Molecular structure of 1-methoxymethylaziridine and methoxymethyldimethylamine and anomeric effects

Igor F. Shishkov,[a] Lyudmila V. Khristenko,[a] Lev V. Vilkov,*[a] Marwan Dakkouri,[b] Gulnara K. Kadorkina,[c] Pavel E. Dormov[c] and Remir G. Kostyanovsky*[c]

[a] *Department of Chemistry, M. V. Lomonosov Moscow State University, 119899 Moscow, Russian Federation. Fax: +7 095 932 8846; e-mail: IFShishkov@phys.chem.msu.ru*
[b] *Department of Electrochemistry, University of Ulm, 89069 Ulm, Germany. Fax: +49 731 502 5409; e-mail: marwan.dakkouri@chemie.uni-ulm.de*
[c] *N. N. Semenov Institute of Chemical Physics, Russian Academy of Sciences, 117977 Moscow, Russian Federation. Fax: +7 095 137 3227; e-mail: kost@center.chph.ras.ru*

10.1070/MC2000v010n06ABEH001359

For 1-methoxymethylaziridine **1** it is proved experimentally (GED) and theoretically that the equilibrium conformers are stabilised by the anomeric effects $n(N) \rightarrow \sigma^*(C–O)$ and $n(O) \rightarrow \sigma^*(C–N)$, whereas in the case of methoxymethyldimethylamine **2** the calculations predict the existence of a conformer appropriate to the $n(N) \rightarrow \sigma^*(C–O)$ effect.

1-Methoxymethylaziridine **1** occupies a special place in the series of alkoxymethylamines because of a dramatic change in the chemical properties on the incorporation of a nitrogen atom into a three-membered ring. Compound **1** cannot be prepared using a standard method for alkoxymethylamine synthesis by the reaction of an amine with formaldehyde in methanol. In the case of aziridine, this reaction gives 1-hydroxymethylaziridine in almost 100% yield.[1,2] As well as **1**, 1-hydroxymethylaziridine does not exhibit an aminomethylating effect,[3–6] which is the most typical property of secondary amine derivatives such as piperidine.[7] Aziridine **1** was prepared for the first time by the alkylation of potassium ethyleneamide with methoxymethyl chloride.[6] An interesting property of **1** is that in the cleavage with acetic anhydride an electrophilic attack occurs almost equiprobably at the N and O atoms [reaction (1)],[6] whereas ordinary alkoxymethylamines are attacked only at the O atom [reaction (2)].

$$\underset{}{MeOCH_2N(CH_2)_2} \xrightarrow[Et_2O,\ -60\ ^\circ C]{(MeCO)_2O} \underset{20\%}{MeCON(CH_2)_2} + \underset{17\%}{MeC(O)OCH_2OMe} + \underset{17\%}{MeC(O)OMe} \quad (1)$$

$$ROCH_2NR_2 \xrightarrow{(MeCO)_2O} MeC(O)OR + MeC(O)OCH_2NR_2 \quad (2)$$

A similar behaviour was observed in electron-impact fragmentation.[6] In the mass spectra at 17 eV, the intensity ratios between the peaks of amine ($>N^+=CH_2$) and oxygen ($MeO^+=CH_2$) fragments were 0.3 and 40 for **1** and 1-methoxymethylpiperidine, respectively. Finally, a noticeable decrease (by 3.4 kcal mol^{-1}) in the inversion barrier of the nitrogen atom was observed in **1** as compared with 1-ethylaziridine.[8,9] A similar decrease in the N inversion barrier was described for 2-methoxymethyl-1,2-oxazolidine.[9]

The above properties of **1** can be explained by stereoelectronic effects with the participation of lone pair electrons for both N[8] and O atoms. These effects will manifest themselves in different conformers as the most favourable molecular conformations.

In this connection, we examined the structure of **1** by gas electron diffraction analysis† and made *ab initio* and DFT calculations for **1** and methoxymethyldimethylamine **2**.

To describe the molecular geometry of **1**, the two torsion angles φ(C–N) and φ(C–O), which correspond to rotation of molecular fragments about the exocyclic bonds CH_2–N and CH_2–O, respectively, were used. The torsion angle φ(C–O) = 0° corresponds to the projection of CH_2–O onto the endocyclic bond C–N. A minus sign denotes the rotation of a CH_2–O unit about the N–CH_2 bond inwards the projection of the CNC angle of the ring (see Scheme 1). The angle φ(C–O) = 0° corresponds

Table 1 Geometry parameters of **1** (bond lengths/Å, bond angles/°) determined by quantum-chemical calculations.[a]

Parameter	B3LYP/6-31G**		B3LYP/cc-pvtz		MP2/6-311G**
	I	II	I	II	I[b]
r[C(2)–N]	1.461	1.461	1.457	1.458	1.465
r(C–C)	1.495	1.490	1.490	1.485	1.495
r[C(4)–N]	1.437	1.459	1.434	1.455	1.440
r[C(4)–O]	1.424	1.401	1.423	1.399	1.420
r[C(8)–O]	1.411	1.421	1.411	1.420	1.414
C–O–C	112.9	111.9	112.8	114.0	110.9
O–C –N	112.7	113.6	113.2	112.0	112.7
C(2)–N– C(4)	118.7	115.8	119.2	115.9	117.3
C(2)–N– C(3)	61.5	61.2	61.5	61.2	61.4
φ(C–N)	–35. 7	87.4	–35 .8	88.8	–35 .0
φ(C–O)	179.9	67.3	179.9	68.6	180.0
$_1$	0.024	0.002	0.023	0.003	0.025
$_2$	0.013	–0 .020	0.012	–0 .021	0.016
E^b/kcal mol^{-1}		0.69		0.1	2.6

[a]In the electron diffraction analysis, the values $_1$ = [C(2)–N] – [C(4)–N] and $_2$ = [C(4)–O] – [C(8)–O] were fixed at 0.023 and 0.012 Å, respectively. [b] $E = E(II) – E(I)$, where $E(I)$ and $E(II)$ are the energies of conformer I and II, respectively.

Table 2 Geometry parameters of the main conformer of **1** (bond lengths/Å, bond angles/°).[a]

Parameter	Value
r[C(4)–O]	1.421 |
r[C(8)–O] [b]	1.409 | (7)
r[C(2)–N]	1.456 |
r[C(4)–N] [b]	1.434 | (9)
$r(C–H)_{av}$	1.098(4)
$r(C–C)^b$	1.500(9)
C–O–C	114.3(22)
O–C –N	113.4(12)
C(2)–N– C(4)	116.8(4)
C(2)–N– C(3)	61.9(4)
φ(C–N)	–11 (4)
φ(C–O)	167(6)
α^c (%)	67(12)
R_f (%)	6.90

[a]Standard deviations are given in parentheses. [b]Dependent parameters. [c]Vapour composition at 300 K. The values of independent geometry parameters of conformer II were taken equal to the corresponding parameters of the main conformer. The torsion angles of conformer II were refined and found to be φ(C–N) = 120(7)° and φ(C–O) = 80(9)°.

† **1** was synthesised according to a published procedure[6] and distilled with sodium metal; bp 75 °C. ^{1}H NMR ($CDCl_3$) δ: 1.28 (m), 1.73 [m, 4H, $(CH_2)_2N$], 3.44 (s, 3H, MeO), 3.70 (s, 2H, NCH_2O). For the gas electron diffraction experiments, samples of **1** were sealed in evacuated (1 Torr) glass ampoules (5 mm in diameter and 50 mm in length) on cooling.

Table 3 Comparison between the main geometry parameters of molecules with XCH_2Y units (X, Y = O, N or F).

XCH_2Y	r(X–C H$_2$)/ Å	r(Me–Y), r(CH$_2$–F)/ Å	X–C H$_2$–Y/ °	C–Y–C /°	Reference
1	1.433(9)	1.410(7)	113.4(12)	114.3(22)	This work
$(MeO)_2CH_2$	1.382(4)	1.432(4)	114.3(7)	114.6(5)	17
Me_2NCH_2F	1.408(13)	1.410(5)	115.9(24)	—	18
Me_2O	—	1.410(3)	—	111.7(0.4)	19
Me_3N	—	1.454(3)	—	110.9(6)	20
MeF	—	1.391(2)	—	—	21

to a conformation with eclipsed Me–O and CH_2–N bonds.

To construct the full energy surface in the HF/6-31G approximation,[10,11] we calculated the energies of pseudo-conformers with the full optimization of all parameters. The angles φ(C–N) and φ(C–O) were fixed within the ranges –30 to 15 0° and 0 to 180°, respectively, at steps of 30°. Two minima were found on the surface of 49 models: conformer I with φ(C–N) = = 30° and φ(C–O) = 180° and conformer II with φ(C–N) = 90° and φ(C–O) = 60° (Scheme 1).

The parameters of these minima were optimised in B3LYP/6-31G**, B3LYP/cc-pvtz and MP2/6-311G** calculations (Table 1). Force fields for each of these conformers were then obtained from the B3LYP/cc-pvtz calculations, and mean-square vibrational amplitudes and perpendicular corrections were computed using the program described in ref. 12.

In the structure analysis of electron diffraction patterns,‡ we assumed that the methyl group and the aziridine unit have C_{3v} and C_{2v} local symmetries, respectively. The valence angles associated with H atoms were fixed at values taken from a quantum-chemical calculation (B3LYP/cc-pvtz). The calculated difference between the C–O interatomic distances in the CH_2O and MeO units, as well as the difference in the endocyclic and exocyclic bonds (C–N), depended only slightly on the method and basis set used (Table 1). Therefore, to decrease the correlation between the main parameters we fixed these differences in the C–O and C–N bond lengths at values obtained from the B3LYP/cc-pvtz calculations. The further refinements of the C–N , C–O and (C–H)$_{av}$ bond lengths, the C–O–C, O–C– N and C–N –C (exo) valence angles and the φ(C–N) and φ(C–O) torsion angles were performed using step-by-step variation[14] and a least-squares technique.[15]

The theoretical conformational composition of 1-methoxymethylaziridine strongly depends on the method and the basis set used in the quantum-chemical calculations (from 100 to 50% of conformer I at room temperature). Therefore, the agreement between experimental data and theoretical data from models in which only conformer I or conformer II was present was examined. The torsion angles φ(C–N) were refined; they were found to be equal to ~0° for conformer I [Figure 1(*a*)] and ~100° for conformer II [Figure 1(*b*)]. The *R*-factors obtained using the two models were 8.1 and 11.2%, respectively.

Table 4 Calculated geometry parameters of methoxymethyldimethylamine **2** (bond lengths/Å, bond angles/°).

Parameter	MP2/6-311++G**	B3pw91/6-311++G**
r[C(4)–N]	1.439	1.431
r[C(1)–N]	1.458	1.449
r[C(3)–N]	1.456	1.446
r[C(4)–O]	1.407	1.404
r[C(12)–O]	1.414	1.403
C(1)–N(2)–C (3)	110.7	112.5
C(1)–N(2)–C (4)	110.9	112.7
N–C (4)–O(11)	108.8	109.1
C(4)–O(11)–C(12)	110.7	112.4
C(1)–N(2)–C (4)–O(11)	66.0	67.7
N(2)–C(4)–O(11)–C(12)	–1 75.6	–173.4

‡ Gas electron diffraction data were recorded on an EMR-100 electron diffraction unit at room temperature. The electron diffraction patterns were photometrically evaluated on an automatic microdensitometer.[13] The averaged intensities were obtained in the ranges $3.0 \leqslant s \leqslant 15.4$ Å^{-1} and $4.6 \leqslant s \leqslant 25.8$ Å^{-1} with the step $s = 0.2$ Å^{-1}.

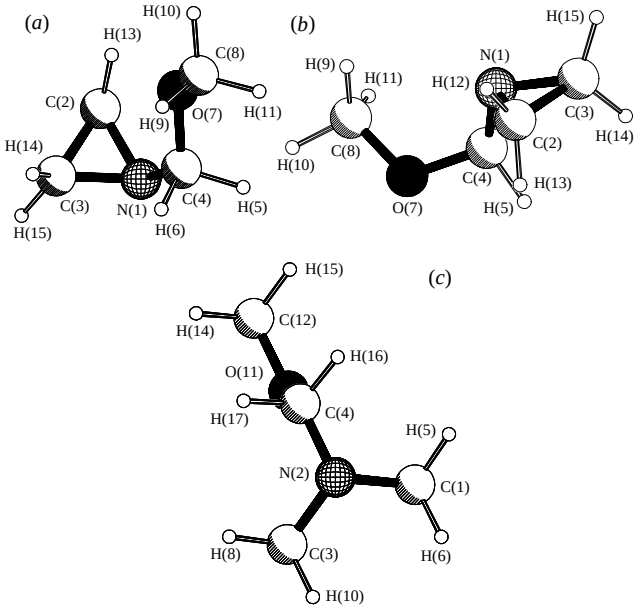


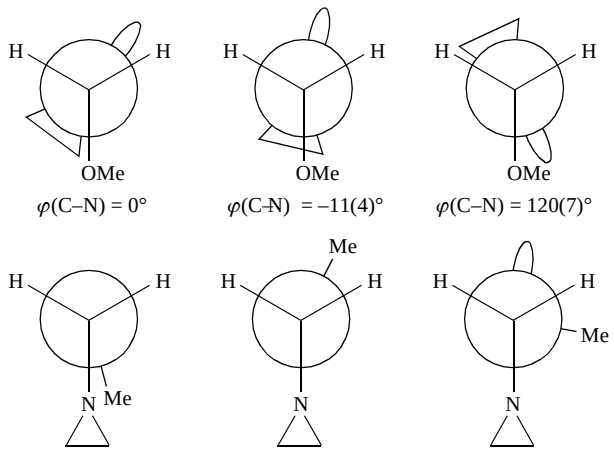
Figure 1 Molecular models: (a) **1**, conformer I, (*b*) **1**, conformer II and (*c*) **2**, conformer I.

Figure 3 shows the experimental radial distribution curve, $f(r)$, the difference curve, $f(r)$, and the theoretically calculated curve for a model with φ(C–N) = –30 ° [model T(2)]. It can be seen that the molecular model with the projection of the C–O bond on the bisector of the CNC angle is inconsistent with the experimental data. In refined conformer I, the dihedral angles φ(C–N) = –1 1(4)° and φ(C–O) = 176(6)°, *i.e.*, the CH_2–O bond is almost projected onto the N–CH_2 bond of the ring, and the aziridine ring and the Me group are in almost *anti* orientation with respect to the C–O bond.

Starting with the estimated initial ratio between conformers I (70%) and II (30%), a final combined refinement of all main parameters, including conformational composition, was performed and the results are shown in Table 2.

Conformer I exhibits shortened O···H(C_{ring}) and O···($C)_{ring}$ distances of 2.11 and 2.56 Å, respectively. The O···($C)_{ring}$ distance to the second carbon atom of the ring is 2.99 Å. The geometry of the main form (conformer I) corresponds to the anomeric effect n(N) → *(C–O), whereas the geometry of conformer II is consistent with the anomeric effect n(O) → → *(C–N). Note that similar results were obtained previously for 1-(tetrahydropyran-2-yl)aziridine on the basis of ^{1}H NMR spectroscopy and dipole moment measurements.[16]

In Table 3 the main geometrical parameters for molecules containing XCH_2Y units (X, Y = O, N or F) are compared. The conformation of $MeOCH_2OMe$ corresponds to a gauche–gauche arrangement of the Me groups.[17] In the molecule Me_2NCH_2F,



Scheme 1

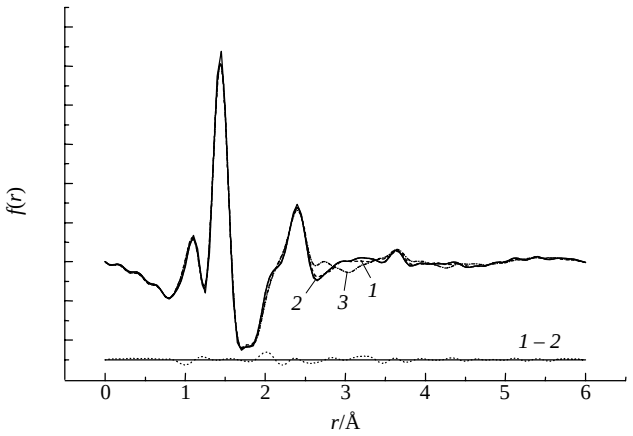


Figure 2 Experimental (*1*) and theoretical (*2*) radial distribution curves with the difference curve for a mixture of two conformers. The theoretical curve (*3*) for a model with the arrangement of the C–N bond along the bisector of the C–N– C angle is also shown.

the C–F bond is projected onto the bisector of the Me_2N angle with a pyramidal configuration of the nitrogen atom.[18] In both of these molecules, the conformations and bond lengths can also be explained by the anomeric effects $n(O) \rightarrow \sigma^*(C\text{–}O)$ and $n(N) \rightarrow \sigma^*(C\text{–}F)$, respectively.

It can be seen in Table 3 that the N–CH_2(O) bond length in **1** is somewhat shorter than the N–Me bond length in Me_3N. The C–O bond lengths in the molecule $MeOCH_2OMe$ are different from each other and from the C–O bond length in Me_2O.[19] In the molecule Me_2NCH_2F, the N–CH_2 bond is shorter than the N–Me bond in Me_3N and the C–F bond is longer than that in MeF.[18,20,21] The valence angles XCH_2Y in the above three molecules, which exhibit an anomeric effect, are considerably greater than tetrahedral angles.

A full energy surface (FES) calculation (B3LYP/6-311++G*) of **2** was also made in order to observe possible differences in the structure and conformation of this molecule. The N(2)–C(4)–O(1 1)–C(1 2) and C(1)–N(2)–C(4)–O (11) torsion angles were varied from 0 to 330° and from 0 to 180°, respectively, in steps of 30°. All remaining parameters were optimised. An analysis of the results showed the presence of two conformers with torsion angles of 180 and 60° for conformer I and 90 and 90° for conformer II, respectively.

In the optimization of the two conformers, the geometrical parameters presented in Table 4 were obtained together with an energy difference between conformers of about 2 kcal mol^{-1}. This large value for the conformer energy difference means that even with allowance for differences in entropy practically only conformer I [Figure 1(*c*)] will be present in the gas phase. In this conformer the H_2C–O bond is oriented in a bisector plane of the Me_2N angle, and the H_2C–N and O–Me bonds are in an *anti* position.

The geometry of conformer I is in agreement with the anomeric effect $n(N) \rightarrow \sigma^*(C\text{–}O)$. Besides, by using the anomeric effect it is possible to explain that the central H_2C–N bond is slightly shorter than the N–Me bond. It should be noticed that we have similar conformers for the torsion about the C–N bond in the molecules of **2** and Me_2NCH_2F.[18] The anomeric effect has smaller influence on the H_2C–O bond. Since polar effects can also take place in the investigated molecules, the interpretation of differences in the designed geometrical parameters can be ambiguous. The valence angle NCO is less than the tetrahedral value (109.5 Å), as can be seen in Table 4. This is inconsistent with the values of XCY angles for molecules listed in Table 3.

The structural analysis of both molecules shows that there is a noticeable difference in the conformational structure of these compounds, which, likely, is revealed in the difference in chemical properties of **1** and **2**.

We are grateful to S. Shlykov and G. Girichev for their assistance in performing electron diffraction experiments.

This study was supported by the Russian Foundation for Basic Research (grant no. 99-03-04004).

References

1 R. G. Kostyanovsky, *Dokl. Akad. Nauk SSSR*, 1960, **135**, 853 [*Dokl. Chem.* (*Engl. Transl.*), 1960, **135**, 1363].
2 R. G. Kostyanovsky, O. A. Yuzhakova and V. F. Bystrov, *Izv. Akad. Nauk SSSR, Otdel. Khim. Nauk*, 1962, 1666 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1962, **11**, 1576).
3 R. G. Kostyanovsky, O. A. Pan'shin and T. Z. Papoyan, *Dokl. Akad. Nauk SSSR*, 1967, **177**, 1099 [*Dokl. Chem.* (*Engl. Transl.*), 1967, **177**, 1160].
4 R. G. Kostyanovsky, R. K. Alekperov, G. K. Kadorkina and I. I. Chervin, *Izv. Akad. Nauk SSSR, Ser. Khim*., 1987, 2523 (*Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1987, **36**, 2343).
5 S. V. Varlamov, G. K. Kadorkina and R. G. Kostyanovsky, *Khim. Geterotsikl. Soedin*., 1988, 390 [*Chem. Heterocycl. Compd.* (*Engl. Transl*.), 1988, **24**, 320].
6 R. G. Kostyanovsky and O. A. Pan'shin, *Izv. Akad. Nauk SSSR, Ser. Khim*., 1965, 740 (*Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1965, **14**, 721).
7 R. G. Kostyanovsky and O. A. Pan'shin, *Izv. Akad. Nauk SSSR, Otdel. Khim. Nauk*, 1963, 182 (in Russian).
8 (*a*) V. F. Bystrov, R. G. Kostyanovsky, O. A. Panshin, A. V. Stepanyants and O. A. Yuzhakova, *Opt. Spektrosk.*, 1965, **19**, 217 (*Opt. Spectrosc. USSR*, 1965, **19**, 122); (*b*) D. G. Gorenstein, *Chem. Rev.*, 1987, **87**, 1047; (*c*) K. B. Wiberg and M. A. Marcko, *J. Am. Chem. Soc.*, 1989, **111**, 4821; (*d*) A. Rastelli and M. Cocchi, *J. Chem. Soc., Faraday Trans.*, 1991, **87**, 249; (*e*) *ACS Symposium Series 539, The Anomeric Effect and Associated Stereoelectronic Effects*, ed. G. R. J. Thatcher, Am. Chem. Soc., Washington, DC, 1993; (*f*) D. Christen, H.-G. Mack, S. Rudinger and H. Oberhammer, *J. Am. Chem. Soc.*, 1996, **118**, 3720.
9 J.-M. Lehn, in *Fortschritte der Chemischen Forschung* (*Topics in Current Chemistry*), band 15, heft 3, Springer-Verlag, Berlin, 1970, p. 311.
10 M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkely, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez and J. A. Pople, *Gaussian 94, Revision D.4*, Gaussian, Inc., Pittsburgh PA, 1995.
11 *SPARTAN version 5.1*, Wavefunction, Inc., Irvine, CA 92612, USA.
12 V. A. Sipachev, *J. Mol. Struct. (Theochem)*, 1985, **121**, 143.
13 M. V. Popik, *Kristallografiya*, 1994, **39**, 332 (*Crystallography Reports*, 1994, **39**, 286).
14 N. I. Sadova, A. A. Ivanov, M. V. Popik, I. F. Shishkov, L. V. Vilkov and Yu. A. Pankrushev, *Zh. Strukt. Khim*., 1989, **30**, 56 [*J. Struct. Chem.* (*Engl. Transl.*), 1989, **30**, 216].
15 B. Andersen, H. M. Seip, T. G. Strand and R. Stolevik, *Acta Chem. Scand*., 1969, **23**, 3224.
16 D. Barbry, D. Couturier and G. Ricart, *J. Chem. Soc., Perkin Trans. 2*, 1982, 249.
17 E. E. Astrup, *Acta Chem. Scand*., 1973, **27**, 3271.
18 D. Christen, H. G. Mack, S. Ruediger and H. Oberhammer, *J. Am. Chem. Soc*., 1996, **118**, 3720.
19 U. Blukis, P. H. Kasai and R. J. Myers, *J. Chem. Phys*., 1963, **38**, 2753.
20 J. E. Wolrab and V. W. Laurie, *J. Chem. Phys*., 1969, **51**, 1580.
21 T. Egawa, S. Yamamoto, M. Nakata and K. Kuchitsu, *J. Mol. Spectrosc*., 1987, **156**, 213.

Received: 12th July 2000; Com. 00/1685