548 **RESEARCH PAPER** SEPTEMBER, 548–551 JOURNAL OF CHEMICAL RESEARCH 2007

# Synthesis and structure determination of 2,3-diphenyl-2*H*-1,4-benzoxazin-2-ol

**Katayoun Marjani, Jafar Asgarian and Mohsen Mousavi***

*Faculty of Chemistry, Teacher Training University, 49 Dr Mofatteh St., Tehran-15614, Iran*

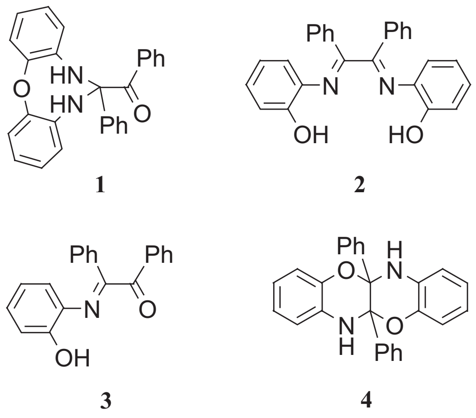
A stable hemiacetal, 2,3-diphenyl-2*H*-1,4-benzoxazin-2-ol, was isolated as the main product from the reaction of benzil and *o*-aminophenol in THF. The structure of the product is confirmed by elemental analysis, common spectroscopic methods, and X-ray crystallographic analysis.

**Keywords:** benzoxazine, hemiacetal, crystal structure, Schiff-base

Condensation of α-diketones and primary amines is an interesting synthetic subject, especially in coordination chemistry[1] since the resulting products, α-diSchiff-bases, are potentially bidentate ligands providing various options to modify electronic and steric effect and coordination properties of nitrogen atoms. Such ligands may be more interesting when having other N, O or S atoms in the suitable position on amine molecule for coordination to the metal ions simultaneously with N atoms of Schiff-base. Therefore, condensation of *o*-aminophenol, 2-aminoethanol and their related compound, possessing S or N atoms instead of O, with α-diketones has often been the subject of synthetic works.[2-6]

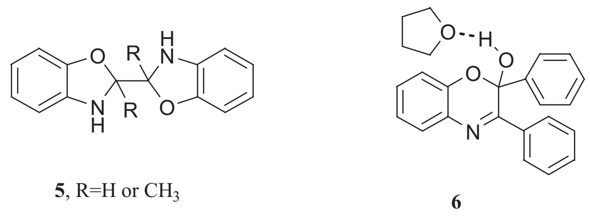
However, there have always been uncertainties in the structure determination of products in these reactions. Some researchers have identified the products of these reactions as open chain Schiff-bases, and have even reported some of their complexes with metal ions,[3-5] but others have considered the product of the same or very similar reactions as five or six membered heterocyclic compounds.[6-9] These later identifications are more reliable since they often were based on more detailed spectroscopic studies and even sometimes on X-ray crystallography.[7,9] Note that some researchers believed in a kind of tautomeric equilibration in solution between these heterocyclic structures and their related open chain Schiff-bases, especially in the presence of metal ions or in alkaline media.[5-8]

In the case of condensation of benzil and *o*-aminophenol itself, previous researchers have been reported different products **1**,[10] **2**,[3] **3**,[4] and **4**[7] (Scheme 1).



**Scheme 1**

The alternative structure **5**, shown in Scheme 2, is also suggested for the product of some closely related reactions.[6]



**Scheme 2**

Here we report a completely different result; a hemiacetal hydrogen bonded to THF in equimolar ratio (structure **6** shown in Scheme 2) which was isolated as main product of the reaction between benzil and *o*-aminophenol in THF and identified by elemental analysis, IR, $^1$H NMR, $^{13}$C NMR, and mass spectroscopy, as well as X-ray crystallographic analysis.

## Experimental

*General method*

Benzil and THF were purchased from Merck and used without further purification; *o*-aminophenol was also purchased from Merck and purified either by sublimation or several recrystallisations from toluene before use. Elemental analysis (CHN) was obtained on Heraeus CHN–O– Rapid Analyser. IR spectrum was recorded with a Perkin-Elmer 843 spectrometer. The mass spectrum was recorded by Finingan-MAT8430 70eV. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker Avance-300 MHz spectrometer employing tetramethylsilane as an internal reference.

*Synthesis of 2,3-diphenyl-2H-1,4-benzoxazin-2-ol,* **6**

*Method (a):* A solution of 2.1 g (10 mmol) benzil and 2.18 g (20 mmol) *o*-aminophenol in THF (20 cm$^3$) was placed in an Erlenmeyer flask (100 cm$^3$) fitted by a simple glass funnel and irradiated in a domestic microwave oven under 100 W power for 30 h (From time to time some solvent was added to save the approximate volume of solvent). Then the solvent was reduced to half, giving a yellowish crystalline product that was collected by filtration, washed with cold THF (3 cm$^3$), and dried *in vacuo* to give **6** (3 g, 73%), m.p. = 142–144°C.

*Method (b):* A solution of 2.1 g (10 mmol) benzil and 2.18 g (20 mmol) *o*-aminophenol in THF (50 cm$^3$) was refluxed for a week. The solvent was evaporated and a dark precipitate was washed several times with petroleum ether. The product was extracted from the residue by chloroform and recrystalised from THF, and gave **6** (2.7 g, 66%).

*Spectroscopy*

Elemental analysis: found C 77.11, H 6.08, N 3.75, $C_{24}H_{23}NO_3$(373.17) requires C 77.19, H 6.21, N 3.75; IR (KBr): 3140 cm$^{-1}$, broad (OH), 1610 (C=N), 1047 (C–O); Mass *m/z* (%): molecular ion was not observed, 196(94) $[Ph–C=N–o–C_6H_4–OH]^+$, 105(14) $[Ph–C=O]^+$, 43(100) $[CH_3C=O]^+$(this fragment probably originated from THF); $^{13}$C NMR(acetone-d$_6$): δ 160.5 ppm (for C double bonded to N), 145.4, 142.4, 137.3, 132.7, 130.3, 129.9, 129.7, 129.3, 128.8, 128.7, 128.4, 127.2, 122.7, 116.9 ppm (14 peaks for carbons of aromatic rings), and 116.9 ppm (for hemiacetalic C); $^1$H NMR(acetone-d$_6$): δ 7.83(d, 2H), 7.62(d, 2H), 7.53(d, 1H), 7.45(s, 1H), 7.3(m, 7H), 7.1(t, 1H), 6.9(d, 1H), and THF peaks at δ 1.75 and 3.6 ppm; $^{13}$C NMR(CDCl$_3$): the same spectrum as in acetone, except six additional small peaks at 27°C which increases to 16 additional peaks at 60°C in the aromatic region from δ 115 to 152 ppm; $^1$H NMR(CDCl$_3$): the same spectrum as in acetone, except for a shift for hydroxyl protons to δ 5 ppm and its broadness, and some additional small peaks beginning at δ 8.23 ppm, ending at δ 6.6 ppm whose area percent increases in higher temperatures (approximately from 20 to 30% from hole under peaks area at 27 and 60°C, respectively.

---

* Correspondent. E-mail address: mooosavi@yahoo.com

*X-ray crystallography*

Crystals of **6** were grown by slow evaporation from THF. Diffraction data were collected on a Bruker SMART 1000 CCD area detector diffractometer with graphite monochromated MoKα. radiation. The structure was solved and refined with the SHELXTL version 5.1 programs. Crystallographic data and selected geometry parameters are presented in Tables 1 and 2, respectively. An ORTEP plot and atom numbering is given in Fig. 1.

The structure of compound **6** is composed of three planar aromatic rings, attached to a six membered oxazine ring, which deviates from planarity due to the presence of a hemiacetal sp$^3$ carbon atom and also an oxygen atom in this ring (Fig. 1). As a result the oxazine ring, at the centre of the molecule, has a half chair conformation (Fig. 2). In this ring, hemiacetal carbon atom retained its tetrahedral geometry. Bond angles around this atom are close to normal sp$^3$ bond angles. The benzoxazine is nearly planar, but the plane of the two phenyl substituents bonded to the imine and hemiacetal carbon atoms are rotated from this plane by angles of about –34° and 77.8°, respectively (Table 2).

The crystal structure of **6** in the solid state is stabilised by strong intermolecular hydrogen bonding between the O–H group of hemiacetal and the oxygen atom of THF molecules (Fig. 3). The packing of the molecules in the solid state is also stabilised by C–H…$\pi$ intermolecular interactions (Fig. 4). Details of hydrogen bonding and C–H…$\pi$ interactions are summarised in Tables 3 and 4, respectively.

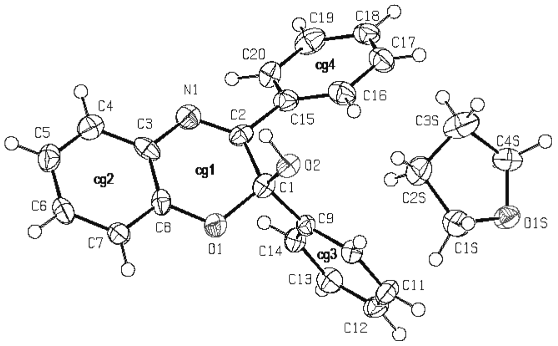


**Fig.1** ORTEP plot of **6** by ellipsoids at 50% probability.

## Result and discussion

Reaction of benzil and *o*-aminophenol in THF was a clean reaction, either in microwave oven under 100 w radiation power or in reflux condition at 70°C or lower, and product was isolated in a simple way. However, raising either radiation power, or refluxing temperature, in each case respectively, was resulted to a mixture of products. Furthermore, applying the same reaction condition for condensation of benzil and

**Table 1** Crystal data and structure refinement

| | |
|---|---|
| Empirical formula | $C_{24}H_{23}NO_3$ |
| Formula weight | 373.43 |
| Temperature | 120(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | Monoclinic |
| Space group | P 21/c |
| Unit cell dimensions | *a* = 10.2545(8) Å α = 90°<br>*b* = 10.7973(8) Å β = 101.408(6)°<br>*c* = 17.7458(14) Å γ = 90° |
| volume | 1926.0(3) Å$^3$ |
| Z | 4 |
| Density (calculated) | 1.288 Mg/m$^3$ |
| Absorption coefficient | 0.085 mm$^{-1}$ |
| F(000) | 792 |
| Crystal size | 0.3 x 0.25 x 0.25 mm |
| Theta range for data collection | 2.03 to 27.00° |
| Index ranges | –13 < = h< = 12, –13< = k< = 13, –22< = 1< = 22 |
| Reflections collected | 18027 |
| Independent reflections | 4177 [R(int) = 0.0469] |
| Completeness to theta = 27.00° | 99.3% |
| Absorption correction | semi-empirical from equivalents |
| Refinement method | Full-matrix least-squares on F$^2$ |
| Data/restraints/parameters | 4177/0/253 |
| Goodness-of-fit on F$^2$ | 1.003 |
| Final R indices [for 2477 rfln with I>2 sigma (I)] | R1 = 0.0590, wR2 = 0.1314 |
| R indices (all data) | R1 = 0.0968, wR2 = 0.1461 |
| Largest diff. peak and hole | 0.896 and -0.295 e. Å$^{-3}$ |

**Table 2** selected bond lengths [Å] and bond angles [°]

| | | | |
|---|---|---|---|
| O(1)–C(8) | 1.355(3) | N(1)–C(2) | 1.273(3) |
| C(1)–C(2) | 1.517(3) | O(1)–C(1) | 1.468(3) |
| N(1)–C(3) | 1.412(3) | C(1)–C(9) | 1.511(3) |
| C(2)–C(15) | 1.518(3) | C(3)–C(8) | 1.406(3) |
| O(2)–C(1) | 1.386(3) | | |
| O(1)–C(1)–C(9) | 102.78(17) | C(8)–O(1)–C(1) | 118.70(17) |
| O(1)–C(1)–C(2) | 109.38(18) | O(2)–C(1)–C(9) | 110.77(18) |
| C(2)–N(1)–C(3) | 116.9(2) | N(1)–C(2)–C(1) | 125.9(2) |
| O(1)–C(1)–C(2)–N(1) | 23.0(3) | N(1)–C(2(–C(15)–C(20) | –34.0(3) |
| O(1)–C(1)–C(9)–C(14) | 77.8(2) | C(1)–O(1)–C(8)–C(7) | –160.67(19) |

**Table 3** Hydrogen bonds for **6** [Å and°]

| D-H...A | d(D-H) | d(D...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|
| O(2)-H(2O)...O(1S) | 0.97 | 1.70 | 2.653(2) | 170 |

Symmetry transformations used to generate equivalent atoms: *x-1,y,z*.

**Table 4** X–H...Cg (Pi-ring) interactions for **6** [Å and °]

| X–H (I)...Cg (J) | d (H...Cg) | <(X-H...Cg) | d(X...Cg) |
|---|---|---|---|
| C (1S)–H (1SB)...Cg (2) $^{(ii)}$ | 3.00 | 141 | 3.797(3) |
| C (12)–H (12A)...Cg (2) $^{(iii)}$ | 2.92 | 139 | 3.678(2) |
| C (18)–H (18A)...Cg (3) $^{(IV)}$ | 2.95 | 148 | 3.774(3) |

Symmetry transformations used to generate equivalent atoms: (ii) 1 + X, Y, Z; (iii) 1–X, 1/2 + Y, 1/2–Z; (IV) X, 3/2–Y,–1/2 + Z
The Cg (J) refers to the ring centre-of-gravity.

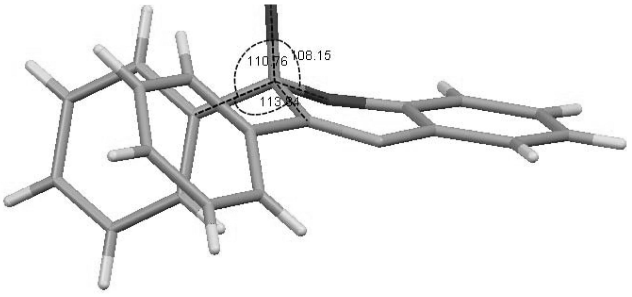


**Fig. 2** Half chair conformation of benzoxazine ring and tetrahedral geometry of sp$^3$ carbon.

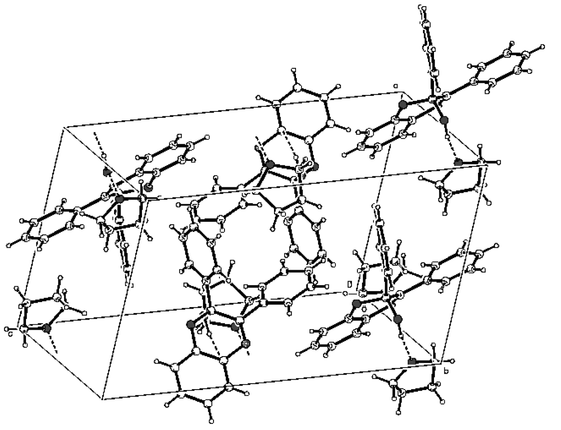


**Fig. 3** A view of molecular packing, hydrogen bonds are shown in dashed lines.

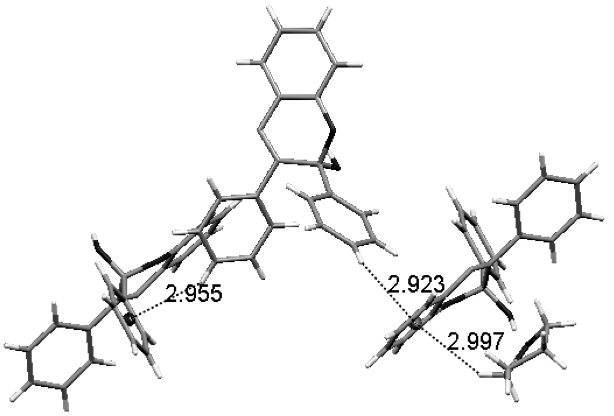


**Fig. 4** C-H... π interactions in the solid state of **6**.

aromatic amines possessing general formula **7** (Scheme 3), led to dark oil mixtures, which was not precipitated after the usual solvent treatments.

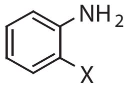
On the other hand, the reaction between benzil and *o*-aminophenol either in benzene, toluene, or chloroform resulted in complex mixtures.

As a simple view, condensation of primary amines with α-diketones has two potential products, mono-imine and di-imine, and depends on the molar ratio of of starting material. Thus, in the condensation of benzil and *o*-aminophenol, either Schiff base **2** or **3** is expected to be the main product of the reaction. But it has been shown earlier[5-9] in similar reactions that the first hypothetically formed imines will be issued to further cyclisation reaction by inter-molecular nucleophilic attack of phenolic oxygen on carbon atom of imine group, so one of the heterocyclic compounds **4** or **6** may be isolated. However, when we have run the reaction in THF either in 1 : 1, 2:1 or even higher molar ratio of *o*-aminophenol to benzil, we only isolated the hemiacetal **6**. This observation was rather unexpected because earlier researchers have not reported this product, and also hemiacetals are usually considered as unstable and unseparateable products; however, more investigation revealed that Murase[6] and Belgodere[8] had earlier obtained some similar hemiacetal products in condensation of *o*-aminophenol and some α-dicarbonyl compounds.

## Conclusion

These observations lead us to assume that the cyclisation of imine to benzoxazine, which could not take place in amines **7** (Scheme 3) except for *o*-aminophenol, is the motivational force of the reaction. Furthermore formation of **4** or **6**, beyond the molar ratio of starting materials, strongly depends on the nature of solvent. THF, capable of hydrogen bonding with hydroxyl group, may stabilise the hemiacetalin structure of monobenzoxazine **6** and prevent it from further reaction to form **4**, because formation of hemiacetal inactivates the carbonyl group against nucleophilic attack by *o*-aminophenol. This is unless an equilibrium, as shown in Scheme 4, opens the benzoxazine ring and liberates the carbonyl group for further reaction.

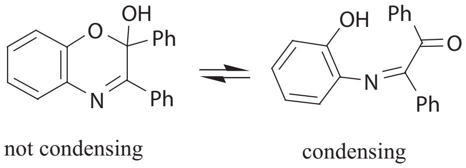
THF, by stabilisation of hemiacetal, prevents the equilibrium proceeding and consequently hemiacetal **6** becomes the final product. Solvents such as benzene, toluene and chloroform are not capable of behaving like this. Therefore in such solvents, unstable hemiacetal falls in equilibration with open chain keto-imine and the carbonyl group becomes free for further nucleophilic attack by *o*-aminophenol; so with a proper molar ratio of the starting material, the final product would be benzoxazinobenzoxazine **4**. The mechanism of stabilisation of hemiacetal by THF apparently occurs mainly through hydrogen bonding between lone pair electrons of solvent and acidic hydrogen of hemiacetal (Fig. 3).



X= *m*-OH, *P*-OH, *o*-OMe, *m*-OMe, *o*-COOH,*o*-OCOCH$_3$

**7**

**Scheme 3**



**Scheme 4**

Evidence for this conception, beyond X-ray crystallography, arises from experiments and spectroscopy. When the reaction runs in THF, the yield of mono-benzoxazine **6** has such predominance that it simply crystallises from the mixture; while in benzene, toluene and chloroform, the product is more complicated and chromatographic methods must be applied to separate the product. Furthermore, when NMR experiments were run in acetone, a solvent capable of hydrogen bonding, the resulting proton and carbon spectra are fully in accord with the mono-benzoxazine structure **6**. On the other hand, in chloroform, the spectra are rather complicated and some additional small peaks appear which follow a regular pattern and their area percentage increases at elevated temperatures as was mentioned in the spectroscopy section. These observations indicate the conversion of hemiacetal **6** to another equilibrating structure in chloroform. Although we do not have enough evidence to assign the second equilibrating structure, but this conversion is an evidence of the instability of **6** in chloroform.

## Supplementary data

CCDC 643815 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data-request/cif.

The authors wish to thank their Teacher Training University for financial support.

*Received 26 June 2007; accepted 20 September 2007*
*Paper 07/4716 doi: 10.3184/030823407X247776*

## References

1 (a) W.A. Welsh, G.J. Reynolds, and P.M. Henry, *Inorg. Chem.*, 1977, **16**, 2558; (b) Franco Sannicolo, *J. Org. Chem.*, 1983, **48**, 2924; (c) C.J. Keleverlaan, F. Hartl and D.J. Stufkens, *J. Organomet. Chem.*, 1998, **561**, 57; (d) S. Mecking, L.K. Johnson, L. Wang, and M. Brookhart, *J. Amer. Chem. Soc.*, 1998, **120**, 888, (e) A. Arquero, M. Canadas, M. Martinez-Ripoll, M.A. Mendiola, and A. Rodriguez, *Tetrahedron*, 1998, **54**, 11271; (f) B. Billdstein, M. Malam, H. Kopacka, M. Fontani and P. Zanello, *Inorg. Chim. Acta*, 2000, **16**, 300; (g) H.A. Zhong, J.A. Labinger and J.E. Bercaw, *J. Amer. Chem. Soc.*, 2002, **124**, 1378; (h) Y. Dong and K. Gai, *J. Braz. Chem. Soc.*, 2006, **17**, 135.
2 B.N. Ghose, *J. Chem. Eng. Data*, 1984, **29**, 237.
3 B.N. Ghose and A.D. Usman, *An. Quim.*, 1988, **84**, 275.
4 A. Schmidpeter and J.H. Winmaier, *Angew. Chem. Int. Ed.***,** 1975, **14**, 489.
5 (a) K. Singh, R.V. Singh and J.P. Tandon, *J. Prakt. Chem.*, 1989, **331**, 525; (b) V.P. Singh, R.V. Singh and J.P. Tandon, *J. Inorg. Biochem*. 1990, **39**, 237.
6 I. Murase, *Bull. Chem. Soc. Jpn.*, (a) 1959, **32**, 827; (b) 1960, **33**, 59.
7 J. Barluenga, F. Aznar, R. Liz, M. Cabal, F.H. Cano, and C. Foces-Foces, *Chem. Ber.*, 1986, **119**, 887.
8 E. Belgodere, R. Bossio, V. Parrini and R. Pepino, *J. Heterocycl. Chem.*, (a) 1977, **14**, 957; (b) 1997, **14**, 994; (c) 1980, **17**, 1625; (d) 1980, **17**, 1629.
9 E. Tauer and K.H. Grellmann, *Chem. Ber.*, 1990, **123**, 1149.
10 F. Kehrmann, *Chem. Ber.*, 1895, **28**, 343.