Pergamon

Tetrahedron Vol. 51, No. 31, pp. 8565-8572, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00471-8

Isoquinuclidine Derivatives from Limonene

Stanislav A. Bakunov[a], Alexey Yu. Denisov[b], Alexey V. Tkachev[a]

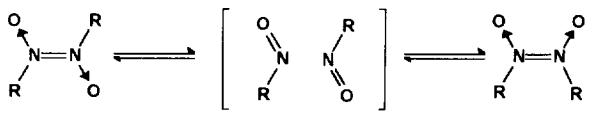
[a] Novosibirsk Institute of Organic Chemistry, Novosibirsk 630090, Russia
[b] Novosibirsk Institute of Bioorganic Chemistry, Novosibirsk 630090, Russia

Abstract: Structure of α-hydroxyl amino oxime derived from monoterpene hydrocarbon limonene was carefully determined using NMR technique and confirmed by chemical transformations. This α-hydroxyl amino oxime derivative of limonene, that was believed to be a simple monocyclic compound, is in fact a derivative of isoquinuclidine.

α-Hydroxyl amino oximes are readily prepared by treatment of the corresponding nitrosochlorides either with free hydroxylamine or hydroxylamine hydrochloride, and a number of α-hydroxyl amino oximes derived from different olefins has been described.[1] When applied to terpene hydrocarbons, this reaction results in functionalized terpene derivatives[2,3,4] which are of interest from the viewpoint of their use in the synthesis of useful organic molecules.[5] The α-hydroxyl amino oxime of the limonene series, described by G.Cusmano at the beginning of the century,[3] was believed to have the normal monocyclic structure, in spite of its unusual chemical behavior.[6] Now we report experimental evidence of the unusual structure of the limonene α-hydroxyl amino oxime **6** that is in fact a derivative of 2-azabicyclo[2.2.2]octane (isoquinuclidine), whose derivatives are of special interest due to their properties.[7]

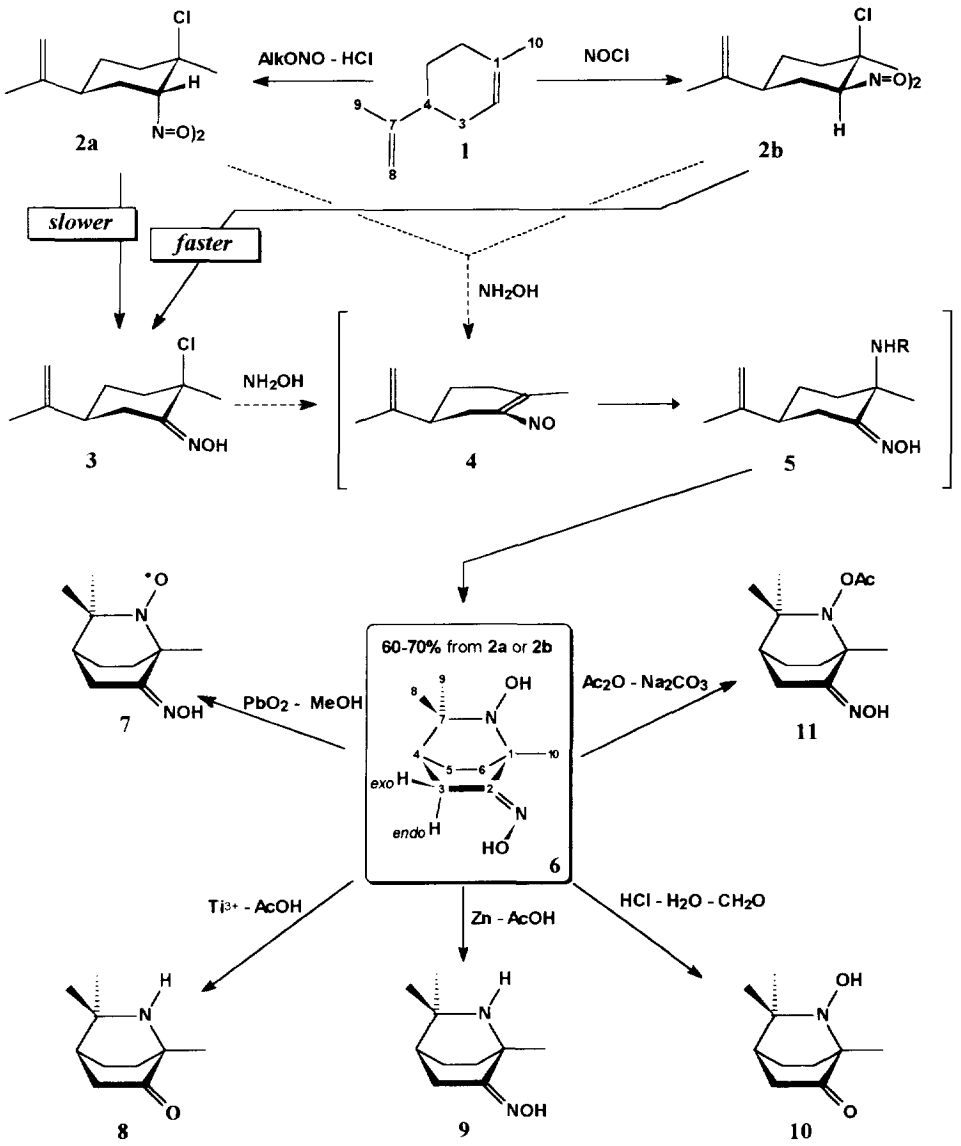
We prepared α-hydroxyl amino oxime **6** according to the standard procedure described as a method for preparing "limonene α-hydroxyl amino oxime"[3] using limonene nitrosochlorides **2a** and **2b** as intermediates.

Nitrosochlorination of limonene **1** is used in the process of making carvone and has been studied previously.[8] We prepared both *trans*- (**2a**)[9] and *cis*- (**2b**)[10] limonene-nitrosochlorides and examined them as starting compounds in the preparation of the bicyclic compound **6**. Unexpectedly, both *cis*- and *trans*-nitrosochlorides display two sets of signals in NMR spectra. Both *trans*- (**2a**) and *cis*- (**2b**) nitrosochlorides are *E*-dimers in the solid state according to IR spectroscopy. When registered immediately after dissolving, the NMR spectrum of each isomer shows one set of signals possessed by the *E*-isomer at the **N=N** double bond of the dimeric nitrosochloride. In a period of 4 hours the NMR spectra show equilibrium mixtures: *E*:*Z*=5:3 for *trans*-isomer (**2a**) and 4:3 for *cis*-isomer (**2b**). Dimeric nitroso compounds with the structural fragment of **N,N'**-azodioxides are known to exist in *E*- and *Z*- forms at the **N=N** bond[11] which can undergo fast interconversion in a solution.[12]



E-dimer monomer *Z*-dimer

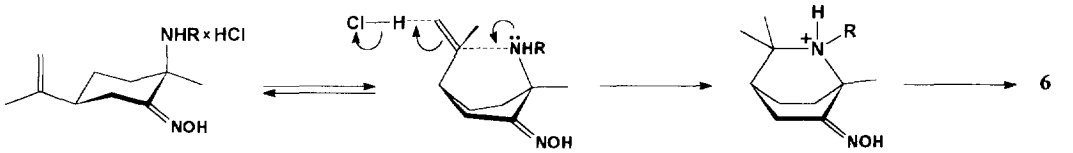
Cis- and *trans*- limonene nitrosochlorides are more stable than other terpenic nitrosochlorides,[13] the *cis*-isomer **2b** is completely transformed to α-chloro oxime **3** in a chloroform solution at room temperature in two weeks, whereas the degree of conversion is only 60% for *trans*-isomer **2a**. Reaction of both *cis*- and *trans*-nitrosochlorides with hydroxylamine results in one and the same compound **6**, the reaction of the *cis*-isomer



The numbering of the C-atoms of the isoquinuclidine derivatives shown on the scheme does not coincide with the numbering of the system according to IUPAC. This numbering scheme is usual for the p-menthane type monoterpenoids and given for NMR interpretation only.

being to some extent faster due to the axial position of proton H^2, which is more favorable for the formation of the corresponding intermediate nitroso olefin **4**.[14]

The chemical structure of the bicyclic product was solved by NMR spectroscopy using the ^{13}C-^{13}C coupling constants. The ^{13}C and ^{1}H NMR data for compound **6** and other limonene derivatives obtained are collected in ***Table 1*** and ***Table 2*** respectively. Signal assignment of the *gem*-dimethyl fragment was carried out using Nuclear Overhauser Effect for compound **11**: irradiation of the H^8 methyl at δ 1.10 ppm (δ_C 23.00 ppm) gave 5% enhancement of the signal at δ 2.78 ppm (H^3-*exo*) and 2% enhancement of the signal at δ 1.81 ppm (H^4). *E*-Configuration of the oxime group in **11** was determined by comparing values of the coupling constants $^1J(C^1\text{-}C^2)$ and $^1J(C^2\text{-}C^3)$ [15] Comparison of the ^{1}H and ^{13}C NMR data for **11** with those of the other bicyclic derivatives obtained shows the same configuration of the oxime moiety in molecules **6,8-10**. In addition, molecular mechanics calculations using MMX program[16] show the *E*-isomers to be *ca.* 2-3 kcal/mol more stable. ^{1}H NMR chemical shifts and proton-proton couplings in compounds **6,8-11** are in agreement with the NMR parameters of a number of known synthetic isoquinuclidine derivatives.[17] Transformations of the α-hydroxylamino oxime into a number of derivatives, including the stable nitroxyl radical **7**,[18] shown on the ***Scheme***, supports the bicyclic structure of the isoquinuclidine type **6** for this compound. Bicyclic compound **6** appears to be due to an intramolecular acid-catalyzed cyclization of intermediate monocyclic α-hydroxyl amino oxime of normal structure (**5, R=OH**), whose formation is postulated as a result of nucleophilic substitution of the chlorine atom *via* corresponding nitroso olefin **4** with the retention of the C^1 configuration.[19] We tried to perform the intramolecular cyclization of other monocyclic limonene derivatives of this type (**5, R=Me, Ph, CH_2Ph**[9,19]) by the action of inorganic acids under various conditions, but our attempts failed and the starting compounds were recovered unchanged. The intramolecular cyclization of the N-hydroxylamino derivative **5** (**R=OH**) is possible due to the low basicity of N-hydroxylamino group. When the limonene nitrosochloride reacts with hydroxylamine, the N-hydroxylamino derivative **5** (**R=OH**) is formed as hydrochloride. This hydrochloride is in equilibrium with the free N-hydroxylamino derivative which can be attacked by hydrogen chloride at the C^8 atom to give the cyclization product:



Corresponding N-alkyl amino oximes **5** (**R=Alk**) are more strong bases by a factor of 10^3-10^4, so the cyclization should be much slower, if at all.

EXPERIMENTAL

General experimental procedures. All the solvents used were reagent quality. Diethyl ether was freshly distilled. Removal of all solvents was carried out under reduced pressure and all commercial reagents were used without additional purification. Analytical TLC plates were **Silufol**® (Silpearl on aluminum foil, Czechoslovakia). Preparative column chromatography was performed on **SiO_2** ("KSK", Russia, 100-200

mesh, air dried and activated at 140°C for 5h). IR spectra were obtained using a **Specord M-80** infrared spectrophotometer. IR spectra for nitrosochlorides **2a** and **2b** were obtained using a ***Bruker* IFS-66** infrared spectrometer. A **Polamat A** polarimeter was used to measure optical rotation at 578 nm. Melting points were obtained using a **Kofler** melting point apparatus. Mass spectra were obtained on a **Finnigan MAT 8200** instrument using the Electron Impact Ionization technique (100-220°C, 70eV). Microanalyses were obtained using a ***Hewlett Packard 185*** analyzer and a ***Carlo Erba 1106*** analyzer. ESR spectrum was recorded using a ***Bruker ESR 300*** instrument.

NMR experiments. ^{1}**H** and ^{13}**C** NMR spectra were recorded at room temperature using a **Bruker AC-200** instrument (^{1}**H** 200.13 MHz, ^{13}**C** 50.32 MHz) locked to the deuterium resonance of the solvent using standard Bruker NMR Software System. The chemical shifts were calculated relative to the solvent signal using as the internal standard: $\delta_{\mathbf{H}}$ 7.24 ppm and $\delta_{\mathbf{C}}$ 76.90 ppm for **$CDCl_3$**, $\delta_{\mathbf{H}}$ 2.55 ppm and $\delta_{\mathbf{C}}$ 39.60 ppm for **DMSO-d_6**. NOE and INADEQUATE experiments were performed on a a **Bruker AM-400** instrument (^{1}**H** 400.13 MHz, ^{13}**C** 100.61 MHz). NOE experiment for **11** was carried out for the deoxygenated solution of the compound in **CD_2Cl_2** (20 mg/ml) ($\delta_{\mathbf{H}}$ 5.32 ppm for **CD_2Cl_2**). Carbon-carbon coupling constants $^{1}J_{CC}$ were measured by a standard version of INADEQUATE with adjustment at 40 Hz, and selective INADEQUATE (INADSEL[20]) with adjustment at 3 Hz was used for measuring of the long-range carbon-carbon couplings;[21] 128K of the memory were used for one spectrum, and digital resolutions were 0.2-0.5 Hz.

Table 1. **^{13}C NMR Data for Compounds 2, 3, 6, 8-11.**

	δC^{i} [a]									
i	***Z*-2a** [b]	***E*-2a** [b]	***Z*-2b** [b]	***E*-2b** [b]	**3** [b]	**6** [c]	**8** [b]	**9** [b]	**10** [b]	**11** [c,d,e]
1	69.42	69.53	70.19	70.19	69.22	59.60*	57.03	51.58*	66.49	60.18
2	67.52	67.14	70.46	69.26	160.13	158.43	211.81	162.89	212.11	156.58
3	29.24	29.52	30.70	31.30	26.89	27.72	40.83	28.25	39.88	27.89
4	37.17	37.05	43.29	43.48	44.22	36.18	37.62	35.13	38.29	36.44
5	26.36	26.30	26.35	26.35	25.39	21.53	22.03	22.33	20.83	21.36
6	37.23	37.23	42.02	41.75	42.96	30.61	28.92	31.25	27.64	31.33
7	148.00	148.09	147.33	147.33	147.64	60.04*	51.24	52.33*	60.79	61.72
8	109.54	109.54	109.97	110.14	110.02	24.15	30.93*	31.05*	28.95	23.00
9	20.61	20.54	20.33	20.24	20.44	29.00	28.76*	29.30*	23.57	29.61
10	29.44	28.96	31.38	30.43	28.35	20.40	19.85	22.16	18.30	20.01

[a] chemical shifts are given in ppm; *c* = 5-10%; assignments marked with an asterisk may have to be reversed; [b] in **$CDCl_3$**; [c] in **DMSO-d_6** ; [d] other signals: δ 18.83 ppm (**$\underline{C}H_3CO$-**) and δ 170.30 ppm (**$CH_3\underline{C}O$-**); [e] $J(C^i\text{-}C^j)$ according to INADEQUATE, Hz: 1,2 = 48.1±0.5; 2,3 = 37.1±0.5; 3,4 = 33±1; 4,5 = 32±1; 5,6 = 32±1; 1,6 = 34.7±0.5; 1,10 = 43.7±0.5; 4,7 = 33.2±0.5; 7,8 = 40.8±0.5; 7,9 = 38.6±0.5; **$\underline{C}H_3\text{-}\underline{C}O$-** = 58±1; according to selective INADEQUATE, the carrier frequency was adjusted at the **C^{10}** resonance: 7,10 = 2.1±0.2; 5,10 = 3.5±0.2.

Table 2. **^{1}H NMR Data for Compounds 6, 8-11.** [a]

H'	δH', ppm (*J*, Hz) [b,c]				
	6	**8**	**9**	**10**	**11**
3*exo*	2.62 *ddd* (19.0, 3.0, 3.0)	2.55 *ddd* (19.0, 3.5, 3.5)	2.83 *ddd* (19.5, 3.5, 3.5)	2.70 *dm* (19.5)	2.73 *ddd* (19.0, 3.5, 3.0)
3*endo*	2.08 *dd* (19.0, 3.0)	1.97 *dd* (19.0, 3.0)	2.29 *dd* (19.0, 3.0)	2.10 *dd* (19.5, 3.0)	2.39 *dd* (19.0, 3.0)
4	1.66 *m* $W_{1/2}$ = 9 Hz	≈1.76	1.69 *m* $W_{1/2}$ = 10 Hz	≈1.85-2.05*	1.74 *dddd* (3.5,2.5,2.5,2.5)
5*exo,endo*	≈1.13-1.55*	≈1.40, ≈1.75	≈1.30-1.65*	≈1.30-1.70*	≈1.28, ≈1.88
6*exo*	≈1.67-1.87*	≈1.95	≈2.03		≈2.00
6*endo*	≈1.67-1.87*	≈1.47 *ddd* (12.5,12.5,2.5)	≈1.77*	≈1.85-2.05*	1.60 *ddd* (13.5,11.5,2.5)
8	1.02 *s*	0.99 *s*	1.09 *s*	1.30 *s*	1.03 *s*
9	1.15 *s*	1.11 *s*	1.20 *s*	1.30 *s*	1.32 *s*
10	1.09 *s*	0.83 *s*	1.13 *s*	1.20 *s*	1.12 *s*
other signals	7.4 *br.s* (N-OH)	1.15 *br.s* (NH)		6.4 *br* $W_{1/2}$ = 60 Hz (NOH)	1.95 *s* (CH_3CO)
	10.3 *br.s* (=NOH)				8.9 *br.s* (=NOH)

[a] ^{1}H NMR data for the monocyclic derivatives **2** and **3** are given in the text below; [b] *c* = 5-10% in the same solvents as for the data given in ***Table 1***, [c] assignments marked with an asterisk may have to be reversed.

(*R*)-(+)-Limonene was purchased from Aldrich Chemical Co. (±)-Limonene (95% purity) was purchased from The Central Institute of Forest Chemistry (N.-Novgorod, Russia). Nitrosochlorination of limonene was carried out by standard methods using gaseous **NOCl** and a **CH_2Cl_2** solution of limonene in the preparation of *cis*-isomer (**2b**) and ***i*-AmONO-HCl** in the preparation of *trans*-isomer (**2a**).[22] Purification of the nitrosochlorides was performed by triple precipitation from chloroform solutions by adding of precold methanol.

(-)-Limonene trans-nitrosochloride, (+)-(**2a**): m.p. 100-101°C; *(±)-Limonene trans-nitrosochloride*, (±)-(**2a**): m.p. 96-98°C. IR (0.25% in **CaF_2**): ν = 1643, 1394, 1198, 1188, 1163, 901, 897 cm^{-1}.

^{1}H NMR (in **$CDCl_3$**):

***E*-dimer** – 5.77 *ddd* 1H, *J* = 5.0, 3.0 and 2.0 Hz (**H^2**); 4.71 *br.s* 2H (**H^8**); ≈2.57 1H (**H^4**); 2.49 *ddd* 1H, *J* = 14.5, 10.0 and 7.0 Hz (**H^6**-*ax.*); 2.18 *ddd* 1H, *J* = 15.0, 12.5 and 5.0 Hz (**H^3**-*ax.*); 1.91 *dddd* 1H, *J* = 15.0, 4.0, 4.0 and 2.0 Hz (**H^3**-*eq.*); 1.68 *br.s* 3H (**H^9**); 1.61 *s* 3H (**H^{10}**).

***Z*-dimer** – 5.71 *ddd* 1H, J = 5.0, 3.0 and 2.0 Hz (**H**^{2}); 4.73 *br.s* 2H (**H**^{8}); ≈2.57 1H (**H**^{4}); 2.52 *ddd* 1H, J = 14.5, 10.0 and 7.0 Hz (**H**^{6}-*ax.*); 2.16 *ddd* 1H, J = 15.0, 12.5 and 5.0 Hz (**H**^{3}-*ax.*); 1.92 *dddd* 1H, J = 15.0, 4.0, 4.0 and 2.0 Hz (**H**^{3}-*eq.*); 1.68 *br.s* 3H (**H**^{9}); 1.65 *s* 3H (**H**^{10}).

(−)-Limonene cis-nitrosochloride, (+)-(**2b**): m.p. 100-102°C; *(-)-Limonene cis-nitrosochloride*, (±)-(**2b**): m.p. 91-92.5°C. IR (0.25% in **CaF$_2$**): ν = 1647, 1456, 1445, 1395, 1286, 1252, 1202, 890 cm^{-1}.

^{1}**H** NMR (in **CDCl$_3$**):

***E*-dimer** – 5.68 *dd* 1H, J = 12.0 and 3.5 Hz (**H**^{2}); 4.77 *ddq* 1H, J = 1.0, 1.0 and 1.0 Hz (**H**^{8}*a*); 4.75 *dq* 1H, J = 1.3 and 1.3 Hz (**H**^{8}*b*); 2.39 *ddd* 1H, J = 12.3, 12.3 and 12.3 Hz (**H**^{3}-*ax.*); 1.73 *dd* 3H, J = 1.3 and 1.0 Hz (**H**^{9}); 1.59 *s* 3H (**H**^{10}).

***Z*-dimer** – 5.53 *dd* 1H, J = 12.0 and 3.5 Hz (**H**^{2}); 4.73 *br.s* 2H (**H**^{8}); 2.31 *ddd* 1H, J = 12.3, 12.3 and 12.3 Hz (**H**^{3}-*ax.*); 1.71 *t* 3H, J = 1.0 Hz (**H**^{9}); 1.70 *s* 3H (**H**^{10}).

(1R,4S*)-1-Chloro-p-menth-7-en-2-one oxime* (**3**), ^{1}H NMR (in **CDCl$_3$**): 8.9 *br.s* 1H (=**NOH**), 4.78 *ddq* 2H, J = 1.5, 1.5 and 1.5 Hz (**H**^{8}), 3.34 *dm* 1H, J = 12.0 Hz, $W_{1/2}$ = 5 Hz (**H**^{3}*eq.*); ≈3.1 *m* 1H, 1.76 *br.s* 6H (**H**^{9} and **H**^{10}).

1,3,3-Trimethyl-2-hydroxy-2-azabicyclo[2,2,2]octan-6-one E-oxime (**6**). A solution of **NH$_2$OH** (prepared by neutralization of **NH$_2$OH**×**HCl**, 3.5 g, 50 mmol with **NaOH**, 2.0 g, 50 mmol) in **MeOH** (40 ml) was added to a suspension of dimeric nitrosochloride **2a** or **2b** (2.0 g, 10 mmol) in **Et$_2$O** (10 ml). The reaction mixture was stirred under reflux for 4 h. White precipitate was collected by filtration, washed with **H$_2$O** (2×10 ml), **MeOH** (2×10 ml), **Et$_2$O** (20 ml), and dried to give 1.3 g (63%) of the *title compound*. Sublimation of the crude product in vacuum afforded an analytical sample with m.p. 228-229°C (decomp.) for racemate and 141-143°C for optically active material (lit.[3] m.p. 145°C); found **C** 60.5, **H** 9.4, **N** 14.1; **C$_{10}$H$_{18}$O$_2$N$_2$** requires **C** 60.58, **H** 9.15, **N** 14.13; MS, *m/z* (%): 198.1369 (**M**$^+$, 33%, calc. for **C$_{10}$H$_{18}$O$_2$N$_2$** 198.1368), 183 (**M**$^+$–**CH$_3$** 17), 181 (100), 122 (11), 108 (19), 95 (40), 81 (19), 55 (11), 42 (16), 41 (19). IR (0.25% in **KBr**): ν = 3310 br. (**O-H**), 1650 (**C=N**) cm^{-1}.

(±)-1,3,3-Trimethyl-2-oxyl-2-azabicyclo[2,2,2]octan-6-one oxime (**7**). Reaction of **6** (0.15 g, 0.76 mmol) with **PbO$_2$** (0.15 g,0.63 mmol) in **MeOH** (5 ml) at room temperature for 30 min. resulted in 0.14 g (98%) of the *title compound* as yellow crystals. Column chromatography of the crude product afforded an analytical sample with m.p. 151-153°C (decomp); found **C** 61.1, **H** 8.9, **N** 14.3; **C$_{10}$H$_{17}$N$_2$O$_2$** requires **C** 60.89, **H** 8.69, **N** 14.20; MS, *m/z* (%): 197.1298 (**M**$^+$, 64; calc. for **C$_{10}$H$_{17}$N$_2$O$_2$** 197.1290), 167 (41), 152 (28), 149 (26), 134 (20), 124 (100), 110 (55), 108 (30), 94 (31), 79 (38), 69 (33), 55 (30), 41 (33). IR (0.25% in **CaF$_2$**): ν = 3310, 1466, 1447, 1369, 1227, 1146, 957, 941 cm^{-1}. ESR spectrum (in **CHCl$_3$**): a^{14}**N** = 14.5 G.

(±)-1,3,3-Trimethyl-2-azabicyclo[2,2,2]octan-6-one (**8**). Reduction of **6** (0.99 g, 5 mmol) with **Ti$_2$(SO$_4$)$_3$** (15% aqueous solution, 30 ml, 10 mmol) in a mixture of dioxane (25 ml), **H$_2$O** (10 ml) and **AcOH** (5 ml) in the presence of **NaOAc** (1.64 g, 20 mmol) for 4 h at room temperature gave 0.70 g (84%) of the *title compound* as white crystals. Sublimation of the crude product in vacuum afforded an analytical sample with m.p. 54.5-55.5°C; found **C** 72.0, **H** 10.5, **N** 8.5; **C$_{10}$H$_{17}$NO** requires **C** 71.81, **H** 10.25, **N** 8.37; MS, *m/z* (%): 167 (**M**$^+$, 5), 139 (65), 124 (95), 110 (89), 98 (100), 96 (27), 70 (19), 57 (20), 42 (30). IR (0.25% in **KBr**): ν = 1708, 1460, 1403, 1383, 1088 cm^{-1}; IR (1% in **CHCl$_3$**): ν = 3310 cm^{-1}.

(±)-1,3,3-Trimethyl-2-azabicyclo[2,2,2]octan-6-one E-oxime (**9**). Reduction of **6** (0.40 g, 2.0 mmol) with **Zn**-dust (1.0 g, 15 mmol) in **AcOH** (6 ml) for 2 h at room temperature resulted in 0.30 g (82%) of the *title compound* as colorless crystals. Sublimation of the crude product in vacuum afforded an analytical sample with m.p. 144.5-145°C; found **C** 66.1, **H** 10.2, **N** 15.4; $C_{10}H_{18}N_2O$ requires **C** 65.90, **H** 9.95, **N** 15.37; MS, *m/z* (%): 182 (M^+, 6), 165.1393 (M^+–**OH**, 100, calc. for $C_{10}H_{17}N_2$ 165.1392), 153 (6), 139 (4), 126 (5), 108 (14), 97 (11), 70 (8), 58 (7), 42 (13). IR (0.25% in **KBr**): ν = 3280, 1650, 1450, 1420, 1375, 1200, 1090, 925 cm^{-1}; IR (1% in $CHCl_3$): ν = 3580 cm^{-1}.

(±)-1,3,3-Trimethyl-2-hydroxy-2-azabicyclo[2,2,2]octan-6-one (**10**). Hydrolysis of **6** (0.99 g, 5 mmol) with aq. CH_2O (40%, 5 ml) and conc. **HCl** (15 ml) for 10 h at reflux resulted in 0.80 g (88%) of the *title compound* which was then sublimated in vacuum to give an analytical sample with m.p. 130-132°C; found **C** 65.8, **H** 9.6, **N** 7.7; $C_{10}H_{17}NO_2$ requires **C** 65.54, **H** 9.35, **N** 7.64; MS, *m/z* (%): 183.1261 (M^+, 6, calc. for $C_{10}H_{17}NO_2$ 183.1259), 155 (57), 140 (30), 138 (100), 126 (68), 86 (19), 82 (32), 73 (17), 55 (28), 42 (62), 41 (58); IR (0.25% in **KBr**): ν = 1725, 1460, 1410, 1180, 1060 cm^{-1}; IR (1% in $CHCl_3$): ν = 3580 cm^{-1}.

(±)-1,3,3-Trimethyl-2-acetoxy-2-azabicyclo[2,2,2]octane-6-one oxime (**11**). A solution of Ac_2O (0.24 ml, 2.5 mmol) in Et_2O (5 ml) was added dropwise at 10°C to a stirred suspension of **6** and Na_2CO_3 (0.13 g, 1.25 mmol) in Et_2O. The reaction mixture was stirred for 2 h at room temperature to give 0.50 g (95%) of the *title compound* with m.p. 167-168°C (CH_2Cl_2); found **C** 59.9, **H** 8.7, **N** 11.6; $C_{12}H_{20}N_2O_3$ requires **C** 59.98, **H** 8.39, **N** 11.66; MS, *m/z* (%): 240.1472 (M^+, 15, calc. for $C_{12}H_{20}N_2O_3$ 240.1474), 223 (10), 198 (61), 183 (17), 182 (13), 181 (100), 124 (8), 108 (9), 95 (21), 81 (13), 79 (9), 67 (8), 55 (8). IR (0.25% in **KBr**): ν = 1745, 1420, 1380, 1230, 1200 cm^{-1}; IR (1% in $CHCl_3$): ν = 3580, 1185, 1005, 945 cm^{-1}.

Acknowledgments: The research described in this publication was made possible in part by Grant No RCS000 from the International Science Foundation and Grant No INTAS-93-1588 from the INTAS Program. The authors thank the Novosibirsk Office of the Soros Foundation for computational support and the Russian Fundamental Science Foundation (grant 94-03-08063) for the financial support of this work.

REFERENCES AND NOTES

1. Volodarsky, L.B.; Tikhonov, A.Ya. *Synthesis* **1986**, 704-715.
2. Francesconi, L.; Cusmano, G. *Gazz. Chim. Ital.* **1909**, 39, II, 105-115 (*Chem. Abstr.* **1911**, *5*, 687).
3. Cusmano, G. *Gazz. Chim. Ital.* **1910**, *40*, I, 602-613 (*Chem. Abstr.* **1911**, *5*, 1406).
4. Cusmano, G. *Gazz. Chim. Ital.* **1910**, *40*, II, 122-131(*Chem. Abstr* **1911**, *5*, 1743). (*b*) Volodarsky, L.B.; Putsykin, Yu.G. *Zh. Org. Khim.* **1967**, *3*, 1686-1694. (*c*) Cusmano, G. *Gazz. Chim. Ital.* **1910**, *40*, II, 525-536 (*Chem. Abstr* **1911**, *5*, 2634).
5. Rukavishnikov, A.V.; Tkachev, A.V.; Volodarsky, L.B.; Pentegova, V.A. *Zh. Org. Khim.* **1989**, *25*, 1665-1671. (*b*) Volodarsky, L.B.; Belova, N.V.; Tikhonov, A.Ya. *SU Pat.* 1.137.716 (23.03.1986), (*Chem. Abstr.* **1986**, *105*, 225812).
6. D'Ambrosio, A. *Gazz. Chim. Ital.* **1932**, *62*, 271-278.

7. Rassat, A.; Rey, P. *Brit.Pat.* 1231380 (12.5.71), (*Chem. Abstr.* **1971**, *75*, 63640). (*b*) Rassat, A.; Rey, P. *Tetrahedron* **1972**, *28*, 741-750. (*c*) Ramey, Ch.E.; Luzzi, J.J. *US Pat.* 3875169 (01.04.1975), (*Chem. Abstr* **1975**, *83*, 10514). (*d*) Ramey, Ch.E.; Luzzi, J.J. *US Pat.* 3879396 (22.04.1975), (*Chem. Abstr* **1975**, *83*, 80429). (*e*) Ramey, Ch.E.; Luzzi, J.J. *US Pat.* 3991012 (06.11.1976), (*Chem. Abstr* **1977**, *86*, 91616). (*f*) Longobardi, M.; Schenone, P.; Bondavalli, F. *US Pat.* 4120857 (17.10. 1978), (*Chem. Abstr* **1979**, *90*, 72079). (*g*) Longobardi, M.; Schenone, P.; Bondavalli, F. Farmaco, Ed. Sci. 1979, 34, 4, 331-337, (*Chem. Abstr* **1979**, *91*, 20282). (*h*) Longobardi, M.; Schenone, P.; Bondavalli, F. Farmaco, Ed. Sci. 1979, 34, 5, 383-389, (*Chem. Abstr* **1979**, *91*, 39284). (*i*) Longobardi, M.; Barganda, A.; Schenone, P.; Filippelli, A.; Tortora, G.; Marrazzo, R.; Marto, E. Farmaco, Ed. Sci. 1986, 46, 2, 151-155.

8. Thomas, A.F.; Bessiere, Y. *Nat. Prod. Rep.* **1989**, *6*, 291-309 and references therein.

9. Carman, R.M; Mathew, P.C.; Saraswathi, G.N.; Singaram B.; Verghese, J. *Aust. J.Chem.* **1977**, *30*, 1323-1335.

10. The *cis*-isomer have not been described earlier, and sometimes limonen-nitrosochloride is drawn as if only one isomer of this compound exists (W.F. Erman, Chemistry of the Monoterpenes, Marcel Dekker Inc., New York, 1985, part A, p. 619). The *cis*- and *trans*-isomers have the same **C**-1 configuration as they are transformed to one and the same α-chloro oxime **3**. Equatorial character of the nitroso group in the *cis*-isomer **2b** is confirmed by the splitting character of the **H**-2 signal in NMR ^{1}**H** spectrum.

11. Boyer, J.H. In *The Chemistry on the Nitro and Nitroso Groups;* Feuer, H. Ed.; Interscience: New York, 1969, part 1, p.215.

12. Wajer, Th.A.J.W.; de Boer, Th.J. *Rec. Trav. Chim. Pays-Bas.* **1972**, *91*, 565-577

13. Tkachev, A.V.; Rukavishnikov, A.V.; Korobejnicheva, T.O.; Gatilov, Yu.V.; Bagrjanskaja, I.Yu. *Zh. Org. Khim.* **1990**, *26*, 1939-1947.

14. Dornow, A.; Jordan, H.D. *Ber.* **1961**, *94*, 76-83.

15. Krivdin, L.B.; Kalabin, G.A. *Prog. Nucl. Magn. Reson. Spectrosc.* **1989**, *21*, 293-448.

16. Rogers, D.W. *Computational Chemistry using the P.C.*; VCH Publishers, Inc.: New York. 1990.

17. Rassat, A; Rey, P. *Tetrahedron* **1972**, *28*, 741-750. (*b*) Battiste, D.R.; Traynham, J.G. *J. Org. Chem.* **1975**, *40*, 1239-1243. (*c*) Rassat, A; Rey, P. *Tetrahedron* **1975**, *31*, 2673-2677. (*c*) Belkacemi, D.; Malpass, J.R. *Tetrahedron* **1993**, *49*, 9105-9116 (and references therein).

18. Volodarsky, L.B., Grigor'ev, I.A. Synthesis of Heterocyclic Nitroxides. In *Imidazoline Nitroxides*; Volodarsky, L.B. Ed.; CRC Press, Inc.: Boca Raton, Florida, 1988, vol. 1, pp. 5-28.

19. Tkachev, A.V.; Rukavishnikov, A.V.; Chibiryaev, A.M.; Denisov, A.Yu.; Gatilov, Yu.V., Bagryanskaya, I.Yu. *Austr. J. Chem.* **1992**, *45*, 1077-1086.

20. Salnikov, G.E. *ABACUS Program Library Catalog.* Spectrospin, Fällanden, 1989.

21. Denisov, A.Yu.; Tkachev, A.V.; Mamatyuk, V.I. *Magn. Reson. Chem.* **1992**, *30*, 95-100.

22. Meinwald, J.; Meinwald, Y.C.; Baker, T.N. *J. Amer. Chem. Soc.* **1964**, *86*, 4074-4080.

(*Received in UK* 6 *February* 1995; *revised* 12 *June* 1995; *accepted* 16 *June* 1995)