Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

11-Nitroso-6,7,10,11,12,13,15,16-octahydro-9*H*-5,8,14,17-tetraoxa-11-azabenzocyclopentadecene

Yurii A. Simonov,[a]* Maria V. Gonta[b] and Arkadii A. Yavolovskii[c]

[a]Institute of Applied Physics, Academy of Sciences of Moldova, Academy Street 5, MD2028 Chisinau, Republic of Moldova, [b]Department of Chemistry, Moldovan State University, Chisinau, Republic of Moldova, and [c]AV Bogatsky Physico-Chemical Institute, National Academy of Sciences of Ukraine, Odessa, Ukraine

Correspondence e-mail: simonov.xray@phys.asm.md

Key indicators

Single-crystal X-ray study
T = 130 K
Mean σ(C–C) = 0.003 Å
R factor = 0.029
wR factor = 0.071
Data-to-parameter ratio = 7.4

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 13 May 2005
Accepted 30 August 2005
Online 7 September 2005

The title compound, $C_{14}H_{20}N_2O_5$, was prepared by the nitrosation of 6,7,10,11,12,13,15,16-octahydro-9*H*-5,8,14,17-tetraoxa-11-azabenzocyclopentadecene. The ligand has an intramolecular C—H···O hydrogen bond, resulting in the formation of a six-membered ring. Apart from the near planar OC_6H_4O segment, the macrocycle contains *gauche* C—N and a mixture of *gauche* and *anti* C—O and C—C linkages. The nitroso group is not involved in any significant intermolecular interactions.

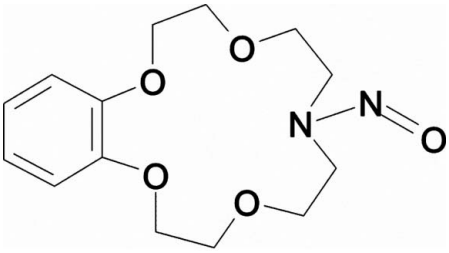
Comment

Aza crown ethers find wide applications in catalysis, chromatographic separation of metal cations and molecular recognition, due to their pronounced complexing abilities (Gokel, 1991; Gokel *et al.*, 2004). Different functionalities, introduced to the N atoms as pendant arms, can tailor the properties of these macrocyclic compounds. Despite potential application as selective complexing agents, these mixed donor–acceptor crown ethers have not been fully examined. A survey of the Cambridge Structural Database (CSD, Version 5.26, plus one 2005 update, 338 445 entries; Allen, 2002) revealed a substantial list of complexes that incorporate monoaza-15-crown-5 as a ligand, covering a range of over 14 metal cations, while only a very few representatives of benzoaza-15-crown ethers (Clegg *et al.*, 1996) and their pendant derivatives (Liu *et al.*, 1998; Chen *et al.*, 1989; Landis *et al.*, 2000; Bian *et al.*, 2001) and complexes have been reported so far.

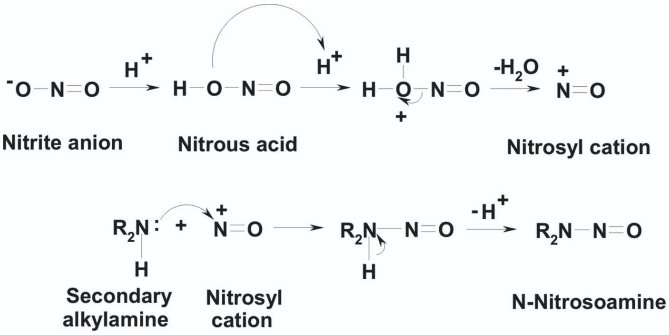
N-Nitroso derivatives are known to possess carcinogenic properties (Lijinsky, 1992), and the route of inhibition of the nitrosation process is currently under discussion (Simonov *et al.*, 2005).

The nitrosation of amines is possible in two ways, namely by endogenous nitrogen oxide (NO) in the conditions of the oxidation reaction and by exogenous nitrites in the acidic medium. The typical reagents for this reaction are sodium nitrite and aqueous solutions of hydrochloric (HCl) or sulfuric (H_2SO_4) acids (this mixture yields nitrous acid, HNO_2). The actual nitrosation reagent is the nitrosyl cation, NO^+, which is formed *in situ*. The nature of the product depends on the nature of the initial amine. Primary alkyl or aryl amines yield diazonium salts. Secondary alkyl or aryl amines yield *N*-nitrosoamines. Tertiary alkyl amines do not react in a useful fashion. Tertiary aryl amines undergo nitrosation of the ring. The scheme shows the route by which secondary amines are transformed to the dangerous *N*-nitroso compounds. Such nitrosamines, like many chemical carcinogens, are thought to promote mutagenesis and carcinogenesis *via* their ability to alkylate specific sites in DNA. For example, these types of nitrosamines undergo enzymatic α-hydroxylation. α-Hydroxy

nitrosamine decomposes to form the alkyl diazonium ion and free alkyl carbocation. The alkyl diazonium salt or carbocations then can react with nucleophilic sites in DNA.



(I)



The task is to develop suitable ways for the effective inhibition of *N*-nitrosation. Among the suitable agents, it was found that the addition of a number of simple alcohols and carbohydrates to reactions of nitrous acid with amines in dilute acidic solution resulted in a reduction in the overall rate constant for *N*-nitrosation, although complete suppression of nitrosation was not achieved (Williams & Aldred, 1982). The results are all consistent with the rapid equilibrium formation of the corresponding alkyl nitrite, which is itself virtually inactive as a direct nitrosating agent. Addition of the two thiols, L-cysteine and *N*-acetylpenicillamine, had a much more marked effect and it was possible to prevent nitrosation of the amine completely in both cases. The O_2^- dianion was also mentioned among the other agents that partially inhibit the *N*-nitrosation of primary and secondary amines (Jourd'heuil *et al.*, 1997).

The title compound, (I), was prepared as a part of study of the products of nitrosation of secondary amines by sodium nitrite in an acidic medium.

Figs. 1 and 2 depict the structure of (I), while selected intramolecular geometric data are listed in Table 1. The shape of the molecule is best described as a dentist-chair, with the five macrocyclic heteroatoms lying approximately in the saddle part (to within 0.16 Å), and with the atoms of the benzene ring located above this plane and the atoms of the nitroso group located below it. The N—N═O moiety is nearly coplanar with the benzene ring, making a dihedral angle of 3.2 (2)°. The macrocyclic cavity is distorted and far from the crown-like shape of benzo-15-crown-5 (Hanson, 1978).

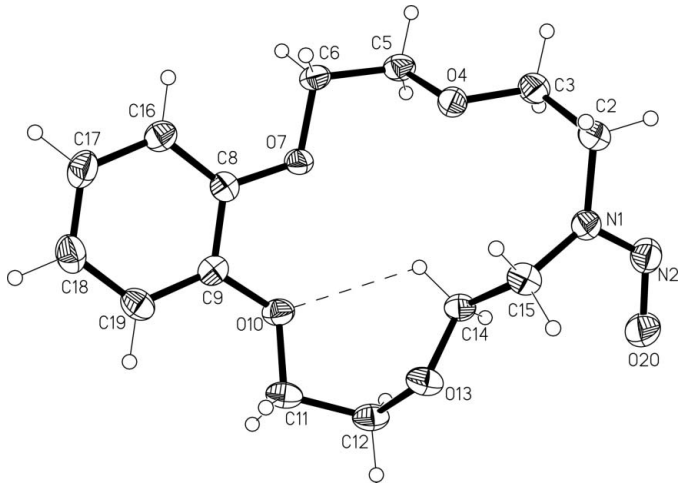


Figure 1
The structure of (I), viewed on the plane of the heteroatoms of the macrocyclic backbone. Displacement ellipsoids are drawn at the 50% probability level. The intramolecular hydrogen bond is shown as a dashed line.

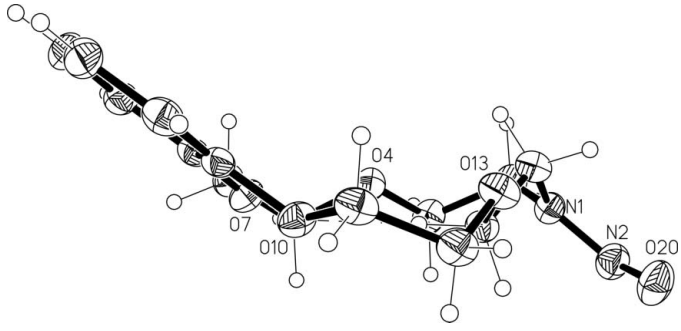


Figure 2
A side view of (I). Displacement ellipsoids are drawn at the 50% probability level.

Atom C14 is involved in an intramolecular C—H···O hydrogen bond with an O atom flanking the aromatic ring, C14···O10 3.090 (2) Å. This bond closes the six-membered intramolecular cycle (Fig. 1). The shape of the macrocyclic ring is similar to that found in 2,3-benzo-10-*N*-(4′-methoxyphenyl)-1,4,7,13-tetraoxa-10-azacyclopentadecane (CSD refcode GIVFIA; Liu *et al.*, 1998), and *N*-(5-bromo-2-hydroxy-3-(hydroxymethyl)benzyl)-benzo-9-aza-15-crown-5 (VEHREF; Chen *et al.*, 1989). The rapprochement of C14 and O10 is probably dictated by the electrostatic repulsion induced by the N-substituent, in the present case by the polarized NO group.

The macrocyclic strand of the molecule displays a series of *anti*, *gauche* and one *cis* torsion angles for the C—C, C—O and C—N bonds (Table 1). The individual *X*—C—C—*X* segments are *gga*, *aga*, *acisa*, *agg*− and *aag*, with a very uncommon distribution of *anti* and *gauche* torsion angles around the heterocyclic framework.

The presence of the NO group in the predominant polarized form is evident from the N1—N2 bond length of 1.314 (2) Å, which is significantly shorter than the expected distance

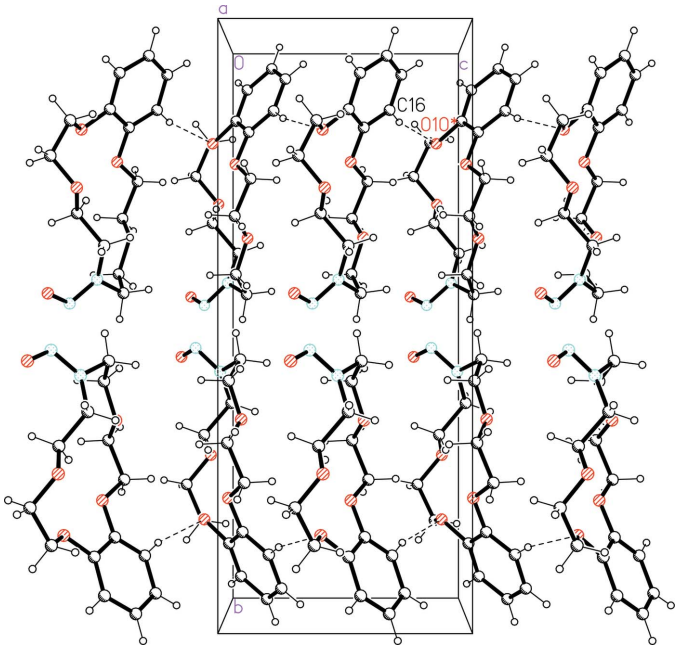


Figure 3
The packing of the molecules in (I) sustained by C—H···O hydrogen bonds. The O atom marked with an asterisk (*) is at the symmetry position $(\frac{1}{2}-x, y, \frac{1}{2}+z)$.

between pyramidal and planar N atoms [1.420 (2) Å; Allen *et al.*, 1987]. The N2—O20 distance is 1.244 (3) Å and the N1—N2—O20 angle is 114.62 (17)°. The geometry of the N—NO group is similar to those observed in related compounds, as is evident from a survey of the CSD. Our search found 121 hits for organic compounds containing an *N*-nitroso group. We selected 55 hits with $R < 0.05$ and analysed the geometry of the *N*-nitroso group, and the results are depicted in Fig. 4. The geometric parameters in (I) fall in the most populated ranges, both for the N—N and N═O bond distances and for the N—N═O angle.

The crystal packing of (I) reveals an intermolecular hydrogen bond of the type C—H···O [C16—H16···O10, with C···O 3.458 (2) Å], which combines the molecules into polar chains running along the *c* direction (Fig. 3). Two neighbouring chains in the unit cell meet each other in a face-to-face fashion *via* their nitroso groups, although specific contacts between them are absent, except for van der Waals contacts.

Experimental

8,9-Benzo-1-aza-4,7,10,13-tetraoxacyclopentadeca-8-ene (2.67 g, 0.01 mol) was dissolved in a minimal amount of acetic acid and then added to an aqueous saturated solution (~5 ml) of sodium nitrite (3.45 g, 0.05 mol). The crude precipitate of (I) was filtered off (yield 2.5 g, 86%; m.p. 353 K). Diffraction-quality crystals were obtained by recrystallization of the crude product from a mixture of ethanol and ethyl acetate (1:2) (m.p. 358–360 K). ^{1}H NMR (DMSO-d_6, 300 MHz, δ, p.p.m.): 2.72 (*m*, 4H, CH_2N), 3.48, 3.80, 4.12 (*m*, 12H, CH_2), 6.67 and 6.74 (*m*, 4H, CH).

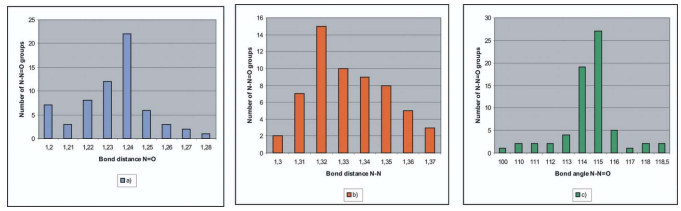


Figure 4
The distribution of the bond distances, (*a*) N═O and (*b*) N—N, and (*c*) the bond angles N—N═O in metal-free *N*-nitroso compounds with $R < 0.05$.

Crystal data

$C_{14}H_{20}N_2O_5$
$M_r = 296.32$
Orthorhombic, $Pca2_1$
$a = 8.3002$ (6) Å
$b = 20.6868$ (14) Å
$c = 8.5584$ (6) Å
$V = 1469.52$ (18) Å^3
$Z = 4$
$D_x = 1.339$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3505 reflections
$\theta = 4$–$25°$
$\mu = 0.10$ mm^{-1}
$T = 130$ (2) K
Prism, colourless
0.25 × 0.20 × 0.20 mm

Data collection

Kuma KM-4 CCD area-detector diffractometer
ω scans
Absorption correction: none
10917 measured reflections
1402 independent reflections
1349 reflections with $I > 2\sigma(I)$
$R_{int} = 0.031$
$\theta_{max} = 25.1°$
$h = -9 \rightarrow 9$
$k = -24 \rightarrow 24$
$l = -10 \rightarrow 7$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.029$
$wR(F^2) = 0.071$
$S = 1.07$
1402 reflections
190 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0543P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.16$ e Å^{-3}
$\Delta\rho_{min} = -0.17$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N2—O20	1.244 (3)	N1—C2	1.459 (3)
N2—N1	1.314 (2)	N1—C15	1.460 (3)
O20—N2—N1	114.62 (17)	C2—N1—C15	123.19 (17)
N2—N1—C2	114.46 (16)	N1—C2—C3	113.25 (17)
N2—N1—C15	121.32 (17)		
N1—C2—C3—O4	68.5 (2)	C9—O10—C11—C12	−158.03 (16)
C2—C3—O4—C5	−173.97 (17)	O10—C11—C12—O13	66.7 (2)
C3—O4—C5—C6	−175.59 (17)	C11—C12—O13—C14	−95.9 (2)
O4—C5—C6—O7	−65.9 (2)	C12—O13—C14—C15	−175.78 (16)
C5—C6—O7—C8	173.99 (15)	O13—C14—C15—N1	158.29 (16)
C6—O7—C8—C9	−174.75 (16)	C14—C15—N1—C2	111.8 (2)
O7—C8—C9—O10	−0.1 (2)	C15—N1—C2—C3	−83.9 (2)
C8—C9—O10—C11	155.22 (16)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C14—H14*A*···O10	0.97	2.52	3.090 (2)	118
C16—H16···O10^{i}	0.93	2.55	3.457 (3)	166

Symmetry code: (i) $-x+\frac{1}{2}, y, z+\frac{1}{2}$.

Determination of the absolute structure has not been carried out, due to the absence of significant anomalous dispersion. H atoms were generated in their ideal positions and their parameters were constrained during the refinement [C—H = 0.97 Å, C—H = 0.93 Å and U_{iso}(H) = 1.2 U_{eq}(C)].

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2000); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2000); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

The authors thank Dr S. Basok for the gift of the initial crown ether, Professor M. Gdaniec for collecting the data, and the Faculty of Chemistry, Adam Mickiewicz University, Poznan, Poland, for the use of their equipment.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
Bian, Z. Q., Li, F. Y., Jin, L. P., Guo, J. Q., Wang, K. Z. & Yang, M. S. (2001). *J. Mol. Struct.* **597**, 121–127.
Chen, Y.-Z., Zhang, J.-G., Zhao, H.-M., Jiang, N. & Wu, D.-X. (1989). *Chin. J. Org. Chem.* p. 132. (In Chinese.)
Clegg, W., Cooper, P. J. & Lockhart, J. C. (1996). *Acta Cryst.* C**52**, 1795–1797.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Gokel, G. W. (1991). *Crown Ethers and Cryptands*. Cambridge: Royal Society of Chemistry.
Gokel, G. W., Leevy, W. M. & Weber, M. E. (2004). *Chem. Rev.* **104**, 2723–2750.
Hanson, I. R. (1978). *Acta Cryst.* B**34**, 1026–1028.
Jourd'heuil, D., Kang, D. & Grisham, M. B. (1997). *Front. Biosci.* **2**, 189–196.
Landis, C. R., Sawyer, R. A. & Somsook, E. (2000). *Organometallics*, **19**, 994–1002.
Lijinsky, W. (1992). *Chemistry and Biology of N-Nitroso Compounds*. Cambridge University Press.
Liu, R. C. W., Fung, P.-S., Xue, F., Mak, T. C. W. & Ng, D. K. P. (1998). *J. Chem. Res. (S)*, pp. 414–415.
Oxford Diffraction (2000). *CrysAlis CCD* and *CrysAlis RED*. Versions 1.163. Oxford Diffraction Ltd., Abingdon, Oxfordshire, England.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Simonov, Y. A., Fonari, M. S., Duca, G. G., Gonta, M. V., Ganin, E. V., Yavolovskii, A. A., Gdaniec, M. & Lipkowski, J. (2005). *Tetrahedron*, **61**, 6596–6601.
Williams, D. L. H. & Aldred, S. E. (1982). *Food Chem. Toxicol.* **20**, 79–81.