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ORIGINAL PAPER

Crystal Structure, Conformation and Vibrational Analysis of a Mannich Base: 2-[(phenylamino) methyl]-isoindole-1,3-dione

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Abstract The crystal structure of 2-[(phenylamino) methyl]-isoindole-1,3-dione, $C_{15}H_{12}N_2O_2$, crystallizes in the triclinic space group $P\bar{1}$ with cell parameters of $a = 7.1176$ (2) Å, $b = 8.5533$ (3) Å, $c = 10.9163$ (4) Å, $\alpha = 95.937$ (2)°, $\beta = 102.975$ (2)°, $\gamma = 108.474$ (2)°, $V = 603.18$ (4) Å^3 and $Z = 2$. This indole derivative is a Mannich base in which a methyl group bridges the molecules of phthalimide and aniline molecules. The dihedral angle between the phthalimide and aniline is 75.47 (3)°. The molecules of the title compound forms a centrosymmetric hydrogen-bonded dimer through a pair of N–H···O hydrogen bonds. C–H···π and an extensive π···π interactions, in addition, stabilize the molecular structure. The compound presented here is V-shaped, the angle at the methyl bridge [N–C–N] being 115.04 (12)°. Present study reports the conformation and hydrogen bonding interactions which play an important role in biological functions. Vibration analysis complement the structure analysed.

Keywords Mannich base · Phthalimide · Aniline · Crystal structure

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Introduction

Mannich reaction is a three-component condensation reaction involving active hydrogen compound, formaldehyde and a secondary or tertiary amine [1, 2]. It is an important C–C bond forming reaction used widely in the synthesis of secondary and tertiary amine derivatives [3, 4]. It is a key step in the synthesis of many bioactive molecules [5]. Mannich base compounds have been reported as potential biological agents. They find applications as anti-tubercular [6], anti-malarial [7], vasorelaxing [8], anti-cancer [9] and analgesic drugs [10]. The crystal structure of 2-[(phenylamino) methyl]-isoindole-1,3-dione {PMID}, a Mannich base compound, reported here is an indole derivative.

Phthalimides [isoindole-1,3-dione] and N-substituted phthalimides belong to an important class of compounds because of their interesting biological activities [11–13]. They exhibit cytotoxicity [14] and anti-HIV activity [15]. Anilines are the simplest and one of the most important aromatic amines used widely in the preparation of polyurethane. It is a starting-product for the manufacture of drugs like paracetamol and several sulfonamide-based drugs. Present study reports the crystal structure of PMID, in which a phthalimide and phenylamine molecules are bridged by a methyl group. This crystal structure has been determined in order to gain a further insight in its chemical and pharmaceutical aspects. The aggregation modes and the hydrogen bonding patterns have been explored.

Experimental

Preparation

Equimolar amount of phthalimide and formaldehyde were dissolved in ethanol and the contents were mixed well at

room temperature. To the clear solution obtained equimolar amount of aniline was added and stirred well. After few days a yellow solid obtained was washed with ethanol several times and dried in the air oven at 333 K. Good quality crystals suitable for X-ray analysis were obtained on crystallizing the product using hot ethanol.

X-ray Diffraction Studies

Single crystal X-ray diffraction data were collected on a Bruker axs CCD area detector [16] using MoKα radiation ($\lambda = 0.71073$ Å) in the range of $2.55° < \theta < 31.0°$ at 273 K. The structure was solved by direct methods using *SHELXS-97* [17] and refined by the full-matrix least-squares methods on F^2 using *SHELXL-97* [17]. Hydrogen atoms were located from the difference Fourier map and their positional and isotropic displacement parameters were refined with a riding model. Summary of the crystal data and structure refinement for the title compound is provided in Table 1. Chemical scheme of the present structure is shown as the inset of Fig. 1. Selected bond lengths and angles are listed in Table 2.

Table 1 Crystal data and structure refinement for PMID

Formula	C_{15} H_{12} N_2 O_2
Formula weight	252.27
Crystal system	Triclinic
Space group	$P\bar{1}$
Cell constants	
a (Å)	7.1176(2)
b (Å)	8.5533(3)
c (Å)	10.9163(4)
α (°)	95.937(2)
β (°)	102.975(2)
γ (°)	108.474(2)
Volume (Å^3)	603.18(4)
Z	2
D_{calc} (mg/m^3)	1.389
μ (MoKα) (mm^{-1})	0.09
F (000)	264
Crystal size (mm)	0.30 × 0.25 × 0.20
Reflections collected	17033
Data/restraints/parameters	4531/0/172
Goodness of fit on F^2	1.04
Final R indices [$I > 2\sigma$(I)]	$R_1 = 0.052$ $wR_2 = 0.139$
R indices (all data)	$R_1 = 0.075$ $wR_2 = 0.159$
$(\Delta\rho)_{min}$, $(\Delta\rho)_{max}$ (e Å^{-3})	−0.30, 0.26
CCDC deposition number	CCDC 728038

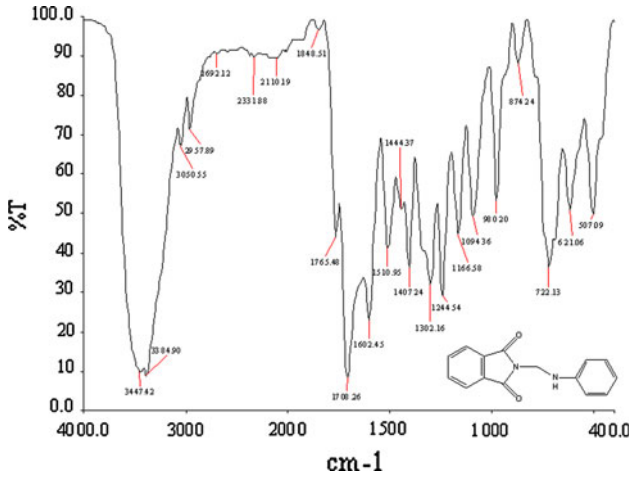

Fig. 1 FTIR spectrum of PMID with an inset for the chemical scheme of PMID

FTIR Studies

The Fourier Transform Infrared (FTIR) spectrum of the compound PMID has been recorded in the range of 400–4000 cm^{-1} using KBr pellet with a Perkin Elmer FTIR spectrophotometer at room temperature. Figure 1 shows the FTIR spectrum of the compound PMID.

Discussion

Structural Studies

The asymmetric unit of the crystal structure presented here consists of one molecule of the 2-[(phenylamino) methyl]-isoindole-1,3-dione {PMID}. An ORTEP-3 [18] diagram of the crystal structure with the atom labelling scheme is shown in Fig. 2. The geometrical parameters of the phthalimide ring system are closer to those values observed in related compounds [19, 20]. The sum of the angle around N1 is 359.83 (10)° indicating sp^2 hybridization. However, the N1–C1 [1.3981(15) Å] and N1–C8 [1.3801(15) Å] distances are intermediate between the average C_{ar}–N sp^3(pyramidal) [1.419(17) Å] and C_{ar}–N sp^2(planar) [1.353(7) Å] distances reported by Allen et al. (1987) [21]. The phthalimide unit is essentially planar making a dihedral angle 75.47(3)° with aniline unit. The compound PMID is V-shaped with an angle 115.04(12)° at the methyl bridge [N–C–N].

The crystal packing of the PMID is stabilized extensively by $\pi\cdots\pi$ and C–H$\cdots\pi$ interactions which are summarized in Table 3. Part of the crystal structure of PMID, depicting the hydrogen-bonding interactions and the formation of hydrogen-bonded motif is shown in Fig. 3. Generally, C–H$\cdots$N intramolecular hydrogen bonds are

Table 2 Selected geometric parameters of PMID (Å, °)

C1–O2	1.1986 (15)
C8–O1	1.2070 (15)
N1–C1	1.3981 (15)
N1–C8	1.3801 (15)
N1–C9	1.4707 (18)
N2–C9	1.23 (2)
N2–C10	1.3963 (18)
C1–N1–C8	111.72 (9)
C1–N1–C9	126.51 (10)
C8–N1–C9	121.60 (10)
C9–N2–C10	122.71 (11)
O2–C1–N1	125.25 (11)
O1–C8–N1	124.50 (11)
N1–C9–N2	115.04 (12)
O2–C1–N1–C9	2.7 (2)
O1–C8–N1–C9	−3.2 (2)
C1–N1–C9–N2	−112.06 (14)
C8–N1–C9–N2	73.08 (16)
N1–C9–N2–C10	75.98 (16)
C9–N2–C10–C15	13.7 (2)
C9–N2–C10–C11	−168.47 (12)

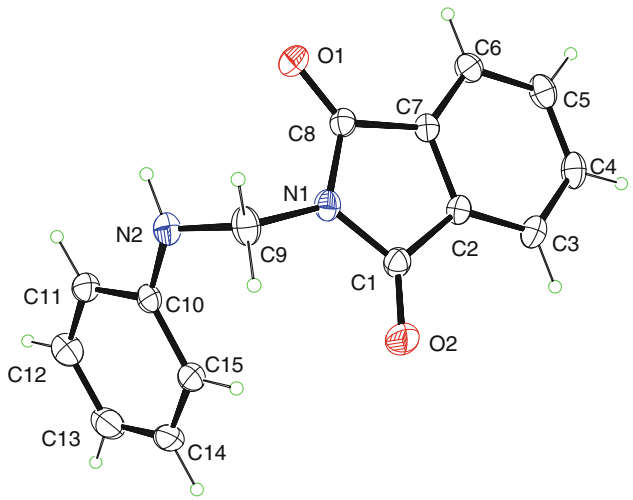

Fig. 2 Molecular structure of PMID, showing 20% probability displacement ellipsoids

Table 3 Hydrogen-bond geometry of PMID (Å, °)

D–H···A	D–H	H···A	D···A	D–H···A
N2–H2···O1^{i}	0.95	2.24	3.1685 (16)	163

Symmetry code: (i) $-x + 2, -y + 1, -z + 1$

observed in majority of the Mannich base compounds [22–24]. However, this kind is absent in the present structure. The molecule of PMID forms centrosymmetric hydrogen–bonded dimers through a pair of N–H···O hydrogen bonds. The hydrogen–bonded ring motif observed can be represented by the graph-set notation $\underline{R}_2^2(12)$ [25, 26]. The succinimide ring at (x, y, z) is linked by aromatic $\pi\cdots\pi$ interactions with the benzene rings (C2–C7) at ($1 - x$, $-y$, $1 - z$) and ($2 - x$, $-y$,$1 - z$), lying in different frameworks, with a centroid separation of 3.6559(8) and 3.6590(8) Å, respectively. Further, the benzene rings (C2–C7) at (x, y, z) and ($2 - x$, $-y$, $1 - z$), lying in different frame works are linked by $\pi\cdots\pi$ stacking interactions with a centroid separation of 3.6596(8) Å. Further, the benzene rings of the aniline molecule at (x, y, z) and ($2 - x$, $1 - y$, $-z$), lying in different frameworks are linked by $\pi\cdots\pi$ stacking interactions with a centroid separation of 3.6919(9) Å. These extensive $\pi\cdots\pi$ interactions (Fig. 3; Table 3) stabilize the crystal packing.

Vibration Studies

The vibrations of various functional groups of the compound PMID were analysed from the FTIR spectrum recorded (Fig. 1). The spectrum reveals the presence of aromatic ring and methyl groups. Sharp bands observed at 3447 and 3384 cm^{-1} is assigned to the ν(N–H) stretching vibrations. The medium band at 3050 cm^{-1} is attributed to aromatic ν(C–H) stretching vibrations. The absorption in the region of 2957 cm^{-1} is due to the ν(C–H) of aliphatic group. The amide band due to ν(C=O) appears at 1765 and 1708 cm^{-1} and amide band due to the δ(N–H) in plane and ν(C–N) vibrations appears at 1510 and 1602 cm^{-1}. The

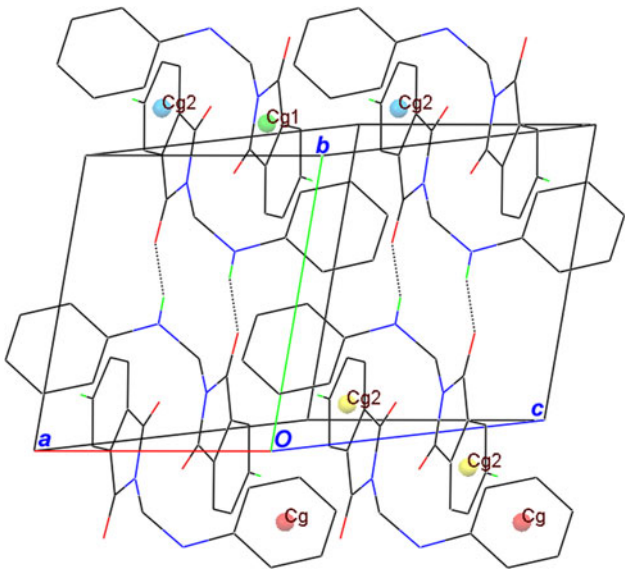

Fig. 3 Part of the crystal structure of PMID, depicting $R_2^2(12)$ hydrogen-bonded ring motif formation. Cg, Cg_1 and Cg_2 represents the centroid of C10-C15; C1, C2, C7, C8, N1 and C2–C7 rings, respectively. (*Dashed lines* represent hydrogen bonds)

medium band at 1094 cm^{-1} is assignable to ν(C–N–C) of the product. The presence of absorption bands in the region 874–722 cm^{-1} is due to out of plane bending vibrations of (C–H) bonds of aromatic ring. The strong absorption band observed at 722 cm^{-1} is due to mono substituted aromatic ring. In plane bending bands appear in the region 1244 cm^{-1}. In general primary amines/amides show two ν(N–H) stretching bands resulting from symmetrical and asymmetrical ν(N–H) stretching and secondary amines/amides show only one absorption band for ν(N–H). Thus, the presence of mono substituted aromatic ring, methyl group and secondary amide group is revealed from the IR spectrum of the ligand [27, 28].

Supplementary Data

Crystallographic data for the structure reported in this work have been deposited with the Cambridge Crystallographic Data Center as the supplementary data, *CCDC No. 728038*. Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223 336033.

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