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ORIGINAL PAPER

Synthesis, Crystallographic and Spectral Studies of 3-(4-(Phenylamino) Phenylamino)Cyclohex-2-Enone

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Abstract The title compound, 3-(4-(phenylamino)phenylamino)cyclohex-2-enone, β-enaminone of 1,3-cyclohexanedione and p-amino diphenylamine ($C_{18}H_{18}N_2O$) was prepared and characterized by ^{1}H-NMR, ^{13}C-NMR, Elemental analysis and IR spectroscopy as well as single crystal X-ray diffraction. These results indicate the predominance of the keto-enol tautomerism. Molecular conformation around the central disubstituted benzene ring is affected by the tautomerism and two steric effects between side molecular groups and mono substituted benzene ring. Electron delocalizations due to these effects have been observed in the molecular structure, the structure being stabilized by some intermolecular hydrogen bonds.

Keywords Schiff base · β-Enaminone · Cyclohexanedione · Crystal structure · Spectroscopic studies · Tautomerism

Introduction

β-Enaminones are a class of enamines which are more stable than the enamines of monocarbonyl compounds due to intramolecular hydrogen bonding. Because of the significant reactivity of the conjugated N–C=C–C=O system, β-enaminones are used as important intermediates in synthetic organic chemistry for the preparation of a large number of heterocyclic compounds [1–8]. β-Enaminones have a wide variety of applications in medicine, biochemistry, coordination chemistry and photonic technologies [9–11]. Some β-enaminones are pharmacologically active and exhibit anticonvulsant activity [12–15].

Despite the importance of β-enaminones as valuable biologically active compounds, their synthesis has received to date little attention. Among them, the most simple and straightforward conventional method is the azeotropic removal of water by refluxing an amine and 1,3-diketone in aromatic solvents. The other methods used for this transformation with various activators such as microwave irradiation, the reaction catalyzed by NaAuCl, bismuth(III) trifluoroacetate, Lanthanum trichloride have been reported [16–20]. β-Enaminones, derived from cyclic 1,3-dicarbonyl compounds, are significantly more stable than acyclic analogs.

When a 1,3-diketone is used in Schiff base synthesis, a more stable β-enaminone derivative is formed by means of isomerization. A keto-enol tautomerism (A $\rightleftharpoons$ B) is observed when only one carbonyl group of 1,3-diketone forms the corresponding ketoimine because of added conjugation, which covers the three carbons of hexane ring. The ketoimine is then converted to β-enaminone form which is stabilized both by the formation of intermolecular hydrogen bonding and resonance [21, 22].

We report here the structure of an β-enaminone, which was obtained by condensation of a diketone, 1,3-cyclohexanedione, and a primary amine, p-amino diphenylamine (Scheme 1).

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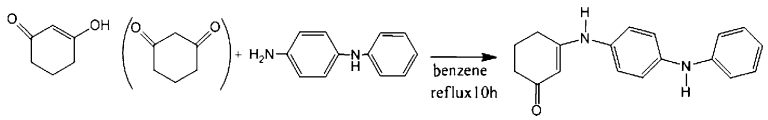


Scheme 1 The reaction of 1,3-cyclohexanedione and p-amino diphenylamine to yield 3-(4-(phenylamino) phenylamino)cyclohex-2-enone

Scheme 2 The other possible structures of the reaction product given in Scheme 1

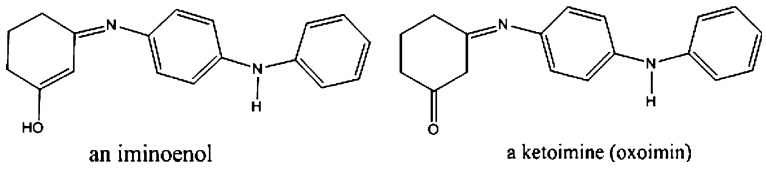
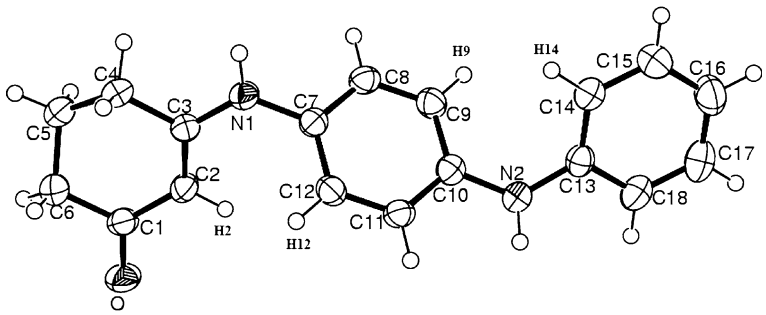


Fig. 1 Molecular structure of the 3-(4-(phenylamino) phenylamino)cyclohex-2-enone, showing 50% probability displacement ellipsoids



The ketoamine, iminoenol and ketoimin form (Schiff base) are the three tautomeric forms of β-enaminones (Scheme 2). However, the enaminone form is generally favored because of increased resonance between sp^3-nitrogen and the carbonyl group [23, 24]. β-enaminones show double-bond stereoisomerism. Previous NMR spectroscopic and **X**-ray crystallographic studies have shown that enaminones exist as either the E-s-E-s-E or as mixture of both conformations, depending on the C-2 substituent the Z-s-Z-s-E conformations [25]. The E and Z forms of enaminones can easily be identified by means of ^{1}H-NMR spectroscopy. The N–H signal of the Z isomer appears at 9–13 ppm while the same signal for the E isomer appears at 4–8 ppm due to strong intermolecular hydrogen bonding [26].

The molecular structure and crystallographic numbering order of the atoms of 3-(4-(phenylamino) phenylamino)cyclohex-2-enone are shown in Fig. 1.

Experimental

Material

All starting compounds and solvents for synthesis were purchased from Across, Aldrich, Sigma and E. Merck. Solvents and all reagents were technical grade and were purified and dried by distillation from appropriate desiccant when necessary. Concentration of solutions after reactions and extractions were achieved using a rotary evaporator at reduced pressure.

Analytical and preparative thin layer chromatography (TLC) was performed on silica gel HF-254 (Merck). Column chromatography was carried out by using 70–230 mesh silica gel (0.063–0.2 min, Merck).

Method

The structures of the compounds in this study were determined by the instruments mentioned below.

All melting points were measured in sealed tubes using an electrothermal digital melting point apparatus (Gallenkamp) and were uncorrected. The investigation of vibrational properties of the β-enaminone was carried out on a Mattson 1000 Model FT-IR Spectrometer within the range of 4000–400 cm^{-1}. The IR sample was prepared as KBr pellet. ^{1}H-NMR, ^{13}C-NMR were recorded on a resolution fourier transform Bruker WH-400 NMR spectrometer with tetramethylsilane as an internal standard. Chemical shifts were reported in ppm relative to the solvent peak. Signals were designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Elemental

microanalyses of the separated solid chelates for C, H, N, were performed with a Elementar Analysensysteme GmbH vario MICRO CHNS analyser.

Synthesis

A mixture of 10 mmol (1.12 g) 1,3-cyclohexanedione and 10 mmol (1.84 g) p-amino-diphenylamine were refluxed in 100 mL benzene using a Dean-Stark apparatus until all water was completely separated. The removal of water is very important because of the back hydrolysis of the enaminone. Benzene was evaporated and the precipitate was extracted with ethanol. The crude product was purified by silica gel column chromatography using a mixture of n-hexane/ethyl acetate mixture as eluent. The product was recrystallized twice from ethanol and obtained as pure crystals. Yield: 58%, mp. 207–208 °C.

Spectroscopic Studies

IR (KBr, cm^{-1}); υ(N–H) 3282 s and 3212 m, υ(Ar–H) 3030 m, υ(C–H) 2995 m and 2946 s and 2860 m, υ(C=O and C=C of enamine) 1680–1490 s and broad, υ(C–N) 1370–1252 s. ^{1}H-NMR ($CDCl_3$); δ ppm, 7.30–7.40 (m, 4H, NH–**Ph**-NH); 7.00–7.10 (m, 5H, **Ph**-NH); 5.95 (s, 1H, enamine N**H**); 5.75 (s, 1H, PhN**H**Ph); 5.50 (s, 1H, vinylic CH); 2.50 (t, 2H, CH_2); 2.40 (t, 2 H, CH_2); 2.00(m, 2 H, CH_2).

Table 1 Crystal data and details of the structure determination of 3-(4-(phenylamino) phenylamino)cyclohex-2-enone

Crystal formula	$C_{18}H_{18}N_2O$
Formula weight	278.34
Crystal dimensions (mm)	0.56 × 0.58 × 0.6
Temp (K)	291(2)
Crystal system	Monoclinic
Space group	$P2_1/c$
a (Å)	9.823(1)
b (Å)	15.625(1)
c (Å)	10.841(1)
β (°)	116.440(8)
Z; D_{calc} (g cm^{-1})	4; 1.24
Range of θ (°)	2.5/26.3
μ (MoKα) (mm^{-1})	0.078
Reflections collected	3,195
Reflections used in refinement	3,019
No. of refined parameters	203
R/R_w values	0.0590/0.1503
GOF	1.0880
Final shift	0.000
$(\Delta\rho)_{min}$, $(\Delta\rho)_{max}$ (e $Å^{-3}$)	0.550, −0.452

^{13}C-NMR (DMSO-d_6); δppm, 97,55 (C-2 vinyl carbon atom); 163.33 (C-3 vinyl carbon atom); 195.68 (C-1 carbonyl carbon atom).

Elemental Analysis calculated (found): C, 77.67 (77.38); H, 6.52 (6.49); N, 10.06 (9.94); O, 5.75 (6.19).

Crystallographic Studies

A summary of the key crystallographic information is given in Table 1. A suitable single-crystal was selected and mounted on an Enraf–Nonius CAD-4 diffractometer. The

Table 2 Some geometrical parameters of 3-(4-(phenylamino)phenylamino) cyclohex-2-enone

Bond lengths (Å)	
O–C1	1.253(2)
N2–C10	1.399(2)
N2–C13	1.401(2)
N1–C3	1.344(2)
N1–C7	1.428(2)
C8–C7	1.376(2)
C3–C2	1.369(2)
C3–C4	1.502(2)
C10–C11	1.392(3)
C10–C9	1.394(2)
C13–C14	1.388(3)
C13–C18	1.392(2)
C1–C2	1.414(3)
C7–C12	1.391(2)
Bond angles (°)	
C10–N2–C13	127.02(16)
C3–N1–C7	126.40(15)
N1–C3–C2	124.49(16)
C11–C10–C9	117.83(17)
C11–C10–N2	118.10(16)
C9–C10–N2	123.99(17)
C14–C13–C18	118.13(18)
C14–C13–N2	123.84(16)
C18–C13–N2	118.01(17)
C3–C2–C1	122.19(17)
C8–C7–C12	118.72(16)
C8–C7–N1	119.87(15)
C12–C7–N1	121.31(16)
O–C1–C2	122.08(17)
Torsion angles (°)	
C7–N1–C3–C2	−7.8(3)
C13–N2–C10–C9	31.8(3)
C10–N2–C13–C14	17.3(3)
C3–N1–C7–C12	−48.6(3)
C3–C2–C1–O	−172.09(18)
N2–C13–C14–C15	178.34(18)

structure was solved by direct methods with SHELXS-97 and refined by least squares on F^2_{obs} with SHELXL-97 [27]. All the hydrogen atoms were located from difference Fourier map and they were refined using riding model.

Some geometrical parameters (bond lengths, bond angles and torsion angles) can be seen in Table 2.

Results and Discussion

The title compound is an enaminone rather than an iminoenol or a ketoimine. In the IR spectrum of this compound, an intense broad band appears at 1,490–1,680 cm^{-1} due to normal carbonyl absorption, the broadness probably arising from the interference of the conjugated C=C absorption of the enamine moiety and the intermolecular hydrogen bonding of the carbonyl moiety. The two bands at 3282 and 3212 cm^{-1} arise from the stretching vibrations of N–H group attached to the conjugated carbonyl group, whereas the absorptions in the region 1,370–1,252 cm^{-1} are due to C–N stretching of the aromatic amino groups. Appearance of the later absorption at shorter wavelengths than the corresponding absorption of aliphatic amines is due to the fact that the force constant of the C–N bond is increased by the resonance with the ring [28].

According to literature data reported for compounds containing the β-enaminone structure [29, 30], the ^1H and ^{13}C NMR data of the prepared β-enaminone compound, clearly possessed the appropriate signals needed to identify these compound unambiguously. In the ^1H NMR spectrum, the NH group between two phenyls appears at δ: 5.95, while the NH of the enaminone group absorbs at δ: 5.75. The downfield shifting in the former case arises due to the conjugation of the NH group with two adjacent phenyl groups. The two phenyl groups also absorb at different fields. The five protons of the phenyl group attached to only one NH group appear upfield in comparison to other aromatic group, probably due to the influence of two NH groups attached at para positions of the later phenyl group. The lone C-2 vinyl hydrogen for the β-enaminone compound appeared as a singlet at 5.50 ppm, with an integral area equivalent to one hydrogen. The ^{13}C NMR results also supported the β-enaminone structure by the observation of signals in the region of 195.68 (C-1 carbonyl carbon atom), 163.33 (C-3 vinyl carbon atom), and 97.55 (C-2 vinyl carbon atom).

The ketoamine (enaminone) form of our compound is distinguished from the ketoimino form by the presence of a single vinylic proton and a single amine proton at δ: 5.50 and 5.75 ppm, respectively.

Elemental analysis is in agreement with the formulae of the β-enaminone.

The discussion related with the crystallographic structure can be given by the following explanations.

The mean planes of the six-membered rings are twisted with respect to each other in order to minimize the steric hinderance (H2···H12 and H9···H14). Indeed, they make an angle of 48.80(6)° and 43.02(6) between the cyclohexanone ring and the phenyl rings and between the two phenyl rings, respectively. The conformation of the molecule can be also affected by the intermolecular hydrogen bonds in Fig. 2. Geometrical details of these hydrogen bonds were given in Table 3. With the help of these donor–acceptor relationship, It can be said that, trans-keto form may be seen in the molecular conformation and this intermolecular tautomeric form may cause thermal and photochromic

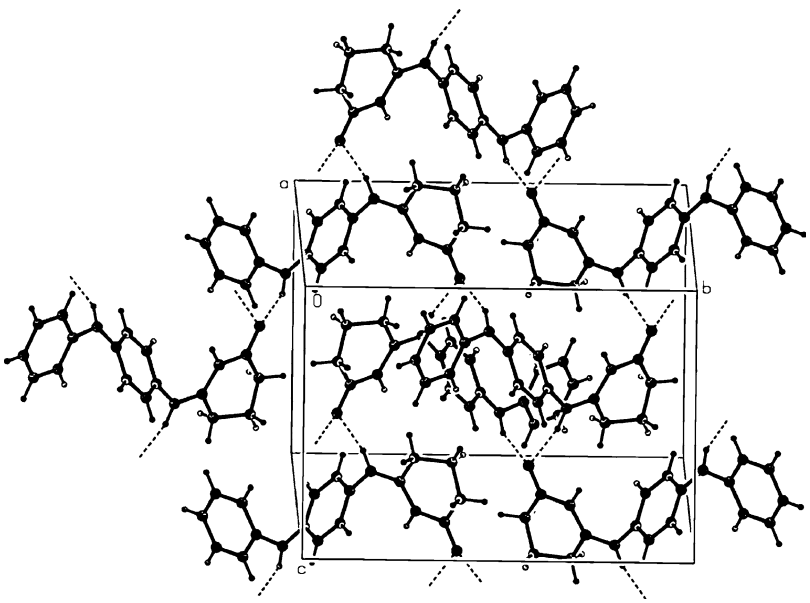


Fig. 2 Packing diagram showing molecular orientation and hydrogen bonded chains

Table 3 Hydrogen bonding geometry (Å, °) for 3-(4-(phenylamino)phenylamino) cyclohex-2-enone

D–H···A	D–H	D···A	H···A	D–H···A
C11–H11···O$^{(1)}$	0.93(2)	3.358(2)	2.655(1)	132.9(1)
N2-H2 N···O$^{(1)}$	0.89(2)	2.942(3)	2.122(27)	151.7(19)
N1–H1 N···O$^{(2)}$	0.91(2)	2.846(2)	1.954(22)	165.3(2)

Symmetry codes: (1) $-x + 1$, $+y + 1/2$, $-z + 1/2 + 1$; (2) x, $-y + 1/2$, $+z - 1/2$

properties in the crystal structure such as molecular cis-keto form [31]. In the molecular structure, the C–O bond length is the most sensitive indicator of the type of tautomeric form. It is a single bond in the case of the enol-imino tautomers while it is shortened in the keto-amino tautomers. A distance of [1.253(2)Å] is observed for the C–O bond length of the title compound, which is slightly longer than the expected value of 1.222 Å for a double bond [32]. According to the enol form and electron delocalizations some bond lengths can be deviated from the expected values [32]. In molecular structures of acyclic β-enaminones, conformational isomerism is usually expected, however, the title compound has a cyclic structure and shows only E isomer. In conjunction with literature data reported for compounds containing the β-enaminone structure the conformation of enaminone can be deduced from their 1H and 13C NMR data [25, 26]. The newly prepared β-enaminone compound, owing to the influence of strong intermolecular hydrogen bonding, exists only as the E-s-E-s-Z conformation (Scheme 1). This is consistent with **X**-ray crystallographic study.

In summary, the X-ray studies confirm the original structural assignments based on spectroscopic techniques and furthermore yield accurate structural parameters which are useful for future biological and pharmaceutical modeling studies.

Supplementary Data

CCDC-657271 contains the supplementary crystallographic data for the compound reported in this paper. These data can be obtained free of charge at http://www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk].

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