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## Molecular Crystals and Liquid Crystals

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### Synthesis, Characterization, and Crystal Structure of 3-(1,2,3,4-Tetrahydroquinazoline-2-yl)phenol—A Ring-Chain Tautomerized 2-Substituted 1,2,3,4-Tetrahydroquinazoline

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# Synthesis, Characterization, and Crystal Structure of 3-(1,2,3,4-Tetrahydroquinazoline-2-yl)phenol—A Ring-Chain Tautomerized 2-Substituted 1,2,3,4-Tetrahydroquinazoline

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*Synthesis, spectroscopic investigations, and X-ray crystal structure of 2-substituted-1,2,3,4-tetrahydroquinazoline ring, obtained from 3-hydroxy benzaldehyde and 2-(aminomethyl)aniline are presented. The X-ray structure and spectroscopic evidence show that the product, which is a ring chain tautomerized Schiff base, appears in a 100% ring form, both in the liquid and in the solid state. The crystal structure of the compound presents a unique supramolecular architecture consisting of hexamers, offering channels of radius 5.79 Å down the c axis.*

*Supplemental materials are available for this article. Go to the publisher's online edition of Mol. Cryst. Liq. Cryst. to view the free supplemental file.*

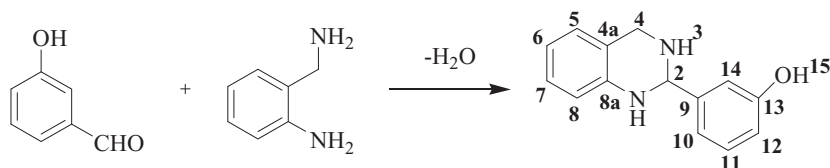
**Keywords** Imine group; quinazoline ring; supramolecular hexamers; tautomerized Schiff base

## 1. Introduction

The ring-chain tautomerism of five- and six-membered 1,3-X,Y-heterocycles (X, Y = O, S, NR) is known to occur in heterocyclic systems closely related to quinazolines, such as 1,3-imidazolidines and piperimidines, and their oxygen-containing analogs, 1,3 and 3,1-benzoxazines [1–6]. The ring-chain tautomerism of 3-substituted tetrahydro- and decahydro-quinazolines has been investigated in the last decade by Fülöp and coworkers [7, 8]. Sinkkonen et al. used NMR spectroscopy to study this phenomenon on a set of 2-substituted 1,2,3,4-tetrahydroquinazolines, derived from 2-aminomethylaniline and various carbonyl compounds [9]. In 2-aryl substituted compounds, the ring-chain ratio has been found to depend on the electronic character of the substituent on the aromatic ring [10–12]. Two X-ray crystal structures of 2,3-substituted [13, 14] and four crystal structures of 2-substituted-1,2,3,4-tetrahydroquinazolines [15] have been reported, which show the existence of a ring conformer in the solid state.

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**Scheme 1.** Synthetic route to the compound (I).

Here, we report the synthesis, spectroscopic, and X-ray crystal structural studies of a new 2-substituted-1,2,3,4-tetrahydroquinazoline compound, synthesized from 3-hydroxy benzaldehyde and 2-(aminomethyl)aniline (Scheme 1), which appears in a 100% ring form both in the liquid and in the solid state. Using NMR spectroscopy, Fülöp et al. [6] had reported 38.0% and 76.9% ring conformer with the products obtained from 2-(aminomethyl) aniline with 4-hydroxy- and 2-hydroxy-benzaldehyde, respectively, in solution. Correa et al. [15] have also synthesized a number of 2-aryl-1,2,3,4-tetrahydroquinazolines in a solvent-free environment. However, a product from 3-hydroxybenzaldehyde has not been reported earlier.

## 2. Experimental

### 2.1. Materials and Instrumentation

C, H, N elemental analysis was obtained with a CHNS-O analyzer flash-EA-1112 series. The melting point was determined with electrically heated apparatus.  $^1\text{H}$  NMR spectrum of compound was recorded on AL-300 FT JEOL spectrometer operating at a frequency of 300 MHz in dimethylsulfoxide ( $\text{DMSO}$ )- $\text{d}_6$  with tetramethylsilane (TMS) as internal reference. The IR spectrum of compound was recorded on Perkin ELMER FT-IR spectrometer in the range  $4000\text{--}400\text{ cm}^{-1}$ . Mass of the compound was recorded on Bruker compass microTOF-Q11. Single crystal structural X-ray diffraction was carried out on a Bruker's Apex-II CCD diffractometer using Mo  $\text{K}\alpha$  ( $\lambda = 0.71069$ ) at room temperature.

### 2.2. Synthesis of [3-(1,2,3,4-Tetrahydroquinazoline-2-yl)phenol]

3-Hydroxy benzaldehyde (1.0 mmol) was added to the methanol solution (60 ml) followed by 2-(aminomethyl)aniline (1.0 mmol). After mixing, the clear solution formed was stirred for 24 hours and later kept undisturbed for 7–8 days. Light yellow crystalline compound is formed. Recrystallization in  $\text{NH}_4\text{OH}$  allowed the isolation of light yellow colored crystals, which were suitable for X-ray diffraction. Yield 68%; Mp:  $148\text{--}150^\circ\text{C}$ ; Calculated for  $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_1$ , (226.27 g/mol): Calculated C, 74.31%; H, 6.24%; N, 12.38%; Found C, 74.42%; H, 6.47%; N, 12.69%; MS:  $m/z$  227.117 [ $\text{M}^+$ , 100%], 210.091 [ $\text{M-OH}^+$ ]. IR (KBr,  $\nu/\text{cm}^{-1}$ ): 3355 (OH), 2932 (C–H), 3266 (N–H), 1606 (C=C).  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO-d}_6$ ):  $\delta = 7.12$  (1H, t,  $J = 8.1, 7.9\text{ Hz}$ ,  $-\text{CH}_{\text{aromatic}}$ ),  $\delta = 6.89$  (3H, m,  $-\text{CH}_{\text{aromatic}}$ ),  $\delta = 6.79$  (1H, d,  $J = 7.5\text{ Hz}$ ,  $-\text{CH}_{\text{aromatic}}$ ),  $\delta = 6.67$  (1H, d,  $J = 7.5\text{ Hz}$ ,  $-\text{CH}_{\text{aromatic}}$ ),  $\delta = 6.56$  (1H, d,  $J = 7.9\text{ Hz}$ ,  $-\text{CH}_{\text{aromatic}}$ ),  $\delta = 6.47$  (1H, t,  $J = 7.9, 8.1\text{ Hz}$ ,  $-\text{CH}_{\text{aromatic}}$ ),  $\delta = 3.67, 3.90$  (dd,  $J = 16.52\text{ Hz}$ ,  $\text{CH}_2$ ),  $\delta = 6.1$  (1H, CH)  $\delta = 9.3$  (1H, OH),  $\delta = 4.9$  (1H, NH),  $\delta = 2.6$  (1H, NH).

**Table 1.** Crystal data and structure refinements for compound

Identification code	shelxl
Empirical formula	C <sub>14</sub> H <sub>14</sub> N <sub>2</sub> O
Formula weight	226.27
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system, space group	Trigonal, R-3
Unit cell dimensions	$a = 33.682(3)$ Å $\alpha = 90^\circ$ $b = 33.682(3)$ Å $\beta = 90^\circ$ $c = 5.4395(4)$ Å $\gamma = 120^\circ$
Volume	5344.1(7) Å <sup>3</sup>
Z, calculated density	18, 1.266 Mg · m <sup>-3</sup>
Absorption coefficient	0.081 mm <sup>-1</sup>
$F(000)$	2160
Crystal size	0.12 × 0.10 × 0.09 mm <sup>3</sup>
Theta range for data collection	2.09° to 28.71°
Completeness to theta	28.71, 99.2%
Absorption correction	Mixed
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data/restraints/parameters	3057/3/163
Final R indices [ $I > 2$ sigma(I)]	R1 = 0.0535, wR2 = 0.0983
R indices (all data)	R1 = 0.1569, wR2 = 0.1311
Largest diff. peak and hole	0.140 e·Å <sup>-3</sup> and -0.177 e·Å <sup>-3</sup>
CCDC number	926959

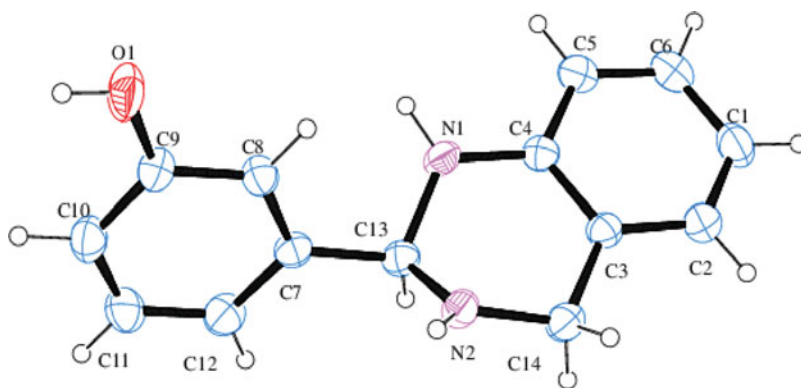
### 2.3. X-Ray Crystallography

X-ray data were collected on a Bruker's Apex-II CCD diffractometer using Mo K $\alpha$  ( $\lambda = 0.71069$ ) at room temperature. Lorentz and polarization effects and empirical absorption corrections were applied using Siemens Area Detector Absorption Correction (SADABS) computer program. The structure was solved by direct methods, using SIR-92 software [16] and refined by full-matrix least squares refinement [17] methods based on F<sup>2</sup>, using SHELX-97. The hydrogen atoms of amines and hydroxyl group were located from the difference Fourier synthesis and were refined isotropically with  $U_{\text{iso}}$  values 1.2 times that of their carrier oxygen and nitrogen atoms, with fixed distances (O–H 0.82 Å and N–H 0.88 Å). All nonhydrogen atoms were refined anisotropically. All other hydrogen atoms were fixed geometrically with their  $U_{\text{iso}}$  values 1.2 times of the phenylene and methylene carbons. The structure shows solvent accessible voids (SAV) of volume 68 Å<sup>3</sup>, which are due to the crystal packing forces, and there is no significant residual electron density. All calculations were performed using Wingx package [18]. The crystal and refinement parameters are given in Table 1.

## 3. Results

### 3.1. Spectroscopic Studies

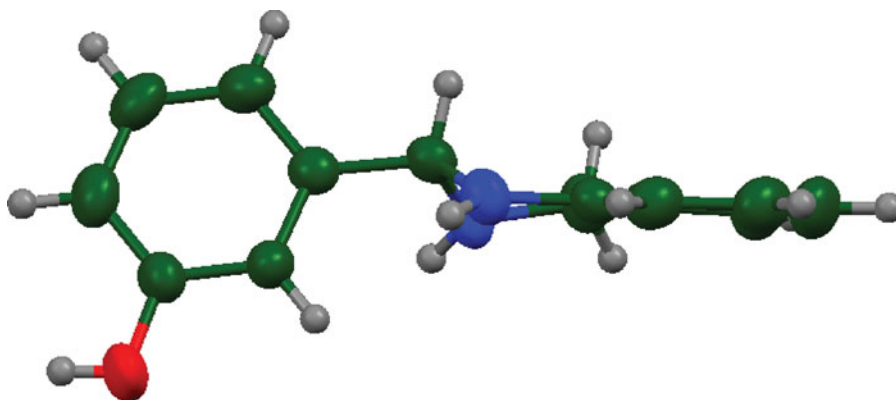
The experimental result for the C, H, N, analysis are in good agreement with those calculated for compound (I) C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O formed in the reaction. The IR spectrum (Fig. S1,



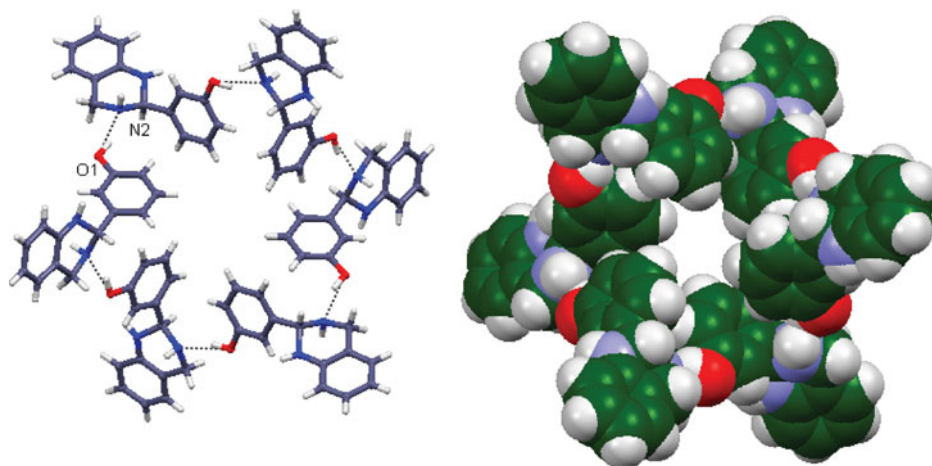
**Figure 1.** Showing Oak Ridge Thermal Ellipsoidal Plot (ORTEP) diagram of compound (I).

Supplemental Material, available online) of this compound shows a broad peak of O—H group present in the region of  $3355\text{ cm}^{-1}$  due to strong hydrogen bonding interactions. The peaks at  $3266, 2932, 1606\text{ cm}^{-1}$  due to presence of N—H, C—H, C=C stretching vibrations, respectively. The mass spectrum (Fig. S2, Supplemental Material, available online) of the compound supports its formation. The base peak at  $227.117$  corresponds to the molecular ion peak. Another peak at  $210.091$  indicates the ionization of meta-substituted —OH group.

$^1\text{H}$  NMR spectrum (Fig. S3, Supplemental Material, available online) of compound was recorded in DMSO. Proton of the —OH group shows a sharp singlet at  $\delta$  9.3 ppm. The proton **1** and **3** of amine group —NH show signals at  $\delta$  4.9 and  $\delta$  2.6 ppm, respectively. Protons **6** and **11** of aromatic ring show triplets at  $\delta$  6.47 ppm and  $\delta$  7.12 ppm, respectively (Fig. S4, Supplemental Material, available online). Protons **8**, **10**, **12** of aromatic ring are showing doublets at  $\delta$  6.67,  $\delta$  6.56,  $\delta$  6.79 ppm. Protons **5**, **7**, **14** are accidentally equivalent and appearing together at  $\delta$  6.89 ppm. Magnetically inequivalent protons of the methylene group at position **4** show two doublets at  $\delta$  3.67 and  $\delta$  3.92 ppm, with  $J$  values of 16.5 Hz and proton of methine group —CH at position **2** shows a singlet at  $\delta$  6.1 ppm. The DMSO solvent also shows absorption at  $\delta$  2.49 ppm and water in the DMSO at  $\delta$  3.3 ppm. The



**Figure 2.** Showing molecular structure of compound where phenyl ring is nearly perpendicular to the quinazoline ring.

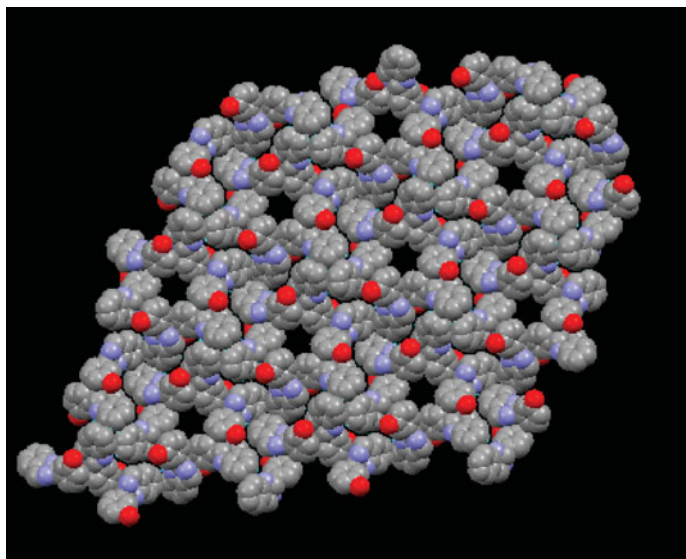


**Figure 3.** H-bonded atoms in compound (**I**) showing a helical channel about the *c* axis.

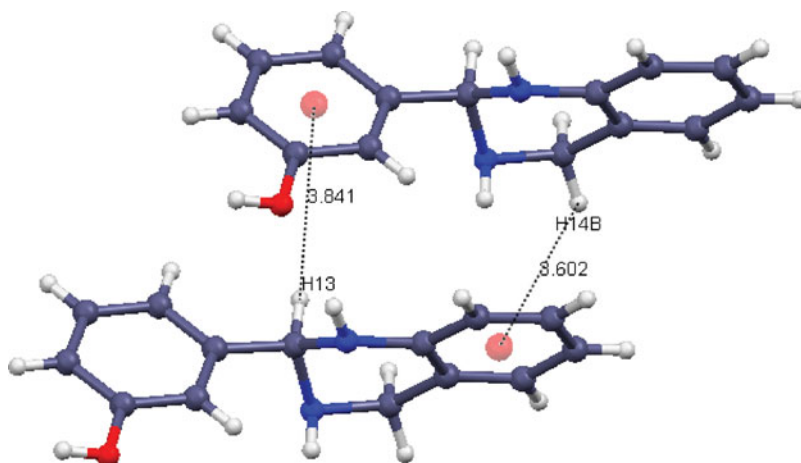
imine proton is absent in the  $^1\text{H}$ -NMR spectrum, which should appear in the range of  $\delta$  8.2–8.5 ppm in the chain form. Therefore, the NMR clearly indicates that the molecule is present in the ring form and not in the chain form in the solution state also. No signal corresponding to the chain form has been seen.

### 3.2. Single Crystal X-Ray Diffraction Studies

The compound crystallizes in the trigonal unit cell having R-3 space group. The ORTEP diagram of the molecule (Fig. 1) shows that compound is a ring-chain tautomerized Schiff



**Figure 4.** Showing channels down the *c* axis formed due to self-assembly of the hexamers.



**Figure 5.** Showing CH– $\pi$  interactions between two different molecules of compound (I).

base and is present in the ring form. All the bond parameters are normal. Tetrahydroquinazoline ring is not planar, because the methine group is significantly out of the plane by 0.53 Å. This ring is perpendicular to the phenol (Fig. 2), which is planar. These two make a dihedral angle of 72° between them. The molecular structure is similar to the earlier reported X-ray crystal structures of four compounds of 2-aryl substituted tetrahydroquinazoline rings [15], which also showed a perpendicular disposition of aryl ring with respect to the tetrahydroquinazoline ring.

Due to presence of OH group at *meta* position, typical intermolecular hydrogen bonding interactions are present. The –OH group is H-bonded to the amine group N2. These interactions give rise to H-bonded hexamers (Fig. 3) positioned about the sixfold axis of rotation, producing a channel of radius about 5.79 Å (Fig. 4) down the *c* axis. This supramolecular arrangement is further supported by the second amine group, along the *c* axis when the amine nitrogen N1 donates H-bond to the phenol oxygen (Table S1, Supplemental Material, available online). There are important CH– $\pi$  interactions also between the methane carbon C13 and the phenol ring and the methylene carbon C14 and the aromatic ring of tetrahydroquinazoline ring, with distances to the centroid being 3.841 Å and 3.602 Å, respectively (Fig. 5). The supramolecular architecture of this crystal structure is very much different from that of its analogous compound with the –OH group at *para* position [15], which crystallizes in an orthorhombic *Pbca* space group. The intermolecular H-bonding interactions between the amine and hydroxyl group produce a linear *zig-zag* chain running along the *b* axis, whereas in 2-(2'-nitrophenyl)-1,2,3,4-tetrahydroquinazoline, N–H···O(NO<sub>2</sub> group) interactions form a linear tape along the *b* axis [15].

#### 4. Conclusions

The condensation product of 3-hydroxybenzaldehyde and 2-benzylamine-aniline has been found to be a tautomerized Schiff base, which is present solely in the ring form, both in the solution and in the solid state. The analogous products with 2-hydroxy and 4-hydroxybenzaldehyde are known to exist as tautomers in solution with 38% and 77% ring form, respectively, whereas the latter appears only in the ring form as solid. Our results in combination with the literature emphasize that the ring form is the only form stable in

the solid state. The presence of another group, capable of H-bonding on the aryl ring at position 2, generates interesting supramolecular arrangements.

## Supplementary Information

NMR, IR, mass along with H-bonding tables. The *cif* and structure factor data are available from Cambridge structure data base, free of cost, ccdc number = 926959.

## Acknowledgments

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