

## A new [(1*R*,2*R*)-1,2-diaminocyclohexane]platinum(II) complex: formation by nitrate–acetonitrile ligand exchange

Richard Pažout,<sup>a\*</sup> Jitka Housková,<sup>a</sup> Michal Dušek,<sup>b</sup>  
Jaroslav Maixner,<sup>a</sup> Jana Cibulková<sup>a</sup> and Petr Kačer<sup>a</sup>

<sup>a</sup>Institute of Chemical Technology, Technická 5, Prague 166 28, Czech Republic, and <sup>b</sup>Institute of Physics, Czech Academy of Sciences, Na Slovance 2, 18221

Prague 8, Czech Republic

Correspondence e-mail: richard.pazout@vscht.cz

Received 17 May 2010

Accepted 17 August 2010

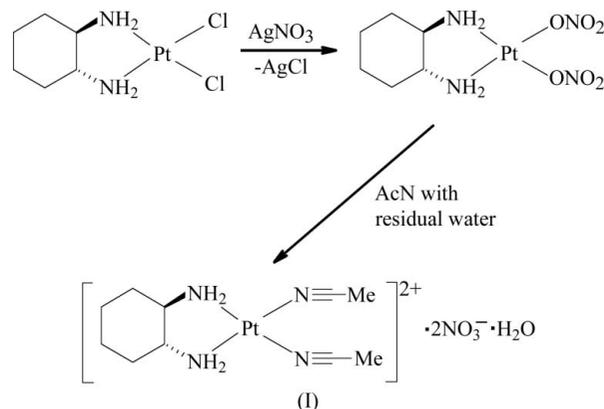
Online 4 September 2010

The title compound, *cis*-diacetonitrile[(1*R*,2*R*)-1,2-diaminocyclohexane- $\kappa^2N,N'$ ]platinum(II) dinitrate monohydrate, [Pt(C<sub>2</sub>H<sub>3</sub>N)<sub>2</sub>(C<sub>6</sub>H<sub>14</sub>N<sub>2</sub>)](NO<sub>3</sub>)<sub>2</sub>·H<sub>2</sub>O, is a molecular salt of the diaminocyclohexane–Pt complex cation. There are two formula units in the asymmetric unit. Apart from the two charge-balancing nitrate anions, one neutral molecule of water is present. The components interact *via* N–H···O and O–H···O hydrogen bonds, resulting in supramolecular chains. The title compound crystallizes only from acetonitrile with residual water, with the acetonitrile coordinating to the molecule of *cis*-[Pt(NO<sub>3</sub>)<sub>2</sub>(DACH)] (DACH is 1,2-diaminocyclohexane) and the water forming a monohydrate.

### Comment

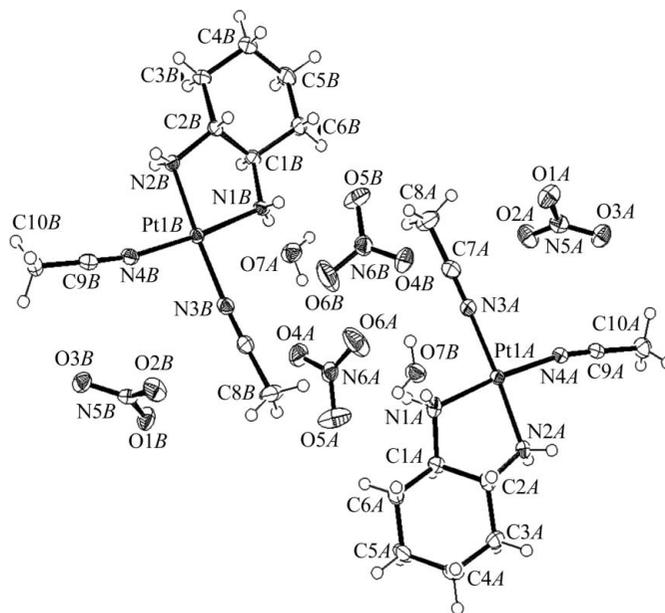
The search for novel platinum-based anticancer complexes remains an expanding area of the contemporary pharmaceutical industry. The driving force for investigations of this group of active anticancer therapeutics is the discovery of more active and less toxic analogues of the chemotherapy complexes used in today's clinical practice (cisplatin, carboplatin, oxaliplatin, *etc.*) (Ho *et al.*, 2003; Galanski *et al.*, 2003; Abu-Surrah & Kettunen, 2006). Some of the novel structures are based on the platinum (1*R*,2*R*)-1,2-diaminocyclohexane (DACH) carrier ligand and various leaving groups bound to the central Pt metal atom. There are several synthetic routes used for the preparation of DACH–platinum-based complexes (Fuentes *et al.*, 2004; Leh & Wolf, 1976). One of the interesting routes for the preparation of oxaliplatin, AP5346 and other DACH–Pt complexes is the synthetic method starting from *cis*-[Pt(NO<sub>3</sub>)<sub>2</sub>(DACH)]. This compound is a valuable precursor of the DACH–Pt-based cytostatics (Pasini *et al.*, 1993). This is prepared by a simple method where *cis*-[PtCl<sub>2</sub>(DACH)], prepared by the quantitative transformation

of DACH with K<sub>2</sub>[PtCl<sub>4</sub>], reacts with silver nitrate. The title compound, (I), crystallizes only from acetonitrile with residual water in such a way that the molecule forms a monohydrate.

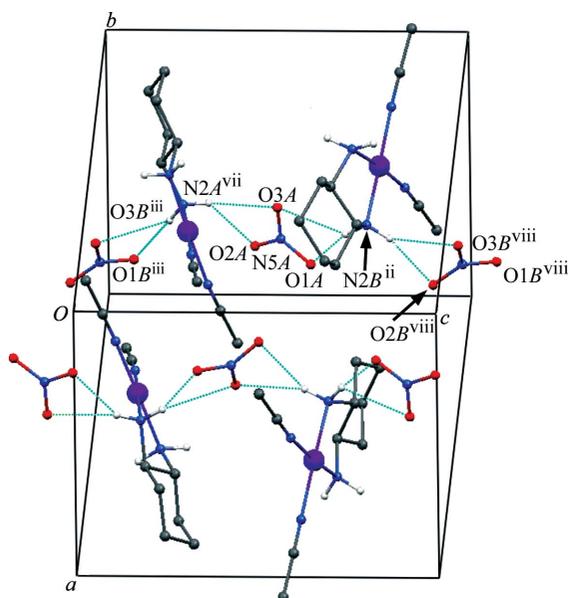


The single-crystal structure of (I) is built up from discrete moieties in the monoclinic space group *P*<sub>2</sub><sub>1</sub>, with two formula units in the asymmetric unit. The [Pt(C<sub>2</sub>H<sub>3</sub>N)<sub>2</sub>(C<sub>6</sub>H<sub>14</sub>N<sub>2</sub>)]<sup>2+</sup> complex cation is formed by one cyclohexane ring with a chair conformation, a five-membered diamine ring, a central Pt atom and two leaving groups of acetonitrile (N≡C–CH<sub>3</sub>). This dication is balanced by two nitrate groups and one neutral water solvent molecule.

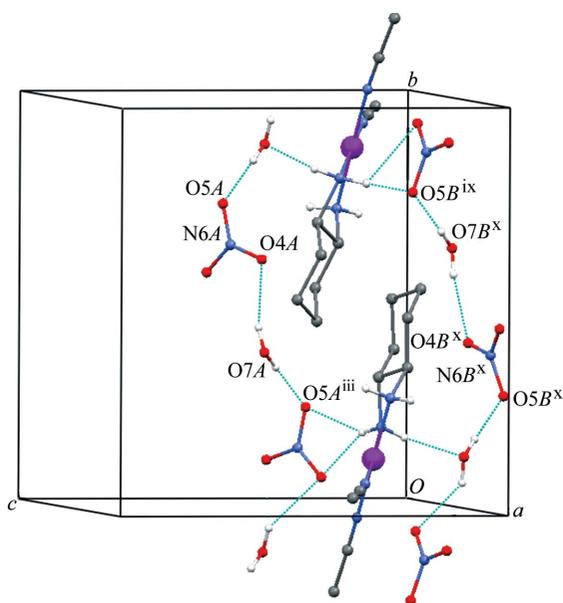
The [Pt(C<sub>2</sub>H<sub>3</sub>N)<sub>2</sub>(C<sub>6</sub>H<sub>14</sub>N<sub>2</sub>)]<sup>2+</sup> cation is nearly planar, with the dihedral angle between the N1A/N2A/N3A/N4A plane and the cyclohexane plane (C3A/C6A/N1A/N2A) being approximately 5°. The Pt1A–N1A bond is shorter than the same bond in *cis*-[PtBr<sub>2</sub>(DACH)] and similar to that in *cis*-[PtCl<sub>2</sub>(DACH)] (Lock & Pilon, 1981). As for the two symmetry-independent cations of (I), they show few significant differences in bond distances and angles, apart from the



**Figure 1**  
The molecular structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.



**Figure 2**  
Bifurcated hydrogen-bonded chains formed by N—H···(O,O) interactions along the *c* axis. H atoms not involved in the hydrogen bonding have been omitted for clarity. [Symmetry codes as in Table 1; additionally, (vii)  $-x, y - \frac{1}{2}, -z + 1$ ; (viii)  $-x + 1, y - \frac{1}{2}, -z + 2$ .]



**Figure 3**  
The formation of two types of hydrogen-bonded chains parallel to the *b* axis. [Symmetry codes as in Table 1; additionally, (ix)  $-x + 1, y + \frac{1}{2}, -z + 1$ ; (x)  $x, y, z - 1$ .]

analogous Pt1—N3—C7 angles, which are 178.6 (3) (cation *A*) and 174.1 (3)° (cation *B*). Comparable torsion angles about the Pt atoms, *e.g.* N4—Pt1—N2—C2, differ by up to 8° in cations *A* and *B*. The N—O bonds in the NO<sub>3</sub> anions lie within expected ranges and these nitrate anions are positioned in such a manner that their O atoms are oriented towards the H atoms of adjacent water molecules and diamine groups, forming hydrogen bonds.

There are three systems of supramolecular chains interacting by hydrogen bonds: one formed by bifurcated N—

H···(O,O) interactions linking an N atom of the diamine group with O atoms of a nitrate anion, and two O—H···O chains linking an O atom of a nitrate anion to the water O atom. The first is parallel to [001] and takes the form (O1B,O3B)<sup>iii</sup>···N2A<sup>vii</sup>···(O2A,O3A)···N5A···(O1A,O3A)···N2B<sup>ii</sup>···(O2B,O3B)<sup>viii</sup>···N5B<sup>viii</sup>···(O1B,O3B)<sup>viii</sup> [all symmetry codes as in Table 1; additionally, (vii)  $-x, y - \frac{1}{2}, -z + 1$ ; (viii)  $-x + 1, y - \frac{1}{2}, -z + 2$ ] (Fig. 2). Also present are chains parallel to [010] (Fig. 3) between a water molecule and nitrate anions, of the form O5A···N6A···O4A···O7A···O5A<sup>iii</sup>; the second chain running parallel to the *b* axis is O5B<sup>ix</sup>···O7B<sup>x</sup>···O4B<sup>x</sup>···N6B<sup>x</sup>···O5B<sup>x</sup> [symmetry codes: (ix)  $-x + 1, y + \frac{1}{2}, -z + 1$ ; (x)  $x, y, z - 1$ ]. Details of hydrogen bonds are given in Table 1 and the C—H···O interactions are considered weak.

## Experimental

For the preparation of the title compound, an aqueous suspension (312 ml) of *cis*-[PtCl<sub>2</sub>(DACH)] (0.041 mol, 15.6 g) was mixed with 1.935 equivalents of AgNO<sub>3</sub> (0.079 mol, 13.5 g) and the reaction mixture was stirred in the absence of light at 318 K for 4 h. The by-product, AgCl, was removed by filtration through an ultra-filter ( $\varnothing = 0.22$  mm; Sigma–Aldrich) and a layer of active carbon. The colourless filtrate was evaporated and dried (Buchi Rotavapor RII rotary evaporator, 318 K, 2 kPa). The resulting white powder, crude *cis*-[Pt(NO<sub>3</sub>)<sub>2</sub>(DACH)], was recrystallized from acetonitrile. Single crystals of *cis*-[Pt(CH<sub>3</sub>CN)<sub>2</sub>(DACH)](NO<sub>3</sub>)<sub>2</sub>·H<sub>2</sub>O, (**I**), suitable for X-ray diffraction analysis, were obtained from a solution of *cis*-[Pt(NO<sub>3</sub>)<sub>2</sub>(DACH)] (3.1 mg, 0.0072 mmol) in acetonitrile (0.24 ml) by spontaneous precipitation under slow programmed cooling.

### Crystal data

[Pt(C<sub>2</sub>H<sub>3</sub>N)<sub>2</sub>(C<sub>6</sub>H<sub>14</sub>N<sub>2</sub>)](NO<sub>3</sub>)<sub>2</sub>·  
H<sub>2</sub>O  
*M<sub>r</sub>* = 533.4  
Monoclinic, *P*2<sub>1</sub>  
*a* = 12.6799 (3) Å  
*b* = 12.0326 (3) Å  
*c* = 11.6791 (2) Å

$\beta = 94.5495$  (17)°  
*V* = 1776.29 (7) Å<sup>3</sup>  
*Z* = 4  
Mo *K*α radiation  
 $\mu = 7.94$  mm<sup>-1</sup>  
*T* = 120 K  
0.49 × 0.20 × 0.10 mm

### Data collection

Oxford Xcalibur Atlas Gemini  
Ultra diffractometer  
Absorption correction: analytical  
[*CrysAlis Pro* (Oxford  
Diffraction, 2008), based on  
expressions derived by Clark &  
Reid (1995)]  
*T<sub>min</sub>* = 0.110, *T<sub>max</sub>* = 0.544

16828 measured reflections  
7866 independent reflections  
7374 reflections with *I* > 3σ(*I*)  
*R<sub>int</sub>* = 0.014

### Refinement

*R*[*F*<sup>2</sup> > 2σ(*F*<sup>2</sup>)] = 0.012  
*wR*(*F*<sup>2</sup>) = 0.030  
*S* = 1.02  
7866 reflections  
480 parameters  
12 restraints

H atoms treated by a mixture of  
independent and constrained  
refinement  
 $\Delta\rho_{\max} = 0.34$  e Å<sup>-3</sup>  
 $\Delta\rho_{\min} = -0.18$  e Å<sup>-3</sup>  
Absolute structure: Flack (1983),  
with 3554 Friedel pairs  
Flack parameter: 0.027 (5)

The title structure exhibits strong pseudosymmetry in the space group *P*2<sub>1</sub>/*c*. Using this symmetry, the cyclohexane ring showed disorder. After refinement in this space group, the *R* factors

**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>
N1A—H1N1A...O7B	0.870 (19)	2.030 (17)	2.892 (3)	171 (2)
N1A—H2N1A...O5A	0.87 (2)	2.44 (2)	3.232 (5)	151 (3)
N1A—H2N1A...O6A	0.87 (2)	2.21 (3)	3.013 (5)	154 (3)
N2A—H1N2A...O2A <sup>i</sup>	0.870 (14)	2.51 (2)	3.190 (4)	136 (2)
N2A—H1N2A...O3A <sup>i</sup>	0.870 (14)	2.207 (11)	3.023 (3)	156 (2)
N2A—H2N2A...O1B <sup>ii</sup>	0.87 (2)	2.05 (2)	2.914 (4)	174 (3)
N2A—H2N2A...O3B <sup>ii</sup>	0.87 (2)	2.54 (3)	3.064 (3)	119.4 (18)
O7A—H1O7A...O5A <sup>iii</sup>	0.80 (3)	2.00 (3)	2.802 (4)	175 (3)
O7A—H2O7A...O4A	0.80 (2)	2.019 (17)	2.757 (5)	153 (3)
N1B—H1N1B...O5B	0.87 (3)	2.32 (3)	3.090 (4)	148 (3)
N1B—H1N1B...O6B	0.87 (3)	2.63 (4)	3.207 (4)	125 (3)
N1B—H2N1B...O7A	0.87 (3)	1.95 (4)	2.813 (4)	171 (5)
N2B—H1N2B...O1A <sup>iv</sup>	0.87 (3)	2.10 (3)	2.936 (4)	160 (2)
N2B—H1N2B...O3A <sup>iv</sup>	0.87 (3)	2.53 (3)	3.238 (3)	140 (3)
N2B—H2N2B...O2B <sup>v</sup>	0.87 (3)	2.43 (4)	3.213 (4)	150 (4)
N2B—H2N2B...O3B <sup>v</sup>	0.87 (3)	2.21 (2)	3.005 (3)	152 (4)
O7B—H1O7B...O5B <sup>vi</sup>	0.80 (3)	2.02 (3)	2.818 (4)	177 (3)
O7B—H2O7B...O4B	0.800 (14)	2.059 (14)	2.846 (5)	168 (3)

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

converged to 0.042, but large anisotropic displacement parameters (ADPs) were shown by the nitrate atoms and three of the six C atoms of the cyclohexane ring. These C atoms were split and the ADPs changed to isotropic, and two chairs appeared with the refinement converging to 0.039 and a goodness-of-fit of 0.023. However, the H atoms of the water molecule and diamine groups were not visible in the difference Fourier map. Therefore, the sample was remeasured at a lower temperature, which showed that the reflections violating the *c*-glide plane condition were real violations, not admixtures present in low-quality data. Therefore, the model was transformed to subgroup  $P2_1$ . For expansion of the structure model, the inversion was used as a merohedral twinning operation. In this case, the volume fraction of the inversion twin is the Flack parameter (Flack, 1983). This parameter refined to a final value of 0.027 (5), which confirms both that the above configuration is the correct absolute structure and that there is no twinning in the crystal structure. The noncentrosymmetric refinement converged to *R* factors close to 0.01, gave reasonable ADPs for the C atoms in the cyclohexane ring and all H atoms were visible in the difference Fourier maps. There are no significant differences between the individual cations in the space groups  $P2_1$  and  $P2_1/c$ , apart from the disorder of the C atoms in the cyclohexane ring shown in  $P2_1/c$  which is non-existent in  $P2_1$ . As to the two cations in the asymmetric unit in  $P2_1$ , they show few significant differences in

bond distances and angles, but several are noted for the torsion angles.

O- and N-bound H atoms were refined with N—H distances restrained to 0.87 (2) Å and O—H distances restrained to 0.80 (3) Å. All other H atoms were positioned geometrically and refined using a riding model, with C—H = 0.96 Å and  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ .

Data collection: *CrysAlis Pro* (Oxford Diffraction, 2008); cell refinement: *CrysAlis Pro* (Oxford Diffraction, 2008); data reduction: *CrysAlis Pro*; program(s) used to solve structure: *SUPERFLIP* (Palatinus & Chapuis, 2007); program(s) used to refine structure: *JANA2006* (Petříček *et al.*, 2006); molecular graphics: *ORTEP-3* (Farrugia, 1999) and *Mercury* (Version 2.3; Macrae *et al.*, 2006); software used to prepare material for publication: *JANA2006*.

This work was supported by grant No. MSM 6046137301 and research programme 2B08021 of the Ministry of Education, Youth and Sports of the Czech Republic, and by grant No. MPO 2A-2TP1/049 from the Ministry of Industry and Trade of the Czech Republic. We also acknowledge institutional research plan No. AVOZ10100521 of the Institute of Physics of the Czech Academy of Sciences.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG3238). Services for accessing these data are described at the back of the journal.

## References

- Abu-Surrah, A. S. & Kettunen, M. (2006). *Curr. Med. Chem.* **13**, 1337–1357.
- Clark, R. C. & Reid, J. S. (1995). *Acta Cryst.* **A51**, 887–897.
- Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
- Flack, H. D. (1983). *Acta Cryst.* **A39**, 876–881.
- Fuertes, M. A., Castilla, J. & Nguewa, P. A. (2004). *Med. Chem. Rev. Online*, **1**, 187–198.
- Galanski, M., Arion, V. B., Jakupec, M. A. & Keppler, B. K. (2003). *Curr. Pharm. Des.* **9**, 2078–2089.
- Ho, Y.-P., Au-Yeung, S. C. F. & To, K. K. W. (2003). *Med. Res. Rev.* **23**, 633–655.
- Leh, F. K. V. & Wolf, W. (1976). *J. Pharm. Sci.* **65**, 315–328.
- Lock, C. J. L. & Pilon, P. (1981). *Acta Cryst.* **B37**, 45–49.
- Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl. Cryst.* **39**, 453–457.
- Oxford Diffraction (2008). *CrysAlis Pro*. Oxford Diffraction Ltd, Yarnton, Oxfordshire, England.
- Palatinus, L. & Chapuis, G. (2007). *J. Appl. Cryst.* **40**, 786–790.
- Pasini, A., Caldriola, C. & Spinelli, S. (1993). *Synth. React. Inorg. Met. Org. Nano-Met. Chem.* **23**, 1021–1060.
- Petříček, V., Dušek, M. & Palatinus, L. (2006). *JANA2006*. Institute of Physics, Czech Academy of Sciences, Prague, Czech Republic.