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2-(4-Bromophenyl)-1,2-dihydropyrimido[1,2-*a*]benzimidazol-4(3*H*)-one and 4-(4-methylphenyl)-3,4-dihydropyrimido[1,2-*a*]benzimidazol-2(1*H*)-one form hydrogen-bonded base-paired dimers

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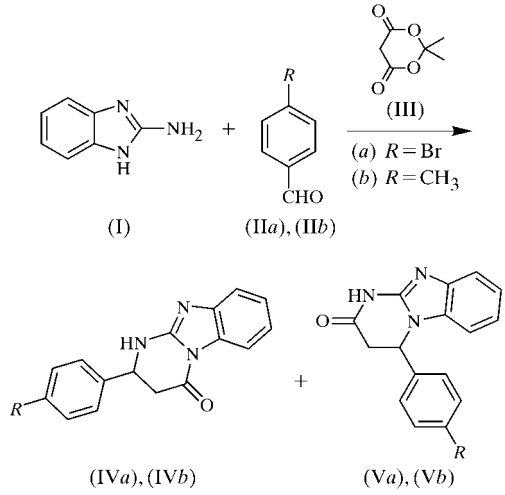
The title compounds, 2-(4-bromophenyl)-1,2-dihydropyrimido[1,2-*a*]benzimidazol-4-(3*H*)-one, $C_{16}H_{12}BrN_3O$, (IV*a*), and 4-(4-methylphenyl)-3,4-dihydropyrimido[1,2-*a*]benzimidazol-2-(1*H*)-one, $C_{17}H_{15}N_3O$, (V*b*), both form $R_2^2(8)$ centrosymmetric dimers *via* N—H···N hydrogen bonds. The N···N distance is 2.943 (3) Å for (IV*a*) and 2.8481 (16) Å for (V*b*), with the corresponding N—H···N angles being 129 and 167°, respectively. However, in other respects, the supramolecular structures of the two compounds differ. Both compounds contain different C—H···π interactions, in which the C—H···π(centroid) distances are 2.59 and 2.47 Å for (IV*a*) and (V*b*), respectively (the latter being a short distance), with C—H···π(centroid) angles of 158 and 159°, respectively. The supramolecular structures also differ, with a short Br···O distance of 3.117 (2) Å in bromo derivative (IV*a*), and a C—H···O interaction with a C···O distance of 3.2561 (19) Å and a C—H···O angle of 127° in tolyl system (V*b*). The dihydropyrimido part of (V*b*) is disordered, with a ratio of the major and minor components of 0.9:0.1. The disorder consists of two non-interchangeable envelope conformers, each with an equatorial tolyl group and an axial methine H atom.

Comment

Benzimidazoles are associated with antiparasitic (Loewe *et al.*, 1978), central nervous system depressant and anti-inflammatory (Yale & Bristol, 1977; Denzel & Hoehn, 1978*a*,*b*) and other pharmacological activities (Berg & Parnell, 1961; Mendzneritskaya *et al.*, 1978; Paget *et al.*, 1969, 1980). Hence, it may be expected that pyrimidobenzimidazoles such as the title compounds, (IV*a*) and (V*b*), might display potent biological activity.

In previous research (Quiroga *et al.*, 1999, and references therein), we have shown that the reaction between heterocyclic amines and benzylidene derivatives of compounds with an active methylene group, such Meldrum's acid, dimedone, malonodinitrile or ethyl cyanoacetate, is a good synthetic procedure to produce fused pyridinic and pyrimidinic systems. Here, we describe two regioisomer compounds obtained from the reaction of 2-aminobenzimidazole, (I), the benzaldehydes (II*a*) and (II*b*), and Meldrum's acid, (III). The isomerism in the reaction is due to the two non-equivalent nucleophilic centres in (I), the NH_2 group and the *endo* N atom. The formation of both products was observed in the two reactions. Related processes with Meldrum's acids are well known (McNab, 1978; Brown *et al.*, 1974). Herein, we describe the X-ray crystal structures for the crystalline derivatives with R = Br, (IV*a*), and R = CH_3, (V*b*).



Compound (IV*a*) (Fig. 1) crystallizes in the monoclinic space group $P2_1/c$ and (V*b*) (Fig. 2) in the triclinic space group $P\overline{1}$. In (V*b*), there is disorder involving the envelope dihydropyrimido part of the molecule, such that the C atom of the envelope lies below and above the mean plane of the other

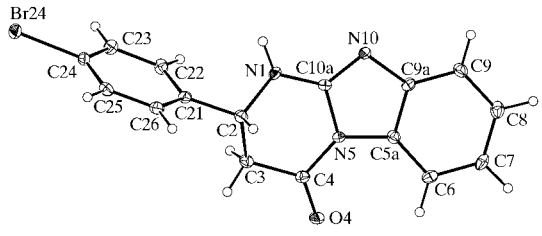


Figure 1
A view of (IV*a*) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

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five ring atoms for the major and minor components, respectively, which are in the ratio 0.9:0.1. This disorder consists of two non-interchangeable conformers, each with an equatorial tolyl group and an axial methine H atom. Thus, two enantiomers are present, since a straightforward 'flip' of the envelope would give an axial tolyl and an equatorial H atom. A view of the two components of the disorder is shown in Fig. 3.

In both compounds, an $R_2^2(8)$ centrosymmetric base-paired dimer (Bernstein *et al.*, 1995) is formed, *via* the N1—H1···N10($2-x, 1-y, -z$) hydrogen bond in (IV*a*) (Fig. 4) and the corresponding N1—H1···N10($2-x, 1-y, 1-z$) hydrogen bond in (V*b*). There is a short Br24···O4($1-x, \frac{1}{2}+y, \frac{1}{2}-z$) contact of 3.117 (2) Å in (IV*a*). In the case of (V*b*), there is a weak C3—H3*A*···O2($2-x, 1-y, 1-z$) hydrogen bond, with a C···O distance of 3.2561 (19) Å and a C3—H3*A*···O2 angle of 127 Å. This latter interaction forms an $R_2^2(8)$ ring. These two ring structures link the molecules into a continuous ribbon which runs parallel to the *b* axis. Alternatively, this ribbon can be regarded as being formed by two antiparallel $C_2^2(10)$ centrosymmetrically related chains (Fig. 5).

The supramolecular structures of the two compounds differ in other respects as well. Both compounds contain different C—H···π(arene) interactions. In (IV*a*), there is a C9—H9···*CgX*($2-x, 1-y, -z$) contact of 2.59 Å, where *CgX* is

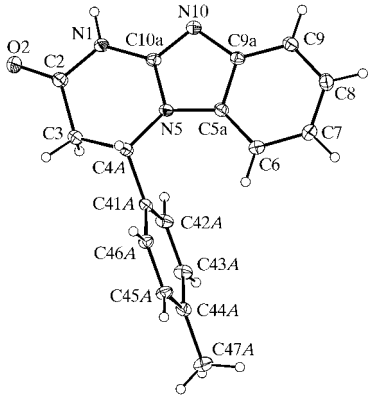

Figure 2
A view of the major component of (V*b*) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

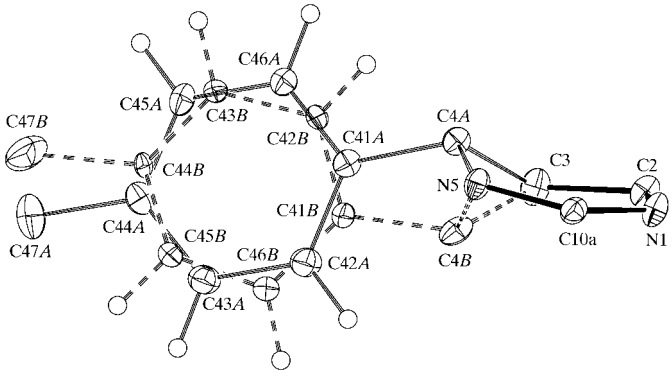

Figure 3
A view of the major and minor components in the disorder of (V*b*). Only the dihydropyrimido part of the molecule and the tolyl groups are shown, and the methyl H atoms have been omitted for clarity.

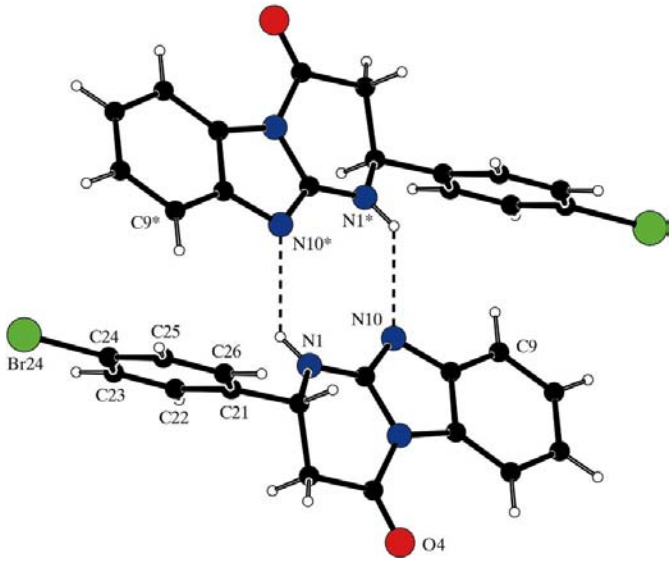

Figure 4
A view of the $R_2^2(8)$ base-paired dimer in (IV*a*).

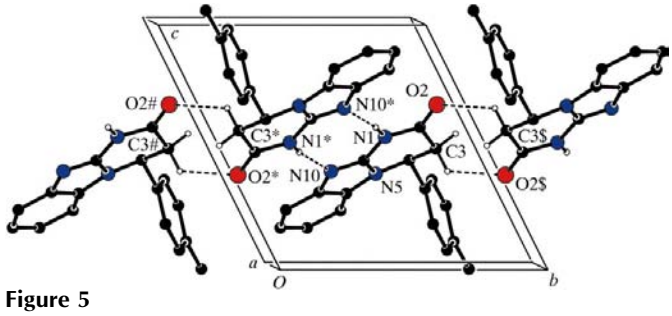

Figure 5
A view of the ribbon structure in (V*b*); only the major component is shown. H atoms not involved in the hydrogen bonding have been omitted for clarity. The molecule labelled * is at ($2-x, 1-y, 1-z$), that labelled # is at ($x, y-1, z$) and that labelled $ is at ($2-x, 2-y, 1-z$).

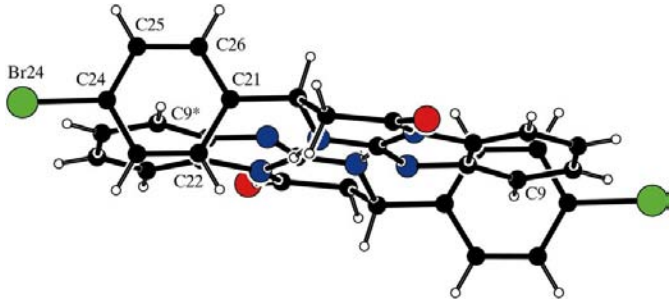

Figure 6
A view of the C—H···π interaction for (IV*a*) perpendicular to the ring at C21; atom C9* is in the molecule at ($2-x, 1-y, -z$).

the centroid of ring *X*, and *X* is the ring C21–C26. The perpendicular distance C9···*CgX* is 2.58 Å and the angle at H9 is 158°. This interaction reinforces the strong N—H···N bond described above, since it involves the same two molecules which are thus linked head-to-tail. This interaction can be seen in Figs. 4 and 6. Thus, in (IV*a*), the main supramolecular structure is the dimer.

In (V*b*), there is a C4*A*—H4*A*···*CgY*(1 − *x*, 1 − *y*, 1 − *z*) contact of 2.47 Å (*Y* is the ring C5a–C9a). The perpendicular distance C4*A*···*CgY* is 2.43 Å and the angle at H4*A* is 159°. This H···π distance is rather short at *ca* 2.40 Å, if C—H is given the neutron value of 1.083 Å. This means that it lies within 0.10–0.15 Å of the values found in some alkynyltetraborate structures (Lindeman *et al.*, 1998). Fig. 7 shows that the molecules are linked head-to-tail by this interaction. The minor component of (V*b*) is not involved in any such interaction. Details of the hydrogen bonding are given in Tables 1 and 2.

Only one similar compound which includes H atoms in the analysis was found in the Cambridge Structural Database (Release 5.22, October 2001; Allen & Kennard, 1993), namely 2,2-dimethyl-1,2,3,4-tetrahydrobenzimidazo[3,2-*a*]pyrimid-4-one (VOBLAZ; Bird *et al.*, 1991). In this structure, an identical dimer to that found for (IV*a*) and (V*b*) is formed, with an N···N distance of 3.037 (3) Å and an angle at H of 175°. There are C—H···O contacts, but these are too long to be classed as weak hydrogen bonds. In addition, there is a C—H···π(arene) contact involving a methyl H atom of 2.79 Å (perpendicular distance 2.78 Å), with an angle at H of 176°. One noticeable feature of this compound which differs markedly from (IV*a*) and (V*b*) is the difference in the angles at the H atoms, which suggests that the interplay between the C—H···π hydrogen bonds, which are very much shorter in (IV*a*) and (V*b*) than in VOBLAZ, may have sufficient strength to distort the N—H···N hydrogen bonds in (IV*a*) and (V*b*).

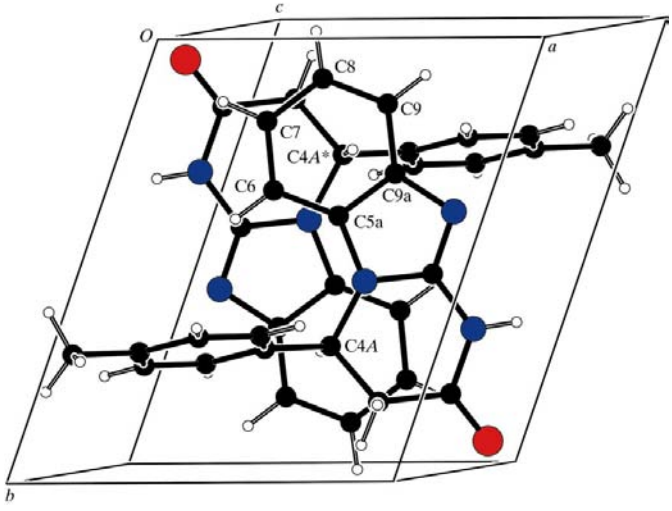

Figure 7
A view of the C—H···π interaction for (V*b*) perpendicular to the ring at C5a; atom C4*A** is in the molecule at (1 − *x*, 1 − *y*, 1 − *z*).

Experimental

A solution of 2-aminobenzimidazole, (I) (2.0 mmol), and an equimolar amount of 4-bromobenzaldehyde, (II*a*), or 4-tolualdehyde, (II*b*), and Meldrum's acid, (III), in ethanol (20 ml) was refluxed for 1–2 h with thin-layer chromatography control. The solvent was then removed and the resulting precipitate was filtered, washed with ethanol, dried and purified by silica-gel chromatography with ethyl acetate as the eluent. The title compounds were eluted in the order (IV) then (V) from the column. Colourless crystals suitable for X-ray diffraction were obtained directly from the chromatographic fractions. (IV*a*): 20% yield, m.p. 577 K; (V*b*): 69% yield, m.p. 506 K.

Table 1
Hydrogen-bonding and contact geometry (Å, °) for (IV*a*).

CgX is the centroid of the C21–C26 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···N10^{i}	0.88	2.30	2.943 (3)	129
C9—H9···*CgX*^{i}	0.95	2.59	3.501 (3)	158

Symmetry code: (i) 2 − *x*, 1 − *y*, −*z*.

Table 2
Hydrogen-bonding and contact geometry (Å, °) for (V*b*).

CgY is the centroid of the C5a–C9a ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···N10^{i}	0.88	1.98	2.8481 (16)	167
C3—H3*A*···O2^{ii}	0.99	2.56	3.2561 (19)	127
C4*A*—H4*A*···*CgY*^{iii}	1.00	2.43	3.419 (16)	159

Symmetry codes: (i) 2 − *x*, 1 − *y*, 1 − *z*; (ii) 2 − *x*, 2 − *y*, 1 − *z*; (iii) 1 − *x*, 1 − *y*, 1 − *z*.

Compound (IV*a*)

Crystal data

$C_{16}H_{12}BrN_3O$
M_r = 342.20
Monoclinic, $P2_1/c$
a = 6.8807 (2) Å
b = 16.2254 (6) Å
c = 13.3379 (5) Å
β = 111.280 (2)°
V = 1387.54 (8) Å^3
Z = 4
D_x = 1.638 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 3046 reflections
θ = 3.0–27.4°
μ = 2.96 mm^{-1}
T = 120 (1) K
Lath, colourless
0.20 × 0.06 × 0.02 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ scans, and ω scans with κ offsets
Absorption correction: multi-scan (*DENZO-SMN*; Otwinowski & Minor, 1997)
T_{min} = 0.589, T_{max} = 0.943
8697 measured reflections
3046 independent reflections
2401 reflections with $I > 2\sigma(I)$
R_{int} = 0.078
θ_{max} = 27.4°
h = −8 → 8
k = −21 → 21
l = −17 → 13

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.114
S = 1.01
3046 reflections
190 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0658P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.71 e Å^{-3}
$\Delta\rho_{min}$ = −1.55 e Å^{-3}

Compound (V*b*)

Crystal data

$C_{17}H_{15}N_3O$	$Z = 2$
$M_r = 277.32$	$D_x = 1.299$ Mg m^{-3}
Triclinic, $P\overline{1}$	Mo $K\alpha$ radiation
$a = 8.1360$ (3) Å	Cell parameters from 3170 reflections
$b = 9.8647$ (4) Å	$\theta = 3.0$–$27.5°$
$c = 10.0975$ (5) Å	$\mu = 0.08$ mm^{-1}
$\alpha = 114.8796$ (13)°	$T = 120$ (1) K
$\beta = 94.9156$ (15)°	Block, colourless
$\gamma = 100.966$ (3)°	0.1 × 0.1 × 0.1 mm
$V = 709.18$ (5) Å^3	

Data collection

Nonius KappaCCD area-detector diffractometer	3170 independent reflections
φ scans, and ω scans with κ offsets	2247 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (*DENZO-SMN*; Otwinowski & Minor, 1997)	$R_{int} = 0.056$
$T_{min} = 0.992$, $T_{max} = 0.992$	$\theta_{max} = 27.5°$
10 703 measured reflections	$h = -10 \rightarrow 10$
	$k = -12 \rightarrow 12$
	$l = -13 \rightarrow 13$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0664P)^2 + 0.0023P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.046$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.120$	$\Delta\rho_{max} = 0.21$ e Å^{-3}
$S = 1.05$	$\Delta\rho_{min} = -0.21$ e Å^{-3}
3170 reflections	
264 parameters	
H-atom parameters constrained	

All H atoms were treated as riding, with C—H = 0.95 Å (phenyl H) for (IV*a*) and 1.00 Å (methine H) for (V*b*). A residual electron-density peak of 0.75 e Å^{-3} was found in the final stages of refinement for (V*b*) at 1.2 Å from C4*A*, 1.45 Å from C3 and 1.63 Å from N5. This suggested that two envelope forms were present for the dihydropyrimido part of the molecule and it was found that this was the case. Since the next difference map peaks were less than 0.3 e Å^{-3}, the nature of the disorder was not immediately obvious. When atom C4*B* was put at the position of the difference map peak, and atom C4*A* and the attached tolyl group were refined with a free variable, such that the combined site-occupancy factors summed to 1.0, then a minor component consisting of C4*B* and a staggered tolyl group overlapping the major component tolyl group was found from the resulting difference map (Fig. 3). The minor component was modelled using appropriate *DFIX* constraints to optimize the position of C4*B* with respect to C4*A*, C3, N5 and C41*B*. *ISOR* and *DELU* constraints were applied to the phenyl-ring atoms of the minor component (*SHELXL*97; Sheldrick, 1997). The ratio of major to minor components is *ca* 0.9:0.1 and consists of two non-interchangeable conformers, each with an axial tolyl group.

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; molecular graphics: *ORTEP*II (Johnson, 1976) and *PLATON* (Spek, 2001); software used to prepare material for publication: *SHELXL*97 and *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. In addition, the authors thank a referee and Dr Chris Glidewell, St Andrews University, for help and discussion in the interpretation of the disorder in (V*b*). We are grateful to COLCIENCIAS and Universidad del Valle for financial support.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1087). Services for accessing these data are described at the back of the journal.

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