Synthesis, crystal structure and spectroscopic properties of a novel tricyclic cinnoline derivative

Yuehua Yuan ^a, Maozhong Tian ^{a,*}, Qiangfeng Yin ^b, Feng Feng ^{a,*}

^a College of Chemistry and Environmental Engineering, Shanxi Datong University, Datong
037009, P. R. China.

^b Product Engineering Department, Chemical Engineering Institute,
East China University of Science and Technology, Shanghai 200237, P. R. China.

* Corresponding author. Tel.: +086-352-7624721; Fax: +086-352-7624721

E-mail address: tmzhong2002@163.com; feng-feng64@263.net

Abstract

A facile, efficient synthesis of the novel cinnoline derivative (*E*)-2,2'-(3-((3-bromophenyl)imino)-5-(*tert*-butyl)-3*H*-pyrrolo[3,2,1-*ij*]cinnoline-2,8-diyl)bis(propan-*an*-2-ol) (**1**) is reported. Richter cyclization of an *o*-ethynenearyldiazonium salt gave the cinnoline derivative which underwent a cyclization reaction to form the unexpected tricyclic compound **1**. The absorption and fluorescence properties of cinnoline **1** were investigated in various solvents. A single crystal of **1** was grown and analyzed by X-ray diffraction analysis. The results showed that the inclusion compound was formed between the host (cinnoline **1**) and the guest (acetone) in the crystal.

Keywords: Cinnoline derivative; Synthesis; Absorption spectra; Fluorescence quantum yields; Single crystal; Hydrogen bond

1. Introduction

Cinnoline derivatives are an important class of heterocyclic compounds showing biological activities [1]. In recent years, a large number of cinnoline compounds were

found to exhibit interesting pharmacological properties including anticancer, anti-inflammatory and antibacterial [2]. Several methods for the synthesis of cinnolines have now been reported [3-5]. The cyclization of *ortho*-alkynylbenzenediazonium salts was discovered by Richter [6]. The chemistry of *ortho*-ethynyl-substituted arenediazonium salts has attracted considerable attention in recent years [7-8]. These substances have proven to be valuable precursors of cinnoline derivatives enabling various types of substituents in the aromatic ring accessible.

In this paper an unexpected tricyclic cinnoline **1** was reported, which was synthesized via the cyclization reaction of an *ortho*-ethynyl-substituted cinnoline derivative under rather mild reaction condition.

2. Experimental

2.1. Materials

All reactions were carried out under a nitrogen atmosphere. All the materials were obtained from commercial suppliers and were used without further purification.

2.2. Instruments

¹H-NMR and ¹³C-NMR spectra were recorded at 400 MHz and 100 MHz, respectively. Chemical shifts (δ) were expressed in ppm relative to TMS and coupling constants (*J*) are in Hz. Matrix-assisted laser desorption/ionization reflectron time-of-flight (MALDI-TOF) mass spectrometry was performed with a BrukerBiflex III mass spectrometer. UV-vis absorption spectra were measured on a PerkinElmer Lambda 35 spectrophotometer in a quartz cell. Fluorescence excitation and emission spectra were recorded by using a Hitachi F 2500 Fluorescence Spectrophotometer in a quartz cell. The crystal data collection of compound **1** was performed on

a CrysAlisPro diffractometer.

3. Results and discussion

3.1. Synthesis of cinnoline **1**

The synthetic strategy to the new cinnoline **1** is depicted in Scheme 1. The reaction between compound **2** and 3-bromoaniline offered cinnoline **1** as an orange solid (51.7%) after purification by column chromatography. Compound **1** was synthesized from the *ortho*-ethenyl substituted cinnoline derivative **2** in good yield (78 %) upon refluxing in THF.

3.2. Spectroscopic properties

The new cinnoline derivative **1** was dissolved in different solvents to enable its spectroscopic properties to be studied (Table S1). The absorption spectra of the cinnoline **1** are similar in shape in these solvents, showing a prominent, broad absorption feature around 388 nm (Fig S1). The excitation and emission maxima of cinnoline **1** have no obvious shift in organic solvents with various polarities (Fig S2). Cinnoline **1** has a maximum of excitation (400-417 nm) and emission (452-455 nm) within a narrow wavelength range in the five solvents.

As seen from the data in Table S1, the fluorescence quantum yields (Φ_f) of cinnoline **1** in different solvents are low which may arise as a result of the possible photoinduced electron transfer from the amino to the tricyclic cinnoline and internal heavy atom effect (bromine atom).

The molar absorption coefficients for cinnoline **1** are high and lie within the range of 1.08×10^4 - $2.38 \times 10^4 \text{ L} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$ in the five solvents. The fact that the molar absorption coefficients are higher than $10^4 \text{ L} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$ indicate that the long-wavelength band of the absorption spectra is a band of charge transfer which occurs as a result from a $\pi \rightarrow \pi^*$ electron transfer during the $S_0 \rightarrow S_1$

transition.

3.3. Single crystal X-ray structural analysis of cinnoline **1**

The ORTEP plot of the molecular structure, with the atom labelling, of cinnoline **1** is showed in Fig. 1. Crystal data and structure refinement for cinnoline **1** were shown in Table S2. The relevant bond lengths and angles are listed in Table S3.

An examination of the deviations from the least-squares planes through the individual rings showed that the rings A (C1—C6), B (C1, C6, C9, C10, N1, N2), and C (C5 – C8, N1) are almost planar. The cinnoline ring systems were planar, with dihedral angle of $4.86(0)^\circ$ between the planes of ring A and ring B. The cinnoline ring systems (the ring A and ring B) and the ring C are almost coplanar [r.m.s. deviation = 0.043 nm]. The plane of the phenyl ring (C22-C25) are twisted out of the plane of central tricyclic cinnoline unit on the one side. The dihedral angle between the plane of phenyl ring (C22-C27) and that of ring A is $71.2(1)^\circ$. Obviously, the bond length of C7–C8 (1.356(3) Å) is in good agreement with a carbon–carbon double bond. The bond length of C9–N2 (1.301(3) Å) is in good agreement with a carbon–nitrogen double bond. Moreover, the bond lengths of C5–C7 (1.448(3) Å), C1–C10 (1.471(3) Å), C9–C10 (1.499(3) Å), C6–N1 (1.360(3) Å), and C8–N1 (1.416(2) Å) are, as expected, shorter than a normal carbon–carbon single bond and carbon-nitrogen single bond due to a conjugation effect. Therefore, it could be suggested that the ring A and ring B is highly conjugated with the C ring.

The molecules are linked into a zigzag one-dimensional chain along the a-axis by intermolecular O—H $\cdots$ O (O(1)—H(1) $\cdots$ O(2))ⁱ: O—H = 0.084 nm, H $\cdots$ O = 0.198 nm, O1 $\cdots$ O4 = 0.2822 (2) nm, O(1)—H(1) $\cdots$ O(2) = 175° , symmetry code: (i) x+1, y, z) hydrogen bonds (Fig S3). The oxygen atom plays a significant role in the crystal packing as O(2) is the acceptor and O(1) is

a donor in one hydrogen bond. The crystal-packing diagram shows that the introduction of two crystallizing acetone molecules in the complex successfully leads to the self assembly of the molecules by intermolecular hydrogen bonds.

4. Conclusion

In conclusion, we have presented the synthesis of a novel and unexpected tricyclic cinnoline **1**. The introduction of two crystallizing acetone molecules in the complex successfully leads to the self assembly of these monomeric units by intermolecular hydrogen bonds. The fluorescence quantum yields of cinnoline **1** are low in various solvents due to the photoinduced electron transfer and internal heavy atom effect (bromine atom).

Acknowledgments

We thank the National Science Foundation of China (project 21175085, 21375083 and 21106044) and the Shanxi Scholarship Council of China (No. 200310) for support of this work.

References

- [1] Li S, Zhao YF, Wang KW, Gao YL, Han JM, Cui BB, Gong P. Discovery of novel 4-(2-fluorophenoxy)quinoline derivatives bearing 4-oxo-1,4-dihydrocinnoline-3-carboxamide moiety as c-Met kinase inhibitors. *Bioorg Med Chem* 2013; 21 (11): 2843-55.
- [2] Khalafy J, Rimaz M, Ezzati M, Prager RH. A Green One-Pot Protocol for Regioselective Synthesis of New Substituted 7,8-Dihydrocinnoline-5(6H)-ones. *Bull Korean Chem Soc* 2012; 33 (9): 2890-6.
- [3] Vinogradova OV, Balova IA, Popik VV. Synthesis and reactivity of cinnoline-fused cyclic enediyne. *J Org Chem* 2011; 76 (16): 6937-41.
- [4] Dey R, Ranu BC. A convenient and efficient protocol for the synthesis of 4(1H)-cinnolones,

1,4-dihydrocinnolines, and cinnolines in aqueous medium: application for detection of nitrite ions.

Tetrahedron 2011; 67 (46): 8918-24.

[5] Muralirajan K, Cheng CH. Rhodium(III)-catalyzed synthesis of cinnolinium salts from azobenzenes and alkynes: application to the synthesis of indoles and cinnolines. Chem-Eur J 2013; 19 (20): 6198-202.

[6] Klenov MS, Ratnikov MO, Churakov AM, Solkan VN, Strelenko YA, Tartakovsky VA. Synthesis of [1,2,5]oxadiazolo[3,4-c]cinnoline 5-oxides. Russ Chem Bull 2011; 60 (3): 536-47.

[7] Zhang GW, Miao JM, Zhao Y, Ge HB. Copper-catalyzed aerobic dehydrogenative cyclization of N-methyl-N-phenylhydrazones: synthesis of cinnolines. Angew Chem Int Ed 2012; 51 (33): 8318-21.

[8] Ball CJ, Gilmore J, Willis MC. Copper-catalyzed tandem C-N bond formation: an efficient annulative synthesis of functionalized cinnolines. Angew Chem Int Ed 2012; 51 (23): 5718-22.

Scheme 1 Synthesis of compound **1**.

Fig. 1 Crystal structure of the **1**/acetone complex with atom numbering. Thermal ellipsoids are plotted at 50% probability level. Hydrogen atoms are omitted for clarity.

Scheme 1

Fig. 1.

Synthesis, crystal structure and spectroscopic properties of a novel tricyclic cinnoline derivative

Yuehua Yuan ^a, Maozhong Tian ^{a,*}, Qiangfeng Yin ^b, Feng Feng ^{a,*}

^a College of Chemistry and Environmental Engineering, Shanxi Datong University, Datong

037009, P. R. China.

^b Product Engineering Department, Chemical Engineering Institute,

East China University of Science and Technology, Shanghai 200237, P. R. China.

An unexpected tricyclic cinnoline derivative (*E*)-2,2'-(3-((3-bromophenyl)imino)-5-(*tert*-butyl)-3*H*-pyrrolo[3,2,1-*ij*]cinnoline-2,8-diyl)bis(prop-2-ol) was synthesized.

The inclusion compound was formed between the tricyclic cinnoline and acetone in the crystal.