Experimental

4-Amino-2-chloro-6,7-dimethoxyquinazoline was synthesized from vanillin *via* multi-step reactions, including methylation, nitration, oxidation, hydrogenation, cyclization, chlorination and amination. The detailed synthetic procedure will be published elsewhere. Single crystals suitable for X-ray diffraction studies were obtained from methanol by slow evaporation of the solvent.

Crystal data

$C_{10}H_{10}ClN_3O_2.CH_4O$
$M_r = 271.70$
Monoclinic
$P2_1/n$
$a = 7.254\,(4)$ Å
$b = 11.914\,(2)$ Å
$c = 14.953\,(2)$ Å
$\beta = 100.34\,(3)°$
$V = 1271.3\,(6)$ Å^3
$Z = 4$
$D_x = 1.419$ Mg m^{-3}
D_m not measured
Mo $K\alpha$ radiation
$\lambda = 0.7107$ Å
Cell parameters from 25 reflections
$\theta = 12.0$–$14.0°$
$\mu = 0.305$ mm^{-1}
$T = 295.2$ K
Needle
$0.72 \times 0.26 \times 0.20$ mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
2573 measured reflections
2402 independent reflections
1779 reflections with $I > 2.5\sigma(I)$
$R_{int} = 0.0117$
$\theta_{max} = 24.97°$
$h = 0 \rightarrow 8$
$k = 0 \rightarrow 14$
$l = -17 \rightarrow 17$
3 standard reflections
every 200 reflections
intensity decay: none

Refinement

Refinement on F
$R = 0.042$
$wR = 0.055$
$S = 1.484$
1779 reflections
163 parameters
$w = 1/[\sigma^2(F_o)]$
$(\Delta/\sigma)_{max} = 0.0280$
$\Delta\rho_{max} = 0.50$ e Å^{-3}
$\Delta\rho_{min} = -0.26$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

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

Cl—C1	1.748 (2)	N1—C1	1.296 (3)
O1—C4	1.366 (2)	N1—C7	1.388 (2)
O1—C9	1.416 (3)	N2—C1	1.330 (3)
O2—C5	1.353 (2)	N2—C2	1.342 (2)
O2—C10	1.416 (3)	N3—C2	1.325 (2)
C4—O1—C9	116.3 (2)	N2—C2—N3	117.4 (2)
C5—O2—C10	118.2 (2)	N2—C2—C8	120.3 (2)
C1—N1—C7	113.9 (2)	N3—C2—C8	122.3 (2)
C1—N2—C2	115.4 (2)	O1—C4—C3	124.9 (2)
Cl—C1—N1	115.4 (2)	O1—C4—C5	114.9 (2)
Cl—C1—N2	113.0 (1)	O2—C5—C4	114.5 (2)
N1—C1—N2	131.6 (2)	O2—C5—C6	125.4 (2)

The hydroxyl H atom of the methanol was located from a difference map. All other H atoms were placed in calculated positions, with NH_2 assumed to be planar. H-atom parameters were not refined.

Data collection: *CAD-4-PC Software* (Enraf–Nonius, 1992). Cell refinement: *CAD-4-PC Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1985). Program(s) used to solve structure: *SIR92* (Altomare, Cascarano, Giacovazzo & Guagliardi, 1993). Program(s) used to refine structure: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

This work was supported by the National Science Foundation (OSR-9452893).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ1177). Services for accessing these data are described at the back of the journal.

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(*E*,*Z*)-2-(2-Chloro-5-nitrostyryl)-1-(1-propenyl)benzimidazole

DANIEL E. BACELO, OSVALDO COX,* LUIS A. RIVERA, MARISOL CORDERO AND SONGPING D. HUANG*

Department of Chemistry, University of Puerto Rico, San Juan, PR 00931, USA. E-mail: huang@zintl.chem.uprr.pr

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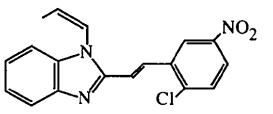
Abstract

The title compound, $C_{18}H_{14}ClN_3O_2$, was synthesized by the condensation of 2-chloro-5-nitrobenzaldehyde with 2-methyl-1-propenylbenzimidazole, and the molecule comprises a 2-chloro-5-nitrobenzene and a 1-(*Z*)-propenylbenzimidazole. The two aromatic moieties are conjugated through the vinyl group. The dihedral angle between the two rings is 1.4 (6)°. The propenyl group lies out of the benzimidazole plane with a dihedral angle of 112.9 (9)°.

Comment

The title compound was synthesized as the precursor to the potential antineoplastic agent 7-(Z)-1-propenyl-3-nitrobenzimidazolo[3,2-*a*]quinolinium chloride. The ^1H and ^{13}C NMR spectra, and elemental analysis data showed that the compound formed is a mixture of two stereoisomers. The title compound, (I), was obtained by fractional crystallization and its identity established by single-crystal X-ray structure analysis. Fig. 1 is the *ORTEP*II (Johnson, 1976) drawing of the title compound.



(I)

The planar aromatic benzimidazole ring has a mean deviation of 0.005 (4) Å. The benzimidazole is conjugated with the phenyl ring through a vinyl group, with a dihedral angle between the two rings of 1.4 (6)°. The propenyl group lies out of the benzimidazole plane with a dihedral angle of 112.9 (9)°. The N2—C1 [1.317 (3) Å], C8—C9 [1.304 (4) Å] and C16—C17 [1.304 (5) Å] bond lengths are consistent with the double-bond assignment. All other bond distances and bond angles are within normal ranges.

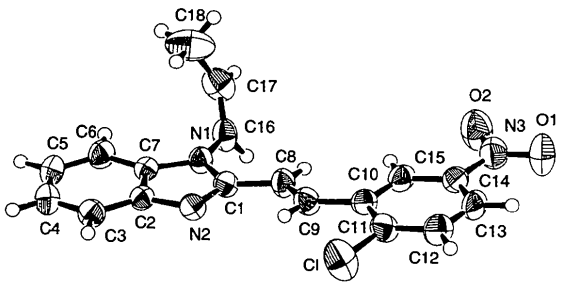


Fig. 1. An *ORTEP*II (Johnson, 1976) representation of compound (I) showing 50% probability displacement ellipsoids.

Experimental

When 2-chloro-5-nitrobenzaldehyde (2.2 g, 12.0 mmol) and 2-methyl-1-propenylbenzimidazole (2.0 g, 12.0 mmol) were refluxed in 30 ml acetic anhydride, a yellow solid was obtained. The crude product (3.2 g, 78% yield) was recrystallized from chloroform to give pale-yellow single crystals (melting point 407–409 K).

Crystal data

$C_{18}H_{14}ClN_3O_2$
M_r = 339.78
Monoclinic
$P2_1/n$
a = 7.956 (1) Å
b = 8.456 (3) Å
c = 24.587 (4) Å
β = 96.15 (2)°
V = 1644.6 (6) Å^3
Z = 4
D_x = 1.372 Mg m^{-3}
D_m not measured
Mo $K\alpha$ radiation
λ = 0.7107 Å
Cell parameters from 25 reflections
θ = 12.0–14.0°
μ = 0.247 mm^{-1}
T = 298.2 K
Needle
0.56 × 0.15 × 0.12 mm
Pale yellow

Data collection

CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
3361 measured reflections
3257 independent reflections
1991 reflections with $I > 3\sigma(I)$
R_{int} = 0.0089
θ_{max} = 24.97°
$h = 0 \rightarrow 9$
$k = 0 \rightarrow 10$
$l = -29 \rightarrow 29$
3 standard reflections
every 200 reflections
intensity decay: none

Refinement

Refinement on F
R = 0.054
wR = 0.073
S = 1.626
1991 reflections
217 parameters
H atoms at calculated positions, not refined
$w = 1/[\sigma^2(F_o) + p^2/4F_o^2]$, where p = 0.030
$(\Delta/\sigma)_{max}$ = 0.0003
$\Delta\rho_{max}$ = 0.38 e Å^{-3}
$\Delta\rho_{min}$ = −0.30 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

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

Cl—C11	1.732 (3)	N2—C1	1.317 (3)
O1—N3	1.232 (4)	N2—C2	1.384 (4)
O2—N3	1.211 (4)	N3—C14	1.469 (4)
N1—C1	1.383 (3)	C8—C9	1.304 (4)
N1—C7	1.387 (4)	C16—C17	1.304 (5)
N1—C16	1.423 (4)		
C1—N1—C7	106.0 (2)	C1—C8—C9	122.4 (3)
C1—N1—C16	127.6 (2)	C8—C9—C10	127.8 (3)
C1—N2—C2	105.0 (2)	C9—C10—C11	121.0 (3)
O1—N3—O2	123.1 (3)	Cl—C11—C10	120.2 (2)
N1—C1—N2	113.1 (2)		

Data collection: *CAD-4-PC Software* (Enraf–Nonius, 1992). Cell refinement: *CAD-4-PC Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1992). Program(s) used to solve structure: *SIR*92 (Altomare, Cascarano, Giacovazzo & Guagliardi, 1993). Program(s) used to refine structure: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: HA1188). Services for accessing these data are described at the back of the journal.

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Absolute Configuration of (+)-α-Methyl-4-carboxyphenylglycine (MCPG), a Metabotropic Glutamate Receptor Antagonist

CLAIRE WILSON,[a]† JUDITH A. K. HOWARD,[a] DAVID E. JANE,[b] DAVID C. SUNTER[c] AND JEFFREY C. WATKINS[b]

[a]*Department of Chemistry, University of Durham, Durham DH1 3LE, England,* [b]*Pharmacology, School of Medical Sciences, University of Bristol, Bristol BS8 1TD, England, and* [c]*Tocris Cookson Ltd, Churchill Building, Langford House, Bristol BS8 1TD, England. E-mail: claire@kemi.aau.dk*

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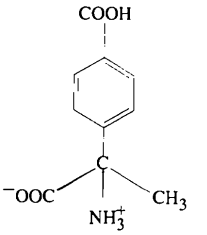
Abstract

The title compound, (+)-MCPG [(+)-α-(4-carboxyphenyl)-α-methylglycine, $C_{10}H_{11}NO_4$], is an antagonist at certain subtypes of metabotropic glutamate (mGlu) receptors. (+)-MCPG has gained widespread acceptance as a tool for probing the physiological role of mGlu receptors in the central nervous system. As a result, mGlu receptors are now known to be involved in processes connected with learning and memory, modulation of synaptic transmission and the transmission of pain responses. (+)-MCPG crystallized in its zwitterionic form. Its absolute configuration was assigned as *S* from X-ray diffraction data collected at 150 K. The refined Flack parameter is consistent with this assignment, although the large e.s.d. associated with it introduces some ambiguity.

Comment

To date, molecular biologists have cloned eight subtypes of metabotropic glutamate (mGlu) receptors, termed $MGlu_{1-8}$ (Pin & Duvoisin, 1995). Although a number of selective agonists have been identified for these receptors, no competitive antagonists were known at the outset of this project. We introduced (+)-α-methyl-4-carboxyphenylglycine [(+)-MCPG] as an antagonist of mGlu receptors present in the neonatal rat spinal cord (Jane *et al.*, 1993; Kemp *et al.*, 1994) and subsequently reported antagonist actions of MCPG on cloned mGlu receptors expressed in Chinese hamster ovary cells (Hayashi *et al.*, 1994). As a result of this work, (+)-MCPG has gained widespread use as a tool for probing the physiological roles of mGlu receptors in the central nervous system (Watkins & Collingridge, 1994; Knöpfel, Kuhn & Allgeier, 1995). The determination of the absolute configuration of (+)-MCPG is therefore an important aid in the design of more potent and selective mGlu receptor antagonists.



(+)-MCPG

(+)-MCPG crystallizes in its zwitterionic form, with the C1, O1 and O2 atoms forming the COO^- group. The two C—O bond lengths are not identical, but differ by 0.021 (4) Å. This may be due to the greater involvement of the O1 atom in hydrogen bonds compared with O2. A similar difference (0.016 Å) was noted in the neutron structure of L-alanine (Lehmann, Koetzle & Hamilton, 1972). The three H atoms of the NH_3^+ group were located in difference Fourier maps and, as for the other H atoms, positional and U_{iso} parameters were refined. All three H atoms are involved in a hydrogen-bonding network, details of the geometry of which are given in Table 2 and Fig. 2.

The Flack absolute structure parameter (Flack, 1983) was refined; expected values are 0 for the correct and +1 for the inverted absolute structure. The refined value

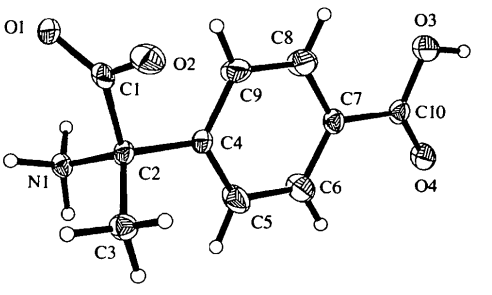


Fig. 1. View showing the labelling of the non-H atoms of (+)-MCPG. Displacement ellipsoids are drawn at the 50% probability level and H atoms are drawn as small circles of arbitrary radii.

† Current address: Department of Chemistry, Aarhus University, Langelandsgade 140, DK-8000 Aarhus C, Denmark.