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Hydrogen-bonded supramolecular motifs in 2-amino-4,6-dimethoxypyrimidinium picrate and pyrimethaminium picrate dimethyl sulfoxide solvate

Kaliyaperumal Thanigaimani,[a] Annamalai Subashini,[a] Packianathan Thomas Muthiah,[a]* Daniel E. Lynch[b]‡ and Ray J. Butcher[c]

[a]School of Chemistry, Bharathidasan University, Tiruchirappalli 620 024, Tamil Nadu, India, [b]Faculty of Health and Life Sciences, Coventry University, Priory Street, Coventry CV1 5FB, England, and [c]Department of Chemistry, Howard University, Washington, DC 20059, USA
Correspondence e-mail: tommtrichy@yahoo.co.in

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In the crystal structures of 2-amino-4,6-dimethoxypyrimidinium 2,4,6-trinitrophenolate (picrate), $C_6H_{10}N_3O_2^+\cdot C_6H_2N_3O_7^-$, (I), and 2,4-diamino-5-(4-chlorophenyl)-6-ethylpyrimidin-1-ium (pyrimethaminium or PMN) picrate dimethyl sulfoxide solvate, $C_{12}H_{14}ClN_4^+\cdot C_6H_2N_3O_7^-\cdot C_2H_6OS$, (II), the 2-amino-4,6-dimethoxypyrimidine and PMN cations are protonated at one of the pyrimidine N atoms. The picrate anion interacts with the protonated cations through bifurcated N—H···O hydrogen bonds, forming $R_2^1(6)$ and $R_1^2(6)$ ring motifs. In (I), Z' = 2. In (II), two inversion-related PMN cations are connected through a pair of N—H···N hydrogen bonds involving the 4-amino group and the uncharged N atom of the pyrimidine ring, forming a cyclic hydrogen-bonded $R_2^2(8)$ motif. In addition to the pairing, the O atom of the dimethyl sulfoxide solvent molecule bridges the 2-amino and 4-amino groups on both sides of the paired bases, resulting in a self-complementary ...*DADA*... array of quadruple hydrogen-bonding patterns.

Comment

Picric acid functions not only as an acceptor to form π-stacking complexes with aromatic biomolecules but also as an acidic ligand to form salts with polar biomolecules through specific electrostatic or hydrogen-bonding interactions (In *et al.*, 1997). Picric acid forms charge-transfer complexes with organic compounds. Crystalline picrates have commonly been used in the preparation of amine derivatives in qualitative organic chemistry (Shriner *et al.*, 1980). Dimethyl sulfoxide (DMSO) is a versatile solvent, which can dissolve various organic substances and can form crystalline solvates in which it is either disordered (Deetz *et al.*, 2000; Harper *et al.*, 2001) or well ordered (TranQui *et al.*, 1998). Hydrogen bonding plays a key role in molecular recognition and crystal engineering research (Desiraju, 1989). Some derivatives of pyrimidines are used as antiviral, antitumor and cardiovascular agents (Atwal *et al.*, 1989). Pyrimethamine is a well known antifolate drug used in the treatment of malaria. In the chemotherapy of malaria and neoplastic diseases, substituted 2,4-diaminopyrimidines are widely employed as metabolic inhibitors of pathways leading to the synthesis of proteins and nucleic acid (Hitchings & Burchall, 1965). Pyrimethamine is also used along with other drugs for the treatment of opportunistic infections in patients suffering from AIDS (Tanaka *et al.*, 2004). The crystal structures of pyrimethamine (Sethuraman & Thomas Muthiah, 2002) and 2-amino-4,6-dimethoxypy-

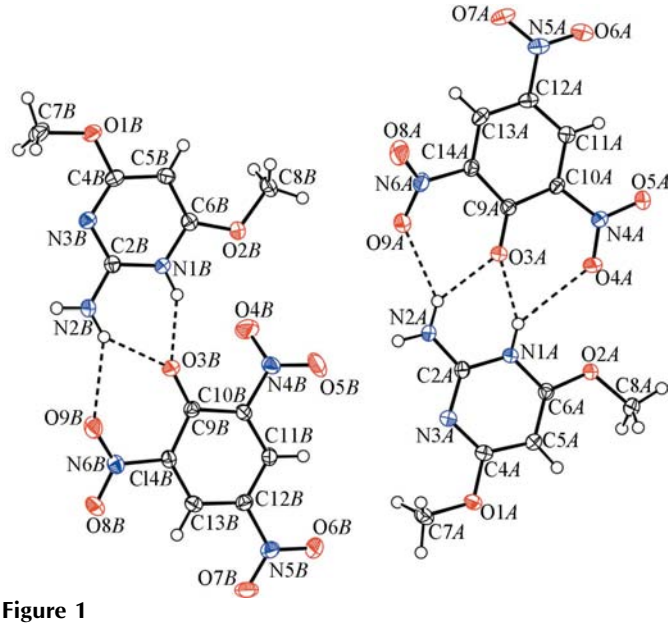

Figure 1
The asymmetric unit of (I), showing 50% probability displacement ellipsoids. Dashed lines indicate hydrogen bonds.

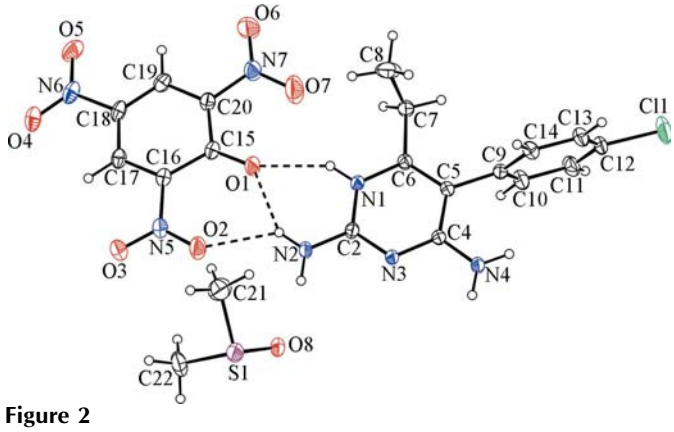

Figure 2
The asymmetric unit of (II), showing 50% probability displacement ellipsoids. Dashed lines indicate hydrogen bonds.

‡ Technical Director, Exilica Limited, The Technocentre, Puma Way, Coventry CV1 2TT, England.

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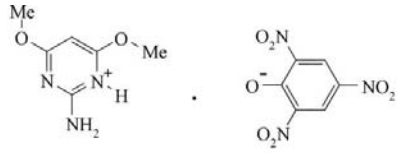
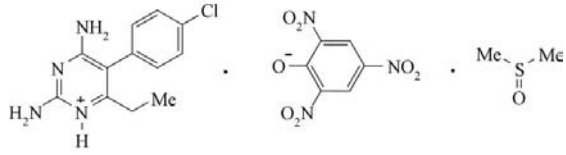
rimidine have also been reported (Low *et al.*, 2002). Hydrogen-bonding patterns in aminopyrimidine–carboxylate salts have been recently reviewed (Schwalbe & Cody, 2006). The crystal structures of 2-amino-4,6-dimethoxypyrimidinium 4-hydroxybenzoate monohydrate (Thanigaimani *et al.*, 2007*a*) and 2-amino-4,6-dimethoxypyrimidinium salicylate (Thanigaimani *et al.*, 2007*b*) have been reported by us. The present study was undertaken to obtain more information regarding patterns of hydrogen bonds in these types of compounds.

ORTEPII (Johnson, 1976) views of the title compounds, (I) and (II), are shown in Figs. 1 and 2, and selected geometric parameters are given in Tables 1 and 3. In (I), the asymmetric unit contains pairs of 2-amino-4,6-dimethoxypyrimidinium cations (*A* and *B*) and picrate anions (*A* and *B*). In (II), the asymmetric unit contains one protonated pyrimethaminium (PMN) cation, one picrate anion and one DMSO solvent molecule. In the two compounds, the pyrimidine rings are protonated at atom N1. Protonation of the pyrimidine base on the N1 site is reflected by an increase in bond angle at N1 [the C2—N1—C6 angle is 120.27 (16)° in cation *A* of (I), 120.44 (16)° in cation *B* of (I) and 121.51 (15)° in (II)] when compared with that at the unprotonated atom N3 [the C2—N3—C4 angle is 116.36 (17)° in cation *A* of (I), 116.42 (18)° in cation *B* of (I) and 117.92 (17)° in (II)]. The key conformational features of the PMN cations are described by two angles. The first is the dihedral angle between the 2,4-diaminopyrimidine and 4-chlorophenyl mean planes. The second is the torsion angle that represents the deviation of the ethyl group from the pyrimidine plane. The dihedral angle between the pyrimidine and benzene ring is 81.05 (10)°, and the C5—C6—C7—C8 torsion angle is −105.3 (2)°. These values are close to those observed in modeling studies of dihydrofolate reductase–pyrimethamine complexes, which indicates that these angles play an important role in the effective docking of the drug molecule in the active site of the enzyme (Sansom *et al.*, 1989).



(I)



(II)

For ions *A* of (I), the phenolate O atom and two of the nitro O atoms (O9*A* and O4*A*) of the picrate anion act as acceptors of bifurcated N—H···O hydrogen bonds with the protonated pyrimidine and amine N atoms of the 2-amino-4,6-dimethoxypyrimidinium cation (Table 2), forming three rings with graph-set notations $R_1^2(6)$, $R_2^1(6)$ and $R_1^2(6)$ (Etter, 1990; Bernstein *et al.*, 1995). A similar type of interaction has been observed in the crystal structure of 2-aminopyrimidinium picrate (Narayana *et al.*, 2008). However, in cation *B* and compound (II), the protonated N atoms (N1*B* and N1) do not form bifurcated hydrogen bonds with the nitro group (O4*B* and O7) of the picrate anion, resulting in only two rings with graph-set notations $R_2^1(6)$ and $R_1^2(6)$ (Table 4). This type of interaction has also been reported in the crystal structure of 2-amino-4,6-dimethylpyrimidinium picrate (Subashini *et al.*, 2006). Ions *A* and *B* form individual chains *via* C—H···O hydrogen bonds. These two chains are interlinked by N—H···O hydrogen bonds to form a supramolecular sheet with graph-set notation $R_6^6(32)$ (Fig. 3).

In (II), the two inversion-related PMN cations are linked through a pair of N—H···N hydrogen bonds invol-

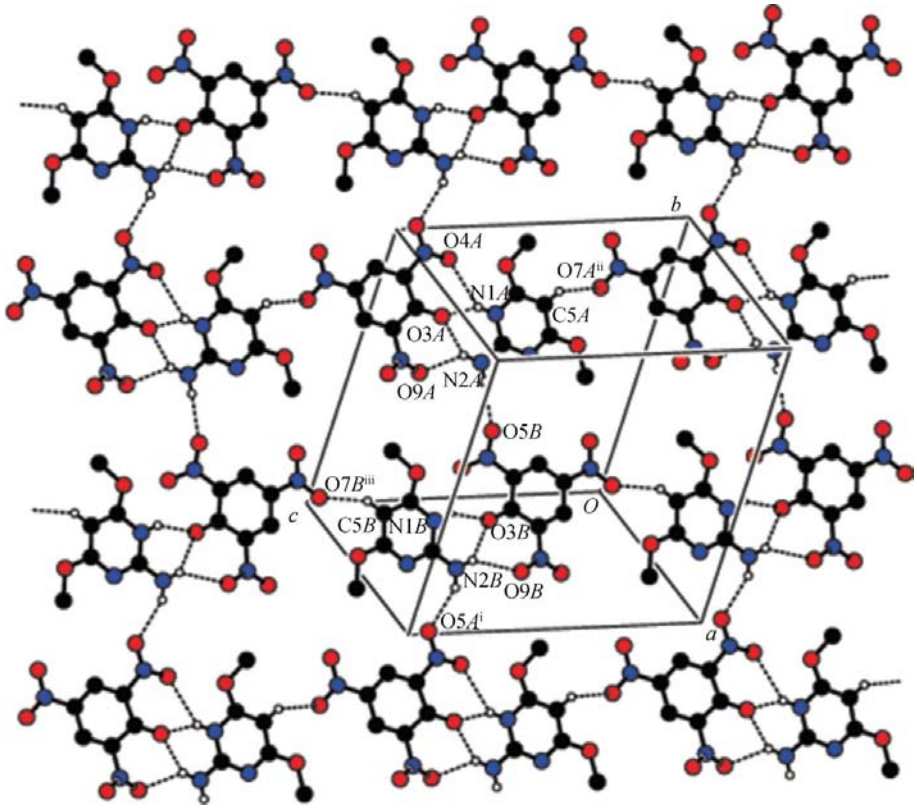


Figure 3
The crystal structure of (I). Dashed lines indicate hydrogen bonds. H atoms not involved in hydrogen bonding have been omitted. [Symmetry codes: (i) $x+1, y-1, z$; (ii) $x, y, z-1$; (iii) $x, y, z+1$.]

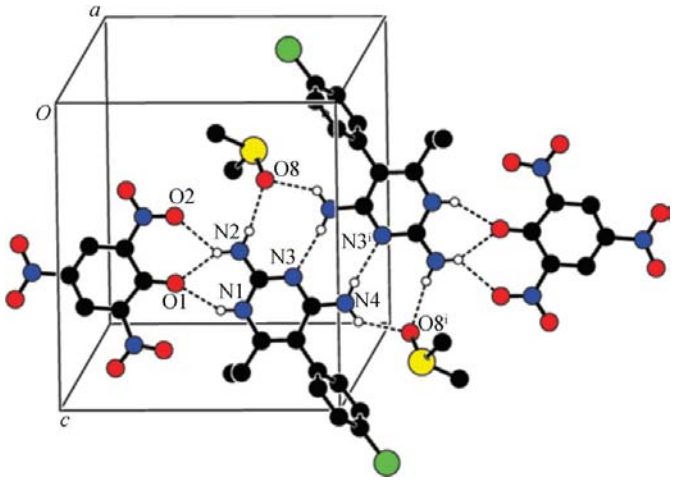


Figure 4
The crystal structure of (II). Dashed lines indicate hydrogen bonds. H atoms not involved in hydrogen bonding have been omitted. [Symmetry code: (i) $-x, -y+2, -z+1$.]

ving the 4-amino group and atom N3 of the pyrimidine ring, generating an $R_2^2(8)$ ring motif. No similar interactions are observed in (I). In addition to the pairing, the O atom from the DMSO solvent molecule bridges the 2-amino and 4-amino groups on either side of the paired bases, resulting in a self-complementary *DADA* (*D* represents a hydrogen-bond donor and *A* a hydrogen-bond acceptor) array of quadruple hydrogen-bonding patterns. The corresponding graph-set notations are $R_3^2(8)$, $R_2^2(8)$ and $R_3^2(8)$ (Fig. 4). This type of ...*DADA*... array of quadruple hydrogen bonds has been observed in PMN carboxylates (Stanley *et al.*, 2005).

In (I), π–π stacking interactions between the aromatic rings are also observed. The pyrimidine ring of 2-amino-4,6-dimethoxypyrimidinium cation *A* forms stacking interactions with the aryl rings of picrate anion *A*, with interplanar and centroid–centroid distances of 3.2953 (7) and 3.8433 (11) Å, respectively, and a slip angle (the angle between the centroid vector and the normal to the plane) of 30.97°. A similar type of stacking is also observed between 2-amino-4,6-dimethoxypyrimidinium cation *B*, which forms stacking interactions with the aryl rings of picrate anion *A*, with interplanar and centroid–centroid distances of 3.3652 (8) and 3.8659 (11) Å, respectively, and a slip angle of 29.49°. These are typical aromatic stacking values (Hunter, 1994).

Experimental

Compound (I) was prepared by mixing a hot methanol solution (20 ml) of 2-amino-4,6-dimethoxypyrimidine (38 mg) and picric acid (57 mg) and warming the solution for half an hour over a water bath. The solution was cooled slowly and kept at room temperature. After a few days, yellow plate-shaped crystals were obtained. Compound (II) was prepared by heating hot methanol solutions of pyrimethamine (62 mg, Shah Pharma Chemicals, India) and picric acid (57 mg, Merck) for 20 min; the solution became turbid. In order to obtain a clear solution, a few drops of DMSO were added. After about a week, thin yellow plates of (II) were obtained.

Compound (I)

Crystal data

$C_6H_{10}N_3O_2^+\cdot C_6H_2N_3O_7^-$
$M_r = 384.28$
Triclinic, $P\overline{1}$
$a = 8.8796$ (2) Å
$b = 13.2847$ (3) Å
$c = 14.1395$ (3) Å
$\alpha = 99.820$ (1)°
$\beta = 100.701$ (1)°
$\gamma = 105.095$ (1)°
$V = 1539.68$ (6) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.14$ mm^{-1}
$T = 120$ K
0.16 × 0.12 × 0.06 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
27465 measured reflections
7048 independent reflections
5725 reflections with $I > 2\sigma(I)$
$R_{int} = 0.039$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.052$
$wR(F^2) = 0.121$
$S = 1.06$
7048 reflections
487 parameters
H-atom parameters constrained
$\Delta\rho_{max} = 0.67$ e Å^{-3}
$\Delta\rho_{min} = -0.40$ e Å^{-3}

Compound (II)

Crystal data

$C_{12}H_{14}ClN_4^+\cdot C_6H_2N_3O_7^-\cdot C_2H_6OS$
$M_r = 555.97$
Triclinic, $P\overline{1}$
$a = 9.3365$ (3) Å
$b = 11.1245$ (3) Å
$c = 13.1861$ (6) Å
$\alpha = 83.779$ (3)°
$\beta = 86.057$ (3)°
$\gamma = 65.784$ (3)°
$V = 1241.24$ (8) Å^3
$Z = 2$
Mo $K\alpha$ radiation
$\mu = 0.30$ mm^{-1}
$T = 200$ K
0.47 × 0.26 × 0.21 mm

Data collection

Oxford Diffraction Gemini diffractometer
Absorption correction: multi-scan (*CrysAlis RED*; Oxford Diffraction, 2007)
$T_{min} = 0.873$, $T_{max} = 0.940$
17314 measured reflections
7722 independent reflections
3648 reflections with $I > 2\sigma(I)$
$R_{int} = 0.029$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.054$
$wR(F^2) = 0.172$
$S = 0.93$
7722 reflections
337 parameters
H-atom parameters constrained
$\Delta\rho_{max} = 1.09$ e Å^{-3}
$\Delta\rho_{min} = -0.60$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °) for (I).

O3*A*—C9*A*	1.251 (2)	O7*B*—N5*B*	1.227 (2)
O4*A*—N4*A*	1.221 (2)	O8*B*—N6*B*	1.233 (2)
O5*A*—N4*A*	1.233 (2)	O9*B*—N6*B*	1.226 (2)
O6*A*—N5*A*	1.229 (3)	N1*A*—C2*A*	1.362 (3)
O7*A*—N5*A*	1.234 (2)	N1*A*—C6*A*	1.367 (2)
O8*A*—N6*A*	1.221 (2)	N3*A*—C4*A*	1.329 (3)
O9*A*—N6*A*	1.230 (2)	N3*A*—C2*A*	1.336 (3)
O3*B*—C9*B*	1.251 (2)	N1*B*—C6*B*	1.365 (3)
O4*B*—N4*B*	1.229 (3)	N1*B*—C2*B*	1.366 (3)
O5*B*—N4*B*	1.224 (3)	N3*B*—C2*B*	1.335 (3)
O6*B*—N5*B*	1.229 (3)	N3*B*—C4*B*	1.328 (3)
C2*A*—N1*A*—C6*A*	120.27 (16)	C2*B*—N1*B*—C6*B*	120.44 (16)
C2*A*—N3*A*—C4*A*	116.36 (17)	C2*B*—N3*B*—C4*B*	116.42 (18)

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

D—H···A	D—H	H···A	D···A	D—H···A
N2A—H2A1···O5B	0.86	2.21	3.047 (3)	165
N1A—H1A···O3A	0.86	1.97	2.720 (2)	145
N1A—H1A···O4A	0.86	2.51	3.226 (2)	142
N1B—H1B···O3B	0.86	1.93	2.707 (2)	149
N2A—H2A2···O3A	0.86	2.03	2.771 (2)	143
N2A—H2A2···O9A	0.86	2.27	2.970 (2)	138
N2B—H2B1···O5A^{i}	0.86	2.24	3.017 (2)	151
N2B—H2B2···O3B	0.86	2.11	2.842 (2)	142
N2B—H2B2···O9B	0.86	2.40	3.134 (2)	144
C7A—H7A2···O6B	0.96	2.48	3.050 (3)	118
C5A—H5A···O7A^{ii}	0.93	2.29	3.100 (2)	146
C5B—H5B···O7B^{iii}	0.93	2.31	3.142 (2)	148
C7B—H7B3···O4A^{iv}	0.96	2.47	3.346 (3)	152

Symmetry codes: (i) $x+1, y-1, z$; (ii) $x, y, z-1$; (iii) $x, y, z+1$; (iv) $-x+1, -y+1, -z+2$.

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

Cl1—C12	1.739 (2)	O5—N6	1.238 (3)
S1—O8	1.4997 (19)	O6—N7	1.194 (3)
S1—C21	1.781 (3)	O7—N7	1.208 (3)
S1—C22	1.773 (3)	N1—C6	1.377 (3)
O1—C15	1.238 (2)	N1—C2	1.360 (3)
O2—N5	1.217 (2)	N3—C2	1.334 (2)
O3—N5	1.229 (2)	N3—C4	1.344 (2)
O4—N6	1.220 (3)		
C21—S1—C22	97.39 (16)	C2—N1—C6	121.51 (15)
O8—S1—C21	105.84 (13)	C2—N3—C4	117.92 (17)
O8—S1—C22	105.76 (15)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1	0.88	2.05	2.827 (2)	147
N2—H2A···O8	0.88	2.08	2.953 (3)	169
N2—H2B···O1	0.88	2.04	2.827 (2)	148
N2—H2B···O2	0.88	2.18	2.862 (2)	134
N4—H4A···N3^{i}	0.88	2.12	2.996 (2)	170
N4—H4B···O8^{i}	0.88	2.05	2.765 (2)	137

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

All H atoms were positioned geometrically and treated as riding. The C—H and N—H bond lengths are 0.93–0.96 and 0.86 Å, respectively, for (I), and 0.95–0.99 and 0.88 Å for (II). The constraint U_{iso}(H) = 1.2U_{eq}(carrier) or 1.5U_{eq}(methyl carrier) was applied as appropriate.

For (I), data collection: *COLLECT* (Hooft, 1998); cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT*; data reduction: *DENZO* and *COLLECT*. For (II), data collection: *CrysAlis CCD* (Oxford Diffraction, 2007); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2007). For both compounds, program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *PLATON*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GZ3155). Services for accessing these data are described at the back of the journal.

References

Atwal, K. S., Rovnyak, G. C., O'Reilly, B. C. & Schwartz, J. (1989). *J. Org. Chem.* **54**, 5898–5907.

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.

Deetz, M. J., Shang, M. Y. & Smith, B. D. (2000). *J. Am. Chem. Soc.* **122**, 6201–6207.

Desiraju, G. R. (1989). In *Crystal Engineering: The Design of Organic Solids.* Amsterdam: Elsevier.

Etter, M. C. (1990). *Acc. Chem. Res.* **23**, 120–126.

Harper, J. K., Dalley, N. K., Mulgrew, A. E., West, F. G. & Grant, D. M. (2001). *Acta Cryst.* C**57**, 64–65.

Hitchings, G. H. & Burchall, J. J. (1965). *Advances in Enzymology*, Vol. 27, edited by F. Nord, p. 417. New York: Interscience.

Hooft, R. (1998). *COLLECT*. Nonius BV, Delft, The Netherlands.

Hunter, C. A. (1994). *Chem. Soc. Rev.* **23**, 101–109.

In, Y., Nagata, H., Doi, M., Ishida, T. & Wakahara, A. (1997). *Acta Cryst.* C**53**, 367–369.

Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Low, J. N., Quesada, A., Marchal, A., Melguizo, M., Nogueras, M. & Glidewell, C. (2002). *Acta Cryst.* C**58**, o289–o294.

Narayana, B., Sarojini, B. K., Prakash Kamath, K., Yathirajan, H. S. & Bolte, M. (2008). *Acta Cryst.* E**64**, o117–o118.

Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*. Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet. pp. 307–326. New York: Academic Press.

Oxford Diffraction (2007). *CrysAlis CCD* and *CrysAlis RED*. Versions 1.171.32.5. Oxford Diffraction Ltd, Abingdon, Oxfordshire, England.

Sansom, C. E., Schwalbe, C. H., Lambert, P. A., Griffin, R. J. & Stevens, M. F. G. (1989). *Biochim. Biophys. Acta*, **995**, 21–27.

Schwalbe, C. H. & Cody, V. (2006). *Crystallogr. Rev.* pp. 267–300.

Sethuraman, V. & Thomas Muthiah, P. (2002). *Acta Cryst.* E**58**, o817–o818.

Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.

Shriner, R. L., Fuson, R. C., Curtin, D. Y. & Morrill, T. C. (1980). *Qualitative Identification of Organic Compounds*, 6th ed., pp. 236–237. New York: Wiley.

Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.

Stanley, N., Muthiah, P. T., Geib, S. J., Luger, P., Weber, M. & Messerschmidt, M. (2005). *Tetrahedron*, **61**, 7201–7210.

Subashini, A., Muthiah, P. T., Bocelli, G. & Cantoni, A. (2006). *Acta Cryst.* E**62**, o3847–o3849.

Tanaka, R., Arai, T. & Hirayama, N. (2004). *Anal. Sci. X*, **20**, x175.

Thanigaimani, K., Muthiah, P. T. & Lynch, D. E. (2007*a*). *Acta Cryst.* C**63**, o295–o300.

Thanigaimani, K., Muthiah, P. T. & Lynch, D. E. (2007*b*). *Acta Cryst.* E**63**, o4555–o4556.

TranQui, D., Fresneau, P. & Cussac, M. (1998). *Acta Cryst.* C**54**, 1152–1154.