Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

4-Aminopyridinium 4-aminobenzoate dihydrate and 4-aminopyridinium nicotinate

Samuel Robinson Jebas,[a]* A. Sinthiya,[b] B. Ravindran Durai Nayagam,[c] Dieter Schollmeyer[d] and S. Alfred Cecil Raj[e]

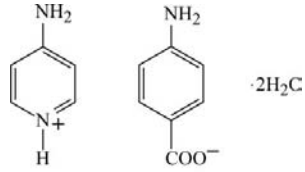
[a]Department of Physics, Karunya University, Karunya Nagar, Coimbatore 641 114, India, [b]Department of Electronics, St Joseph's College, Tiruchirappalli 620 002, India, [c]Department of Chemistry, Pope's College, Sawyerpuram 628 251, Tamilnadu, India, [d]Institut für Organische Chemie, Universität Mainz, Duesbergweg 10-14, 55099 Mainz, Germany, and [e]Department of Physics, St Joseph's College, Tiruchirappalli 620 002, India
Correspondence e-mail: jebas2@gmail.com

Received 28 April 2009
Accepted 3 June 2009
Online 30 June 2009

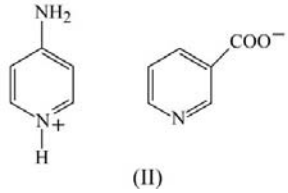
In the title compounds, 4-aminopyridinium 4-aminobenzoate dihydrate, $C_7H_6NO_2^-\cdot C_5H_7N_2^+\cdot 2H_2O$, (I), and 4-aminopyridinium nicotinate, $C_5H_7N_2^+\cdot C_6H_4NO_2^-$, (II), the aromatic N atoms of the 4-aminopyridinium cations are protonated. In (I), the asymmetric unit is composed of two 4-aminopyridinium cations, two 4-aminobenzoate anions and four water molecules, and the compound crystallizes in a noncentrosymmetric space group. The two sets of independent molecules of (I) are related by a centre of symmetry which is not part of the space group. In (I), the protonated pyridinium ring H atoms are involved in bifurcated hydrogen bonding with carboxylate O atoms to form an $R_1^2(4)$ ring motif. The water molecules link the ions to form a two-dimensional network along the $(10\bar{1})$ plane. In (II), an intramolecular bifurcated hydrogen bond generates an $R_1^2(4)$ ring motif and inter-ion hydrogen bonding generates an $R_4^2(16)$ ring motif. The packing of adduct (II) is consolidated *via* N—H···O and N—H···N hydrogen bonds to form a two-dimensional network along the $(10\bar{2})$ plane.

Comment

4-Aminopyridine (fampridine) is used clinically in the treatment of Lambert–Eaton myasthenic syndrome and multiple sclerosis because by blocking potassium channels it prolongs action potentials, thereby increasing transmitter release at the neuromuscular junction (Judge & Bever, 2006; Schwid *et al.*, 1997; Strupp *et al.*, 2004). The structure of 4-aminopyridine was first reported by Chao & Schempp (1977) and a redetermination was reported by Anderson *et al.* (2005). 4-Aminobenzoic acid acts as a bacterial cofactor involved in the biosynthesis of folic acid, which is a constituent of the vitamin B complex and is found in animal and plant tissues (Robinson, 1966; Zoroddu *et al.*, 1996). Two polymorphs of 4-aminobenzoic acid have been re-investigated recently, namely the α-form (Athimoolam & Natarajan, 2007) and the β-form (Gracin & Fischer, 2005). We have already reported the crystal structure of the salt of 4-aminobenzoic acid and nicotinic acid (Jebas & Balasubramanian, 2006). Nicotinic acid (vitamin B3) is pyridine-3-carboxylic acid, also known as niacin. It is a lipid-lowering agent widely used to treat hypertriglyceridemia by the inhibition of lipolysis in adipose tissues (Athimoolam & Rajaram, 2005). The crystal structure of nicotinic acid was first determined by photographic methods (Wright & King, 1953), and a redetermination was reported by Kutoglu & Scheringer (1983). The crystal structures of isonicotinic acid (Takusagawa & Shimada, 1976), 2-aminonicotinic acid (Dobson & Gerkin, 1997), 6-aminonicotinic acid hydrochloride (Giantsidis & Turnbull, 2000) and 2-(methylsulfanyl)nicotinic acid (Basavoju *et al.*, 2005) have been reported. The nicotinic acid complex with 5-methylpyrazine-2-carboxylic acid 4-oxide is a commonly used drug for the treatment of hypercholesterolemia (Lorenzen *et al.*, 2001). Coordination complexes of nicotinic acid with metals such as Sn possess antitumour activity greater than that of the well known cisplatin or doxorubicin (Gielen *et al.*, 1992). The enzyme nicotinic acid mononucleotide adenyltransferase is essential for the synthesis of nicotinamide adenine dinucleotide in all living cells and is a potential target for antibiotics (Kim *et al.*, 2004). As an extension of our systematic study of hydrogen-bonding patterns of 4-aminopyridine with carboxylic acids, 4-aminopyridinium 4-aminobenzoate dihydrate, (I), and 4-aminopyridinium nicotinate, (II), have been synthesized and their crystal structures are presented here.



(I)



(II)

The asymmetric unit of (I) (Fig. 1) consists of two 4-aminopyridinium cations protonated at aromatic ring atoms N4*B* and N4*D*, two 4-aminobenzoate anions with the carboxyl groups deprotonated, and four water molecules, while that of (II) contains one 4-aminopyridinium cation protonated at aromatic ring atom N1 and one nicotinate anion with the carboxyl group deprotonated (Fig. 2). Compound (I) crystallizes in a noncentrosymmetric space group. The bond lengths and angles of the protonated 4-aminopyridinium ion in (I) and (II) are comparable with the values reported earlier for 4-aminopyridine in its protonated form (Fun *et al.*, 2009*a*,*b*). There is a significant decrease in the length of the C1*B*—N7*B*

 doi:10.1107/S0108270109021106

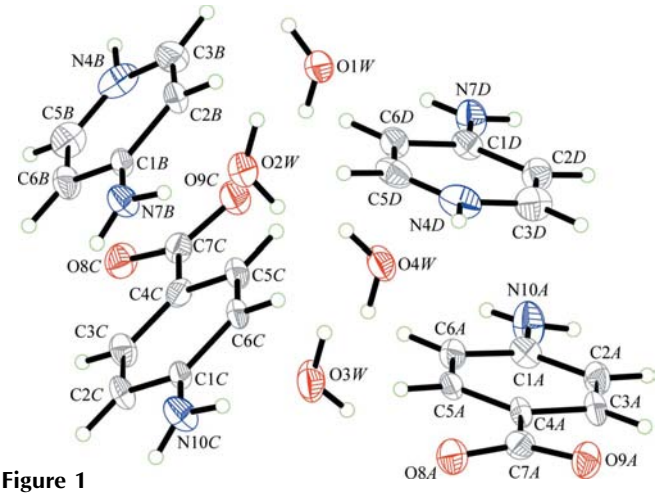


Figure 1
The asymmetric unit of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

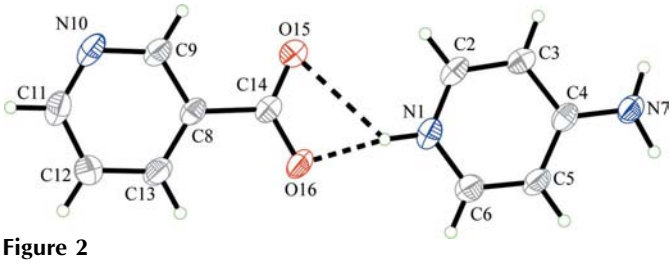


Figure 2
The asymmetric unit of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. Bifurcated intramolecular hydrogen bonding with a ring of motif $R_1^2(4)$ is shown as dashed lines.

bond, which is 1.313 (5) Å in (I) compared with 1.3597 (18) Å in the neutral 4-aminopyridine molecule (Anderson *et al.*, 2005). The bond lengths and angles in 4-aminobenzoic acid and nicotinic acid are comparable with values reported previously (Gracin & Fischer, 2005; Jebas *et al.*, 2006; Kutoglu & Scheringer, 1983; Jebas & Balasubramanian, 2006). 4-Aminopyridine is protonated in (I) and (II) to form salts, with the H atom from the carboxyl group of 4-aminobenzoic acid in (I) transferred to atoms N4*B* and N4*D* of 4-aminopyridine in (I), and the H atom from the carboxyl group of nicotinic acid transferred to atom N1 of 4-aminopyridine in (II). The protonation is evidenced by the widening of the internal angles (C3*B*—N4*B*—C5*B* and C3*D*—N4*D*—C5*D*) of the pyridine rings to 120.5 (4)° in molecule *B* and 120.4 (3)° in molecule *D* of (I), and of the C2—N1—C6 angle to 120.52 (19)° in molecule (II), compared with 115.25 (13)° in unprotonated 4-aminopyridine (Anderson *et al.*, 2005; Chao & Schempp, 1977). Similar protonation is observed in various 4-aminopyridine–acid complexes, such as 4-aminopyridinium hydrogen succinate (Fun *et al.*, 2009*a*) and bis(4-aminopyridinium) bis(hydrogen oxalate) monohydrate (Fun *et al.*, 2009*b*).

In (I), the dihedral angles formed by the carboxylate groups (O8*A*—C7*A*—O9*A*—C4*A* and O8*C*—C7*C*—O9*C*—C4*C*) of

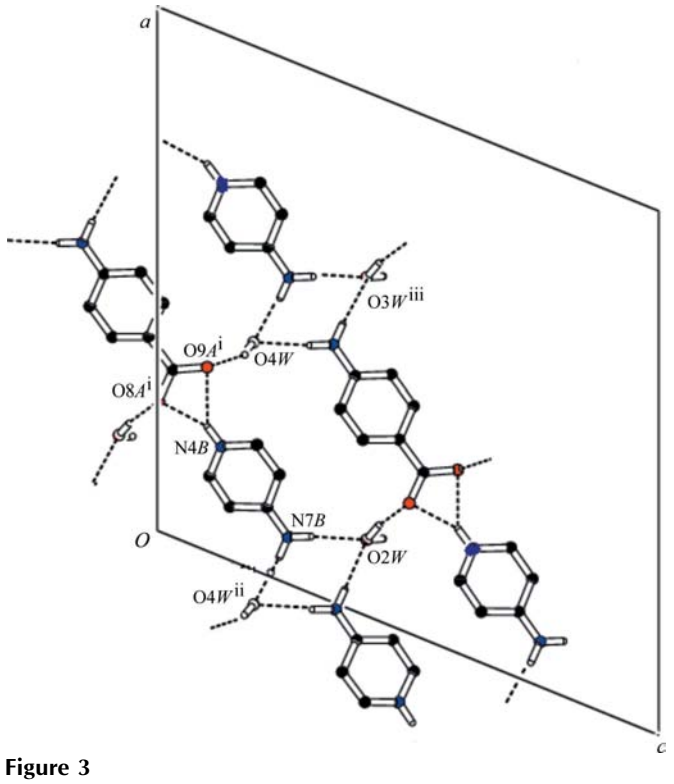


Figure 3
A view of the two-dimensional hydrogen-bonded network of (I), showing the aggregation of the $R_1^2(4)$ hydrogen-bonding motif. Hydrogen bonds are shown as dashed lines. [Symmetry codes: (i) $x, 1-y, -\frac{1}{2}+z$; (ii) $-\frac{1}{2}+x, \frac{1}{2}+y, z$; (iii) $\frac{1}{2}+x, -\frac{1}{2}+y, z$.]

the aminobenzoate anions with the attached benzene rings (C1*A*–C6*A* and C1*C*–C6*C*) are 8.21 (18) and 5.92 (18)°, respectively, indicating that they are twisted slightly from the mean planes of the benzene rings. The two pyridinium rings (C1*B*–C3*B*/N4*B*/C5*B*/C6*B* and C1*D*–C3*D*/N4*D*/C5*D*/C6*D*) in (I) are twisted from away each other, forming a dihedral angle of 55.25 (19)°, and the two 4-aminobenzoate anions are twisted away from each other with a dihedral angle of 47.78 (18)°. The nicotinate and 4-aminopyridinium ions are oriented at an angle of 9.04 (7)° in (II).

The hydrogen-bonding pattern of (I), involving 20 different intermolecular hydrogen bonds, is shown in Fig. 3. The carboxylate O atoms of the 4-aminobenzoate anion act as acceptors of bifurcated N—H···O hydrogen bonds with the protonated aromatic ring N atom of the 4-aminopyridinium cation (Table 2), forming a ring with the graph-set notation $R_1^2(4)$ (Bernstein *et al.*, 1995). In addition to the bifurcated hydrogen bonding linking the cations with the anions, the water molecules play a crucial role in linking the cations with the anions, as well as linking adjacent cations. In the crystal packing of (I) (Fig. 3), the moieties are linked by N—H···O and O—H···O hydrogen bonds to form a two-dimensional network along the $(10\bar{1})$ plane. In (II), the carboxylate O atoms of the nicotinate anion act as acceptors of bifurcated N—H···O hydrogen bonds with the protonated aromatic ring N atom of the 4-aminopyridinium cation (Table 4), forming a ring with the graph-set notation $R_1^2(4)$. One of the amino H atoms are involved in an N—H···O hydrogen bond with an

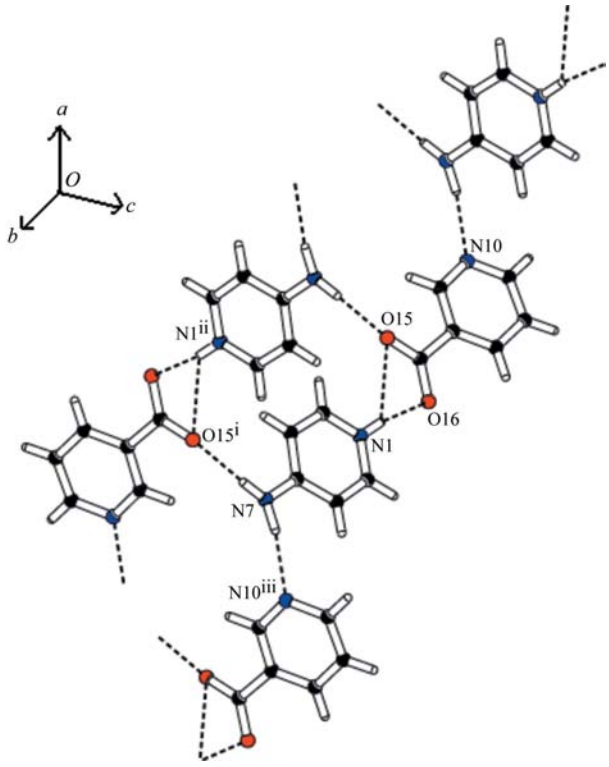


Figure 4
A two-dimensional hydrogen-bonded view of (II), showing the $R_1^2(4)$ and $R_4^2(16)$ ring motifs. Hydrogen bonds are shown as dashed lines. [Symmetry codes: (i) $1-x, \frac{1}{2}+y, \frac{1}{2}-z$; (ii) $1-x, -\frac{1}{2}+y, \frac{1}{2}-z$; (iii) $-1+x, \frac{1}{2}-y, -\frac{1}{2}+z$.]

inversion-related anion to complete a centrosymmetric loop of graph-set motif $R_4^2(16)$ (Fig. 4). The packing of adduct (II) is consolidated *via* N—H···O and N—H···N hydrogen bonds to form a two-dimensional network along the $(10\overline{2})$ plane.

Experimental

Compound (I) was prepared by dissolving 4-aminopyridine (0.094 g, 1 mmol) in water (10 ml) and 4-aminobenzoic acid (0.169 g, 1 mmol) in ethanol (10 ml). The solutions were mixed and the mixture was stirred well for 3 h. Colourless crystals of (I) were obtained by slow evaporation of the solution over a period of one month. Compound (II) was prepared by dissolving 4-aminopyridine (0.094 g, 1 mmol) in ethanol and nicotinic acid (0.123 g, 1 mmol) in water. The nicotinic acid solution was added dropwise to the 4-aminopyridine solution. The clear solution obtained was allowed to evaporate slowly. Colourless crystals of (II) suitable for X-ray diffraction were obtained after two weeks.

Compound (I)

Crystal data

$C_5H_7N_2^+\cdot C_7H_6NO_2^-\cdot 2H_2O$
M_r = 267.29
Monoclinic, *Cc*
a = 18.9692 (18) Å
b = 7.8092 (4) Å
c = 19.5944 (19) Å
β = 112.213 (4)°
V = 2687.2 (4) Å^3
Z = 8
Cu *K*α radiation
μ = 0.84 mm^{-1}
T = 193 K
0.38 × 0.32 × 0.16 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Absorption correction: ψ scan (*CORINC*; Draeger & Gattow, 1971)
T_{min} = 0.741, T_{max} = 0.877
4793 measured reflections
2557 independent reflections
2334 reflections with $I > 2\sigma(I)$
R_{int} = 0.045
3 standard reflections
frequency: 60 min
intensity decay: 2%

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.055
$wR(F^2)$ = 0.156
S = 1.05
2557 reflections
344 parameters
14 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.28 e Å^{-3}
$\Delta\rho_{min}$ = −0.37 e Å^{-3}
Absolute structure: Flack (1983), with 2236 Friedel pairs
Flack parameter: 0.2 (3)

Compound (II)

Crystal data

$C_5H_7N_2^+\cdot C_6H_4NO_2^-$
M_r = 217.23
Monoclinic, $P2_1/c$
a = 11.9645 (17) Å
b = 8.2635 (5) Å
c = 11.305 (3) Å
β = 111.854 (7)°
V = 1037.4 (3) Å^3
Z = 4
Cu *K*α radiation
μ = 0.82 mm^{-1}
T = 193 K
0.26 × 0.19 × 0.13 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Absorption correction: ψ scan (*CORINC*; Draeger & Gattow, 1971)
T_{min} = 0.815, T_{max} = 0.901
2068 measured reflections
1960 independent reflections
1837 reflections with $I > 2\sigma(I)$
R_{int} = 0.022
3 standard reflections
frequency: 60 min
intensity decay: 2%

Table 1
Selected bond angles (°) for (I).

C5*B*—N4*B*—C3*B*	120.5 (4)	C5*D*—N4*D*—C3*D*	120.4 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1*W*—H1*W*···O9*A*^{i}	0.96	1.84	2.763 (4)	159
O1*W*—H2*W*···O9*C*	0.96	1.83	2.767 (4)	165
O2*W*—H3*W*···O8*A*^{ii}	0.97	1.80	2.760 (4)	170
N4*B*—H4*B*···O8*A*^{i}	0.88	1.99	2.808 (5)	153
N4*B*—H4*B*···O9*A*^{i}	0.88	2.18	2.936 (5)	143
N4*D*—H4*D*···O8*C*^{iii}	0.88	2.09	2.883 (5)	150
N4*D*—H4*D*···O9*C*^{iii}	0.88	2.08	2.859 (5)	146
O2*W*—H4*W*···O8*C*^{iii}	0.97	1.83	2.748 (4)	156
O3*W*—H5*W*···O8*C*^{iii}	0.96	1.80	2.754 (4)	169
O3*W*—H6*W*···O8*A*	0.96	1.80	2.741 (4)	166
N7*B*—H7*B*···O2*W*	0.88	2.09	2.965 (4)	173
N7*B*—H7*C*···O4*W*^{iv}	0.88	2.09	2.967 (5)	172
N7*D*—H7*D*···O2*W*^{v}	0.88	2.10	2.973 (5)	173
N7*D*—H7*E*···O1*W*	0.88	2.06	2.938 (4)	174
O4*W*—H7*W*···O9*C*	0.97	1.85	2.768 (4)	156
O4*W*—H8*W*···O9*A*^{vi}	0.96	1.78	2.740 (4)	179
N10*A*—H10*A*···O3*W*^{v}	0.88	2.21	3.085 (5)	176
N10*A*—H10*B*···O4*W*	0.88	2.14	3.015 (4)	176
N10*C*—H10*C*···O3*W*	0.88	2.12	3.000 (5)	177
N10*C*—H10*D*···O1*W*^{vii}	0.88	2.26	3.136 (5)	178

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

Table 3
Selected geometric parameters (Å, °) for (II).

N1—C2	1.339 (3)	C14—O15	1.246 (3)
N1—C6	1.350 (3)	C14—O16	1.255 (2)
C2—N1—C6	120.52 (19)	O16—C14—C8	116.37 (18)
O15—C14—C8	117.64 (17)		

Table 4
Hydrogen-bond geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O16	0.92	1.77	2.680 (2)	169
N1—H1···O15	0.92	2.49	3.131 (2)	127
N7—H7A···N10^{i}	0.98	2.07	3.027 (3)	166
N7—H7B···O15^{ii}	0.89	1.94	2.814 (2)	168

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

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.062$	146 parameters
$wR(F^2) = 0.220$	H-atom parameters constrained
$S = 1.13$	$\Delta\rho_{max} = 0.35$ e Å^{-3}
1960 reflections	$\Delta\rho_{min} = -0.38$ e Å^{-3}

In (I) and (II), H atoms bonded to C and N atoms were positioned geometrically and treated as riding, with C—H = 0.95 Å and N—H = 0.88 Å, and with U_{iso}(H) = 1.2U_{eq}(C,N). The water H atoms were initially located in a difference Fourier map and were then refined with restraints of 0.97 (1) and 1.54 (1) Å, respectively, applied to the O—H and H···H distances. In the final cycles of refinement, the positions of the water H atoms were constrained to ride on their parent atoms, with U_{iso}(H) = 1.5U_{eq}(O).

For both compounds, data collection: *CAD-4 EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD-4 EXPRESS*; data reduction: *CORINC* (Draeger & Gattow, 1971); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 2009).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3319). Services for accessing these data are described at the back of the journal.

References

Anderson, F. P., Gallagher, J. F., Kenny, P. T. M. & Lough, A. J. (2005). *Acta Cryst.* E**61**, o1350–o1353.
Athimoolam, S. & Natarajan, S. (2007). *Acta Cryst.* C**63**, o514–o517.
Athimoolam, S. & Rajaram, R. K. (2005). *Acta Cryst.* E**61**, o2764–o2767.
Basavoju, S., Reddy, C. M. & Desiraju, G. R. (2005). *Acta Cryst.* E**61**, o822–o823.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Chao, M. & Schempp, E. (1977). *Acta Cryst.* B**33**, 1557–1564.
Dobson, A. J. & Gerkin, R. E. (1997). *Acta Cryst.* C**53**, 1427–1429.
Draeger, M. & Gattow, G. (1971). *Acta Chem. Scand.* **25**, 761–762.
Enraf–Nonius (1994). *CAD-4 EXPRESS*. Enraf–Nonius, Delft, The Netherlands.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Fun, H.-K., John, J., Jebas, S. R. & Balasubramanian, T. (2009*a*). *Acta Cryst.* E**65**, o748–o749.
Fun, H.-K., John, J., Jebas, S. R. & Balasubramanian, T. (2009*b*). *Acta Cryst.* E**65**, o765–o766.
Giantsidis, J. & Turnbull, M. M. (2000). *Acta Cryst.* C**56**, 334–335.
Gielen, M., Khloufi, A. E., Biesemans, M. & Willem, R. (1992). *Polyhedron*, **11**, 1861–1868.
Gracin, S. & Fischer, A. (2005). *Acta Cryst.* E**61**, o1242–o1244.
Jebas, S. R. & Balasubramanian, T. (2006). *Acta Cryst.* E**62**, o5621–o5622.
Jebas, S. R., Balasubramanian, T. & Light, M. E. (2006). *Acta Cryst.* E**62**, m1818–m1819.
Judge, S. & Bever, C. (2006). *Pharmacol. Ther.* **111**, 224–259.
Kim, H.-L., Yoon, H.-J., Ha, J. Y., Lee, B. I., Lee, H. H., Mikami, B. & Suh, S. W. (2004). *Acta Cryst.* D**60**, 948–949.
Kutoglu, A. & Scheringer, C. (1983). *Acta Cryst.* C**39**, 232–234.
Lorenzen, A., Stannek, C., Lang, H., Andrianov, V., Kalvinsh, I. & Schwabe, U. (2001). *Mol. Pharmacol.* **59**, 349–357.
Robinson, F. A. (1966). *The Vitamin Co-factors of Enyzyme Systems*, pp. 541–662. London: Pergamon.
Schwid, S. B., Petrie, M. D., McDermott, M. P., Tierney, D. S., Mason, D. H. & Goodman, A. D. (1997). *Neurology*, **48**, 817–821.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.
Strupp, M., Kalla, R., Dichgans, M., Fraitinger, T., Glasauer, S. & Brandt, T. (2004). *Neurology*, **62**, 1623–1625.
Takusagawa, F. & Shimada, A. (1976). *Acta Cryst.* B**32**, 1925–1927.
Wright, W. B. & King, G. S. D. (1953). *Acta Cryst.* **6**, 305–317.
Zoroddu, M. A., Dallocchio, R. & Mosca, S. (1996). *Polyhedron*, **15**, 277–283.