Acta Crystallographica Section E
Structure Reports
Online

ISSN 1600-5368

1-Hydroxy-6,7-dimethoxy-8-nitro-1,2,3,4-tetrahydroisoquinoline

Nuria Roqué-Rosell,[a]‡ Pablo Cironi,[a,b] Xavier Solans,[c] Fernando Albericio[a,d] and Mercedes Álvarez[a,b]*

[a]Biomedical Research Institute, Barcelona Scientific Park-University of Barcelona, Josep Samitier 1-5, E-08028 Barcelona, Spain, [b]Laboratory of Organic Chemistry, Faculty of Pharmacy, University of Barcelona, E-08028 Barcelona, Spain, [c]Departament de Cristal.lografia, Universitat de Barcelona, Martí i Franquès, sn, E-08028 Barcelona, Spain, and [d]Department of Organic Chemistry, University of Barcelona, E-08028 Barcelona, Spain

‡ Current address: Biological and Biophysical Chemistry Section, Department of Chemistry, Imperial College, South Kensington Campus, Exhibition Road, London SW7 2AZ, England

Correspondence e-mail: xavier@geo.ub.es

Received 24 April 2006
Accepted 8 May 2006

The title compound, $C_{11}H_{13}N_2O_5$, was obtained during the preparation of 3,4-dihydro-6,7-dimethoxy-8-nitroisoquinoline from 3,4-dihydro-6,7-dimethoxyisoquinoline using NO_2BF_4 as a source of NO_2^+. $^1H/^{13}C$ NMR and X-ray analysis confirm the presence of a hydroxy group at position 1. The structure consists of layers of molecules parallel to the $(12\overline{1})$ plane.

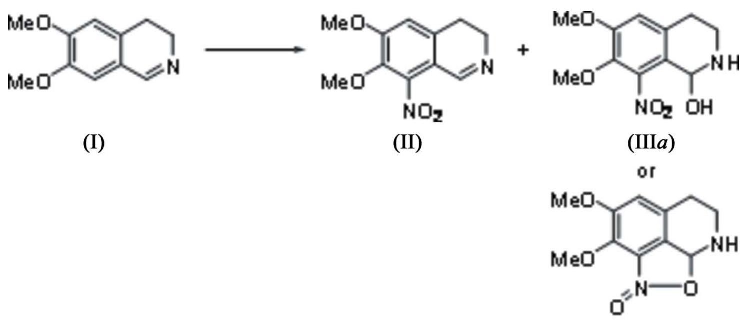
Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.003 Å
R factor = 0.040
wR factor = 0.097
Data-to-parameter ratio = 19.7

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Comment

3,4-Dihydroisoquinolines have been used as building blocks in the synthesis of natural products. Specifically, the cycloaddition of quinolinium derivatives from 3,4-dihydroisoquinolines to triple bonds, for the formation of pyrrole derivatives, has been described as a key step in the synthesis of lamellarins (Banwell *et al.*, 1997; Cironi *et al.*, 2003; Cironi, Cuevas *et al.*, 2004). As a result of the important pharmacological properties of lamellarins (Cironi, Albericio & Álvarez, 2004), the synthesis of these marine alkaloids and analogues represents a target in drug discovery.



(I) **(II)** **(III*a*)** or **(III*b*)**

In an attempt to increase the restricted commercial availability of 3,4-dihydroisoquinolines, several routes for their synthesis have been tested. As a result of the tendency of the heterocycle to be aromatic and the reactivity as electrophile of the carbon–nitrogen double bond, 3,4-dihydroisoquinolines are poor substrates upon modification of their aromatic ring (McCoubrey & Mathieson, 1951). The nitration of compound (I) in position 8 was achieved using nitronium tetrafluoroborate, NO_2BF_4. However, the formation of a hydrated side-product (III) could not be avoided under the different conditions tested. Analysis by ^1H NMR, ^{13}C NMR and MS–ESI+ suggested two possible structures, (III*a* or III*b*). Whilst both compounds (III*a*) and (III*b*) would show similar resonance patterns in ^1H NMR and ^{13}C NMR, the MS–ESI+ spectrum obtained suggested the (III*b*) structure. However, suitable crystals were obtained, which has allowed us to identify the product as (III*a*). A possible explanation is that,

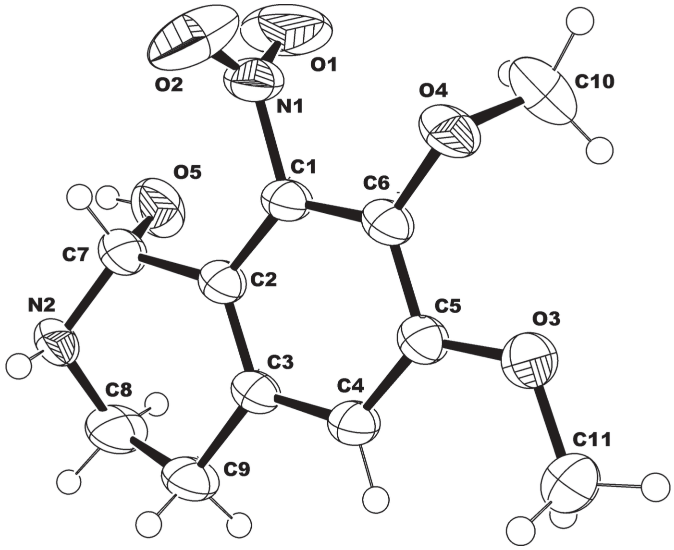


Figure 1
View of (III*a*), showing the labelling of the non-H atoms. Displacement ellipsoids are drawn at the 50% probability level and H atoms are drawn as small circles of arbitrary radius.

during the recording of the MS spectra, dehydration of (III*a*) could easily occur, to give the 238 [$M + 1 - H_2O$] peak, which corresponds to $M + 1$ of (III*b*).

The piperidine ring has a half-chair form, with atoms N2 and C8 out of the plane defined by the remaining four atoms. Atoms C1 and C4 are located as equatorial substituents, while O5 occupies an axial site. The molecules are packed in layers parallel to the ($12\overline{1}$) plane. The short contact O2···O2($1 - x$, $-y$, $-z$) [2.785 (2) Å] is in the range of intermolecular distances among nitro groups (range: 2.765–3.036 Å, CSD Database, November 2005 version; Allen, 2002).

Experimental

A solution of (I) (1 g, 5.2 mmol) in an anhydrous mixture of acetonitrile (MeCN) and dichloromethane (DCM) (25 ml, 7:1) was added dropwise to 25 ml of a 0.36 M nitronium tetrafluoroborate solution in an anhydrous mixture of MeCN–DCM (5:4) at 248 K. The reaction mixture was stirred at 248 K for 3.5 h and then allowed to reach room temperature. Ice was added, the solution basified with NH_3 (32%, pH 11) and extracted with DCM. The solvent was removed under vacuum and the residue containing a mixture of products was purified by flash silica column chromatography. Elution with DCM–MeOH (99:1) afforded (II) (540 mg, 52% yield) and (IIIa) (156 mg, 14% yield). (IIIa) was obtained as a pale-yellow oil. Colourless single crystals of (IIIa) suitable for X-ray analysis were obtained by recrystallization from DCM at 277 K. ^1H NMR (400 MHz, $CDCl_3$): δ 6.78 (*s*, 1H, H-5), 6.14 (*d*, *J* = 4.4 Hz, 1H, H-1), 4.18 (*m*, 1H, H-3α), 3.95 (*m*, 1H, H-3β), 3.93 (*s*, 3H, OCH_3), 3.91 (*s*, 3H, OCH_3), 3.01 (*d*, *J* = 4.4 Hz, 1H OH), 2.98 (*m*, 1H, H-4α), 2.11 (*m*, 1H, H-4β). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.1 (*s*, $COCH_3$), 144.5 (*s*), 139.9 (*s*, $COCH_3$), 131.4 (*s*), 119.0 (*s*, C-8a), 113.6 (*d*, C-5), 87.4 (*d*, C-1), 62.1 (*q*, OCH_3), 57.4 (*t*, C-3), 56.2 (*q*, OCH_3), 27.8 (*t*, C-4). HPLC-MS (ESI+): [C18, H_2O-CH_3CN (0,1% HCOOH) gradient 0-100% CH_3CN in 15 min]: r_t 7.3 min; m/*z* 238 [$M + 1 - H_2O$]$^+$.

Crystal data

$C_{11}H_{14}N_2O_5$
$M_r = 254.24$
Triclinic, $P\overline{1}$
$a = 8.587$ (7) Å
$b = 8.636$ (5) Å
$c = 8.746$ (14) Å
$\alpha = 80.04$ (9)°
$\beta = 64.67$ (8)°
$\gamma = 85.18$ (6)°
$V = 577.4$ (11) Å^3
$Z = 2$
$D_x = 1.462$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 0.12$ mm^{-1}
$T = 293$ (2) K
Prism, colourless
$0.4 \times 0.2 \times 0.2$ mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
3356 measured reflections
3356 independent reflections
2298 reflections with $I > 2\sigma(I)$
$\theta_{max} = 30.0°$
3 standard reflections
frequency: 120 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.097$
$S = 1.08$
3356 reflections
170 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0292P)^2 + 0.1026P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.23$ e Å^{-3}
$\Delta\rho_{min} = -0.18$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—N1	1.196 (2)	N2—C7	1.4151 (19)
O2—N1	1.2129 (18)	N2—C8	1.439 (2)
N1—C1	1.480 (3)		
O1—N1—O2	124.10 (15)	C7—N2—C8	112.20 (12)
O1—N1—C1	119.21 (16)	C6—C1—N1	115.14 (13)
O2—N1—C1	116.68 (15)	C2—C1—N1	120.82 (13)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O5—H5O···N2^{i}	0.832 (17)	2.056 (18)	2.870 (5)	166.2 (17)

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

H atoms bonded to C atoms were placed in geometrically calculated positions and refined using a riding model, with C—H = 0.96–0.98 Å and $U_{iso}(H) = 1.2U_{eq}(C)$. The coordinates of the H atom bonded to nitrogen were refined but $U_{iso}(H)$ was set at $1.2U_{eq}(N)$. The hydroxyl H atom was refined freely.

Data collection: *CAD-4-PC* (Kretschmar, 1996); cell refinement: *CAD-4-PC*; data reduction: *CFEO* (Solans, 1978); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1998); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1998); molecular graphics: *ORTEP-3.2* (Brueggemann & Schmid, 1990); software used to prepare material for publication: *PLATON* (Spek, 2003).

The authors acknowledge PharmaMar SAU (Madrid), CICYT (BQU 2003–00089, PETRI 95–0658OP), the Generalitat de Catalunya (Grup Consolidat and Centre de Referència en Biotecnologia), and the Barcelona Science Park for their support.

o2286 Roqué-Rosell *et al.* • $C_{11}H_{14}N_2O_5$ *Acta Cryst.* (2006). E**62**, o2285–o2287

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.

Banwell, M., Flynn, B. & Hockless, D. (1997). *Chem. Commun.* pp. 2259–2260.

Brueggemann, R. & Schmid, G. (1990). *ORTEP-3.2*. PC version. University of Ulm, Germany.

Cironi, P., Albericio, F. & Álvarez, M. (2004). *Progress in Heterocyclic Chemistry*, Vol. 16, edited by G. W. Gribble & J. A. Joule, ch. 1, pp. 1-26. Oxford: Pergamon.

Cironi, P., Cuevas, C., Albericio, F. & Álvarez, M. (2004). *Tetrahedron*, **60**, 8669–8675.

Cironi, P., Manzanares, I., Albericio, F. & Álvarez, M. (2003). *Org. Lett.* **5**, 2959–2962.

Kretschmar, M. (1996). *CAD-4-PC*. Version 2.0. PC version of *CAD-4 Software* (Version 5.0). University of Tübingen, Germany.

McCoubrey, A. & Mathieson, D. W. (1951). *J. Chem. Soc.* pp. 2851–2853.

Sheldrick, G. M. (1998). *SHELXS97*, *SHELXL97* and *CIFTAB* (release 97-2). University of Göttingen, Germany.

Solans, X. (1978). *CFEO*. University of Barcelona, Spain.

Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.

Acta Cryst. (2006). E**62**, o2285–o2287 Roqué-Rosell *et al.* • $C_{11}H_{14}N_2O_5$ **o2287**