

# Methyl (SR)-10-chloro-1,2,3,4,5,6-hexahydro-6-hydroxy-8-methoxy-1-methyl-1,9-phenanthroline-6-carboxylate

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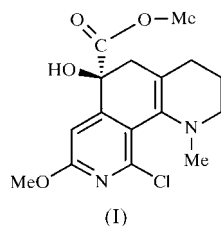
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In the title compound, C<sub>16</sub>H<sub>19</sub>ClN<sub>2</sub>O<sub>4</sub>, the pyridine ring is nearly planar, the piperidine ring is non-planar and the cyclohexane ring adopts a screw-boat conformation. The carboxylate group makes a dihedral angle of 80.9 (2)° with the least-squares plane through the cyclohexane ring.

## Comment

The synthesis and biological evaluation of conformationally restricted analogues of nicotine and anabasine have attracted much attention (Catka & Leete, 1978; Kanne *et al.*, 1986; Kanne & Abood, 1988; Vernier *et al.*, 1998). The anabasine analogue with a piperidine ring has recently been screened as an agonist of neuronal acetylcholine receptors (nAChRs) and, more interestingly, the nicotine analogue with a pyrrolidine ring is currently under clinical trial for the treatment of Parkinson's disease and pain (Vernier *et al.*, 1998). In this context, Sarkar *et al.* (2000) recently reported a domino-reaction-based flexible strategy for the synthesis of the two

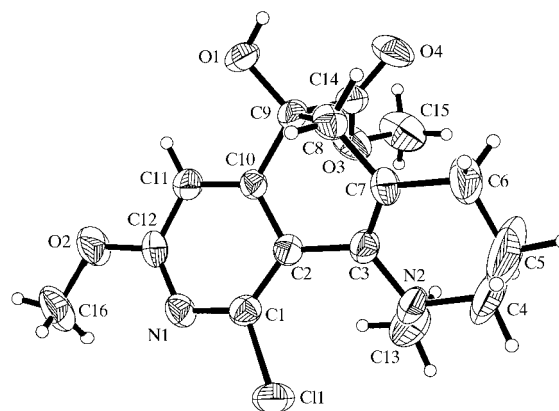


analogues and synthesized the title compound, (I). The presence of a methoxy group at a proper position in the pyridine ring of the bridged analogues is the key to better selectivity as nAChR agonists. An X-ray crystal structure determination of (I) was undertaken to confirm the position of

the methoxy group in the pyridine ring and the results are presented here.

In compound (I), the bond lengths and angles show normal values and are comparable with those of a related structure previously studied by Sarkar *et al.* (1999). The pyridine ring is nearly planar, with a maximum deviation of  $-0.039$  (3) Å for C2. The chloro group deviates by  $0.252$  (1) Å, and the methoxy group is twisted through  $2.2$  (3)°, relative to the least-squares plane of the pyridine ring.

The piperidine ring is not planar, with atoms C4 and C5 deviating by  $0.196$  (7) and  $-0.223$  (8) Å, respectively. The puckering parameters (Cremer & Pople, 1975) are  $Q_2 = 0.265$  (5) Å,  $Q_3 = 0.188$  (5) Å,  $\varphi_2 = 260.8$  (10)°,  $Q_T = 0.325$  (6) Å and  $\theta_2 = 54.7$  (9)°. The methyl group, C13, deviates by  $0.802$  (5) Å from the least-squares plane of the piperidine ring.



**Figure 1**

The molecular structure of (I) showing 30% probability displacement ellipsoids and the atom-numbering scheme. H atoms are drawn as small spheres of arbitrary radii.

The cyclohexane ring adopts a screw-boat conformation, with the following deviations of atoms from their least-squares plane: C10  $-0.071$  (3), C2  $-0.202$  (3), C8  $-0.365$  (4), C7  $0.063$  (3), C3  $0.212$  (3) and C9  $0.363$  (3) Å. This is also confirmed by the puckering parameters  $Q_2 = 0.571$  (3) Å,  $Q_3 = 0.182$  (3) Å,  $\varphi_2 = 210.8$  (3)°,  $Q_T = 0.600$  (3) Å and  $\theta_2 = 72.3$  (3)°.

The hydroxy group is in the least-squares plane through the cyclohexane ring, while this plane makes dihedral angles of  $20.1$  (2),  $23.5$  (2) and  $80.9$  (2)° with the least-squares planes through the pyridine ring, the piperidine ring and the carboxylate group, respectively.

## Experimental

To a stirred solution of the  $\alpha$ -diazoester (140 mg, 0.38 mmol) in dry benzene under an argon atmosphere at ambient temperature, a catalytic amount of Rh<sub>2</sub>(OAc)<sub>4</sub> was added. After stirring the mixture for 24 h, the solvent was removed *in vacuo* and the residue was purified by flash chromatography (alumina; ethyl acetate–petroleum ether, 20:80). Recrystallization from a dichloromethane–diethyl ether–petroleum ether (3:3:1) solution afforded 80 mg (62%) of (I) as yellow–green crystals.

## Crystal data

$C_{16}H_{19}ClN_2O_4$   
 $M_r = 338.78$   
 Triclinic,  $P\bar{1}$   
 $a = 9.2081$  (4) Å  
 $b = 9.4835$  (4) Å  
 $c = 11.1287$  (6) Å  
 $\alpha = 100.574$  (1)°  
 $\beta = 101.751$  (1)°  
 $\gamma = 111.882$  (1)°  
 $V = 846.14$  (7) Å<sup>3</sup>

$Z = 2$   
 $D_x = 1.330$  Mg m<sup>-3</sup>  
 Mo  $K\alpha$  radiation  
 Cell parameters from 3323 reflections  
 $\theta = 2.0$ – $28.3$ °  
 $\mu = 0.25$  mm<sup>-1</sup>  
 $T = 293$  (2) K  
 Slab, yellow–green  
 $0.46 \times 0.36 \times 0.22$  mm

## Data collection

Siemens SMART CCD area-detector diffractometer  
 $\omega$  scans  
 Absorption correction: empirical (SADABS; Sheldrick, 1996)  
 $T_{\min} = 0.895$ ,  $T_{\max} = 0.948$   
 6088 measured reflections

3990 independent reflections  
 2299 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.057$   
 $\theta_{\text{max}} = 28.2$ °  
 $h = -12 \rightarrow 12$   
 $k = -12 \rightarrow 12$   
 $l = -12 \rightarrow 14$

## Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.076$   
 $wR(F^2) = 0.209$   
 $S = 0.94$   
 3990 reflections  
 212 parameters

H-atom parameters constrained  
 $w = 1/[\sigma^2(F_o^2) + (0.1071P)^2]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\text{max}} < 0.001$   
 $\Delta\rho_{\text{max}} = 0.63$  e Å<sup>-3</sup>  
 $\Delta\rho_{\text{min}} = -0.62$  e Å<sup>-3</sup>

Table 1

Selected geometric parameters (Å, °).

N1–C12	1.314 (4)	C3–C7	1.349 (4)
N1–C1	1.343 (4)	C6–C7	1.514 (4)
N2–C3	1.418 (4)	C7–C8	1.503 (4)
N2–C4	1.450 (5)	C8–C9	1.524 (4)
C2–C10	1.415 (4)	C9–C10	1.524 (4)
C2–C3	1.485 (4)		
C3–N2–C4	113.9 (3)	O1–C9–C10	108.4 (2)
C7–C3–N2	124.0 (3)	C8–C9–C10	106.8 (2)
C3–C7–C8	119.0 (3)	O1–C9–C14	107.7 (2)
C7–C8–C9	108.4 (2)		
C10–C2–C3–C7	31.6 (4)	C1–N1–C12–C11	–3.1 (4)
C1–C2–C3–N2	35.9 (4)	C16–O2–C12–N1	1.7 (4)
C10–C2–C3–N2	–149.6 (3)	C10–C9–C14–O4	–173.2 (3)

After checking their presence in the difference map, all H atoms were geometrically fixed and allowed to ride on their attached atoms, with C–H = 0.93–0.97 Å and O–H = 0.82 Å, and  $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{O})$  and  $1.2U_{\text{eq}}(\text{C})$ .

Data collection: SMART (Siemens, 1996); cell refinement: SAINT (Siemens, 1996); data reduction: SAINT; program(s) used to solve structure: SHELXTL (Sheldrick, 1997); program(s) used to refine structure: SHELXTL; molecular graphics: SHELXTL; software used to prepare material for publication: SHELXTL, PARST95 (Nardelli, 1995) and PLATON (Spek, 1990).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1492). Services for accessing these data are described at the back of the journal.

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