Mendeleev Commun., 2002, 12(5), 189–192

Sterically hindered nitrogen inversion in five-membered cyclic hydrazines†

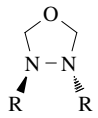
Sergey V. Usachev,[a] Grygorii A. Nikiforov,[b] Yurii A. Strelenko,[c] Pavel A. Belyakov,[c] Ivan I. Chervin[a] and Remir G. Kostyanovsky*[a]

[a] *N. N. Semenov Institute of Chemical Physics, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 095 938 2156; e-mail: kost@.chph.ras.ru*
[b] *N. M. Emanuel Institute of Biochemical Physics, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 095 137 4101; e-mail: komissarova@polymer.chph.ras.ru*
[c] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 095 135 5328; e-mail: strel@ioc.ac.ru*

10.1070/MC2002v012n05ABEH001626

We found that $(Pr^iNH)_2$ with MeCHO form only pyrazoline 1 because of the competitive crotonization of the latter followed by reaction with hydrazine; pyrazoline 2, pyrazolidinones 6 and 9, pyrazolidinol 8 and pyrazolidine 7, in which the inversion of nitrogen atoms is hindered by bulky Pr^iN substituents, were prepared for the first time, and the inversion barriers were determined.

An idea of the sterically hindered inversion of nitrogen[2] was successfully implemented[3] using 1,3,4-oxadiazolidines as an example. Enantiomers **A** and **B** were chromatographically separated on chiral and achiral phases, respectively, followed by studying the kinetics of racemization and epimerization, respectively. Table 1 summarises the inversion barrier of nitrogen atoms in these compounds (*cf.* previously estimated lower limits of the barriers[2–5]).

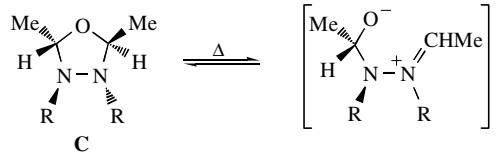


A, **B**

Table 1 Activation parameters of the nitrogen inversion barriers in 1,3,4-oxadiazolidines.[3]

Compound	R	$\Delta G^{\#}_{inv}$ /kJ mol^{-1} at 56 °C	$\Delta S^{\#}$/J K^{-1} mol^{-1}
A	*tert*-Butyl	131.8	–93
B	$MeO_2C(Et)(Me)C$	112 and 107.2	–

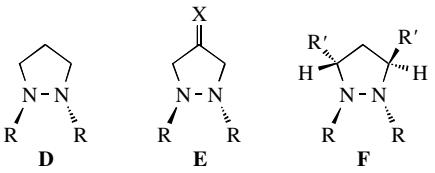
Compound **A** exhibited a high negative value of the entropy of activation[3] (Table 1), which is not typical of the pyramidal inversion of nitrogen.[6] Thus, a dissociative mechanism of inversion with CH_2–O bond cleavage and the formation of an intermediate methyleneiminium ion was assumed [as in the case of the thermal enantiomerization of Tröger bases ($\Delta S^{\#}$ = = –168 J K^{-1} mol^{-1})[7]]. This inversion mechanism was supported by structural data,[5] which are indicative of the possibility of the anomeric effect $n(N) \rightarrow \sigma^*(CO)$ in **A** and its hydrazine-methylating effect on amines with CH_2–O bond cleavage.[8] The dissociative inversion in **A** can be unambiguously supported by the absence of enantiomerization of 2,5-dimethyl-1,3,4-oxadiazolidine **C** with bulky N-substituents R, which prevent the formation of the meso form‡ (Scheme 1).



C

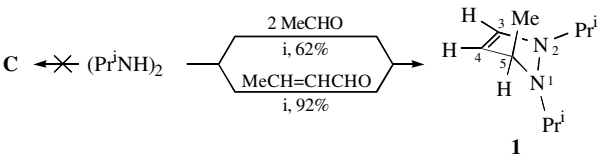
Scheme 1

As compared with compounds **A** and **B**, it is expected that the configurational stability of nitrogen atoms can be increased on the removal of the possibility of dissociative inversion in pyrazolidines with bulky N-substituents **D** or **E** (R = Pr^i, Bu^t). The inversion of nitrogen atoms in 1,3,4,5-tetraalkylpyrazolidines **F** can be completely sterically hindered.§



D **E** **F**

In this work, we attempted to synthesise some compounds of the above types. The syntheses of 2,3,4,5-tetraalkyl-1,3,4-oxadiazolidines **C** in 60–70% yields by the reactions of *N*,*N*′-dimethylhydrazine with aldehydes RCHO (R = H, Me, Pr or Bu)[9] and *N*,*N*′-diethylhydrazine with acetaldehyde[10] were described previously. However, we found that pyrazoline **1** was formed in the reaction of *N*,*N*′-diisopropylhydrazine with acetaldehyde under the same conditions[10] instead of expected product **C** (R = Pr^i) (Scheme 2).



1

Scheme 2 *Reagents and conditions:* i, in *n*-pentane, 1 h at 7–8 °C.

This is evidently due to steric hindrances in the reaction of a substituted hydrazine with acetaldehyde, which gives crotonaldehyde by a more rapid competitive condensation reaction. Crotonaldehyde with hydrazine forms product **1**. Indeed, pyrazoline **1** can be directly prepared by the reaction with crotonaldehyde (Scheme 2). It is interesting that a pyrazoline by-product (in up to 5% yield) was detected in the reaction of less sterically hindered *sym*-diethylhydrazine, whereas the corresponding oxadiazolidine[9] is the main product (Scheme 3). This is a general reaction.

The hydrogenation of pyrazolines **1** and **2** with $NaBH_4$ and $LiAlH_4$ was studied; however, we failed to prepare desired pyrazolidines. Therefore, we tested other reactions for the synthesis of them. Pyrazolidine **7** was obtained in accordance with Scheme 4.

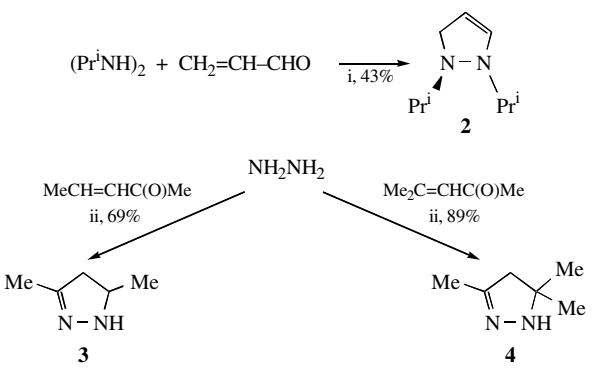
Pyrazolidin-4-ol **8** and pyrazolidin-4-one **9** were prepared in accordance with Scheme 5.

The NMR spectra of pyrazoline **1** suggest that the protons of diastereotopic Me groups in both of the Pr^i substituents are non-equivalent.¶ This can be explained by the fact that the ring conformation is fixed by the methyl substituent at the asymmetric C-5 atom. The arrangement of protons at C-3 and C-5 close to a planar W-zigzag is possible only at an unusual a-orientation (as evidenced by the spin–spin coupling constant

† Asymmetric nitrogen. Part 86, previous communication see ref. 1.

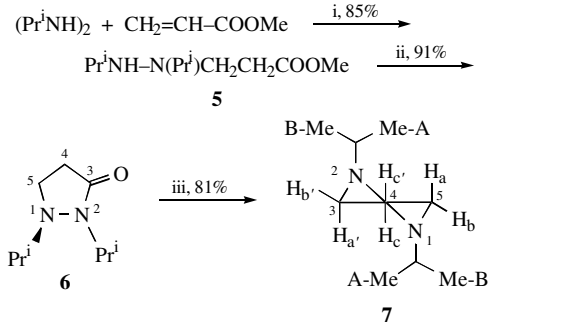
‡ Compounds of the type **C** (R = Me, Et) were described.[9]

§ Pyrazolidines **D** (R = H, PhCO),[11] **E** (X = CH_2, R = CO_2Et),[12] (X = = Me_2C, R = CO_2Et)[13,14] and **F** (R = H, R′ = Me)[15] were described.



Scheme 3 *Reagents and conditions*: i, in *n*-pentane, 45 min at 15–20 °C; ii, in MeOH, 45 min at 10–20 °C.

$^4J_{(H3)(H5)} = -1.5$ Hz).¶ Then, at the a-orientation of an isopropyl substituent at N-1 and the planarization of the enamine atom N-2, substituents at N-1, N-2 and C-5 are most mutually distant. Indeed, the MM2 calculation supported the above molecular conformation with the dihedral angle $\varphi_{H(4),C(4),C(5),H(5)} = 38°$. The value of $^4J_{(H3)(H5)} = -1.5$ Hz, which was found from the angle dependence of the spin–spin coupling constant,[16] is consistent with the experimental value.¶



Scheme 4 *Reagents and conditions*: i, 3 h at 100–105 °C; ii, 3 h at 75–80 °C in MeOH/Cat MeONa; iii, $LiAlH_4$ in THF, 2 h at 65 °C.

In the case of pyrazoline **2**, a flat screen for N-1 inversion is produced because of the flattening of the enamine N-2 atom. Thus, according to NMR spectra, its inversion is hindered in the NMR time scale at 20 °C (^{1}H NMR: 5-CH$_2$ $\Delta\nu_{HH} = 160$ Hz; ^{13}C {^{1}H} NMR: 1-Pr^i, $\Delta\nu_{Me_2C} = 160$ Hz, 2-Pr^i broadened signal of Me$_2$C at 19.47 ppm). Pyrazolidinone **6** exhibits such a steric inversion hindrance (Figures 1 and 2).¶ The inversion barrier of the 1-N atom was found at the signals coalescence temperature

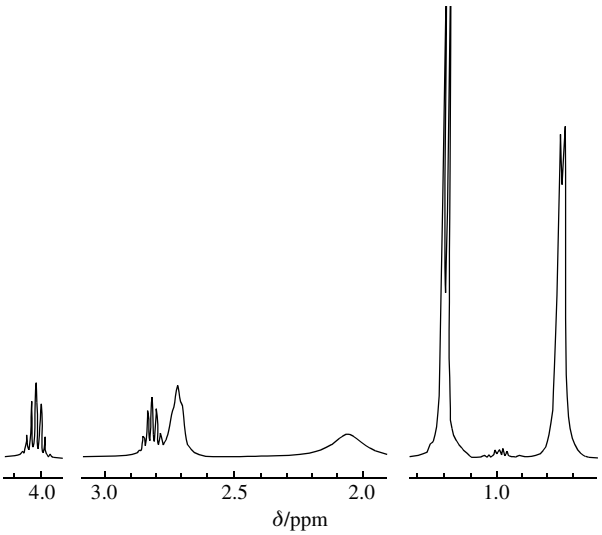
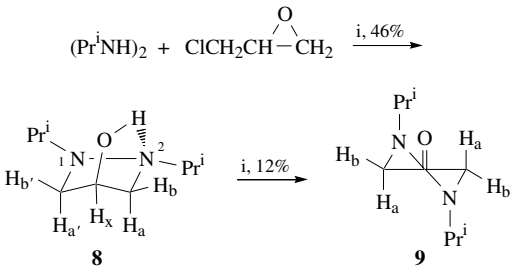


Figure 1 ^{1}H NMR spectrum of compound **6** (400.13 MHz) in [$^2H_6$]benzene at 20 °C.



Scheme 5 *Reagents and conditions*: i, MeCN, K_2CO_3, 20 h at 90 °C; ii, DCC in DMSO, 10 h at 20 °C.

for the protons at C-4 ($\Delta\nu = 204$ Hz in [$^2H_6$]benzene) to be $\Delta G^{\#} = 60.8$ kJ mol^{-1} at 30 °C, which is higher by 12.2 kJ mol^{-1} than that of 1,2-dibenzylpyrazolidin-3-one at –32 °C.[17] Previously,[18] the inversion of nitrogen in substituted diazetidin-3-ones was studied. For example, $\Delta G^{\#} = = 79.7$ kJ mol^{-1} for

¶ ^{1}H and ^{13}C NMR spectra were measured on Bruker WM-400 (400.13 and 100.61 MHz, respectively) and Bruker AM-300 spectrometers (300.13 and 75.43 MHz respectively).

1 prepared in accordance with Scheme 2, 62% yield, bp 38–40 °C (5 Torr). ^{1}H NMR ($CDCl_3$) δ: 0.96 (d, 3H, 1-NCH*Me*$_A$, ^3J 6.4 Hz), 1.03 (d, 3H, 1-NCH*Me*$_B$, ^3J 6.4 Hz), 1.02 (d, 3H, 2-NCH*Me*$_A$, ^3J 6.6 Hz), 1.05 (d, 3H, 5-CH–*Me*, ^3J 6.4 Hz), 1.09 (d, 3H, 2-NCH*Me*$_B$, ^3J 6.6 Hz), 2.82 (hept, 1H, 1-NC*H*, ^3J 6.4 Hz), 2.94 (hept., 1H, 2-NC*H*, ^3J 6.6 Hz), 3.72 (ddq, 1H, 5-CH, ^3J 6.4 Hz, ^3J 2.6 Hz, ^4J –1.5 Hz), 4.74 (dd, 1H, 4-CH, ^3J 3.8 Hz, ^3J 2.6 Hz), 5.87 (dd, 1H, 3-CH, ^3J 3.8 Hz, ^4J –1.5 Hz). ^{13}C NMR ($CDCl_3$) δ: 16.35 and 19.03 (2q, 1-NCH*Me*$_A$*Me*$_B$, ^1J 125.0 Hz), 18.63 and 19.74 (2q, 2-NCH*Me*$_A$*Me*$_B$, ^1J 125.0 Hz), 25.01 (q, 5-C–*Me*, ^1J 125.0 Hz), 54.42 (d, 1-NCH, ^1J 137.3 Hz), 56.30 (d, 2-NCH , ^1J 137.3 Hz), 59.76 (d, 5-CH, ^1J 135.4 Hz), 106.71 (d, 4-CH, ^1J 170.7 Hz), 132.36 (d, 3-CH, ^1J 175.5 Hz, ^3J 7.6 Hz, $^3J = {}^2J = 3.8$ Hz). Found (%): C, 70.85; H, 12.49; N, 16.20. Calc. for $C_{10}H_{20}N_2$ (%): C, 71.38; H, 11.96; N, 16.65.

2 prepared in accordance with Scheme 3, 43% yield, bp 56–58 °C (20 Torr). ^{1}H NMR ($CDCl_3$, at 20 °C) δ: 0.98 (d, 6H, 1-NCH*Me*$_2$, ^3J 6.7 Hz), 1.05 (d, 6H, 1-NCH*Me*$_2$, ^3J 6.7 Hz), 2.77 (hept, 1H, 1-NCH, ^3J 6.7 Hz), 3.02 (hept, 1H, 2-NCH, ^3J 6.7 Hz), 3.69 (br. s, 2H, 3-CH$_2$), 4.89 (m, 1H, 4-CH), 5.90 (m, 1H, 5-CH). ^{13}C NMR ([$^2H_6$]benzene at 20 °C) δ: 17.73 (q, 1-NCH*Me*$_A$, ^1J 125.7 Hz), 19.34 (q, 1-NCH*Me*$_B$, ^1J 125.7 Hz), 19.60 (q, 2-NCH*Me*$_A$, ^1J 125.7 Hz), 19.77 (q, 2-NCH*Me*$_B$, ^1J 125.7 Hz), 55.37 (tq, 5-CH$_2$, ^1J 139.3 Hz, $^2J = {}^3J = 4.2$ Hz), 56.40 (d, 1-NCH, ^1J 139.1 Hz), 57.83 (d, 2-NCH, ^1J 139.6 Hz), 104.40 (ddt, 4-CH, ^1J 170.8 Hz, ^2J 8.9 Hz, ^3J 4.4 Hz), 134.84 (ddq, 3-CH, ^1J 174.3 Hz, ^2J 8.9 Hz, ^3J 4.5 Hz). Found (%): C, 70.30; H, 12.01; N, 17.90. Calc. for $C_9H_{18}N_2$ (%): C, 70.08; H, 11.76; N, 18.16.

3 prepared in accordance with Scheme 3, 69% yield, bp 70–73 °C (30 Torr). ^{1}H NMR ([$^2H_6$]benzene at 20 °C) δ: 0.85 (d, 3H, 3-Me, ^3J 6.7 Hz), 0.97 (s, 3H), 1.75 (dd, 1H, CH$_2$, ^2J 15.8 Hz, ^3J 9.8 Hz), 2.18 (dd, 1H, ^2J 15.8 Hz, ^3J 9.1 Hz), 3.67 (m, 1H, CH, ^3J 6.7 Hz), 7.50 (s, 1H, NH). Found (%): C, 61.39; H, 10.38; N, 28.23. Calc. for $C_5H_{10}N_2$ (%): C, 61.19; H, 10.26; N, 28.58.

4 prepared in accordance with Scheme 3, 89% yield, bp 67–70 °C (31 Torr). ^{1}H NMR ([$^2H_6$]benzene at 20 °C) δ: 0.97 (s, 6H, 5-Me), 1.02 (s, 3H, 3-Me), 1.71 (s, 2H, 4-CH$_2$), 7.85 (s, 1H, NH). Found (%): C, 64.85; H, 10.50; N, 24.65. Calc. for $C_6H_{12}N_2$ (%): C, 64.24; H, 10.78; N, 24.98.

5 prepared in accordance with Scheme 4 and separated by chromatography (SiO_2 40/60 μ. Eluent: $CHCl_3$–acetone, 9:1 by volume), 85% yield, $n_{20}^D = 1.5689$. ^{1}H NMR ($CHCl_3$ at 20 °C) δ: 0.90 (d, 6H, CH*Me*), 0.96 (d, 6H, CH*Me*), 2.47 (t, 2H, CH$_2$COO), 2.68 (t, 2H, CH$_2$N), 2.84 (q, 1H, C*H*Me), 2.94 (q, 1H, C*H*Me), 3.63 (s, 3H, OMe). Found (%): C, 59.72; H, 10.89; N, 13.87. Calc. for $C_{10}H_{22}N_2O_2$ (%): C, 59.37; H, 10.96; N, 13.85.

6 prepared in accordance with Scheme 4 and separated by chromatography (SiO_2 40/60 μ. Eluent: ethyl acetate), 91% yield. ^{1}H NMR ([$^2H_6$]benzene at 70 °C) δ: 0.75 (br. d, 6H, 1-NCH*Me*$_2$, ^3J 6.1 Hz), 1.20 (d, 6H, 2-NCH*Me*$_2$, ^3J 6.9 Hz), 2.07 (br. m, 2H, 4-CH$_2$), 2.71 (br. m, 2H, 5-CH$_2$), 2.81 (hept, 1H, 1-NCH, ^3J 6.7 Hz), 4.02 (hept, 1H, 2-NCH, ^3J 6.8 Hz). ^{13}C NMR {1H} ([$^2H_8$]toluene, 20 °C) δ: 15.0 (br. s, 1-CH*Me*-A), 20.0 (br. s, 3H, 1-NCH*Me*-B), 20.0 (br. s, 6H, 2-NCH*Me*$_2$), 32.2 (s, 4-C), 43.62 (s, 2-NCH), 172.84 (s, 3-C); at 80 °C: 17.6 (br. s, 1-NCH*Me*$_2$) and 19.97 (s, 2-NCH*Me*$_2$). Found (%): C, 63.68; H, 10.46; N, 16.78. Calc. for $C_9H_{18}N_2O$ (%): C, 63.49; H, 10.66; N, 16.45.

1,2-dibenzyl-1,2-diazetidin-3-one.[18(c)] The inversion in picrate **6** and iodomethylates **6** and **7** is blocked because of the protonation and quaternization of the N-1 atom.¶

The NMR spectra of pyrazolidine **7** (Figure 3)¶ are indicative of the C_2 molecular symmetry (six groups of signals in the ^{1}H NMR spectrum and five signals in the ^{13}C {1H} NMR spectrum) and the hindered inversion of nitrogen atoms (the non-equivalence of geminal H_a and H_b protons and protons and carbons in A-Me and B-Me groups of isopropyl substituents, as well as in the case of 1,3,4-oxadiazolidines with bulky N-substituents[2–4]). The activation parameters of nitrogen inversion were found from a full line shape analysis:†† $\Delta G^{\#}_{inv}$ = = 67.7±1.1 kJ mol^{-1} at 25 °C, $\Delta H^{\#}$ = 61.1 kJ mol^{-1} and $\Delta S^{\#}$ = = –22.2±3.3 J K^{-1} mol^{-1}. The inversion barrier is higher than that of 1,2,4,4-tetramethylpyrazolidine[6] by 21.2 kJ mol^{-1}.

The NMR spectra of pyrazolidin-4-ol **8** exhibited the non-equivalence of all ring protons and carbons, as well as of the Pr^i substituents.¶ An analysis of the ring protons five-spin system (Figure 4)¶ demonstrated that it consists of two sub-spectra of the ABX type associated with the long-range spin–spin coupling constant ^4J. The latter and the ratio between the values of ^3J¶ suggest that the most stable molecular conformation of compound **8** corresponds to that shown in Scheme 5. Similarly to compound **7**, the activation parameters of nitrogen inversion in compound **8** were found: $\Delta G^{\#}$ = 69.2±0.3 kJ mol^{-1} at 25 °C, $\Delta H^{\#}$ =63.8±0.5 kJ mol^{-1} and $\Delta S^{\#}$ = –18.0±1.0 J K^{-1} mol^{-1}.

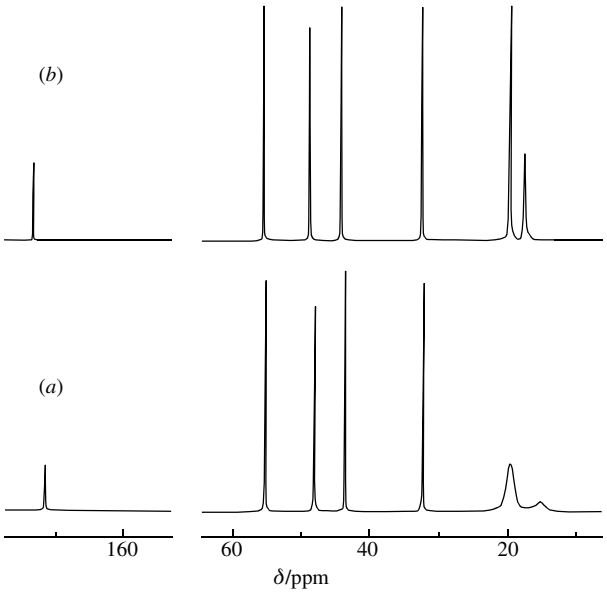


Figure 2 ^{13}C NMR spectra of compound **6** (100.61 MHz) in [$^2H_8$]toluene at 20 °C.

As judged from NMR spectra,¶ the nitrogen inversion in compound **9** is hindered at 20 °C, and the molecule exhibits the C_2 symmetry, as is the case in compound **7** and 1,3,4-oxadiazolidines.[2–4]

Thus, we synthesised pyrazolidines with bulky N-substituents. We found that compound **6** forms a stable picrate, and compounds **6** and **7** form iodomethylates.¶ As expected, the enantiomerization of **7** and **8** occurs at low entropies of activation, *i.e.*, by normal pyramidal inversion rather than a dissociative mechanism, as in the case of **A** (Table 1). It is well known[2–4] that the nitrogen inversion barrier in **A** is higher than that in 3,4-diisopropyl-1,3,4-oxadiazolidine by 50.5 kJ mol^{-1}. Consequently, an increase in inversion barriers up to 120 kJ mol^{-1} or higher may be expected in 1,2-di-*tert*-butyl analogues of **7**–**9**. Thus, they are promising for separation into enantiomers under normal conditions.

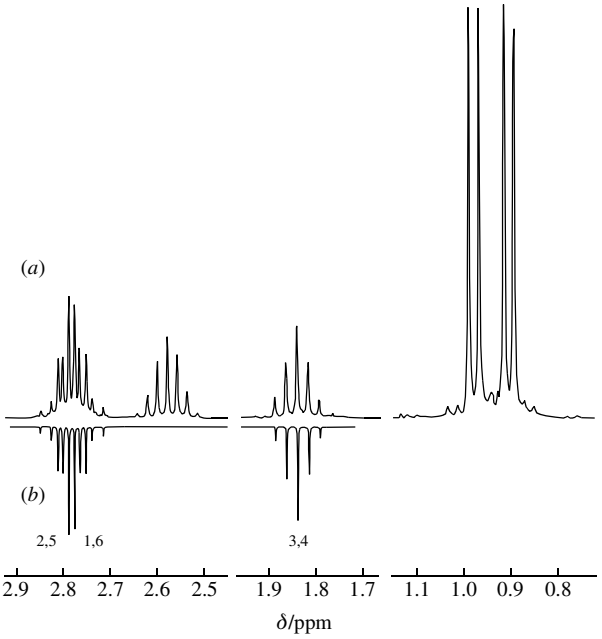


Figure 3 ^{1}H NMR spectra of compound **7**: (*a*) experimental (300.13 MHz, in [$^2H_6$]acetone at –20 °C) and (*b*) calculated by CALM.

Iodomethylate **6**: mp 190–191 °C (acetone), 77.5% yield. ^{1}H NMR (CD_3CN at 20 °C) δ: 1.33 (d, 3H, 1-NCH*Me*-A, ^3J 6.6 Hz), 1.45 (d, 3H, 1-NCH*Me*-B, ^3J 6.6 Hz), 1.46 (d, 6H, 2-NCH*Me*, ^3J 6.3 Hz), 2.76 and 2.86 (m, 2H, 4-CH_2), 3.61 (s, 3H, 1-N–Me), 3.93 and 4.31 (m, 2H, 5-CH_2), 4.22 (hept, 1H, 1-NCH, ^3J 6.6 Hz), 4.30 (hept, 1H, 2-NCH, ^3J 6.3 Hz). Found (%): C, 38.09; H, 6.48; N, 8.61. Calc. for $C_{10}H_{21}IN_2O$ (%): C, 38.47; H, 6.78; N, 8.97.

Picrate **6**: mp 146–147 °C (acetone), 97% yield. ^{1}H NMR ([$^2H_6$]acetone at 20 °C) δ: 1.33 (d, 3H, 1-NCH*Me*-A, ^3J 6.5 Hz), 1.45 (d, 3H, 1-NCH*Me*-B, ^3J 6.5 Hz), 1.46 (d, 6H, 2-NCH*Me*$_2$, ^3J 6.2 Hz), 2.79 and 2.86 (m, 2H, 4-CH_2), 4.05 and 4.15 (m, 2H, 5-CH_2), 4.14 (hept, 1H, 1-NCH, ^3J 6.5 Hz), 4.17 (hept, 1H, 2-NCH, ^3J 6.2 Hz), 8.85 (s, 2H, C_6H_2). Found (%): C, 44.94; H, 5.81; N, 18.06. Calc. for $C_{15}H_{21}N_5O_8$ (%): C, 45.11; H, 5.29; N, 17.54.

7 prepared in accordance with Scheme 4 and separated by chromatography (SiO_2 40/60 μ. Eluent: ethyl acetate), 81% yield. ^{1}H NMR ([$^2H_6$]acetone at –20 °C) δ: 0.91 (d, 6H, 2Me-A, ^3J 6.3 Hz), 0.98 (d, 6H, 2Me-B, ^3J 6.3 Hz), 1.84 (quint, 2H, $H_cH_{c'}$, $^2J_{cc'}$ = –14.5 Hz, $^3J_{ca'}$ = $^3J_{c'a}$ = = 8.35 Hz, $^3J_{ca}$ = $^3J_{c'a'}$ = 7.44 Hz, $^3J_{cb'}$ = $^3J_{c'b}$ = 6.59 Hz, $^3J_{cb}$ = $^3J_{c'b'}$ = = 6.18 Hz), 2.58 (hept, 2H, 2HC), 2.77 (m, 2H, $H_bH_{b'}$, ^2J –11.23 Hz), 2.80 (m, 2H, $H_aH_{a'}$, ^2J –11.23 Hz). ^{13}C NMR ([$^2H_6$]acetone at 20 °C) δ: 20.56 (qqd, Me-A, ^1J 124.0 Hz, ^3J 4.9 Hz, ^2J 1.4 Hz), 22.07 (qqd, Me-B, ^1J 125.0 Hz, ^3J 5.0 Hz, ^2J 2.1 Hz), 26.84 (t quint, 4-CH_2, ^1J 130.0 Hz, ^2J 2.3 Hz), 48.25 (tdt, 3-CH_2, 5-CH_2, ^1J 137.0 Hz, ^3J = ^2J = 3.3 Hz), 55.36 (dm, 2CHN, ^1J 132.0 Hz, ^3J 4.2 Hz). Found (%): C, 69.40; H, 13.10; N, 17.67. Calc. for $C_9H_{20}N_2$ (%): C, 69.17; H, 12.90; N, 17.93.

Iodomethylate **7**: mp 159–160 °C (acetone), 45% yield. ^{1}H NMR ([$^2H_6$]acetone at 20 °C) δ: 1.22 (d, 3H, 1-NCH*Me*, ^3J 6.7 Hz), 1.28 (d, 3H, 1-NCH*Me*, ^3J 6.4 Hz), 1.45 (d, 3H, 2-NCH*Me*, ^3J 6.5 Hz), 1.55 (d, 3H, 2-NCH*Me*, ^3J 6.4 Hz), 2.24 and 2.36 (m, 2H, 4-CH_2), 3.41 (m, 1H, 3-CH_2), 3.47 (m, 1H, 3-CH_2), 3.46 (s, 3H, 2-NMe), 3.73 (m, 1H, 5-CH_2), 4.04 (m, 1H, 5-CH_2), 3.98 (hept, 1H, 2-NCH, ^3J 6.6 Hz), 4.34 (hept, 1H, 1-NCH, ^3J 6.6 Hz). Found (%): C, 39.97; H, 8.01; N, 9.71. Calc. for $C_{10}H_{23}IN_2$ (%): C, 40.27; H, 7.77; N, 9.39.

8 prepared in accordance with Scheme 5, 63% yield, bp 103–105 °C (10 Torr). ^{1}H NMR ([$^2H_6$]acetone at –20 °C) δ: 0.89 (d, 3H, 1-NCH*Me*-A, ^3J 6.5 Hz), 0.95 (d, 3H, 1-NCH*Me*-B, ^3J 6.5 Hz), 0.94 (d, 3H, 2-NCH*Me*-A, ^3J 6.5 Hz), 1.03 (d, 3H, 2-NCH*Me*-B, ^3J 6.5 Hz), 2.61 (hept, 1H, 1-NCH, ^3J 6.5 Hz), 2.94 (hept, 1H, 2-NCH, ^3J 6.5 Hz), 2.72 (dd, 1H, H_a, $^2J_{ab}$ –12.23 Hz, $^3J_{ax}$ 5.40 Hz), 2.79 (ddd, 1H, H_c, $^2J_{cd}$ –11.96 Hz, $^3J_{cx}$ 3.33 Hz, ^4J 0.52 Hz), 2.94 (hept, 1H, 2-NCH, ^3J 6.5 Hz), 2.97 (dd, 1H, H_d, $^2J_{dc}$ –11.96 Hz, $^3J_{dx}$ 6.22 Hz), 3.09 (ddd, 1H, H_b, dddd, 1H, H_x, $^3J_{xb}$ 6.89 Hz, $^3J_{xd}$ 6.22 Hz, $^3J_{xa}$ 5.40 Hz, $^3J_{xc}$ 3.33 Hz). ^{13}C {^{1}H} NMR ([$^2H_6$]DMSO at 20 °C) δ: 20.0 (1-NCH*Me*-A), 20.7 (1-NCH*Me*-B), 21.3 (2-NCH*Me*-A), 21.7 (2-NCH*Me*-B), 54.3 (1-NCH), 54.5 (2-NCH), 55.8 (1-NCH_2), 56.5 (2-NCH_2), 73.2 (CHO). Found (%): C, 62.87; H, 11.42; N, 16.56. Calc. for $C_9H_{20}N_2O$ (%): C, 62.75; H, 11.70; N, 16.26.

9 prepared in accordance with Scheme 5 and separated by chromatography (SiO_2 40/60 μ. Eluent: ethyl acetate), 12% yield. ^{1}H NMR ([$^2H_6$]toluene at 20 °C) δ: 0.74 (d, 6H, 2Me-A, ^3J 6.4 Hz), 0.85 (d, 6H, 2Me-B, ^3J 6.4 Hz), 2.50 (hept, 2H, 2Me, ^3J 6.4 Hz), 2.82 (m, 4H, 2CH_2, AB spectrum, $\Delta\nu$ 100 Hz, ^2J –18.4 Hz); for Pr^i groups, $\Delta\nu$ 24.8 Hz at 20 °C, and 18.7 at 90 °C. Found (%): C, 63.31; H, 10.60; N, 16.07. Calc. for $C_9H_{18}N_2O$ (%): C, 63.49; H, 10.66; N, 16.45.

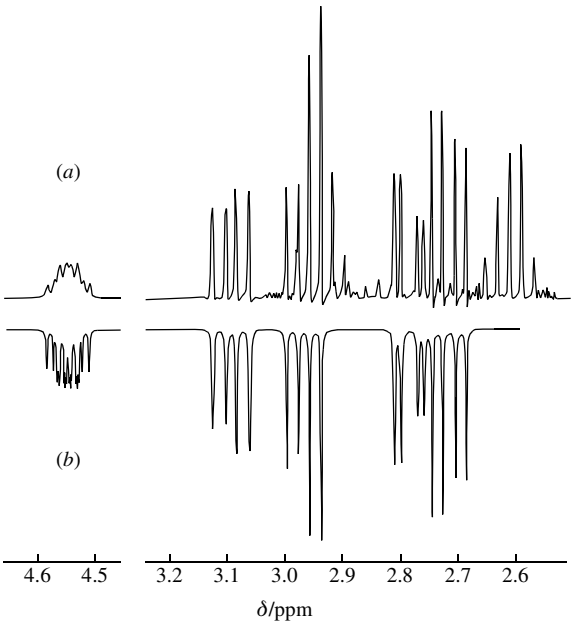


Figure 4 ^{1}H NMR spectra of compound **8**: (*a*) experimental (300.13 MHz, in [$^2H_6$]DMSO at 20 °C) and (*b*) calculated by CALM.

†† Full line shape analysis in the ^{13}C {^{1}H} NMR spectra (75.43 MHz) was performed based on a Bloch equation modified for chemical exchange.[19] The spectra of the A-Me and B-Me groups of pyrazolidines **7** (in [$^2H_5$]pyridine) and **8** (in [$^2H_6$]DMSO) were measured at different temperatures (Table 2).

Table 2 Temperature of spectral measurements and the lifetime of exchanged states.

Compound			
7		**8**	
T/K	τ/s	*T*/K	τ/s
301.6	0.41671	301.9	0.16150
307.0	0.24156	307.7	0.09577
312.0	0.14942	313.2	0.05831
318.0	0.09176	319.2	0.02576
324.0	0.05787	325.0	0.02343
330.0	0.03587	331.0	0.01534
336.0	0.02413	336.9	0.01005
342.0	0.01577	342.9	0.00641
347.9	0.01115	348.8	0.00455
354.4	0.00780	354.6	0.00303
360.5	0.00558	360.5	0.00215
367.2	0.00412	372.5	0.00099
373.9	0.00296		

The signal coalescence temperatures are 348 and 328 K for compounds **7** and **8**, respectively. Temperature was calibrated using an external standard.[20] Bruker software (DISNMR on ASPECT-3000 with Adacos and XWinNMR on PC with Linux) was used for data processing. The spectra were converted using the CODER 7 program (A. O. Krasavin: http://nmr.ioc.ac.ru/coder7.zip). The computation was performed by the DYNNMR integration program.[21] The cross-relaxation times were measured at each temperature.

References

1 R. G. Kostyanovsky, V. Schurig, O. Trapp, K. A. Lyssenko, B. A. Averkiev, A. V. Prosyanik, G. K. Kadorkina and V. R. Kostyanovsky, *Mendeleev Commun*., 2002, 137.
2 R. G. Kostyanovsky, P. Rademacher, Yu. I. El'natanov, G. K. Kadorkina, G. A. Nikiforov, I. I. Chervin, S. V. Usachov and V. R. Kostyanovsky, *Izv. Akad. Nauk. Ser. Khim.*, 1997, 1346 (*Russ. Chem. Bull.*, 1997, **46**, 1291).
3 R. G. Kostyanovsky, G. K. Kadorkina, V. R. Kostyanovsky, V. Schurig and O. Trapp, *Angew. Chem., Int. Ed. Engl.*, 2000, **39**, 2938.
4 (*a*) V. J. Baker, A. R. Katritzky, J.-P. Majoral, S. F. Nelsen and R. J. Hintz, *J. Chem. Soc., Chem. Commun.*, 1974, 823; (*b*) V. J. Baker, A. R. Katritzky and J.-P. Majoral, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1191.
5 R. G. Kostyanovsky, G. K. Kadorkina, V. N. Voznesensky, I. I. Chervin, M. Yu. Antipin, K. A. Lyssenko, E. V. Vorontzov, V. T. Bakhmutov and P. Rademacher, *Mendeleev Commun.*, 1996, 69.
6 J.-M. Lehn, *Fortschr. Chem. Forsch.*, 1970, **15**, 311.
7 O. Trapp and V. Schurig, *J. Am. Chem. Soc.*, 2000, **122**, 1424.
8 (*a*) B. Zwanenburg and W. E. Weening, *Recl. Trav. Chem. Pays-Bas*, 1965, **84**, 408; (*b*) B. Zwanenburg, W. E. Weening and J. Strating, *Recl. Trav. Chim. Pays-Bas*, 1964, **83**, 877.
9 L. Eberson and K. Person, *Acta Chem. Scand.*, 1964, **18**, 721.
10 E. L. Bushle, A. M. Moore and F. Y. Wisclogle, *J. Am. Chem. Soc.*, 1943, **65**, 29.
11 T. Abe, R. Machida, Y. Kukamoto and S. Aoyang, *Jpn. Patent* 02 67,269 (*Chem. Abstr.*, 1990, **113**, 115298).
12 M. Chang and R. J. Crawford, *Can. J. Chem.*, 1981, **59**, 2556.
13 G. N. le Fevre and R. J. Crawford, *J. Am. Chem. Soc.*, 1986, **108**, 1019.
14 R. J. Crawford, D. M. Cameron and H. Tokunaga, *Can. J. Chem.*, 1974, **52**, 4025.
15 R. J. Crawford, A. Mushra and R. J. Dummel, *J. Am. Chem. Soc.*, 1966, **88**, 3959.
16 S. Sternhell, *Quart. Rev.*, 1969, **23**, 236.
17 J. Elguero, C. Marzin and D. Tizane, *Org. Magn. Res.*, 1969, **1**, 249.
18 (*a*) E. Fahz, W. Fisher, A. Jung, L. Sauer and A. Mannshreck, *Tetrahedron Lett*., 1967, 161; (*b*) E. C. Taylor, N. F. Haley and R. J. Clemens, *J. Am. Chem. Soc.*, 1981, **103**, 7743; (*c*) G. Lawton, Ch. J. Moody, Ch. J. Pearson, and D. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1987, 885.
19 R. A. Sack, *Mol. Phys.*, 1958, **1**, 163.
20 A. L. van Geet, *Anal. Chem.*, 1970, **42**, 679.
21 A. V. Shastin, T. I. Godovikova, S. P. Golova, M. V. Povorin, D. E. Dmitriev, M. O. Dekaprilevich, Yu. A. Strelenko, L. N. Khmel'nitskii and B. L. Korsunskii, *Khim. Geterotsikl. Soedin.*, 1995, 679 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1995, **31**, 601].

Received: 2nd July 2002; Com. 02/1952