Bis[1-(*p*-chlorophenyl)-5-iso-propylbiguanide-$\kappa^2 N^2, N^4$]nickel(II) dichloride dimethylformamide solvate

F. Bentefrit,^{a} P. Lemoine,^{b} D. Nguyen-Huy,^{a} G. Morgant^a and B. Viossat^{b,c}*

^{a}Laboratoire de Cristallochimie Bioinorganique, Faculté des Sciences Pharmaceutiques et Biologiques, Université de Paris XI, 5 rue J. B. Clément, 92296 Châtenay Malabry Cedex, France, ^{b}Laboratoire de Cristallographie et RMN Biologiques, Faculté des Sciences Pharmaceutiques et Biologiques, Université de Paris V, UMR 8015 CNRS, 4 avenue de l'Observatoire, 75270 Paris Cedex 06, France, and ^{c}Laboratoire de Chimie Générale, Faculté de Médecine et de Pharmacie, 34 rue du Jardin des Plantes, BP199, 86005 Poitiers Cedex, France

Correspondence e-mail: viossat@pharmacie.univ-paris5.fr

The asymmetric unit of the title compound, [Ni(C$_{11}$H$_{16}$Cl-N$_5$)$_2$]Cl$_2$·C$_3$H$_7$NO, contains one monomeric nickel(II) complex cation, two Cl$^-$ anions and one dimethylformamide solvent molecule. The Ni atom is coordinated to each of two 1-(*p*-chlorophenyl)-5-isopropylbiguanide (proguanil) ligands *via* two N atoms. The complex exhibits a square-planar coordination, with the Ni atom lying 0.021 (2) Å out of the basal plane. The crystal packing is characterized by several hydrogen bonds.

Comment

Proguanil, or 1-(*p*-chlorophenyl)-5-isopropylbiguanide, an antimalarial drug used worldwide, is characterized by different tautomeric forms, one of which is stabilized upon complexation. This fact prompted us to synthesize new complexes of 3*d* elements with a view to modulating the pharmacological properties of the free ligand. The asymmetric unit of the title compound, (I), consists of one Ni^{II} atom, two proguanil ligands, two Cl$^-$ anions and one dimethylformamide (DMF) solvent molecule.

(I)
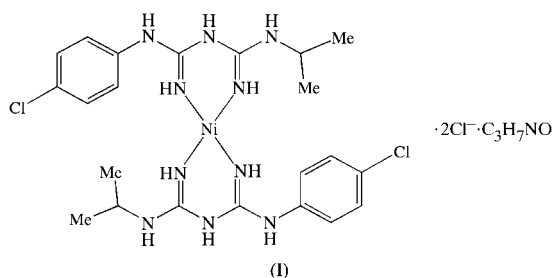
The Ni^{II} atom exhibits a square-planar coordination, built from two bidentate proguanil ligands *via* biguanidyl atoms N2

and N4 in the first ligand and biguanidyl atoms N22 and N24 in the second ligand (Fig. 1). The same square-planar geometry was observed in bis(2-guanidinobenzimidazole)nickel(II) dinitrate (Barba-Behrens *et al.*, 1996) and bis(biguanidino)-nickelate(II):6,7-dimethoxyquinazoline-2,4(1*H*,3*H*)-dione (Bishop *et al.*, 2002). The Ni—N bond lengths are all equivalent [within 2 s.u.; mean 1.864 (3) Å] and the angles at the Ni atom are in the range 89.6 (1)–90.5 (1)° (Table 1). These values agree with those found in bis(*N,N*-dimethylbiguanide)nickel(II) salicylate (Lemoine *et al.*, 1996) and bis-(*N,N*-dimethylbiguanide)nickel(II) monohydroxide chloride (Lemoine *et al.*, 1999). The Ni atom lies 0.021 (2) Å out of the basal plane (*P1*; atoms N2/N4/N22/N24). The N2—C7—N3—C8—N4 and N22—C27—N23—C28—N24 atom sequences have nearly planar geometries (mean planes *P2* and *P3*, respectively), allowing delocalization of the π-electron system along them. The Ni^{II} atom is displaced 0.244 (4) and −0.459 (4) Å out of planes *P2* and *P3*, and the dihedral angle between these two planes is 32.05 (1)°. The Ni/N2/C7/N3/C8/N4 ring can be regarded as having a boat shape, with atoms Ni and N3 on the same side of the N2/C7/C8/N4 (*P4*) plane [0.234 (5) and 0.018 (5) Å, respectively]. The geometry is the same for the Ni/N22/C27/N23/C28/N24 ring, with atoms Ni and N23 being −0.380 (5) and −0.145 (5) Å, respectively, from plane *P5* (N22/C27/C28/N24). These configurations are similar to those described for bis(2-guanidinobenzimidazole)nickel(II) dinitrate (Barba-Behrens *et al.*, 1996). The dihedral angle between plane *P2* and its attached phenyl ring (C1–C6) is 70.0 (1)°, and the corresponding dihedral angle for *P3* and C21–C26 is 76.3 (1)°. The two halves of each biguanide group are planar, with atom C7 lying 0.011 (4)° out of plane *P6*
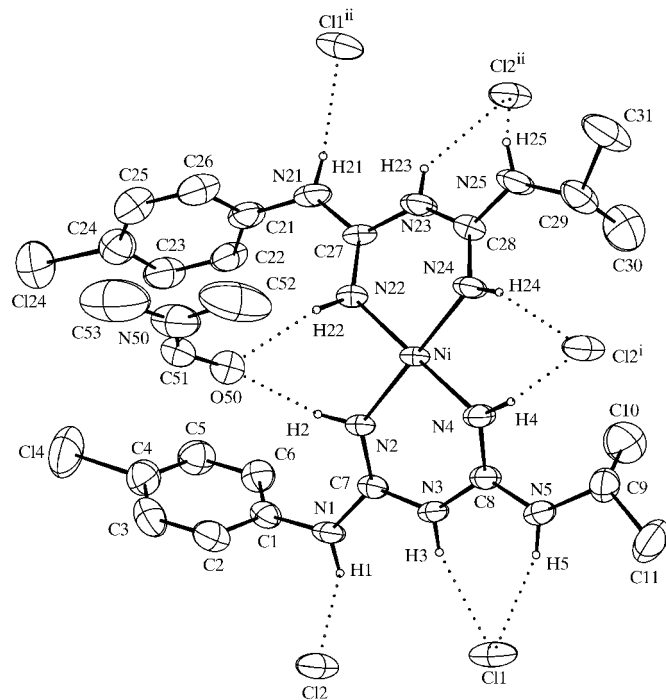

Figure 1
A *CAMERON* (Watkin *et al.*, 1996) drawing of the molecule of (I), showing the atom-numbering system and hydrogen bonding (dotted lines). Displacement ellipsoids are shown at the 50% probability level for non-H atoms. [Symmetry codes: (i) −*x*, −*y*, −*z*; (ii) ½ − *x*, ½ + *y*, −*z*.]

(N1/N2/N3) and atom C8 lying 0.001 (4) Å out of plane $P7$ (N3/N4/N5) [the corresponding out-of-plane distances for the other group are 0.002 (4) Å for atom C27 and plane $P8$ (N21/ N22/N23), and 0.011 (4) Å for atom C28 and plane $P9$ (N23/ N24/N25)]. The dihedral angle between planes $P6$ and $P7$ is 5.9 (3)° and that between planes $P8$ and $P9$ is 15.0 (3)°. Thus, the biguanide moiety in each bidentate proguanil ligand is almost planar. In contrast, the corresponding dihedral angle between the homologous Ni atoms in the crystal structure of 1-(p-chlorophenyl)-5-isopropylbiguanide hydrochloride (Brown, 1967) is 58.9°, a value that is characteristic of a non-planar molecule. In (I), the corresponding distances in the two proguanil ligands are all equivalent (within 3 s.u.) except for the C9—C11 [1.503 (5) Å] and C29—C31 [1.530 (5) Å] distances in the terminal methyl groups. The C1—N1—C7—N2 [−4.5 (5)°] and C9—N5—C8—N4 [17.0 (6)°] torsion angles in the first proguanil ligand, and the C21—N21—C27—N22 [−3.3 (7)°] and C29—N25—C28—N24 [−13.0 (6)°] torsion angles in the second ligand, show that this conformation remains synperiplanar upon metallation. The same conformation was found for the corresponding atomic set in PdCl₂(proguanil) (Bentefrit *et al.*, 2002), but in proguanil hydrochloride (Brown, 1967), the conformation was anti-periplanar (the C—N—C—N torsion angles being 164.1 and 164.5°). The DMF solvent molecule exhibits some disorder in the terminal methyl groups, as shown by its U_{eq} values. The crystal packing is characterized by several intra- and inter-molecular hydrogen bonds, which involve, in particular, the DMF solvent molecule with each ligand of the same complex (Table 2 and Fig. 2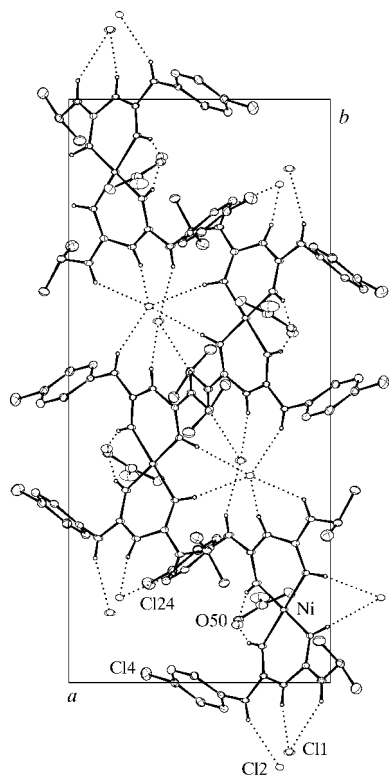), in contrast to the hydrogen bonds ob-served in bis(biguanidino)nickelate(II)–6,7-dimethoxyquin-azoline-2,4(1H,3H)-dione, in which the dimethyl sulfoxide solvent molecule acts as a bridge between two neighbouring complexes (Bishop *et al.*, 2002). In (I), atom Cl1 participates in three hydrogen bonds to two proguanil entities, while atom Cl2 is involved in five hydrogen bonds to three different complexes.

In addition, the crystalline cohesion is ensured by numerous van der Waals contacts, the shortest being C26···C52[iii] [3.41 (2) Å; symmetry code: (iii) $\frac{1}{2} + x, \frac{1}{2} - y, z$].

Experimental

The title compound was obtained by dissolving proguanil hydro-chloride in DMF to a concentration of 0.2 mol l⁻¹ (4×10^{-4} mol) and adding nickel chloride hexahydrate in DMF to a concentration of 0.1 mol l⁻¹ (2×10^{-4} mol). This hydrochloric mixture was neutra-lized with a sodium hydroxide solution (4×10^{-4} mol). After mixing and heating (323 K) for 2 h and slow evaporation, orange crystals were obtained under ambient pressure.

Crystal data

[Ni(C₁₁H₁₆ClN₅)₂]Cl₂·C₃H₇NO	D_m measured by flotation in
$M_r = 710.18$	CHCl₃/CH₂Cl₂
Monoclinic, $P2_1/a$	Mo $K\alpha$ radiation
$a = 10.824$ (5) Å	Cell parameters from 25
$b = 24.12$ (1) Å	reflections
$c = 13.180$ (3) Å	$\theta = 7.0$–11.1°
$\beta = 95.42$ (3)°	$\mu = 0.92$ mm⁻¹
$V = 3426$ (2) Å³	$T = 293$ (2) K
$Z = 4$	Parallelepiped, orange
$D_x = 1.377$ Mg m⁻³	$0.45 \times 0.37 \times 0.10$ mm
$D_m = 1.38$ Mg m⁻³	

Data collection

Enraf–Nonius CAD-4	3270 reflections with $I > 2\sigma(I)$
diffractometer	$R_{int} = 0.061$
$\omega/2\theta$ scans	$\theta_{max} = 25.0°$
Absorption correction: multi-scan	$h = -12 \rightarrow 12$
(*SADABS*; Sheldrick, 1996;	$k = 0 \rightarrow 28$
Blessing, 1995)	$l = -15 \rightarrow 15$
$T_{min} = 0.648$, $T_{max} = 0.883$	3 standard reflections
11 970 measured reflections	frequency: 60 min
6000 independent reflections	intensity decay: 2%

Table 1
Selected geometric parameters (Å, °).

Ni—N4	1.859 (3)	N4—C8	1.307 (4)
Ni—N22	1.861 (3)	N5—C8	1.327 (4)
Ni—N2	1.866 (3)	N21—C27	1.351 (4)
Ni—N24	1.869 (3)	N23—C27	1.358 (4)
N1—C7	1.367 (4)	N23—C28	1.370 (4)
N2—C7	1.293 (4)	N24—C28	1.299 (4)
N3—C7	1.357 (4)	N25—C28	1.345 (4)
N3—C8	1.368 (4)		
N4—Ni—N22	177.55 (13)	N2—C7—N1	124.2 (3)
N4—Ni—N2	89.65 (12)	N3—C7—N1	114.2 (3)
N22—Ni—N2	90.53 (12)	N4—C8—N5	125.3 (3)
N4—Ni—N24	90.23 (12)	N4—C8—N3	120.1 (3)
N22—Ni—N24	89.58 (13)	N5—C8—N3	114.5 (3)
N2—Ni—N24	179.79 (13)	N22—C27—N21	125.1 (3)
C7—N2—Ni	130.0 (2)	N22—C27—N23	121.1 (3)
C7—N3—C8	126.5 (3)	N21—C27—N23	113.8 (3)
C8—N4—Ni	129.9 (2)	N24—C28—N25	125.6 (3)
C27—N22—Ni	128.5 (3)	N24—C28—N23	120.1 (3)
C28—N24—Ni	128.6 (3)	N25—C28—N23	114.3 (3)
N2—C7—N3	121.6 (3)		

Figure 2
The packing of the unit cell of (I), projected along the c axis.

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

$D-\mathrm{H}\cdots A$	$D-\mathrm{H}$	$\mathrm{H}\cdots A$	$D\cdots A$	$D-\mathrm{H}\cdots A$
N1—H1$\cdots$Cl2	0.86	2.54	3.184 (3)	133
N2—H2$\cdots$O50	0.86	2.19	2.981 (4)	153
N3—H3$\cdots$Cl1	0.86	2.39	3.212 (3)	161
N4—H4$\cdots$Cl2$^{\mathrm{i}}$	0.86	2.54	3.394 (3)	170
N5—H5$\cdots$Cl1	0.86	2.48	3.253 (3)	149
N21—H21$\cdots$Cl1$^{\mathrm{ii}}$	0.86	2.36	3.138 (3)	151
N22—H22$\cdots$O50	0.86	2.13	2.957 (4)	160
N23—H23$\cdots$Cl2$^{\mathrm{ii}}$	0.86	2.62	3.358 (3)	145
N24—H24$\cdots$Cl2$^{\mathrm{i}}$	0.86	2.61	3.454 (3)	169
N25—H25$\cdots$Cl2$^{\mathrm{ii}}$	0.86	2.67	3.213 (3)	123
N2—H2$\cdots$O50	0.86	2.19	2.981 (4)	153
N22—H22$\cdots$O50	0.86	2.13	2.957 (4)	160

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

Refinement

Refinement on F^2	H-atom parameters constrained
$R(F) = 0.040$	$w = 1/[\sigma^2(F_o^2) + (0.0724P)^2]$
$wR(F^2) = 0.110$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 0.96$	$(\Delta/\sigma)_{max} = 0.001$
6000 reflections	$\Delta\rho_{max} = 0.37$ e Å^{-3}
417 parameters	$\Delta\rho_{min} = -0.69$ e Å^{-3}

All H atoms were placed at idealized positions as riding atoms (aromatic C—H = 0.93 Å, methine C—H = 0.93 Å, methyl C—H = 0.96 Å and N—H = 0.86 Å). A disordered model was applied for the DMF solvent molecule based on a 60:40 distribution of the $\mathrm{NMe_2}$ group over two sites related by a pseudo-twofold axis.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *XCAD*4 (Harms &

Wocadlo, 1995); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *CAMERON* (Watkin *et al.*, 1996); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

References

Altomare, A., Cascarano, G., Giacovazzo, G., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.

Barba-Behrens, N., Vasquez-Olmos, A., Castillo-Blum, S. E., Hojer, G., Meza-Hojer, S. & Hernandez, R. M. (1996). *Transition Met. Chem.* **21**, 31–37.

Bentefrit, F., Tomas, A., Morgant, G., Nguyen-Huy, D., Lemoine, P. & Viossat, B. (2002). *Z. Kristallogr. New Cryst. Struct.* **217**, 505–506.

Bishop, M. M., Lindoy, L. F., Skelton, B. W. & White, A. H. (2002). *J. Chem. Soc. Dalton Trans.* pp. 377–382.

Blessing, R. H. (1995). *Acta Cryst.* A**51**, 33–38.

Brown, C. J. (1967). *J. Chem. Soc. A*, pp. 60–65.

Enraf–Nonius (1994). *CAD-4 EXPRESS*. Enraf–Nonius, Delft, The Netherlands.

Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.

Harms, K. & Wocadlo, S. (1995). *XCAD*4. University of Marburg, Germany.

Lemoine, P., Chiadmi, M., Bissery, V., Tomas, A. & Viossat, B. (1996). *Acta Cryst.* C**52**, 1430–1436.

Lemoine, P., Tomas, A., Viossat, B. & Prangé, T. (1999). *Z. Kristallogr. New Cryst. Struct.* **214**, 369–370.

Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.

Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.

Watkin, D. J., Prout, C. K. & Pearce, L. J. (1996). *CAMERON*. Chemical Crystallography Laboratory, Oxford, England.