Acta Crystallographica Section C
**Crystal Structure Communications**
ISSN 0108-2701

# 6-(4-Methoxybenzylamino)purin-3-ium chloride

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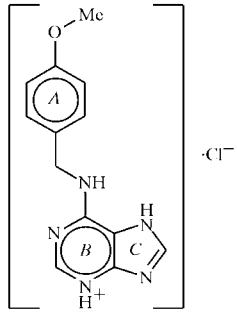
Received 6 May 2004
Accepted 8 July 2004
Online 11 August 2004

The title compound, $C_{13}H_{14}N_5O^+\cdot Cl^-$, belongs to the group of aromatic cytokinins. These compounds affect a variety of important physiological processes in plants and animals as well as in bacteria, including cell division, differentiation and senescence. The structure consists of a 6-(4-methoxybenzylamino)purinium cation and a $Cl^-$ anion. The cation moiety exists as the N3-protonated N7 tautomer. The cation contains nearly planar benzene and purine ring systems, with a dihedral angle of 77.46 (5)°. The crystal structure is stabilized by $N_{amino}-H\cdots N_{purine}$ hydrogen bonds connecting two adjacent molecules, thus forming centrosymmetric dimers.

## Comment

Cytokinins are an important class of plant growth regulators, defined by their ability to promote cell division in tissue culture in the presence of auxins. Virtually all naturally occurring cytokinins identified to date are adenine derivatives, substituted at the N6 position with an isoprenoid or aromatic side chain (Letham & Palni, 1983). They occur widely in plants, as well as in animals and bacteria, and affect a variety of important physiological processes, including cell division, differentiation and senescence. One very active and easily obtainable cytokinin is 6-benzylaminopurine (Bap), widely used in plant biotechnology (Strnad, 1997). Nevertheless, Bap has disadvantages in some crops, causing heterogeneity in growth and inhibition of rooting. One way of finding an alternative to Bap is to test Bap derivatives (Werbrouck *et al.*, 1996).

However, Bap and its derivatives are important compounds not only for plant biotechnology and agriculture. An additional modification of a cytokinin molecule could lead to a dramatic change of its action in growth and development control. Surprisingly, additionally C2/N9-substituted Bap derivatives have been discovered which specifically inhibit Cdc-2 and related kinases. One of the inhibited kinases, the p34cdc2/cyclin B kinase, is a key mitotic factor which is highly conserved and strongly implicated in cell cycle transition in all eucaryotic cells. The compounds have a strong inhibitory function, with the ability to arrest cells at specific points in the cell cycle (Veselý *et al.*, 1994). The total lack of inhibitory effect of C2/N9-substituted Bap derivatives on major kinases, such as cAMP- and cGMP-dependent kinases, protein kinase C and others, suggests that they might be useful tools for cell cycle studies. These cytokinin derivatives also exhibit strong antimitotic and anticancer activities, based on their ability to block plant and animal cell division at specific levels (G1/S, G2/M) of the cell cycle. This specificity can result in the development of a new class of cytostatic agents, *viz*. plant cytokinin analogues, which are especially potent towards cell lines with a dysfunction of the endogenous CDK inhibitors (Havlíček *et al.*, 1997; Kryštof *et al.*, 2002). Thus, the development of new cytokinin derivatives might consequently be of great practical importance. Our recent search for naturally occurring aromatic cytokinins in plants led to the discovery of four new very active endogenous plant hormone substances, identified as 6-(2-methoxybenzylamino)purine (*ortho*-methoxytopolin), 6-(3-methoxybenzylamino)purine (*meta*-methoxytopolin) and their 9-$\beta$-D-ribofuranosyl derivatives (Tarkowská *et al.*, 2003). Subsequently, a group of their synthetic analogues has been prepared in order to study various aspects of their biological activity. One of these analogues is the compound presented in this study, (I).




(I)

The crystal structure of (I) consists of a 6-(4-methoxybenzylamino)purinium cation and a $Cl^-$ anion (Fig. 1 and Table 1). The structure of the cation is similar to those determined for 6-benzylaminopurinium bromide (BapH; Umadevi *et al.*, 2001), 6-(3-chlorobenzylamino)purinium chloride (3-ClBapH; Maloň *et al.*, 2001) and 6-(4-chlorobenzylamino)purinium perchlorate (4-ClBapH; Maloň *et al.*, 2002). The cation contains nearly planar benzene (*A*) and pyrimidine (*B*) ring systems, and an ideally planar imidazole (*C*) ring, with maximum deviations from the planes of six-membered ring *A*, six-membered ring *B* and five-membered ring *C* of 0.0083 (19), 0.0105 (18) and 0.0019 (18) Å, respectively, for atoms C10, C4 and C8 (Nardelli, 1995). The atoms of the purine ring system (*B*+*C*) deviate slightly from planarity, the greatest deviation being 0.0200 (18) Å for atom C5. Rings *B* and *C* are nearly coplanar, with a dihedral angle of 1.50 (6)°, whilst the dihedral angles between planes *A* and *B*, and between *A* and the purine ring system (*B*+*C*) are 77.89 (6) and 77.46 (5)°, respectively.

The cation of (I) is protonated at the N3 and N7 positions of the purine ring, in contrast with the free base, where the

  DOI: 10.1107/S0108270104016749 

protonation occurs on the N9 position. This change in protonation causes changes in the interatomic parameters within the purine ring, mainly in the C—N—C angles. To date, 31 structures of both organic and organometallic compounds with the 6-benzylaminopurine moiety have been deposited with the Cambridge Structural Database (Version 5.25; Allen, 2002), of which only three organic structures represent the N3-protonated N7 tautomer (Umadevi *et al.*, 2001; Maloň *et al.*, 2001, 2002). The C2—N3—C4, C8—N7—C5 and C8—N9—C4 angles in the molecular structure of (I) are 117.01 (16), 106.58 (16) and 103.02 (15)°, respectively. These values are comparable with those found for BapH and 3-ClBapH (Table 3). On the other hand, these angles differ significantly from those found for Bap (Raghunathan *et al.*, 1983) and 6-(2-chlorobenzylamino)purine (2-ClBap) (Maloň *et al.*, 2001), *i.e.* in the N9-protonated electroneutral forms. The torsion angles C6—N6—C9—C10, C9—N6—C6—C5 and N6—C9—C10—C15 are −129.5 (2), 178.99 (17) and 49.7 (3)°, respectively.

The positive charge of the cation of (I) is neutralized by a $Cl^-$ anion. The crystal structure is stabilized by N3—H3···N9$^{i}$ hydrogen bonds connecting two adjacent cation molecules [Fig. 2 and Table 2; symmetry code: (i) $-x, 2-y, 1-z$], thus forming centrosymmetric dimers. Further hydrogen bonds connect H6···Cl1 and H7···Cl1 (Fig. 1).

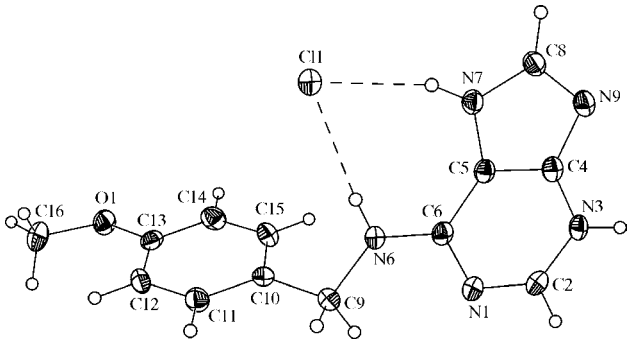



**Figure 1**
The molecular structure of (I), showing the atom-numbering scheme and the N—H···Cl hydrogen bonding (dashed lines). Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

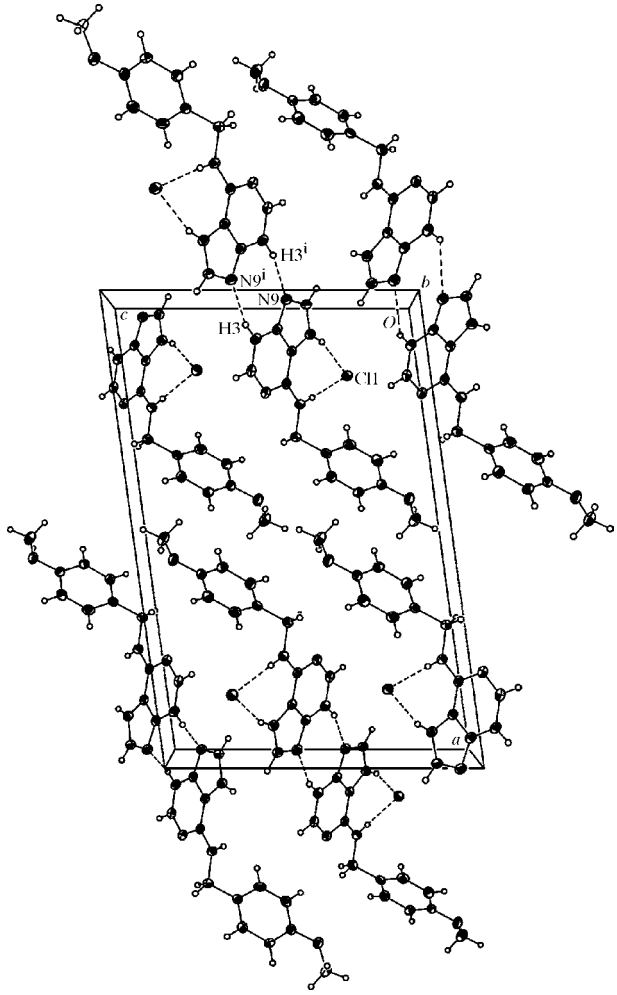



**Figure 2**
Part of the crystal structure of (I), showing the hydrogen bonding (dashed lines) and molecular pairing [symmetry code: (i) $-x, 2-y, 1-z$].

## Experimental

The title compound was synthesized using a procedure similar to that of Tarkowská *et al.* (2003). Colourless crystals of (I) suitable for single-crystal X-ray analysis were obtained by recrystallization from 2 *M* HCl. Elemental analysis (ThermoFinnigen Flash EA 1112 CHN Analyzer) calculated for $C_{13}H_{14}ClN_5O$: C 53.52, H 4.84, N 24.01%; found: C 53.45, H 4.80, N 23.94%.

*Crystal data*

| | |
|---|---|
| $C_{13}H_{14}N_5O^+\cdot Cl^-$ | $D_x$ = 1.450 Mg m$^{-3}$ |
| $M_r$ = 291.74 | Mo $K\alpha$ radiation |
| Monoclinic, $P2_1/c$ | Cell parameters from 3161 reflections |
| $a$ = 20.224 (5) Å | $\theta$ = 2.7–29.0° |
| $b$ = 4.991 (5) Å | $\mu$ = 0.29 mm$^{-1}$ |
| $c$ = 13.365 (5) Å | $T$ = 100 (2) K |
| $\beta$ = 97.727 (5)° | Prism, colourless |
| $V$ = 1336.8 (15) Å$^3$ | 0.30 × 0.30 × 0.20 mm |
| $Z$ = 4 | |

*Data collection*

| | |
|---|---|
| Oxford Diffraction Xcalibur2 diffractometer, with Sapphire2 CCD area-detector | 1858 reflections with $I > 2\sigma(I)$ |
| | $R_{int}$ = 0.030 |
| | $\theta_{max}$ = 25.0° |
| Rotation method, $\omega$ scan | $h = -24 \rightarrow 24$ |
| 7109 measured reflections | $k = -5 \rightarrow 5$ |
| 2327 independent reflections | $l = -13 \rightarrow 15$ |

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| N1—C2 | 1.315 (2) | C5—N7 | 1.372 (2) |
| N1—C6 | 1.361 (2) | C5—C6 | 1.411 (3) |
| C2—N3 | 1.342 (2) | N6—C6 | 1.325 (2) |
| N3—C4 | 1.367 (2) | N6—C9 | 1.458 (2) |
| C4—N9 | 1.365 (2) | N7—C8 | 1.344 (2) |
| C4—C5 | 1.374 (3) | C8—N9 | 1.331 (2) |
| | | | |
| C2—N1—C6 | 118.89 (17) | C4—C5—C6 | 120.63 (17) |
| N1—C2—N3 | 126.17 (18) | C8—N7—C5 | 106.58 (16) |
| C2—N3—C4 | 117.02 (16) | N9—C8—N7 | 113.56 (17) |
| N9—C4—C5 | 111.90 (17) | C8—N9—C4 | 103.01 (15) |
| N3—C4—C5 | 119.55 (17) | | |
| | | | |
| C9—N6—C6—C5 | 178.99 (17) | N6—C9—C10—C15 | 49.7 (3) |
| C6—N6—C9—C10 | −129.5 (2) | | |

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N3—H3···N9$^{i}$ | 0.88 | 2.05 | 2.883 (2) | 158 |
| N6—H6···Cl1 | 0.88 | 2.35 | 3.226 (2) | 171 |
| N7—H7···Cl1 | 0.88 | 2.23 | 3.063 (2) | 158 |

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

**Table 3**
Comparative geometrical parameters (°) for selected cytokinin derivatives containing the 6-benzylaminopurine moiety.

| Compound | C2—N3—C4 | C8—N7—C5 | C8—N9—C4 |
|---|---|---|---|
| 4MeOBapH† | 117.02 (16) | 106.58 (16) | 103.01 (15) |
| BapH‡ | 118.2 (7) | 107.4 (6) | 103.5 (6) |
| 3ClBapH§ | 117.6 (2) | 106.8 (2) | 102.60 (18) |
| 2ClBap¶ | 111.32 (14) | 103.68 (15) | 106.19 (14) |
| Bap†† | 110.70 | 103.90 | 106.41 |

† This work, where 4MeOBapH is the 6-(4-methoxybenzylamino)purinium cation. ‡ Umadevi *et al.* (2001), where BapH is the 6-benzylaminopurinium cation. § Maloň *et al.* (2001), where 3ClBapH is the 6-(3-chlorobenzylamino)purinium cation. ¶ Maloň *et al.* (2001), where 2ClBap is 6-(2-chlorobenzylamino)purine. †† Raghunathan *et al.* (1983), where Bap is 6-benzylaminopurine.

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | H-atom parameters constrained |
| $R[F^2 > 2\sigma(F^2)] = 0.035$ | $w = 1/[\sigma^2(F_o^2) + (0.044P)^2]$ |
| $wR(F^2) = 0.082$ | where $P = (F_o^2 + 2F_c^2)/3$ |
| $S = 1.02$ | $(\Delta/\sigma)_{max} = 0.001$ |
| 2327 reflections | $\Delta\rho_{max} = 0.20$ e Å$^{-3}$ |
| 181 parameters | $\Delta\rho_{min} = -0.16$ e Å$^{-3}$ |

All H atoms were found from difference Fourier maps and refined using a riding model, with C—H distances of 0.95 and 0.99 Å, N—H distances of 0.88 Å, and $U_{iso}$(H) = 1.2$U_{eq}$(CH, $CH_2$ and NH) or 1.5$U_{eq}$($CH_3$).

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2003); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2003); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*III (Johnson & Burnett, 1996); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1995).

The financial support of this work by the Grant Agency of the Czech Republic (GAČR) (grant Nos. 203/04/1168 and 203/02/0436) and the ASCR (grant No. IBS4055304) is gratefully acknowledged.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: TR1094). Services for accessing these data are described at the back of the journal.

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