to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *XP* (Siemens, 1994). Software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1235). Services for accessing these data are described at the back of the journal.

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7-(Carboxymethyl)-6-chloropurine Ethyl Ester†

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Abstract

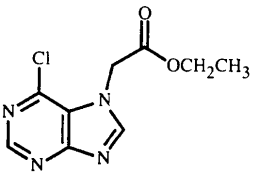
Alkylation of 6-chloropurine using ethyl bromoacetate gives a mixture of regioisomers from which the title compound, $C_9H_9ClN_4O_2$, was isolated in crystalline form. The ethyl acetate fragment attached at N7 avoids steric hindrance by emerging from the ring almost orthogonally. Two ring C atoms donate weak intermolecular hydrogen bonds to the carbonyl O12 and ring N3 atoms.

† Alternative name: ethyl 6-chloropurine-7-acetate.

Comment

Peptidic nucleic acids (PNAs) have important and profound DNA molecular recognition properties (Hyrup & Nielsen, 1996). The achiral uncharged backbone of PNA is composed of covalently linked *N*-(2-aminoethyl)-glycine units to which are attached the heterocyclic bases of DNA through carboxymethyl bridging groups. Since modifications to the PNA bases attract sustained interest in efforts to extend the molecular recognition properties of PNAs, we selected the purine base hypoxanthine as a candidate for incorporation into PNAs. A useful role for hypoxanthine has been as a universal base in polymerase chain reaction (PCR) (Ohtsuka *et al.*, 1985), where the base is attached through the N9 atom to 2′-deoxyribose in oligonucleotide primers. The isomeric α-^{7}H nucleoside, where the N7 of hypoxanthine is connected to α-configured 2′-deoxyribose, displays interesting DNA recognition properties when incorporated into triplex-forming oligonucleotides (Marfurt *et al.*, 1996).

An evaluation of PNAs containing hypoxanthine linked through N9 and N7 necessitates efficient synthesis of protected building blocks of both regioisomers. A general but by no means sole route to PNA building blocks requires attachment of a carboxymethyl substituent, usually as its ethyl ester, to the appropriate heterocyclic base. Direct alkylation of hypoxanthine using ethyl bromoacetate in the presence of potassium carbonate gives peralkylated products with the major component, diethyl 3,7-hypoxanthyldiacetate, isolable in 61% yield (Sood *et al.*, 1998*a*). Direct alkylation of 6-chloropurine can attach substituents at positions N9 or N7 to give a mixture of regioisomers (Dalby *et al.*, 1993). Subsequent hydrolysis or displacement of the chloro group at C6 can then provide hypoxanthine or O6-protected precursors. Reaction of 6-chloropurine with ethyl bromoacetate gave a separable mixture of N9 and N7 regioisomers from which the title compound, (1), was isolated in crystalline form. We undertook the crystal structure determination to establish that the ethyl acetate side chain was indeed attached at N7 in (1).



(1)

Compared with 9-(carboxymethyl)-2,6-dichloropurine ethyl ester, (2) (Chan *et al.*, 1995), the removal of the 2-chloro substituent and the change of regioisomer cause sizeable alternating changes in the internal angles of the six-membered ring: increases of 1.1 (2), 2.4 (2) and 1.5 (2)° at N1, N3 and C5, respectively, and decreases of 1.9 (3), 2.7 (2) and 0.4 (2)° at C2, C4 and C6,

respectively. In the five-membered ring, the internal angle at N7 has increased by 1.5 (2)°, while that at N9 has decreased by 1.6 (2)°. The ethyl acetate fragment at N7 avoids steric hindrance by emerging almost orthogonally, with C8—N7—C10—C11 106.1 (2)° and C11—O13—C14—C15 76.3 (2)°. The side chain of (1) differs both in its relationship to the heterocycle and in its conformation compared with (2) and with other alkyl carboxymethyl-substituted purines: hypoxanthine (Sood *et al.*, 1998*a*), 2,6-diazidopurine (Sood *et al.*, 1997*a*), 2,6-diaminopurine (Sood *et al.*, 1997*b*), adenine (Flensburg & Egholm, 1994) and 6-amino-2-methoxypurine (Sood *et al.*, 1998*b*). The C11—O12 bond in (1) is antiperiplanar to N7—C10, which causes O13 to be nearly eclipsed with the ring, whereas the carbonyl oxygen is adjacent to the ring in (2) and in all other members of the series. The conformation about O13—C14 is uniquely synclinal in (1); in the comparison structures, the ethyl acetate side chain is fully extended from C10 to the end. In the absence of NH groups, there is weak hydrogen-bond donation by C2 and C8 (Table 2) forming chains parallel to **b**.

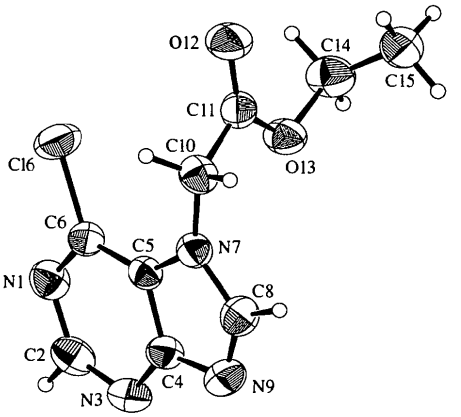


Fig. 1. *ORTEP*II view (Johnson, 1976) of the molecule of (1) with its numbering scheme. Displacement ellipsoids are shown at the 50% probability level.

Experimental

Potassium carbonate (3.78 g, 27.4 mmol) and ethyl bromoacetate (4.59 g, 22.8 mmol) were added to a solution of 6-chloropurine (3.52 g, 22.8 mmol) in dry acetonitrile (25 ml) and the mixture stirred for 48 h under argon at room temperature. The product mixture was filtered, the solvent evaporated and the residue purified by flash chromatography. 9-(Carboxymethyl)-6-chloropurine ethyl ester, (2), was eluted first using ethyl acetate. Further elution using ethyl acetate/methanol (4:1) gave the title compound, 7-(carboxymethyl)-6-chloropurine ethyl ester, (1). Compound (2) was isolated (3.58 g, 65%, m.p. 367–368 K) and recrystallized from methanol; TLC (ethyl acetate): R_f 0.43; IR (KBr disc): ν_{max} 3107, 2938, 1733, 1566, 1500, 1438, 1344, 1105, 909 cm^{-1}; ^1H NMR [250.1 MHz; $(CD_3)_2SO$]: δ (p.p.m.) 1.20 (*t*, 3H, J = 7.1 Hz, CH_3), 4.19 (*q*, 2H, J = 7.1 Hz, CH_2O), 5.27 (*s*, 2H, CH_2N), 8.68 (*s*, 1H, H-2), 8.79 (*s*, 1H, H-8); ^{13}C NMR [62.9 MHz; $(CD_3)_2SO$]: δ (p.p.m.) 14.1 (CH_3), 44.5 (CH_2O), 61.9 (CH_2N), 130.7 (C-5), 148.1 (C-8), 149.4 (C-4), 152.0 (C-2), 152.2 (C-6), 167.6 (CO); MS (EI): *m/z* (I_r) 242 (M + H, 12%), 240 (M + H, 27%), 167 (100%), 140 (18%), 86 (20%), 77 (36%); analysis calculated for $C_9H_9ClN_4O_2$: C 44.9, H 3.8, Cl 14.7, N 23.3%; found: C 45.0, H 3.4, Cl 14.8, N 23.3%. The title compound (1) was isolated (1.48 g, 27%, 380–383 K) and recrystallized from methanol; TLC (ethyl acetate): R_f 0.32; IR (KBr disc): ν_{max} 3120, 2933, 1733, 1599, 1562, 1500, 1440, 1340, 1195, 939 cm^{-1}; ^1H NMR [250.1 MHz; $(CD_3)_2SO$]: δ (p.p.m.) 1.20 (*t*, 3H, J = 7.1 Hz, CH_3), 4.22 (*q*, 2H, J = 7.1 Hz, CH_2O), 5.45 (*s*, 2H, CH_2N), 8.84 (*s*, 1H, H-2), 8.92 (*s*, 1H, H-8); ^{13}C NMR [62.9 MHz; $(CD_3)_2SO$]: δ (p.p.m.) 14.2 (CH_3), 48.0 (CH_2O), 62.0 (CH_2N), 122.6 (C-5), 142.6 (C-4), 151.6 (C-8), 152.2 (C-2), 161.7 (C-6), 168.2 (CO); MS (EI): *m/z* (I_r) 242 (M + H, 14%), 240 (M + H, 40%), 167 (100%), 140 (16%), 86 (25%), 77 (28%); analysis calculated for $C_9H_9ClN_4O_2$: C 44.9, H 3.7, Cl 14.8, N 23.3%; found: C 45.0, H 3.7, Cl 14.5, N 23.1%.

Crystal data

$C_9H_9ClN_4O_2$
M_r = 240.65
Monoclinic
$P2_1/c$
a = 7.7244 (6) Å
b = 9.9912 (14) Å
c = 13.820 (3) Å
β = 91.006 (11)°
V = 1066.4 (3) Å^3
Z = 4
D_x = 1.499 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.54178 Å
Cell parameters from 25 reflections
θ = 22.1–40.7°
μ = 3.134 mm^{-1}
T = 293 (2) K
Hexagonal
0.35 × 0.20 × 0.20 mm
Pale yellow

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical *via* ψ scans (North *et al.*, 1968)
T_{min} = 0.463, T_{max} = 0.534
3928 measured reflections
1898 independent reflections

1733 reflections with $I > 2\sigma(I)$
R_{int} = 0.050
θ_{max} = 66.94°
h = 0 → 9
k = −11 → 11
l = −16 → 16
3 standard reflections
frequency: 120 min
intensity decay: 3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.034
$wR(F^2)$ = 0.082
S = 1.071
1898 reflections
182 parameters
All H atoms refined
$w = 1/[\sigma^2(F_o^2) + (0.0286P)^2 + 0.2806P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.225 e Å^{-3}
$\Delta\rho_{min}$ = −0.256 e Å^{-3}
Extinction correction: *SHELXL*93
Extinction coefficient: 0.0068 (4)
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

C6—Cl6	1.730 (2)		
C6—N1—C2	117.38 (14)	N1—C6—C5	121.06 (14)
N3—C2—N1	127.9 (2)	C8—N7—C5	105.05 (14)
C2—N3—C4	113.44 (14)	N9—C8—N7	114.9 (2)
N3—C4—C5	123.84 (14)	C8—N9—C4	104.24 (13)
C6—C5—C4	116.36 (15)		
C8—N7—C10—C11	106.1 (2)	N7—C10—C11—O13	−19.7 (2)
N7—C10—C11—O12	161.3 (2)	C11—O13—C14—C15	76.3 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2···O12^{i}	0.94 (2)	2.51 (2)	3.324 (2)	145 (2)
C8—H8···N3^{ii}	0.96 (2)	2.49 (2)	3.442 (2)	173 (2)

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

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *CADABS* (Gould & Smith, 1986). Program(s) used to solve structure: *MULTAN*84 (Main *et al.*, 1984). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: HA1208). Services for accessing these data are described at the back of the journal.

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2,6-Dimethyl-3,7-diphenyl-2,6-naphthyridine-1,5(2*H*,6*H*)-dione

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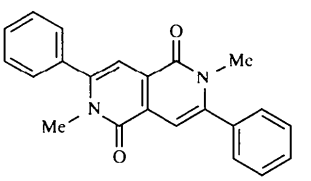
Abstract

The title compound, $C_{22}H_{18}N_2O_2$, has a center of symmetry and the parameters of half of each of the two independent molecules have been determined. The naphthyridine ring is planar; the coplanarity of the naphthyridine ring and the phenyl rings is hindered by the *N*-methyl groups. The dihedral angles between the rings are 51.8 (2) and 61.5 (2)° in the two independent molecules.

Comment

It has been reported that an aminolysis product of a Pechmann dye [(*E*)-5,5′-diphenyl-3,3′-bifuranylidene-2,2′-dione] is supposed to be a γ-dilactam or a naphthyridinedione (Klingsberg, 1954). A γ-dilactam has been obtained from a Pechmann dye (Kollenz *et al.*, 1996), but the formation of the naphthyridinedione has not been reported. In the present study, the title compound, (I), was prepared from 3,7-diphenylpyrano[4,3-*c*]pyran-1,5-dione, since aminolysis of the Pechmann dye gave the target compound in very poor yield.



(I)