Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

The molecular and supramolecular structures of the isomeric compounds 5,7-dimethoxyimidazo[1,2-*c*]pyrimidine and 7-methoxy-1-methylimidazo[1,2-*a*]pyrimidin-5(1*H*)-one

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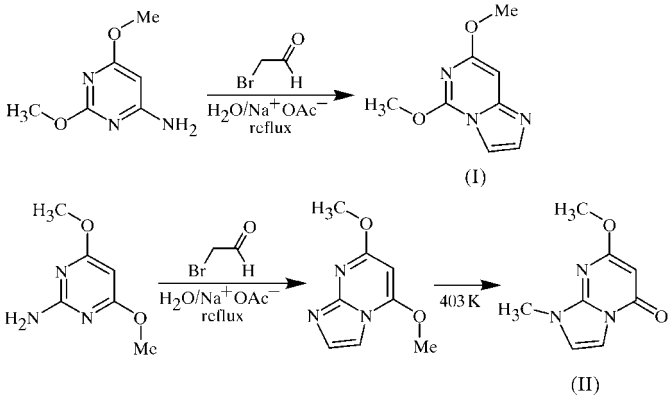
Received 6 May 2003
Accepted 12 May 2003
Online 11 June 2003

The supramolecular structures of the isomeric compounds 5,7-dimethoxyimidazo[1,2-*c*]pyrimidine, $C_8H_9N_3O_2$, (I), and 7-methoxy-1-methylimidazo[1,2-*a*]pyrimidin-5(1*H*)-one, $C_8H_9N_3O_2$, (II), are determined by weak C—H···N and C—H···O hydrogen bonds in (I), which generate alternating linked centrosymmetric $R_2^2(8)$ and $R_2^2(10)$ rings that form a ribbon running parallel to the *c* axis, and by C—H···O bonds in (II), which link the molecules into sheets comprising centrosymmetric $R_2^2(10)$ and $R_4^4(22)$ rings.

Comment

Imidazopyrimidine derivatives are a group of fused heterocyclic systems of particular interest due to their resemblance to the ubiquitous biologically important purine, and thence



their potential as antimetabolites showing useful biological activities. In fact, some imidazo[1,2-*a*]pyrimidines have shown antifungal (Rival *et al.*, 1991) and anti-inflammatory/analgesic activities (Sacchi *et al.*, 1997). In this paper, we report the molecular and supramolecular structures of two isomeric examples of such fused heterocyclic derivatives, namely 5,7-dimethoxyimidazo[1,2-*c*]pyrimidine, (I), and 7-methoxy-1-methylimidazo[1,2-*a*]pyrimidin-5(1*H*)-one, (II). The former was prepared by reaction of commercial 4-amino-2,6-dimethoxypyrimidine with bromoacetaldehyde (Quijano *et al.*, 1994). The latter was obtained in good yield by fusion of the crystalline intermediate 5,7-dimethoxyimidazo[1,2-*a*]pyrimidine, which was prepared by reaction of commercial 2-amino-4,6-dimethoxypyrimidine with bromoacetaldehyde.

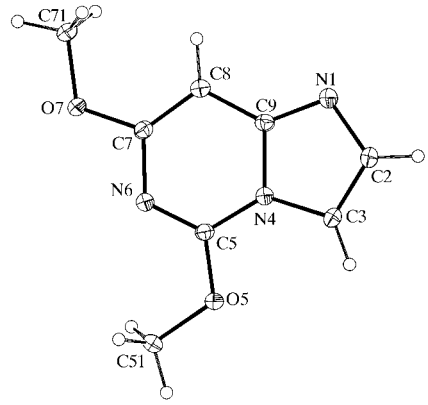


Figure 1
A view of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

There are no unusual bond lengths or angles in (I) and (II), however, the bond distances along the fused heterocycle perimeter of (I) show a clear alternation in single- and double-bond character, pointing to the low aromatic nature of this compound (Table 1). In both compounds, the six- and five-membered rings are planar, with the angles between the rings being 1.40 (10) and 3.13 (12)° in (I) and (II), respectively. In (I), the torsion angles about the C5—O5 and C7—O7 bonds show that the methoxy groups are coplanar with the ring system. In (II), however, the torsion angles about the C7—O7 bond show that the methoxy group is tilted out of the plane of the ring system (Table 3).

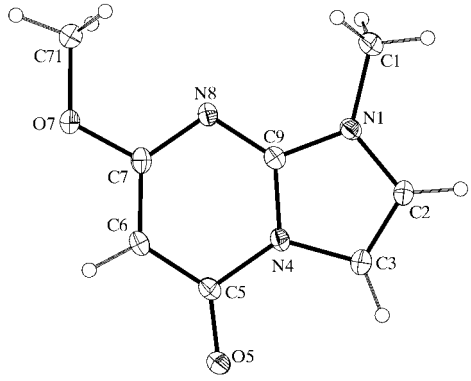


Figure 2
A view of (II) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

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 DOI: 10.1107/S0108270103010266

In the absence of any donors for conventional hydrogen bonds, the supramolecular structures are controlled by the formation of weak C—H···N and C—H···O hydrogen bonds in (I) and by weak C—H···O hydrogen bonds in (II). In the case of (I), these bonds are weaker than in (II), as evidenced by the C8···N1 and C3···O5 distances of 3.476 (2) and 3.391 (2) Å, respectively, in (I), and the C3···O5 and C2···O5 distances of 3.104 (3) and 3.339 (3) Å, respectively, in (II); details of the hydrogen bonding are given in Tables 2 and 4.

In (I), the molecules are linked to form one-dimensional ribbons of centrosymmetric dimers which run parallel to the *c* axis (Fig. 3). Atom C8 in the molecule at (*x*, *y*, *z*) acts as a hydrogen-bond donor, *via* atom H8, to ring atom N1 in the molecule at ($-x$, $1-y$, $1-z$), so generating a centrosymmetric $R_2^2(8)$ ring (Bernstein *et al.*, 1995) centred at (0, $\frac{1}{2}$, $\frac{1}{2}$). Atom C3 in the molecule at (*x*, *y*, *z*) acts as a hydrogen-bond donor, *via* atom H3, to methoxy atom O5 in the molecule at ($-x$, $1-y$, $-z$), so generating a centrosymmetric $R_2^2(10)$ ring centred at (0, $\frac{1}{2}$, 0). Alternatively, the molecules can be viewed as being linked head-to-tail by two centrosymmetrically related $C_2^2(10)$ chains. There are no other direction-specific contacts in the structure.

In (II), atom C2 in the molecule at (*x*, *y*, *z*) acts as a hydrogen-bond donor, *via* atom H2, to atom O5 in the molecule at (x, $\frac{3}{2}-y$, $\frac{1}{2}+z$), so generating a $C(6)$ chain which runs parallel to the *c* axis (Fig. 4). This chain is produced by the action of the *c*-glide plane at $y=\frac{3}{4}$. This chain is then linked to an antiparallel chain produced by the action of centres-of-symmetry to form a corrugated ribbon which lies approximately parallel to the (010) plane. In the crosslink, atom C3 in the molecule at (*x*, *y*, *z*) acts as a hydrogen-bond donor, *via* atom H3, to atom O5 in the molecule at ($1-x$, $1-y$, $1-z$), so generating a centrosymmetric $R_2^2(10)$ ring centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$). An $R_4^4(22)$ ring centred at ($\frac{1}{2}$, $\frac{1}{2}$, 1) is also formed involving six

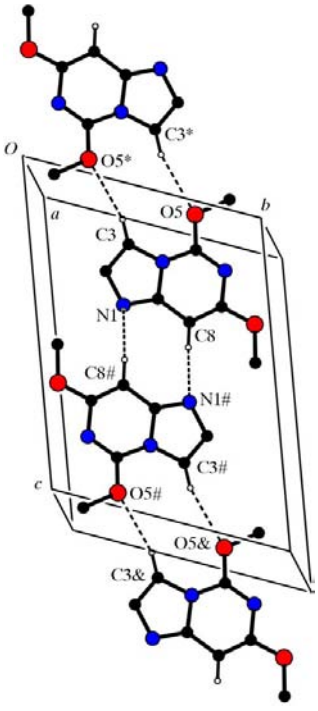

Figure 3
View of the ribbon structure running parallel to the *c* axis in (I). Atoms marked with an asterisk (*), hash (#) or ampersand (&) are at the symmetry positions ($-x$, $1-y$, $-z$), ($-x$, $1-y$, $1-z$) and (x, y, $1+z$), respectively.

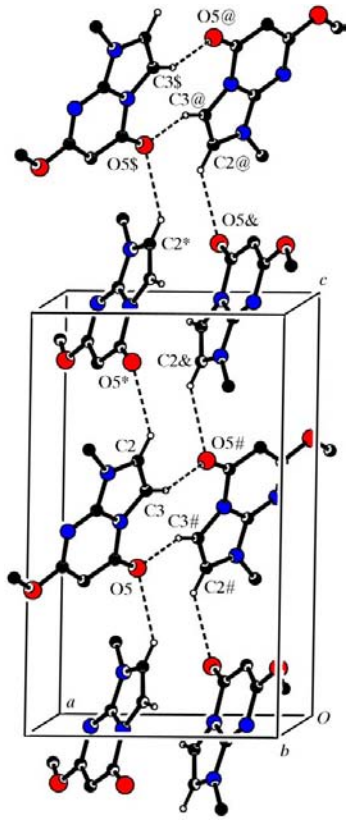

Figure 4
View of the part of the sheet structure formed in (II) by two antiparallel $C(6)$ chains linked by centrosymmetric $R_2^2(10)$ and $R_4^4(22)$ rings. Atoms marked with an asterisk (*), hash (#), ampersand (&), dollar sign ($) or 'at' sign (@) are at the symmetry positions (x, $\frac{3}{2}-y$, $\frac{1}{2}+z$), ($1-x$, $1-y$, $1-z$), ($1-x$, $-\frac{1}{2}+y$, $\frac{3}{2}-z$), (x, y, $1+z$) and ($1-x$, $1-y$, $2-z$), respectively.

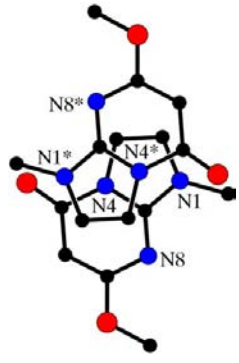

Figure 5
View of the stacking of the molecules in (II), showing the positon of atom N4 almost directly above the centroid of the five-membered ring. The molecule labelled with an asterisk (*) is at the symmetry position ($1-x$, $1-y$, $1-z$).

molecules, with four C2—H2···O5 and two C3—H3···O5 interactions. In this ring, two molecules donate and accept one interaction each, two accept two interactions to the same atom and two donate two interactions *via* two different H atoms each (Fig. 4). These ribbons are then linked *via* further C3—H3···O5 crosslinks, extending the structure parallel to the *b* axis, thereby forming corrugated sheets which lie in the (100) plane.

The molecules stack above each other such that atom N4 of the five-membered ring lies almost directly above the centroid of the five-membered ring at $(1-x, 1-y, -z)$. The inter-centroid distance is 3.5221 (14) Å, the perpendicular distance between the centroid of one ring and the plane of the other is 3.301 Å, and the offset between centroids is 1.228 Å. A view of the stacking is shown in Fig. 5, while Fig. 6 shows a stereoview of the three-dimensional structure formed by the interaction of the sheets, together with the molecular stacking.

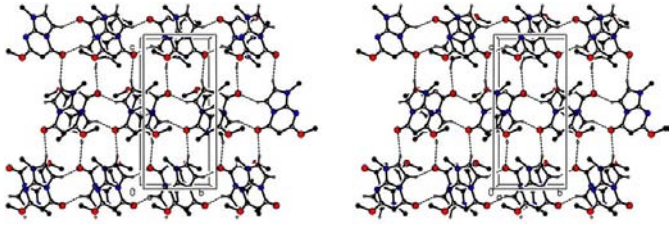

Figure 6
Stereoview of the three-dimensional structure of (II), viewed down the *a* axis.

Experimental

For the preparation of 5,7-dimethoxyimidazo[1,2-*c*]pyrimidine, (I), a mixture of bromoacetaldehyde diethyl acetal (6.9 ml, 45.4 mmol) and water (25 ml) was treated with concentrated hydrochloric acid (2.5 ml) and heated until a homogeneous solution was obtained. The pH was adjusted to 5–6 with solid sodium acetate and the resulting solution was added dropwise to a suspension of 4-amino-2,6-dimethoxypyrimidine (0.51 g, 3.2 mmol) in water (13 ml) containing sodium acetate (0.27 g, 3.2 mmol). The mixture was refluxed for 20 min and, after cooling, 1 *N* NaOH was added until a pH of 8 was achieved. The crude reaction mixture was extracted with dichloromethane. The extract was dried over anhydrous sodium sulfate and the solvent removed *in vacuo*. The residue was chromatographed on a silica-gel flash column to afford 0.214 g (1.19 mmol, 37%) of compound (I). ^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ 3.92 (*s*, 3H, CH_3O-7), 4.21 (*s*, 3H, CH_3O-5), 6.37 (*s*, 1H, H-8), 7.42 (*s*, 2H, H-2 and H-3); ^{13}C NMR (75 MHz, $CDCl_3$/TMS): δ 55.26, 55.87, 82.19, 107.02, 134.03, 148.13, 150.05 and 160.56. Recrystallization from ethyl acetate produced a crystalline sample suitable for single-crystal X-ray diffraction analysis (m.p. 387 K).

7-Methoxy-1-methylimidazo[1,2-*a*]pyrimidin-5(1*H*)-one, (II), was prepared using a procedure similar to that used for the preparation of compound (I). 5,7-Dimethoxyimidazo[1,2-*a*]pyrimidine (150 mg, 0.837 mmol) (m.p. 399 K) was obtained from 2-amino-4,6-dimethoxypyrimidine (1.64 g, 10.3 mmol) and bromoacetaldehyde diethyl acetal (6.25 ml, 41.2 mmol) (reaction time: 40 min). ^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ 4.03 (*s*, 3H, CH_3O-7), 4.08 (*s*, 3H, CH_3O-5), 5.67 (*s*, 1H, H-6), 7.34 (*d*, J = 1.7 Hz, 1H, H-3), 7.42 (*d*, J = 1.7 Hz, 1H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$/TMS): δ 54.35, 56.72, 77.12, 105.87, 132.06, 149.06, 156.36 and 165.12. This compound was placed in a Pyrex tube and heated in an oil bath at 403 K for 20 min. During this period, melting and resolidification of the starting material was observed. The solid residue was directly recrystallized from ethyl acetate to afford 113 mg (0.631 mmol, 75% yield) of compound (II) as crystals suitable for X-ray diffraction analysis (m.p. 449 K). ^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ 3.67 (*s*, 3H, CH_3N), 3.89 (*s*, 3H, CH_3O), 5.39 (*s*, 1H, H-6), 6.86 (*d*, J = 3.1 Hz, 1H, H-2), 7.48 (*d*, J = 3.1 Hz, 1H, H-3). ^{13}C NMR (75 MHz, $CDCl_3$/TMS): δ 31.51, 54.28, 80.01, 106.89, 118.28, 145.72, 158.97 and 170.37.

Compound (I)

Crystal data

$C_8H_9N_3O_2$	Z = 2
M_r = 179.18	D_x = 1.484 Mg m^{-3}
Triclinic, $P\overline{1}$	Mo $K\alpha$ radiation
a = 3.8798 (3) Å	Cell parameters from 1756 reflections
b = 8.9183 (6) Å	θ = 3.5–27.4°
c = 12.6224 (11) Å	μ = 0.11 mm^{-1}
α = 69.426 (3)°	T = 120 (2) K
β = 83.093 (4)°	Block, colourless
γ = 79.189 (4)°	0.22 × 0.14 × 0.10 mm
V = 400.94 (5) Å^3	

Data collection

Nonius KappaCCD diffractometer	R_{int} = 0.058
φ scans, and ω scans with κ offsets	θ_{max} = 27.4°
6415 measured reflections	$h = -5 \rightarrow 4$
1756 independent reflections	$k = -11 \rightarrow 11$
1182 reflections with $I > 2\sigma(I)$	$l = -16 \rightarrow 16$

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.053	$w = 1/[\sigma^2(F_o^2) + (0.0751P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2)$ = 0.134	$(\Delta/\sigma)_{max} < 0.001$
S = 1.03	$\Delta\rho_{max}$ = 0.31 e Å^{-3}
1756 reflections	$\Delta\rho_{min}$ = −0.32 e Å^{-3}
120 parameters	

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

N1—C9	1.324 (2)	C5—O5	1.3335 (19)
N1—C2	1.384 (2)	O5—C51	1.455 (2)
C2—C3	1.353 (3)	N6—C7	1.379 (2)
C3—N4	1.388 (2)	C7—O7	1.358 (2)
N4—C5	1.364 (2)	C7—C8	1.362 (2)
N4—C9	1.402 (2)	O7—C71	1.4398 (19)
C5—N6	1.292 (2)	C8—C9	1.412 (2)
C9—N1—C2	104.59 (15)	C5—N6—C7	117.12 (14)
C3—C2—N1	112.94 (16)	O7—C7—C8	125.53 (15)
C2—C3—N4	104.55 (15)	O7—C7—N6	109.84 (14)
C5—N4—C3	132.45 (14)	C8—C7—N6	124.63 (15)
C5—N4—C9	120.28 (14)	C7—O7—C71	116.35 (13)
C3—N4—C9	107.23 (13)	C7—C8—C9	116.92 (16)
N6—C5—O5	123.74 (15)	N1—C9—N4	110.69 (14)
N6—C5—N4	123.52 (15)	N1—C9—C8	131.85 (16)
O5—C5—N4	112.75 (14)	N4—C9—C8	117.44 (15)
C5—O5—C51	116.14 (13)		
N6—C5—O5—C51	0.4 (2)	C8—C7—O7—C71	1.9 (3)
N4—C5—O5—C51	−179.47 (15)	N6—C7—O7—C71	−178.37 (14)

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

D—H···A	D—H	H···A	D···A	D—H···A
C8—H8···N1^{i}	0.95	2.59	3.476 (2)	155
C3—H3···O5^{ii}	0.95	2.50	3.391 (2)	157

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

Compound (II)

Crystal data

$C_8H_9N_3O_2$
$M_r = 179.18$
Monoclinic, $P2_1/c$
$a = 8.5917$ (6) Å
$b = 6.7484$ (5) Å
$c = 14.3054$ (14) Å
$\beta = 91.648$ (3)°
$V = 829.09$ (12) Å^3
$Z = 4$
$D_x = 1.436$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1855 reflections
$\theta = 3.3$–27.5°
$\mu = 0.11$ mm^{-1}
$T = 120$ (2) K
Plate, colourless
0.30 × 0.28 × 0.02 mm

Data collection

Nonius KappaCCD diffractometer
φ scans, and ω scans with κ offsets
6217 measured reflections
1855 independent reflections
993 reflections with $I > 2\sigma(I)$
$R_{int} = 0.087$
$\theta_{max} = 27.5°$
$h = -11 \rightarrow 10$
$k = -8 \rightarrow 8$
$l = -13 \rightarrow 18$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.052$
$wR(F^2) = 0.122$
$S = 0.94$
1855 reflections
120 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0513P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.29$ e Å^{-3}

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

N1—C9	1.350 (3)	C5—O5	1.244 (3)
N1—C2	1.380 (3)	C5—C6	1.393 (3)
N1—C1	1.456 (3)	C6—C7	1.378 (3)
C2—C3	1.349 (3)	C7—N8	1.346 (3)
C3—N4	1.401 (3)	C7—O7	1.354 (3)
N4—C9	1.363 (3)	O7—C71	1.437 (3)
N4—C5	1.428 (3)	N8—C9	1.328 (3)
C9—N1—C2	108.71 (18)	C6—C5—N4	112.10 (19)
C9—N1—C1	124.14 (19)	C7—C6—C5	121.7 (2)
C2—N1—C1	127.10 (19)	N8—C7—O7	117.0 (2)
C3—C2—N1	109.1 (2)	N8—C7—C6	125.9 (2)
C2—C3—N4	105.82 (19)	O7—C7—C6	117.1 (2)
C9—N4—C3	109.22 (18)	C7—O7—C71	117.10 (18)
C9—N4—C5	121.30 (18)	C9—N8—C7	112.43 (18)
C3—N4—C5	129.39 (19)	N8—C9—N1	126.2 (2)
O5—C5—C6	129.7 (2)	N8—C9—N4	126.6 (2)
O5—C5—N4	118.16 (19)	N1—C9—N4	107.17 (18)
N8—C7—O7—C71	−9.1 (3)	C6—C7—O7—C71	171.5 (2)

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

D—H···A	D—H	H···A	D···A	D—H···A
C3—H3···O5^{i}	0.95	2.22	3.104 (3)	153
C2—H2···O5^{ii}	0.95	2.57	3.339 (3)	139

Symmetry codes: (i) $1-x, 1-y, 1-z$; (ii) $x, \frac{3}{2}-y, \frac{1}{2}+z$.

Compound (I) crystallized in the triclinic system; space group $P\overline{1}$ was assumed and confirmed by the analysis. Compound (II) crystallized in the monoclinic system; space group $P2_1/c$ was determined by the systematic absences. For both compounds, H atoms were treated as riding atoms, with C—H distances of 0.95 (aromatic) and 0.98 Å (CH_3).

For both compounds, data collection: *KappaCCD Server Software* (Nonius, 1997); cell refinement: *DENZO–SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO–SMN*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL*97 and *WordPerfect* macro *PRPKAPPA* (Ferguson, 1999).

X-ray data were collected at the EPSRC, X-ray Crystallographic Service, University of Southampton; the authors thank the staff for all their help and advice. JNL thanks NCR Self-Service, Dundee, for grants which have provided computing facilities for this work.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: LN1168). Services for accessing these data are described at the back of the journal.

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