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# The Crystal Structure of 1-[2-(furan-2-yl)-6-methyl-1,2,3,4-tetrahydroquinolin-4-yl]Pyrrolidin-2-one

Luis A. Vizcaya · Asiloé J. Mora · Gerzon E. Delgado · Ali Bahsas · Uriel Mora · Vladimir V. Kouznetsov

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**Abstract** The title compound,  $C_{18}H_{20}N_2O_2$ , a potential pharmaceutical agent, crystallizes in the monoclinic P2<sub>1</sub>/n space group with unit cell parameters a = 11.157 (7) Å, b = 8.776 (6) Å, c = 16.460 (11) Å,  $\beta = 103.08$  (3)°. The tetrahydroquinoline ring system formed by the fusion of the benzene ring and the piperidine ring via two carbon atoms is coplanar, with the later adopting a sofa conformation. The pyrrolidine group in position 4 adopts an envelope conformation. Dimers related by inversion centers and linked by hydrogen bonds of the type N–H···O form cycles described by the graph set  $R_2^2(16)$ . Additionally, the dimers connect through weak hydrogen bonds of the type C–H···O with graph set C(10) to form chains extending along [001].

**Keywords** X-ray crystal structure · Hydrogen bonding · Tetrahydroquinoline · Diels–Alder

## Introduction

Tetrahydroquinoline derivatives compounds present a wide range of biological activities, which has been reported

L. A. Vizcaya · A. J. Mora · G. E. Delgado (⊠) Laboratorio de Cristalografía, Departamento de Química, Facultad de Ciencias, Universidad de Los Andes, Mérida 5101, Venezuela e-mail: gerzon@ula.ve

A. Bahsas

U. Mora · V. V. Kouznetsov Escuela de Química, Universidad Industrial de Santander, Bucaramanga, Colombia recently. This includes, antimalarial [1], antitumoral [2], antioxidant [3], antipsychotics [4], Alzheimer's treatment [5], anti-breast cancer [6], and antimycobacterial agents [7], among others. In last decades, there has been much interest in the search of new synthetic routes for the preparation of tetrahydroquinolin framework [8–12], which is present in several natural products and pharmaceutical agents.

The imino Diels–Alder reaction, also called the Povarov reaction [13], between aldimines and electron-rich alkenes is maybe the most used synthetic route for the tetrahydroquinolines preparation. Recently, the synthesis of tetrahydroquinoline using the Povarov reaction has been reported to be catalyzed by various Lewis or Brönsted acid catalysts [14]. This method allows the preparation of quinoline derivatives with several degrees of structural diversity.

The present work reports the crystal structure of the tetrahydroquinoline derivative **1**, namely 1-[2-(furan-2-yl)-6-metyl-1,2,3,4-tetrahydroquinolin-4-il]pirrolydin-2-one, which was prepared by the imino Diels–Alder reaction (Scheme 1) [14].

## Experimental

## Preparation

1-[2-(furan-2-yl)-6-metyl-1,2,3,4-tetrahydroquinolin-4-il] pirrolydin-2-one **1**, was synthesized by a Diels–Alder reaction (Scheme 1) which is explained elsewhere [14]. Yield was 80%. X-ray quality crystals were obtained from a solution of chloroform after slow evaporation (m.p.: 467–468 K).

X-ray Crystallography

Brown transparent rectangular crystal (0.4, 0.3, 0.2 mm) was used for data collection. Diffraction data were

Laboratorio de Resonancia Magnética Nuclear, Departamento de Química, Facultad de Ciencias, Universidad de Los Andes, Mérida 5101, Venezuela

collected at 295 (2) K on a Nicolet P3/F diffractometer [15] equipped with graphite-monochromatized MoK<sub> $\alpha$ </sub> radiation ( $\lambda = 0.71073$  Å). The data were corrected for Lorentz-polarization and absorption effects [15]. The structure was solved by direct methods using the SHELXS97 program [16] and refined by a full-matrix least-squares calculation on F<sup>2</sup> using SHELXL97 [16]. All H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, with C–H distances of 0.93 (aromatic) and 0.96 Å (methyl), and with U<sub>iso</sub>(H) = 1.5 (1.2 for aromatic H atoms) times U<sub>eq</sub>(C).

Crystallographic data for the structure reported here have been deposited with the Cambridge Crystallographic Data Centre (Deposition No. CCDC-818541). The data can



Scheme 1 Chemical synthesis of the title compound by the imino Diels-Alder reaction

Table 1 Crystal data, data collection and structure refinement

| Chemical formula                           | C <sub>18</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub> |
|--|---|
| Formula weight                             | 296.36  |
| Crystal system                             | Monoclinic  |
| Space group                                | P2 <sub>1</sub> /n  |
| <i>a</i> (Å)                               | 11.157 (7)  |
| <i>b</i> (Å)                               | 8.776 (6)   |
| <i>c</i> (Å)                               | 16.460 (11)   |
| β (°)                                      | 103.08 (3)  |
| V (Å <sup>3</sup> )                        | 1569.9 (18)   |
| Z  | 4   |
| $d_x (g cm^{-3})$                          | 1.254   |
| F (000)                                    | 632   |
| $\mu (\mathrm{mm}^{-1})$                   | 0.08  |
| $\theta$ range (°)                         | 2.01–27.43  |
| hkl range                                  | $-13 \le h \le 13$  |
|  | $-3 \le k \le 10$   |
|  | $-18 \le 1 \le 19$  |
| Reflections                                |   |
| Collected                                  | 5677  |
| Unique (R <sub>int</sub> )                 | 2811 (0.082)  |
| With I > $2\sigma(I)$                      | 1266  |
| Refinement method                          | Full-matrix least-squares on $F^2$                            |
| Number of parameters                       | 199   |
| $R(F) [I > 2\sigma(I)]$                    | 0.076   |
| wR(F) $[I > 2\sigma(I)]$                   | 0.237   |
| Goodness of fit on $F^2$                   | 1.045   |
| Max/min $\Delta \rho$ (e Å <sup>-3</sup> ) | 0.35/-0.37  |

be obtained free of charge via http://www.ccdc.cam. ac.uk/perl/catreq.cgi (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam. ac.uk).



Fig. 1 Asymmetric unit with anisotropic ellipsoid representations, together with atom labeling scheme [17]. The *ellipsoids* are drawn at 50% probability level, hydrogen atoms are depicted as spheres with arbitrary radii

Table 2 Selected geometrical parameters (Å, °)

| N1-C2        | 1.454 (6)  |
|--------------|------------|
| N1-C19       | 1.397 (6)  |
| N2-C13       | 1.450 (6)  |
| N2-C4        | 1.440 (6)  |
| N2-C16       | 1.349 (6)  |
| C4-N2-16     | 121.7 (3)  |
| C4-N2-13     | 124.5 (3)  |
| C3–C2–C9     | 111.9 (3)  |
| C9-C2-C3-C4  | 179.1 (4)  |
| N1-C2-C3-C4  | -57.4 (4)  |
| N1-C2-C9-O1  | -66.4 (5)  |
| O1–C9        | 1.374 (6)  |
| O1–C12       | 1.372 (9)  |
| O2–C16       | 1.218 (6)  |
| C2–C3        | 1.526 (6)  |
| C2–C9        | 1.485 (6)  |
| C2-C3-C4     | 109.2 (3)  |
| C13-C14-C15  | 104.9 (4)  |
| N1-C2-C9     | 111.0 (4)  |
| C13-N2-C4-C3 | -46.8 (5)  |
| C16-N2-C4-C3 | 139.0 (4)  |
| C2-C3-C4-N2  | -171.6 (3) |
|              |            |

#### **Results and Discussion**

The tetrahydroquinoline compound 1,  $C_{18}H_{20}N_2O_2$ , crystallizes in the monoclinic space group P2<sub>1</sub>/n. The efficiency of the crystal packing reaches 66.9%. Table 1 shows the crystallographic data and structure refinement parameters of 1. A diagram of the asymmetric unit including the atom numbering scheme is shown in Fig. 1 [17].

In the title compound, the bond distance N1–C19 is shorter than the bond distance N1–C2 by 0.061(1) Å (see Table 2 and Fig. 1) as seen in three related structures:

Table 3 Hydrogen bonds geometry (Å, °) Cg1 and Cg2 are the centroid of the benzene and furanic rings, respectively

| D–H…A                                | D–H        | Н…А       | D…A                      | D–H…A                    |
|--------------------------------------|------------|-----------|--------------------------|--------------------------|
| N1-H1····O2 <sup>(i)</sup>           | 0.86       | 2.56      | 3.168 (5)                | 129                      |
| C12-H12····O2 <sup>(ii)</sup>        | 0.93       | 2.31      | 3.148 (9)                | 150                      |
| C4–H4…O2                             | 0.98       | 2.42      | 2.812 (5)                | 103                      |
| C5-H5N2                              | 0.93       | 2.56      | 2.893 (6)                | 102                      |
| C2–H2····Cg1 <sup>(iii)</sup>        | 0.98       | 2.73      | 3.689 (5)                | 168                      |
| C11–H11····Cg2 <sup>(iv)</sup>       | 0.97       | 3.20      | 3.683 (6)                | 151                      |
| Symmetry codes:                      | (i) -x +   | 1, -y +   | 1, -z + 1;               | (ii) $x - \frac{1}{2}$ , |
| $-y + \frac{1}{2}, z + \frac{1}{2};$ | (iii) -x + | - 2, -y + | · 2, -z; <sup>(iv)</sup> | -x + 5/2,                |
| v 1/2 7 1/2                          |            |           |                          |                          |

Fig. 2 The packing diagram for the title compound. Hydrogen bonds are denoted by *dashed lines* 

DISHIW [18], IXAHOE [19] and MHXHQV [20], reported in the CSD database [21]. This shortening is attributed to resonance effects between the benzene ring and the free electron pair of N1, giving a double bond character to N1–C19. The same shortening is seen in bond N2–C16 of the pyrrolidine ring, where the resonance effect is with the adjacent double bond of the carbonyl group.

The furanic and pyrrolidine rings at positions 2 and 4, respectively, are equatorial to the piperidine ring [22] making angles with this ring of 83.3° and 79.8°, respectively. In the piperidine ring, the presence of a plane through C3 and C9 indicates this ring adopts a sofa conformation [23], C3 is 0.373 Å out of the average piperidine plane. This conformation is also seen in 2,4-substituted tetrahydroquinolines such as: MABTHQ [24] and MHXHQV [20]. On the other hand, the pyrrolidine ring shows a plane passing through C14 and bisecting the bond N2–C16, which indicates that this ring adopts the envelope conformation.

The crystalline structure is stabilized by two intramolecular and two intermolecular hydrogen bonds. The geometrical parameters of these hydrogen bonds are summarized in Table 3 and Fig. 2.

Two intramolecular hydrogen bonds [C4–H4…O2 and C5–H5…N2] anchor the pyrrolidine substituent in such a



Fig. 3 The intermolecular hydrogen bonds,  $N-H\cdots O$  and  $C-H\cdots O$ , of the title compound. H atoms not involved in hydrogen bonding have been omitted for clarity



way as to make it bisecting to the tetrahydroquinoline ring system. Dimers related by inversion centers, and strongly linked by hydrogen bonds of the type N–H···O [N1···O2<sup>(i)</sup> 3.168 (5) Å, N1–H1···O2<sup>(i)</sup> 129°], are described by the graph set symbol R<sup>2</sup><sub>2</sub>(16) [25]. These dimers connect through non-conventional C–H···O [C12···O2<sup>(ii)</sup> 3.148 (9) Å, C12–H12···O2<sup>(ii)</sup> 150°] hydrogen bonds to form extended chains running along the [001], with graph set symbol C(10) (see Fig. 3). Additional C–H··· $\pi$  [C2···Cg1<sup>(iii)</sup> and C11···Cg2<sup>(iv)</sup>] hydrogen bonds help to keep the chains together, in which H atoms from the piperidine ring interact with the delocalized  $\pi$  electrons of the furanic and benzene rings of neighboring chains.

In conclusion, the title compound has been prepared from the imino Diels–Alder reaction. The tetrahydroquinoline ring system formed by the fusion of the benzene ring and the piperidine ring via two carbon atoms is coplanar, with the later adopting a sofa conformation. The pyrrolidine group in position 4 adopts an envelope conformation. The molecular structure and crystal packing is stabilized by intermolecular N–H···O and C–H···O hydrogen bonds.

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