, Ph). ^{13}C NMR spectrum, δ, ppm: 37.9 ($C_{(1)}$ and $C_{(5)}$), 45.11 (CH_3), 55.9 ($C_{(6)}$ and $C_{(8)}$), 69.8 ($C_{(2)}$ and $C_{(4)}$), 71.8 ($C_{(9)}$), 126.1, 127.8, 128.9, and 141.6 ($C_{(Ph)}$). Mass spectrum, *m/z* (I_{rel}, %): 233 (M^+ (100), 232 (38), 216 (27), 190 (20), 184 (8), 170 (10), 133 (34), 128 (35), 105 (38), 91 (15), 77 (16). Found, %: C 72.20; H 8.23; N 5.91. $C_{14}H_{19}NO_2$. Calculated, %: C 72.10; H 8.16; N 6.01.

The mother liquor, after removing the *cis* isomer of **4**, was evaporated, and the residue was crystallized from ether to give the *trans*-isomer of **4** (0.12 g, 3%); mp 180°C. R_f 0.42 (acetone). IR spectrum (KBr, ν, cm^{-1}): 3410 and 3220 br. (OH). Mass spectrum, *m/z* (I_{rel}, %): 233 [M^+] (100). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.12 (3H, s, CH_3); 2.37 (2H, m, H-1 and H-5); 2.42 (2H, d, ^2J =11.4, H-6 and H-8); 3.00 (2H, d, ^2J =11.4, H-6 and H-8); 4.02 (2H, dd, $^2J = 10.9$, $^3J = 2.3$, H-2 and H-4); 4.54 (2H, dd, $^2J = 10.9$, $^3J = 2.3$, H-2 and H-4); 7.30-7.50 (5H, m, C_6H_5). ^{13}C NMR spectrum, δ, ppm: 38.3 ($C_{(1)}$ and $C_{(5)}$), 46.5 (CH_3), 58.3 ($C_{(6)}$ and $C_{(8)}$), 67.4 ($C_{(2)}$ and $C_{(4)}$), 71.3 ($C_{(9)}$), 125.4, 128.0, 129.1, 142.4 ($C_{(Ph)}$). Found, %: C 71.92; H 8.27; N 5.85. $C_{14}H_{19}NO_2$. Calculated, %: C 72.10; H 8.27; N 6.01.

The ether mother liquor after separation of the crystalline mixture of the *cis*- and *trans*-isomers of **4** was evaporated to give an amber yellow sticky oil (2.0 g) which was separated by chromatography on a silica gel column (d = 3, h =17 cm, eluant acetone) to give consecutively product **3** (0.28 g, 6%) and product **2** (0.6 g, 15%).

8-Hydroxymethyl-6-methyl-8a-phenylpiperidino[4,5-*d*]dioxane (3), colorless crystals; mp 88-90°C, R_f 0.84 (acetone). IR spectrum (KBr, ν, cm^{-1}): 3210 (OH). Mass spectrum, *m/z* (I_{rel}, %): 263 [M^+]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.57 (1H, br. s, H-8); 2.34 (3H, s, CH_3); 2.83-3.05 (6H, m, H_2-5,5, H_2-7,7, and $\underline{CH_2}OH$); 3.53 (1H, br. d, ^2J = 11.6, H_2-4); 3.61 (1H, dd, ^2J = 11.6, ^3J = 2.6, H-4); 3.90 (1H, m, H-8a); 4.75 and 4.83 (2H, two d, ^2J = 6.1, H_2-2,2); 7.28-7.50 (5H, m, C_6H_5). ^{13}C NMR spectrum, δ, ppm: 35.1 ($C_{(8)}$), 46.1 (CH_3), 47.1 ($C_{(4a)}$). 55.2 ($C_{(5)}$), 57.2 ($C_{(7)}$), 65.8 (C-OH), 66.2 ($C_{(4)}$), 77.7 (C_{quat}-O), 89.4 ($C_{(2)}$), 126.5, 127.5, 128.4, 129.3, and 140.7 ($C_{(Ph)}$). Found, %: 68.21; H 8.16; N 5.28. $C_{15}H_{21}NO_3$. Calculated, %: C 68.44; H 7.99; N 5.32.

6-Methyl-8a-phenylpiperidino[4,5-*d*]dioxane (2); mp 60-62°C (in [3] the mp of the hydrochloride only is given, 323°C (dec.)), R_f 0.76 (acetone). Mass spectrum, *m/z* (I_{rel}, %): 233 [M^+] (7), 174 (38), 128 (5), 105 (11), 77 (12), 57 (13), 44 (100). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.80 (2H, m, H_2-8,8); 2.37 (3H, s CH_3); 2.50-3.20 (5H, m, H_2-5,5 and H_2-7,7 and H-4a); 3.60 (1H, br. d, ^2J = 11.5, H_2-4,4); 3.80 (1H, dd, ^2J = 11.5, ^3J = 2.5, H-4); 4.77 and 4.83 (2H, two d, ^2J = 6.5, H_2-2,2); 7.30 (5H, m, Ph).

Oxidative Condensation of the Tetrahydropyridines 1a,b with Formaldehyde in the Presence of MnO_2 (Modified Prins Reaction). A mixture of 4-aryltetrahydropyridine **1a,b** (10 mmol), manganese dioxide (5 g, 50 mmol), formaldehyde (as a 37% aqueous solution) (3 ml, 30 mmol), and conc. H_2SO_4 (3 ml) was boliled for 7 h. 20% Sodium hydroxide was added to the cold reaction mass to pH 9, and the mixture was extracted with benzene. The solvent was evaporated in vacuum and the residue was chromatographed on a silica column with acetone as eluant. Product **5a** (0.84 g, 31%) was obtained from phenyltetrahydropyridine and product **5b** (1.0 g, 35%) was obtained from 4-tolyltetrahydropyridine.

2-Methyl-5-phenyl-6-oxa-2-azabicyclo[3.2.1]octan-4-one (5a). A thick, colorless oil, R_f 0.7 (acetone). IR spectrum (nujol mull), ν, cm^{-1}: 1680 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.51 (3H, s, CH_3); 3.00 (1H, t, ^2J = 12.6, H_a-8); 3.16 (1H, br. d, ^2J = 12.6, H_e-8); 3.73 (1H, t, ^2J = 10.7, H_a-7); 4.00 (1H, m, H_e-1); 4.12 (1H, d, ^2J = 9.5, H_a-3); 4.23 (1H, br. d, ^2J = 10.7, H_e-7); 4.42 (1H, br. d, ^2J =9.5, H_e-3); 7.30-7.50 (5H, m, C_6H_5). Mass spectrum, *m/z* (I_{rel}, %): 217 [M^+] (16), 202 (43), 187 (15), 131 (12), 105 (100), 77 (37). Found, %: C 71.7; H 7.03; N 6.52. $C_{13}H_{15}NO_2$. Calculated, %: C 71.89; H 6.91; N 6.45.

2-Methyl-5-(4-tolyl)-6-oxa-2-azabicyclo[3.2.1]octan-4-one (5b). A thick, colorless oil, R_f 0.7 (acetone). IR spectrum (nujol mull), ν, cm^{-1}: 1675 (C=O). Mass spectrum, *m/z* (I_{rel}, %): 231 [M^+] (7), 216 (36), 203 (6), 188 (28), 172 (34), 160 (38), 145 (12), 119 (100), 91 (45). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.39 (3H, s, CH_3); 2.51 (3H, s, CH_3); 2.98 (1H, t, ^2J = 12.9, H_a-8); 3.16 (1H, br. d, ^2J =12.9, H_a-8); 3.76 (1H, t, ^2J =10.9, H_a-7); 4.07 (1H, m, H_e-1); 4.10 (1H, d, ^2J = 9.4, H_a-3); 4.20 (1H, br. d, ^2J = 10.9, H_e-7); 4.40 (1H, br. d, ^2J = 9.4, H_e-3); 7.27 and 7.86 (4H, AX'BX' system, ^3J = 7.2, ^4J = 1.1, Ar). ^{13}C NMR spectrum, δ, ppm: 22.6 (CH_3 in Ar), 40.3 ($C_{(1)}$), 40.8 (N-CH_3), 55.8 ($C_{(8)}$), 70.2 ($C_{(7)}$), 86.7 ($C_{(3)}$), 129.7 ($C_{(5)}$), 129.3, 130.5, 144.3, 145.4 (C_{arom}). Found, %: C 73.01; H 7.49; N 5.90. $C_{14}H_{17}NO_2$. Calculated, %: C 72.72; H 7.36; N 6.06.

Oxidative Aromatization of the Tetrahydropyridines 1a,b. A mixture of 4-phenyltetrahydropyridine **1a** (0.5 g, 2.9 mmol) and manganese dioxide (2.5 g, 29 mmol) in toluene (100 ml) was boiled for 3 h. The manganese dioxide was filtered off and washed on the filter with chloroform (50 ml). The combined filtrates were evaporated in vacuum and the residue was separated by column chromatography on silicagel with 1:1 ether: hexane as eluant to give 4-phenylpyridine, **6a**, (0.2 g, 45%), R_f = 0.5 (ether); mp 76-78°C [12]. The mass spectrum and ^{1}H NMR spectra were identical to those cited in [5].

Analogously from the tetrahydropyridine **1b** (0.5 g, 2.7 mmol) 4-(*p*-tolyl)pyridine **6b** was obtained (0.19 g, 42%), R_f 0.5 (ether); mp 43-45°C.

^{1}H NMR spectrum, δ, ppm, (*J*, Hz): 2.40 (3H, s, Me); 7.25 and 7.50 (4H, AA'XX' system, ^3J =7.1, ^4J = 1.1, Ar); 7.61 and 8.63 (AA'BB' system, ^3J =7.1, ^4J = 1.1, H_{het}). Mass spectrum, *m/z* (I_{rel}, %): 169 [M^+] (100), 168 (43), 155 (95), 91 (20). Found, %: C 84.98; H 6.67; N 8.01. $C_{12}H_{11}N$. Calculated, %: 85.21; H 6.51; N 8.28.

We thank the Russian Fund for Fundamental Research for financial support of this work (grants nos. 99-03-32940a and 00-15-97359).

REFERENCES

1. A. T. Soldatenkov, A. V. Temesgen, K. B. Polyanskii, S. A. Soldatova, N. M. Kolyadina, N. I. Golovtsov, and N. D. Sergeeva, *Khim. Geterotsikl. Soed.,* 552 (2003).
2. C. J. Schmidle and R.C. Mansfield, US Pat. 2748140; *Chem. Abstr.,* **51,** 2880 (1957).
3. A. F. Casy, A. V. Simmonds, and D. Staniforth, *J. Org. Chem.,* **37**, 3189 (1972).
4. A. T. Soldatenkov, A. W. Temesgen, I. A. Bekro, T. P. Khristoforova, S. A. Soldatova, and B. N. Anissimov, *Mendeleev Commun.,* 243 (1997).
5. A. T. Soldatenkov, A. W. Temesgen, L. N. Kuleshova, and V. N. Khrustalev, *Mendeleev Commun.,* 193 (1998).
6. A. T. Soldatenkov, A. W. Temesgen, I. A. Bekro, S. A. Soldatova, and B. N. Anissimov, *Mendeleev Commun.,*137 (1998).
7. F. H. Allen and O. Kennard, *Chem. Des. Autom. News*, 31 (1993).
8. A. F. Casy and F. Ogungbamila, *Heterocycles,* **16**, 1913 (1981).
9. A. T. Soldatenkov, K. B. Polyanskii, A. W. Temesgen, S. A. Soldatova, N. D. Sergeeva, N. D. Kolyadina, and N. N. Lobanov, *Mendeleev Commun.,* 27 (2001).
10. S. P. Korshunov and L. I. Vereshchagin, *Uspekhi Khimii,***35**, 2255 (1966).
11. L. M. Sheldrick, SHELXTL, Version 5. *Software Reference Manual. Siemens Industrial Automation, Inc.* Madison (1994).
12. A. E. Chichibabin and D. I. Rochko, *Zh. RFKhO,* **62**, 1201 (1930).