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N,3-Dimethyl-3-(perhydro-1,3,2-dioxazepin-2-yl)butanamide: synthesis and crystal structure†

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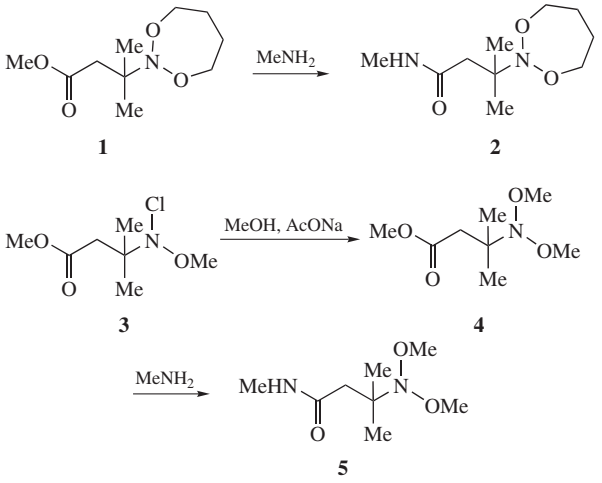
XRD study of crystals of *N*,3-dimethyl-3-(perhydro-1,3,2-dioxazepin-2-yl)butanamide and *N*,3-dimethyl-3-(*N*′,*N*′-dimethoxyamino)-butanamide showed that both of them have similar conformations and similar high degree of nitrogen pyramidality in O–N–O fragment.

In *N*,*N*-dialkoxy-*N*-*tert*-alkylamines, two geminal alkoxy groups at the nitrogen atom cause high configurational stability of the trivalent nitrogen.[2–4] Due to this, such a dialkoxyamino fragment can serve as a chirality centre.[4] The cyclic analogues such as 1,3,2-dioxazolidines,[5] perhydro-1,3,2-dioxazines,[5] perhydro-1,3,2-dioxazepines[6,7] and perhydro-1,3,6,2-trioxazocines[8] were also obtained. The structure of some perhydro-1,3,2-dioxazines was investigated by XRD,[9] however, the real structural parameters of perhydro-1,3,2-dioxazepines and acyclic *N*,*N*-dialkoxyamines remained unknown.

To estimate such data, we converted the liquid ester **1** into crystalline amide **2** (Scheme 1).‡ For more information, we converted acyclic analogue, *N*,*N*-dialkoxyamino ester **4**, into solid amide **5** in the same manner (Scheme 1).‡ The *N*,*N*-dimethoxyamine **4** has been synthesised by methanolysis of *N*-chloro-*N*-methoxyamino derivative **3** in the presence of AcONa. This procedure of alcoholysis of *N*-chloro-*N*-alkoxyamines is more selective than earlier described method.[2]



Scheme 1

The XRD study of compounds **2** and **5** (Figures 1 and 2)§ revealed that in both of them the N(1) atoms of O–N–O geminal

† Geminal systems. Part 60. For the previous part, see ref. 1.

‡ N,*3-Dimethyl-3-(perhydro-1,3,2-dioxazepin-2-yl)butanamide* **2**. The solution of methyl 3-(perhydro-1,3,2-dioxazepin-2-yl)-3-methylbutanoate **1**[6] (0.366 g, 1.684 mmol) in $MeNH_2$ (3 ml) in a sealed tube was kept at 30 °C for 25 days, then $MeNH_2$ was evaporated, the residue was crystallized from hexane, giving 0.322 g (88%) of compound **2** as colourless crystals, mp 82–83 °C (hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.24 (s, 6H, Me_2C), 1.95–2.02 (m, 4H, $OCH_2CH_2CH_2CH_2O$), 2.46 (s, 2H, CH_2), 2.81 (d, 3H, NH*Me*, ^3J 4.8 Hz), 3.75–3.95 (m, 4H, $NOCH_2$), 6.32 (br. s, 1H, NH). Found (%): C, 55.61; H, 9.42; N, 12.82. Calc. for $C_{10}H_{20}N_2O_3$ (%): C, 55.53; H, 9.32; N, 12.95.

*Methyl 3-(*N,N*-dimethoxyamino)-3-methylbutanoate* **4**. To the cold (–32 °C) solution of AcONa (0.305 g, 3.727 mmol) in MeOH (3 ml), methyl 3-(*N*-chloro-*N*-methoxyamino)-3-methylbutanoate **3**[2] (0.364 g, 1.863 mmol) was added. The reaction mixture was heated to 13 °C within 15 h, then methanol was evaporated *in vacuo*. The residue was extracted with Et_2O (15 ml), the extract was concentrated, the residue was stirred with hexane (8 ml) and $NaHCO_3$ (0.1 g), then the hexane phase was separated and evaporated *in vacuo*, giving 0.322 g (90%) of the product **4** as colourless liquid, n_D^{25} 1.4250, identified by ^{1}H NMR spectroscopy with authentic sample.[2] ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.23 (s, 6H, Me_2C), 2.55 (s, 2H, CH_2), 3.67 (s, 3H, CO_2Me), 3.75 [s, 6H, $N(OMe)_2$].

N,*3-Dimethyl-3-(*N′,N′*-dimethoxyamino)butanamide* **5** was obtained similarly to compound **2**, yield 81%, colourless crystals, mp 61–62 °C (hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.23 (s, 6H, Me_2C), 2.45 (s, 2H, CH_2), 2.83 (d, 3H, NH*Me*, ^3J 5.4 Hz), 3.78 [s, 6H, $N(OMe)_2$], 6.12 (br. s, 1H, NH). MS (FAB), *m*/*z*, [I_{rel} (%)]: 191 $[M+H]^+$ (45), 190 $[M]^+$ (17), 159 $[M-OMe]^+$ (100). Found (%): N, 14.65. Calc. for $C_8H_{18}N_2O_3$ (%): N 14.72.

§ *Crystal data for* **2**: $C_{10}H_{20}N_2O_3$, M = 216.21, monoclinic, space group $P2_1/c$, a = 11.837(6), b = 10.510(6) and c = 9.610(5) Å, β = 100.49(5)°, V = 1175.6(11) Å^3, F(000) = 472, d_{calc} = 1.22 g cm^{-3}, Z = 4, μ = 0.09 mm^{-1}.

Crystal data for **5**: $C_8H_{18}N_2O_3$, M = 190.24, rhombic, space group *Pbca*, a = 10.5134(14), b = 9.5173(8) and c = 22.191(2) Å, V = 2220.4(4) Å^3, F(000) = 832, d_{calc} = 1.138 g cm^{-3}, Z = 8, μ = 0.086 mm^{-1}.

Data were measured using an Xcalibur 3 diffractometer (298 K, graphite-monochromated MoKα radiation, $2\theta/\theta$ scan, $2\theta_{max}$ = 52°). The structures were solved by direct method using the SHELX-97 program package.[13] Refinement against F^2 in an anisotropic approximation (the hydrogen atoms isotropic in the riding model) by a full matrix least-squares method for 2248 reflections was carried out to wR_2 = 0.089 [R_1 = 0.067 for 755 reflections with $F > 4\sigma(F)$, S = 0.82] for **2**, for 2182 reflections was carried out to wR_2 = 0.076 [R_1 = 0.040 for 1215 reflections with $F > 4\sigma(F)$, S = 0.99] for **5**.

CCDC 764202 and 784347 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2011.

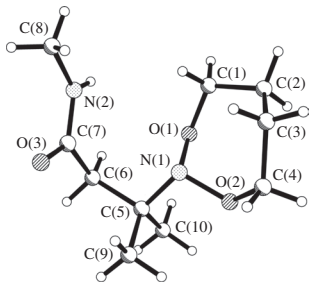


Figure 1 The molecular structure of compound **2**. Selected bond lengths (Å) and bond angles (°): O(1)–N(1) 1.432(4), O(2)–N(1) 1.441(4), N(1)–C(5) 1.471(4), C(5)–C(9) 1.497(5), C(5)–C(10) 1.547(5); O(1)–N(1)–O(2) 104.1(3), O(1)–N(1)–C(5) 104.9(3), O(2)–N(1)–C(5) 106.1(3).

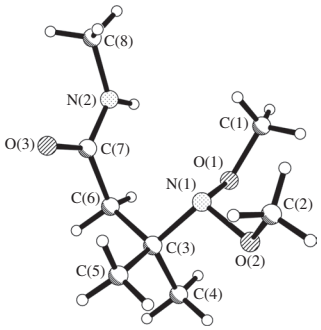


Figure 2 The molecular structure of compound **5**. Selected bond lengths (Å) and bond angles (°): O(1)–N(1) 1.4221(14), O(2)–N(1) 1.4363(15), O(1)–C(1) 1.4171(18), O(2)–C(2) 1.421(2), N(1)–C(3) 1.4926(18), C(3)–C(4) 1.532(2), C(3)–C(5) 1.521(2), C(3)–C(6) 1.529(2); O(1)–N(1)–O(2) 104.88(10), O(1)–N(1)–C(3) 104.82(10), O(2)–N(1)–C(3) 105.76(11).

fragment have strongly pyramidal configuration. The sum of bond angles centered at this nitrogen atom ($\Sigma\beta$) is 315.1(2)° in **2** and 315.4(2)° in **5**, the deviation of the N(1) from the plane of atoms bonded with the N(1) atom (h_N) is equal to 0.579(4) Å in **2** and 0.578(1) Å in **5**. Therefore, the degree of nitrogen pyramidality in both cyclic **2** and acyclic **5** are close.

Note that the degree of nitrogen pyramidality in relative *N*,3-dimethyl-3-(perhydro-1,3,2-dioxazin-2-yl)butanamide is slightly lower ($\Sigma\beta$ is 317.5°).[9]

Similar situation is observed for the O–N–N^+ geminal system. In methyl 2-[*N*-(1-pyridinio)-*N*-methoxyamino]-2-methylpropanoate perchlorate $\Sigma\beta$ is 322.8° and h_N is equal to 0.531 Å.[10] On the other hand, in tetramethoxyhydrazine,[11] the nitrogen pyramidality degree is greater ($\Sigma\beta$ is 306.0°).

Perhydro-1,3,2-dioxazepine ring in compound **2** adopts chair conformation similarly to perhydro-1,3,2-dioxazines.[9] The O(1), C(1), O(2), C(3) and C(4) atoms are coplanar and the C(2) and N(1) atoms deviate from this plane in opposite directions by 0.760(5) and 0.887(4) Å, respectively. Common parts of both compounds **2** and **5** have similar conformations. In *N*,*N*-dimethoxyamine **5**, both *N*-methoxy groups are directed towards the lone electron pair (Lp) of the N(1) atom [the C(1)–O(1)–N(1)–Lp(N1) and the C(9)–O(2)–N(1)–Lp(N1) torsion angles are 36° and –8°, respectively].

In perhydro-1,3,2-dioxazepine **2**, the substituent at the N(1) atom has equatorial orientation [the C(1)–O(1)–N(1)–C(5) torsion angle is 157.7(3)°]. Methyl groups at the C(9) and C(10) atoms have sc-conformation and ap-conformation relatively to the Lp of the N(1) atom [the Lp(N1)–N(1)–C(5)–C(9) and the Lp(N1)–N(1)–C(5)–C(10) torsion angles are –57° and –178°, respectively]. In *N*,*N*-dimethoxyamine **5** the C(4) methyl group has ap-conformation to the Lp(N1) [the Lp(N1)–N(1)–C(3)–C(4) torsion angle is 179°]. Some difference in lengths of Me–C bonds is observed for **5** [the C(3)–C(4) bond length is 1.532(2) Å, the C(3)–C(5) bond length is 1.521(2) Å]. This may be due to C(3)–C(4) bond elongation caused by the $n_{N(1)} \rightarrow \sigma^*_{C(3)–C(4)}$ anomeric interaction. In compound **2**, the similar $n_{N(1)} \rightarrow \sigma^*_{C(5)–C(10)}$ anomeric interaction must have taken place causing some difference in Me–C bonds [the C(5)–C(10) bond length is 1.547(5) Å, the C(5)–C(9) bond length is 1.497(2) Å]. Interestingly, that in *N*,3-dimethyl-3-(perhydro-1,3,2-dioxazin-2-yl)butanamide both Me–C bonds are equal in length.[9]

The N–O bond lengths in perhydro-1,3,2-dioxazepine **2** and *N*,*N*-dimethoxyamine **5** are considerably shorter [the N(1)–O(1) and N(1)–O(2) bonds lengths are 1.432(4) Å and 1.441(4) Å, respectively, in **2**, 1.4221(14) Å and 1.4363(15) Å, respectively, in **5**] compared to the N–OMe bond in MeNHOMe (1.496 Å).[12] Probably it may be explained by the $n_{O(1)} \rightarrow \sigma^*_{N(1)–O(2)}$ and $n_{O(2)} \rightarrow \sigma^*_{N(1)–O(1)}$ anomeric interactions. Similar situation was observed in methyl 2-[*N*-(1-pyridinio)-*N*-methoxyamino]-2-methylpropanoate perchlorate,[10] where the N–OMe bond is shortened to 1.414 Å due to the $n_{O(Me)} \rightarrow \sigma^*_{N–N^+}$ anomeric effect.

The C(5)–C(6)–C(7)–N(2) fragment of **2** has sc–ac–ap conformation. The N(1)–C(5)–C(6)–C(7), C(5)–C(6)–C(7)–N(2) and C(6)–C(7)–N(2)–C(8) torsion angles are –48.7(5)°, 110.5(4)° and –179.8(3)°, respectively. Similarly, in *N*,*N*-dimethoxyamine **5**, the C(3)–C(6)–C(7)–N(2) methylamide fragment has ap-conformation with respect to the C(3)–C(4) bond. The C(4)–C(3)–C(6)–C(7) and C(3)–C(6)–C(7)–N(2) torsion angles are –170.43(13)° and 110.55(15)°, respectively.

In the crystal, molecules of perhydro-1,3,2-dioxazepine **2** are linked in the chains along the (001) crystallographic direction due to intermolecular hydrogen bonds N(2)–H(2)···O(3′) (x, $0.5-y$, $-0.5+z$) (H···O, 2.01 Å; N–H···O, 162°).

Analogously, molecules of *N*,*N*-dimethoxyamine **5** in the crystal are linked in the chains along the *b* crystallographic direction due to intermolecular hydrogen bonds N(2)–H(2A)···O(3′) ($1.5-x$, $0.5+y$, z) (H···O, 2.05 Å; N–H···O, 157°).

Thus, the comparison of molecular structures of perhydro-1,3,2-dioxazepine **2** and acyclic *N*,*N*-dimethoxyamine **5** demonstrates that the structural parameters for O–N–O fragment and their neighbouring environment are similar.

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