Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Methyl 1-benzoyl-3-hydroxy-4-methoxy-1,2,3,4-tetrahydroquinoline-2-carboxylate

Michel Evain,[a]* Mickaël Pauvert,[b] Sylvain Collet[b] and André Guingant[b]

[a]Institut des Matériaux Jean Rouxel, 2 rue de la Houssinière, BP 32229, 44322 Nantes Cedex 3, France, and [b]Laboratoire de Synthèse Organique, UMR CNRS 6513, Faculté des Sciences et des Techniques, 2 rue de la Houssinière, BP 92208, 44322 Nantes Cedex 3, France

Correspondence e-mail: michel.evain@cnrs-imn.fr

Key indicators

Single-crystal X-ray study
T = 150 K
Mean σ(C–C) = 0.002 Å
R factor = 0.058
wR factor = 0.124
Data-to-parameter ratio = 21.3

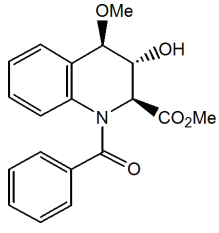
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 25 March 2004
Accepted 31 March 2004
Online 17 April 2004

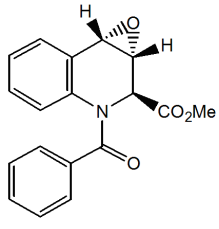
The title compound, $C_{19}H_{19}NO_5$, is the result of a regioselective nucleophilic epoxide ring-opening performed with methanol on a 1,2,3,4-tetrahydroquinoline 3,4-epoxide bearing a related *trans* ester functionality. The relative stereochemistry of the resulting diol has shown that the the three adjacent substituents are mutually *trans* disposed. In the crystal structure, centrosymmetric hydrogen-bonded dimers are observed.

Comment

1,2,3,4-Tetrahydroquinolines of non-natural origin have been shown to display a broad range of activities in diverse domains of industrial and pharmacological interest (Katritzky *et al.*, 1996). The 1,2,3,4-tetrahydroquinoline motif is also present in natural alkaloids, in which it constitutes the basic framework or is part of the polycyclic core of the molecule. Representative alkaloids recently synthesized are the antiviral virantmycine (Steinhagen & Corey, 1999) and the first non-peptide antagonists for the bradykinin B1 and B2 receptors, martinellic acid and martinelline (Dawei *et al.*, 2001; Sniser *et al.*, 2001; Powell & Batey, 2002). In the context of new drugs discovery, the structures of these natural products may be employed as a guiding principle for the elaboration of libraries of analogues with more potent activities (Breinbauer *et al.*, 2002).



(I)



(II)

In the course of an investigation aimed at preparing such analogues, the title compound, (I), was regio- and stereoselectively synthesized (quantitative yield) by exposure of the 2-carboxymethyl-1,2,3,4-tetrahydroquinoline-3,4-epoxide, (II), to methanol at room temperature. By contrast to most other epoxide ring-opening reactions, it is worth mentioning that no catalyst was required to perform this transformation. Although the stereochemistry of the epoxide precursor (II) could not be assigned with certainty, it was assumed, based on the work of Kratzel and collaborators (Kratzel *et al.*, 1994; Hiessböck & Kratzel, 1996; Hiessböck *et al.*, 1999), that the epoxide and ester functionalities were *trans* disposed. In order to ascertain the stereochemical relationships of the C2, C3 and C4 substituents in both (I) and (II), compound (I) was subjected to X-ray crystal structure analysis.

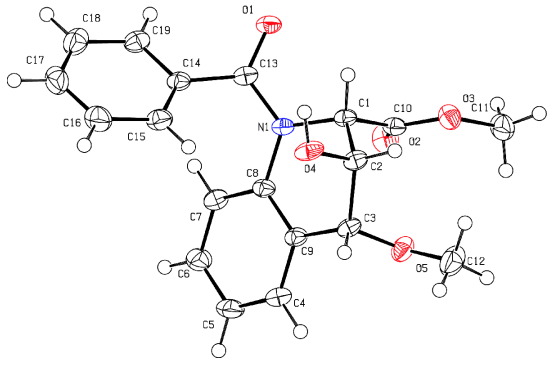


Figure 1
The molecular structure of (I), showing 50% probability displacement ellipsoids. H atoms have been omitted for clarity.

The molecular structure of (I) is shown in Fig. 1. It can be seen that the substituents at C2 and C3, and at C3 and C4, have *trans* arrangements. Since the stereoselective methanol-induced epoxide ring-opening certainly arose *via* an S_N2-type mechanism, the observed relative stereochemistries in the title compound (I) confirm the anticipated *trans* relative stereochemistry in epoxide (II).

It is also worth noticing that, in the crystal structure, molecules are paired through inversion centres by means of hydrogen bonds; see Table 1 for details.

Experimental

To a solution of methyl 1-benzoyl-1,2-dihydroquinoline-2-carboxylate (Cobb & McEwen, 1955; Collins & Henshall, 1958; 680 mg, 2.32 mmol) in CH_2Cl_2 (20 ml) at 253 K was added *m*CPBA (600 mg, 3.5 mmol) in small portions. The reaction mixture was maintained at 253 K and stirred for 4 h. After the mixture was allowed to warm to room temperature it was filtered through a pad of celite. The filtrate was washed with saturated $NaHCO_3$ solution (3 × 20 ml) and brine (10 ml), dried over $MgSO_4$ and evaporated. The crude product was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 1:1) to give the desired epoxide compound, (II) (556 mg, 78%) as white crystals (m.p. 392–393 K). A solution of epoxide (II) (570 mg, 1.85 mmol) in dry methanol (15 ml) was stirred at room temperature for 48 h. The solvent was then evaporated to give the title compound, (I) (630 mg, 100%), as a white solid (m.p. 407–409 K). Crystals of (I), suitable for X-ray diffraction analysis, were grown by slow isothermal evaporation of a CH_2Cl_2 solution.

Crystal data

$C_{19}H_{19}NO_5$
M_r = 341.4
Monoclinic, $P2_1/c$
a = 13.0672 (4) Å
b = 6.7829 (3) Å
c = 19.2623 (8) Å
β = 97.381 (3)°
V = 1693.14 (12) Å^3
Z = 4
D_x = 1.339 Mg m^{-3}
Mo Kα radiation
Cell parameters from 8343 reflections
θ = 2.9–30.0°
μ = 0.10 mm^{-1}
T = 150 K
Thick plate, colourless
0.23 × 0.16 × 0.06 mm

Data collection

Nonius KappaCCD diffractometer
φ and ω scans
Absorption correction: none
27588 measured reflections
4886 independent reflections
3228 reflections with $I > 2\sigma(I)$
R_{int} = 0.076
θ_{max} = 29.8°
$h = -18 \rightarrow 18$
$k = -9 \rightarrow 9$
$l = -26 \rightarrow 26$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.058
$wR(F^2)$ = 0.124
S = 1.44
4886 reflections
229 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(I) + 0.001936I^2]$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.51 e Å^{-3}
$\Delta\rho_{min}$ = −0.44 e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O4—H1O4···O1^{i}	0.858 (19)	1.926 (19)	2.7724 (14)	169 (2)

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

The H atom of the hydroxyl group was located in a Fourier difference map and refined isotropically. H atoms attached to C atoms were included in calculated positions and treated as riding atoms; C—H = 0.97 Å and U_{iso}(H) = 1.2U_{eq}(C).

Data collection: *COLLECT* (Nonius, 1998); cell refinement: *COLLECT*; data reduction: *EVALCCD* (Nonius, 1998); program(s) used to solve structure: *SHELXTL* (Sheldrick, 1995); program(s) used to refine structure: *JANA*2000 (Petricek & Dusek, 2000); molecular graphics: *DIAMOND* (Brandenburg & Berndt, 1999); software used to prepare material for publication: *JANA*2000.

References

Brandenburg, K & Berndt, M. (1999). *DIAMOND*. Crystal Impact GbR, Bonn, Germany.
Breinbauer, R., Vetter, I. R. & Waldmann, H. (2002). *Angew. Chem. Int. Ed.* **41**, 2878–2890.
Cobb, R. L. & McEwen, W. E. (1955). *J. Am. Chem. Soc.* **77**, 5042–5048.
Collins, R. F. & Henshall, T. (1958). *J. Am. Chem. Soc.* **80**, 159–161.
Dawei, M., Chengfeng, X., Jiqing, J. & Jianhua, Z. (2001). *Org. Lett.* **3**, 2189–2191.
Hiessböck, R. & Kratzel, M. (1996). *Heterocycles*, **43**, 873–882.
Hiessböck, R., Wolf, C., Richter, E., Hitzler, M., Chiba, P., Kratzel, M. & Ecker, G. (1999). *J. Med. Chem.* **42**, 1921–1926.
Katritzky, A. R., Rachwal, S. & Rachwal, B. (1996). *Tetrahedron*, **52**, 15031–15070.
Kratzel, M., Hiessböck, R. & Völlenkle, H. (1994). *Monatsh. Chem.* **125**, 963–969.
Nonius (1998). *COLLECT* and *EVALCCD*. Nonius BV, Delft, The Netherlands.
Petricek, V. & Dusek, M. (2000). *JANA*2000. Institute of Physics, Prague, Czech Republic.
Powell, D. A. & Batey, R. A. (2002). *Org. Lett.* **4**, 2913–2916.
Sheldrick, G. M. (1995). *SHELXTL*. Version 5.0. Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Sniser, B. B., Ahn, Y. & O'Hare, S. M. (2001). *Org. Lett.* **3**, 4217–4220.
Steinhagen, H. & Corey, E. J. (1999). *Org. Lett.* **1**, 823–824.