

2,12-Dichloro-10,20-diphenyl-5,7,15,17-tetrahydro-6*H*,16*H*-dibenzo[*d,l*][1,9,2,6,10,14]dioxotetraazacyclohexadecine-6,16-dione solvate as a potential macrocyclic hexadentate ligand

Victor N. Khrustalev,^{a*} Eugene A. Komissarov^a and Oleg V. Kulikov^b

^aX-Ray Structural Centre, A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 Vavilov Street B-334, Moscow 119991, Russian Federation, and ^bMedicinal Chemistry Department, A. V. Bogatsky Physico-Chemical Institute of NAS of Ukraine, Lustdorfskaya doroga 86, 65089 Odessa, Ukraine

Correspondence e-mail: vkh@xray.ineos.ac.ru

Received 30 March 2007

Accepted 30 April 2007

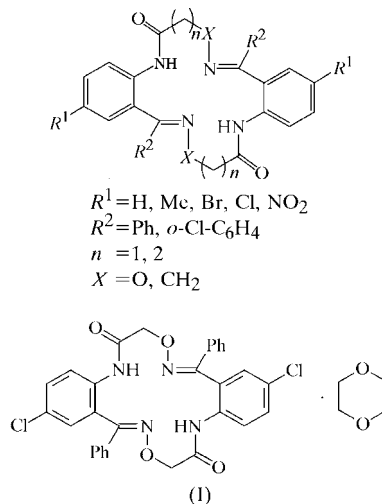
Online 14 June 2007

The macrocyclic title compound crystallizes as a dioxane solvate, $C_{30}H_{22}Cl_2N_4O_4 \cdot C_4H_8O_2$, with two independent formula units in the unit cell. The observed *syn* conformation is controlled by both intramolecular N—H...O hydrogen bonds and intermolecular C—H... π interactions. The relative macrocyclic inner bore is estimated to be 4.19 Å. In the crystal structure, molecules form dimers *via* intermolecular C—H... π interactions, and these dimers are, in turn, linked to form columns along the *a* axis by intermolecular C—H...O hydrogen bonds. Both X-ray diffraction analysis and density functional theory (DFT) calculations reveal that the macrocycle possesses very high flexibility. This property, as well as the presence of six donor atoms accessible for coordination, makes the title macrocycle a very promising ligand for complexation with the majority of transition metals.

Comment

Azamacrocyclic compounds are interesting macrocyclic objects with regard to their spatial structures, their self-assembly, chemical and coordination properties, and their biological activity (Hiraoka, 1978; Gokel & Korzeniowski, 1982; Gokel, 1991; Cooper, 1992; Bradshaw *et al.*, 1993; Lehn, 1995; Bradshaw & Izatt, 1997; Kulikov *et al.*, 2005). Recently, we have reported on the synthesis, crystal structure (Dvorkin *et al.*, 1985; Andronati *et al.*, 2005) and chemical properties (Kulikov *et al.*, 2003), in particular, complexation with lanthanides (Pavlovsky *et al.*, 2004; Rusakova *et al.*, 2005), of the 16- and 18-membered dibenzodioxatetraaza macrocycles shown in the scheme. We present here the investigation, by

experimental and theoretical methods, of the structural features of the macrocycle of the title solvate, (I), which are relevant to its complexation capabilities.



Two independent macrocycles, together with two dioxane molecules, are found in the asymmetric unit of (I), *i.e.* the macrocyclic ligand crystallizes as a solvate with dioxane in a 1:1 ratio. The structure of the macrocycles of (I) are shown in Fig. 1. The main difference between the two macrocyclic molecules is only in the relative orientations of the phenyl groups (Fig. 2). Therefore, for the most part, only the geometry and conformation of one of the independent macrocycles is discussed.

The macrocycle of compound (I) has two O- and four N-donor atoms in the macrocyclic ring, two fused chloro-

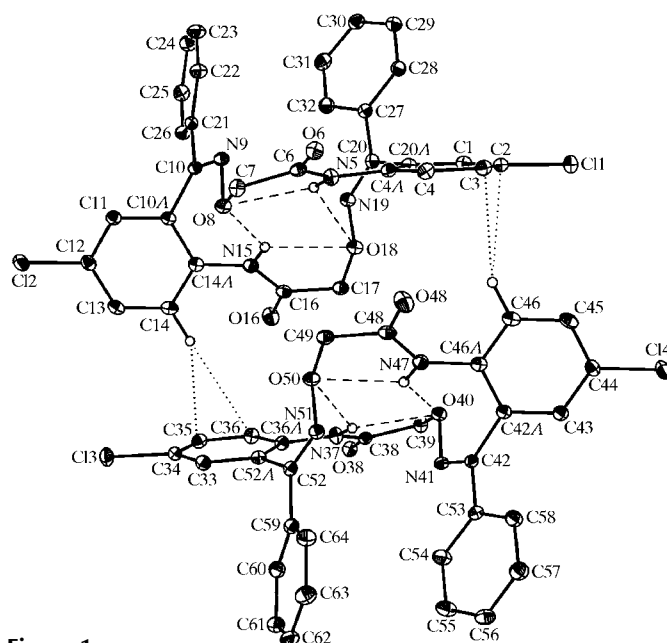


Figure 1

The two independent macrocycles of (I), showing the dimer formation *via* intermolecular C—H... π interaction (dotted lines). Intramolecular N—H...O hydrogen bonds are shown as dashed lines. The atom-numbering scheme is shown and displacement ellipsoids are drawn at the 40% probability level. The two dioxane solvent molecules and most of the H atoms have been omitted for clarity.

substituted benzene rings, and two carbonyl and two phenyl groups in the side chains. The bond lengths and angles fall within the expected ranges. The *syn* configuration at the C=N bond is unchanged compared with that in the starting material, *viz.* 2-chloroacetamidobenzophenone *syn*-oxime. Both amide groups have *E* configurations, which are apparently determined by intramolecular N—H···O hydrogen bonds (Table 1). It is noteworthy that the formation of an intramolecular hydrogen bond between a H atom of the amide group and the oxime O atom in a sterically unfavoured seven-membered ring has also been found in the previously described molecular structure of 5-bromo-2-propenoylaminobenzophenone *syn*-oxime (Andronati *et al.*, 2005). The angle between the planes formed by the two fused benzene rings is 79.0 (3)°. The phenyl substituents at atoms C10 and C20 are *syn* relative to the macrocyclic core. The interplanar angle between these phenyl rings is 37.2 (3)° [24.3 (3)° for the second independent macrocycle].

The conformational assignment for the macrocycle of (I) is close to $t-c-g^- - t-c-g^- - c-t-t-c-g^- - t-c-g^- - c-t$ ($t = 180^\circ$, $c = 0^\circ$ and $g = \pm 60^\circ$). The overall idealized symmetry of the macrocyclic ligand is C_2 , but the two bridged chains between the fused aromatic rings adopt different conformations. Although most of the corresponding dihedral angles of these chains are within 5° of each other, there are three dihedral angles which deviate considerably (Table 2). Moreover, except for the C6—C7—O8—N9 and C16—C17—O18—N19 torsion angles, the dihedral angles of the C4A/N5/C6/C7/O8/N9/C10/C10A chain around one side of the molecule are somewhat smaller in absolute value than the dihedral angles of the C14A/N15/C16/C17/O18/N19/C20/C20A chain along the other side of the molecule. The flexibility of the macrocycle allows it to adopt such an essentially puckered conformation, which is stabilized by both intramolecular N—H···O hydrogen bonds and intermolecular C—H··· π interactions (see below).

The intramolecular distances O8···O18 [3.979 (3) Å], N5···N15 [4.120 (3) Å] and N9···N19 [3.853 (3) Å] can be used to estimate the inner hole size of the macrocyclic ring. The dimensions of the macrocyclic bore, estimated to be twice as large as the mean distance from the donor atoms to their

centroid, is 4.19 Å, and is thus sufficiently large to accommodate many transition metal ions.

In the crystal structure, the two independent molecules of (I) form dimers *via* intermolecular C—H··· π interactions [H14A···C35 = 2.68 Å, H14A···C36 = 3.02 Å, H46A···C3 = 2.74 Å and H46A···C2 = 3.05 Å; these distances are given for the C14—H14A and C46—H46A bond lengths normalized to 1.05 Å (Fig. 1)]. The dimers, in turn, are linked into columns along the *a* axis by two intermolecular C—H···O hydrogen bonds (Table 1 and Fig. 3). The dioxane molecules apparently occupy the cavities between these columns in the unit cell and are bound to them *via* weak intermolecular C—H···O hydrogen bonds.

We used the *PRIRODA* program (Laikov, 1997) to perform quantum-chemical calculations for two different conformations of (I), namely *syn*, which is realised in the crystal, and *anti*. The geometry optimizations were carried out using the PBE generalized gradient function with C_1 symmetry and the TZ2P valence basis set. Vibration frequencies were used to characterize stationary points as minima. According to the calculations, both conformations correspond to minima of the potential energy surface, with a very small energy difference of

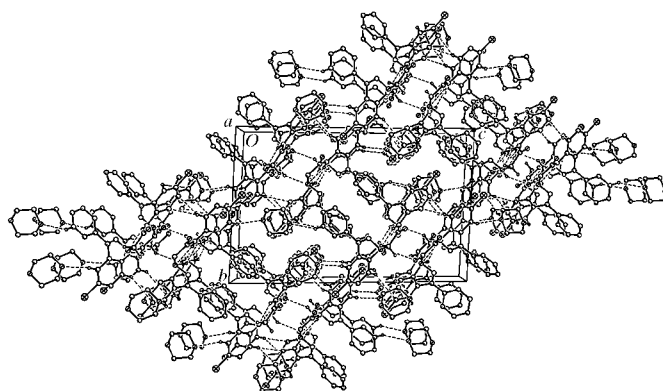


Figure 3
A packing diagram for (I), viewed along the *a* axis, showing the columns of dimers of the macrocycles and the arrangement of the dioxane solvent molecules. The orientation of the lower-occupancy disordered dioxane molecule is not presented. Only H atoms participating in the formation of hydrogen bonds are shown and hydrogen bonds are drawn as dashed lines.

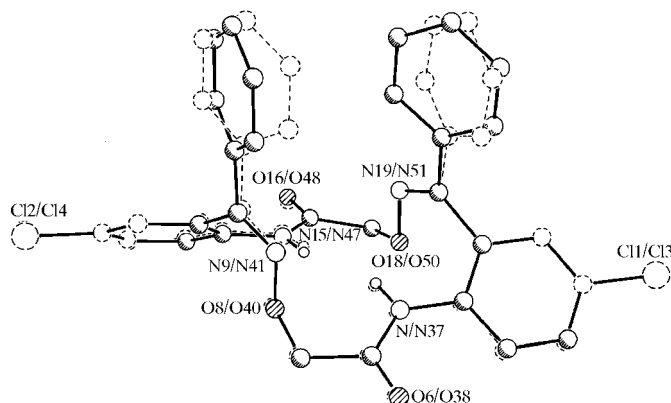


Figure 2
An overlay diagram, demonstrating the structural differences between the two symmetry-independent macrocyclic molecules of (I).

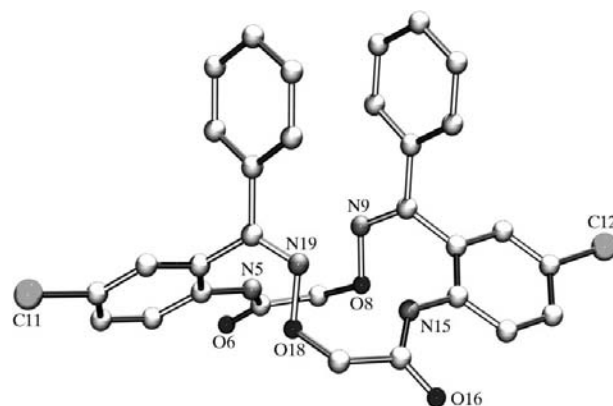


Figure 4
The calculated *syn* conformation for the macrocycle of (I).

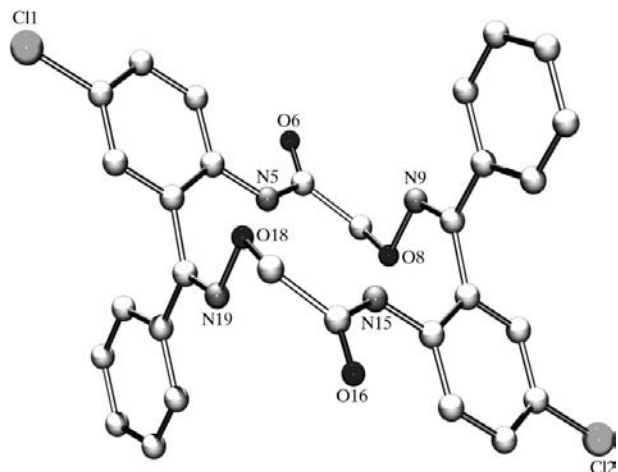


Figure 5
The calculated *anti* conformation for the macrocycle of (I).

2.2 kcal mol⁻¹ (1 kcal mol⁻¹ = 4.184 kJ mol⁻¹). It is very important to note that both the calculated *syn* and *anti* conformations of the macrocycle of (I) (Figs. 4 and 5) have intrinsic C₂ and C_s symmetries, respectively. We attribute the observed distortions of the macrocycle of (I) from C₂ symmetry in the crystal to the aforementioned intra- and intermolecular interactions. The results obtained prove that the macrocycle of (I) is highly flexible.

Thus, the data presented above show that the studied macrocycle of the title solvate, (I), is a good potential hexadentate ligand for complexation with transition metals. The presence of six donor atoms accessible for coordination and the high flexibility of the molecule, which allows it to adopt various conformations, make this compound a very promising ligand for complexation with the majority of transition metals. These investigations are currently in progress.

Experimental

A solution of NaOH (0.619 g, 15.48 mmol) in water (10 ml) was added dropwise with stirring to a solution of 2-chloroacetamidobenzophenone *syn*-oxime (5.0 g, 15.48 mmol) in dioxane (10 ml), and the mixture was stirred at room temperature overnight. The white solid that formed was separated by filtration. The crude product was purified by recrystallization from dioxane to give (I) as the dioxane solvate (yield 1.82 g, 41%; m.p. 589–590 K). ¹H NMR (DMSO-*d*₆): δ 4.44–4.73 (*dd*, *J* = 15.6 and 55.7 Hz, 4H), 7.10–7.58 (*m*, 16H), 9.83 (*s*, 2H); MS *m/z*: 572 (22) [*M*⁺], 270 (7), 257 (100), 228 (21), 192 (7); IR (CHCl₃, ν, cm⁻¹): 3400, 3000, 1680, 1600, 1500. Single crystals of solvate (I) suitable for X-ray structural analysis were grown from a dioxane solution by slow evaporation at room temperature.

Crystal data

C ₃₀ H ₂₂ Cl ₂ N ₄ O ₄ ·C ₄ H ₈ O ₂	γ = 92.476 (2)°
<i>M_r</i> = 661.52	<i>V</i> = 3034.1 (3) Å ³
Triclinic, <i>P</i> 1̄	<i>Z</i> = 4
<i>a</i> = 9.6834 (6) Å	Mo Kα radiation
<i>b</i> = 14.2960 (8) Å	μ = 0.27 mm ⁻¹
<i>c</i> = 22.2970 (13) Å	<i>T</i> = 120.0 (2) K
α = 92.389 (2)°	0.30 × 0.25 × 0.20 mm
β = 99.896 (3)°	

Data collection

Bruker SMART 1000 CCD area-detector diffractometer	31338 measured reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 1998)	14551 independent reflections
<i>T</i> _{min} = 0.928, <i>T</i> _{max} = 0.944	10236 reflections with <i>I</i> > 2σ(<i>I</i>)
	<i>R</i> _{int} = 0.025

Refinement

<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)] = 0.046	28 restraints
<i>wR</i> (<i>F</i> ²) = 0.126	H-atom parameters constrained
<i>S</i> = 1.02	Δρ _{max} = 0.56 e Å ⁻³
14551 reflections	Δρ _{min} = -0.37 e Å ⁻³
874 parameters	

Table 1

Hydrogen-bond geometry (Å, °).

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
N5—H5A...O8	0.88	2.28	2.734 (2)	112
N5—H5A...O18	0.88	2.48	3.043 (2)	122
N5—H5A...N9	0.88	2.44	2.990 (2)	121
N5—H5A...N19	0.88	2.59	3.232 (2)	131
N15—H15A...O8	0.88	2.30	2.935 (2)	129
N15—H15A...O18	0.88	2.30	2.740 (2)	111
N37—H37A...O40	0.88	2.28	2.737 (2)	112
N37—H37A...O50	0.88	2.42	3.001 (2)	124
N37—H37A...N41	0.88	2.45	2.974 (2)	119
N37—H37A...N51	0.88	2.60	3.235 (2)	130
N47—H47A...O40	0.88	2.37	2.985 (2)	128
N47—H47A...O50	0.88	2.28	2.731 (2)	112
C1—H1A...O65 ⁱ	0.95	2.50	3.200 (2)	130
C7—H7A...O38 ⁱⁱ	0.99	2.31	3.206 (2)	150
C11—H11A...O74 ⁱⁱⁱ	0.95	2.45	3.284 (3)	147
C33—H33A...O71 ⁱⁱ	0.95	2.55	3.241 (4)	130
C39—H39B...O6 ^v	0.99	2.36	3.236 (2)	148
C43—H43A...O68 ^v	0.95	2.37	3.249 (2)	154
C57—H57A...O71 ^v	0.95	2.52	3.349 (4)	146

Symmetry codes: (i) *x*, *y* - 1, *z*; (ii) *x* + 1, *y*, *z*; (iii) -*x* + 1, -*y* + 1, -*z*; (iv) *x* - 1, *y*, *z*; (v) -*x* + 1, -*y* + 1, -*z* + 1.

Table 2

Selected torsion angles (°).

C20A—C4A—N5—C6	-162.32 (17)	C52A—C36A—N37—C38	157.50 (17)
C4A—N5—C6—C7	-172.34 (16)	C36A—N37—C38—C39	175.66 (16)
N5—C6—C7—O8	-4.5 (2)	N37—C38—C39—O40	5.1 (2)
C6—C7—O8—N9	-73.11 (17)	C38—C39—O40—N41	71.96 (17)
C7—O8—N9—C10	-159.68 (14)	C39—O40—N41—C42	162.55 (14)
O8—N9—C10—C10A	0.8 (2)	O40—N41—C42—C42A	-4.0 (2)
N9—C10—C10A—C14A	-66.2 (2)	N41—C42—C42A—C46A	73.0 (2)
C10—C10A—C14A—N15	3.6 (3)	C42—C42A—C46A—N47	-5.7 (2)
C10A—C14A—N15—C16	-145.44 (18)	C42A—C46A—N47—C48	151.21 (18)
C14A—N15—C16—C17	-177.46 (16)	C46A—N47—C48—C49	177.25 (17)
N15—C16—C17—O18	-16.0 (2)	N47—C48—C49—O50	11.2 (2)
C16—C17—O18—N19	-69.74 (18)	C48—C49—O50—N51	72.36 (18)
C17—O18—N19—C20	-162.92 (14)	C49—O50—N51—C52	160.72 (14)
O18—N19—C20—C20A	4.1 (2)	O50—N51—C52—C52A	-1.3 (2)
N5—C4A—C20A—C20	6.3 (2)	N37—C36A—C52A—C52	-3.4 (3)
N19—C20—C20A—C4A	-75.8 (2)	N51—C52—C52A—C36A	69.3 (2)

H atoms were placed in calculated positions and refined using a riding model, with C—H = 0.95 or 0.99 Å and N—H = 0.88 Å, and with fixed displacement parameters [*U*_{iso}(H) = 1.2*U*_{eq}(C,N)]. The asymmetric unit contains two dioxane solvent molecules, one of which is disordered over two sites with occupancies of 0.6 and 0.4. 28 distance restraints were used to fit the ideal chair conformations for both orientations of the disordered dioxane molecule. 73 reflections, with experimentally observed *F*² deviating significantly from the theoretically calculated *F*², were omitted from the refinement.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT-Plus* (Bruker, 1998); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1998); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: LN3049). Services for accessing these data are described at the back of the journal.

References

- Andronati, S. A., Simonov, Yu. A., Pavlovsky, V. I., Kulikov, O. V., Gdanec, M. & Mazepa, A. V. (2005). *Russ. J. Gen. Chem.* **75**, 915–922.
- Bradshaw, J. S. & Izatt, R. M. (1997). *Acc. Chem. Res.* **30**, 338–345.
- Bradshaw, J. S., Krakowiak, K. E. & Izatt, R. M. (1993). In *Aza-Crown Macrocycles*. New York: Wiley.
- Bruker (1998). *SAINT-Plus* (Version 6.01) and *SMART* (Version 5.059). Bruker AXS Inc., Madison, Wisconsin, USA.
- Cooper, S. R. (1992). In *Crown Compounds: Toward Future Applications*. Weinheim: VCH.
- Dvorkin, A. A., Malinowsky, T. I., Simonov, Yu. A., Andronati, S. A., Kuzmina, A. V. & Yavorsky, A. S. (1985). *Acta Cryst.* **C41**, 796–798.
- Gokel, G. W. (1991). In *Crown Ethers and Cryptands*. Cambridge: Royal Society of Chemistry.
- Gokel, G. W. & Korzeniowski, S. H. (1982). In *Macrocyclic Polyether Syntheses*. Berlin: Springer.
- Hiraoka, M. (1978). In *Crown Compounds: Their Characteristics and Applications*. Tokyo: Kodansha.
- Kulikov, O. V., Pavlovsky, V. I. & Andronati, S. A. (2005). *Chem. Heterocycl. Compd.* **462**, 1763–1795.
- Kulikov, O. V., Pavlovsky, V. I., Mazepa, A. V. & Andronati, S. A. (2003). *Chem. Heterocycl. Compd.* **430**, 566–573.
- Laikov, D. N. (1997). *Chem. Phys. Lett.* **281**, 151–156.
- Lehn, J.-M. (1995). In *Supramolecular Chemistry: Concepts and Perspectives*. Weinheim: VCH.
- Pavlovsky, V. I., Kulikov, O. V., Ruskova, N. V., Andronati, S. A. & Korovin, Yu. V. (2004). *Russ. Chem. Bull.* **53**, 791–794.
- Ruskova, N. V., Pavlovsky, V. I., Kulikov, O. V., Andronati, S. A., Korovin, Yu. V. & Kost, S. S. (2005). *Russ. J. Inorg. Chem.* **50**, 1516–1520.
- Sheldrick, G. M. (1998). *SADABS* (Version 2.01) and *SHELXTL* (Version 5.10). Bruker AXS Inc., Madison, Wisconsin, USA.