2-Thioxo-1,2-dihydrobenzo[d][1,3]thiazin-4-one: Synthesis, Crystal Structure and Its Photoinduced Proton Transfer Reaction

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ABSTRACT  2-Thioxo-1,2-dihydrobenzo[d][1,3]thiazin-4-one (TDBTO), a new thiazin-one derivative, was synthesized and investigated. The crystal structure of TDBTO (C₈H₅NOS₂, Mr = 193.8) was determined by single-crystal X-ray diffraction. The crystal belongs to the triclinic system, space group \( P\overline{1} \) with \( a = 6.946(3) \), \( b = 7.402(3) \), \( c = 8.954(4) \) Å, \( \alpha = 66.931(7) \)º, \( \beta = 89.866(7) \)º, \( \gamma = 72.289(7) \)º, \( V = 399.8(3) \) Å³, \( Z = 2 \), \( M_r = 195.25 \), \( D_r = 1.622 \) g/cm³, \( \mu = 0.606 \) mm⁻¹, \( F(000) = 200 \), \( R = 0.0361 \) and \( wR = 0.1032 \). There exist intermolecular hydrogen bond of N(1)–H(1A)···O(1) and weak C(6)–H(6A)···O(1) contact in the structure as well as face-to-face \( \pi-\pi \) stacking interactions between the benzene ring and the thiazin ring of an adjacent benzo-thiazin unit. The photoinduced proton transfer reaction, transforming the initial thione into thiol form, was found, and the latter form was characterized by UV absorption spectra, fluo-rescence spectra and infrared spectra.

Keywords: 2-thioxo-1,2-dihydrobenzo[d][1,3]thiazin-4-one, photoinduced proton-transfer, crystal structure

1 INTRODUCTION

The photochemistry of thiocarbonyl compounds has been intensively studied over the recent decades[1–10]. Photoinduced single proton transfer reactions conversing a thione form of a compound to the corresponding thiol form have been previously observed for a number of heterocycles, such as 2(1H)-pyridinethione[8], 3(2H)-pyridazinethione[9] and 2(1H)-quinolinethione[11]. Photoinduced double proton transfer reactions were observed for three molecules: dithiooximide[4], 2,6-dithiopurine[6] and 2,4-dithiouracil[7]. Recently, triple proton transfer has even been observed in trithiocyanuric acid by Maciej J. Nowak[2]. To the best of our knowledge, no other examples of such intramolecular proton transfer from thione to thiol are reported.

Thiazin and its derivatives have provoked interest and investigation because of their biological activities[12–16]. An essential prerequisite for understanding the interactions of such molecule in various chemical and biological environments is the know-
ledge of its physicochemical properties, and the most basic information concerns the molecular structure of the compound. In the present paper, we report a new derivative compound of TDBTO. The crystal structure and its photoinduced single proton transfer reaction were studied. Intermolecular hydrogen bonds and face-to-face $\pi-\pi$ stacking interactions are found in the molecule. There also exists photochemical single proton transfer reaction, transforming the initial thione form into the thiol tautomer upon UV irradiation.

2 EXPERIMENTAL

2.1 Materials and apparatus

All the reagents were used as received from Shanghai Chemicals Group Company. Solvents of analytical grade were redistilled before use to ensure that there was no fluorescence impurity. ESI-MS data were obtained on a Bruker ESQUIRE-3000plus LC-MS/MS spectrometer and elemental analysis was performed on a CE Instruments EA 1110. Corrected fluorescence spectra were taken on a Hitachi F-4500 fluorescence spectrophotometer with excitation and emission slits of 5.0/5.0 nm, and absorption spectra were scanned on a Shimadzu UV224012PC absorption spectrophotometer. The solid-state infrared spectra were recorded on a Nicolet AVATAR FT-IR360 spectrometer by using pressed KBr pellet. $^1$H NMR and $^{13}$C spectra were acquired in DMSO-$d_6$ on a Varian Unity 400MHz spectrometer using TMS as an internal standard. Melting point was determined with a X-4 micromelting point apparatus without correction. Photoreactions were carried out in solvents, such as ethanol (1.0 $\times$ 10$^{-5}$ mol·dm$^{-3}$), at an ambient temperature under irradiation at 365 nm from an ultraviolet lamp in a ZF1-II ultraviolet analyzer. All experiments were conducted at room temperature of ca. 25 °C.

2.2 Synthesis and characterization

The synthetic route for compound TDBTO is shown in Scheme 1.

2-Aminobenzoic acid (58 mmol, 7.95 g) and carbon disulfide (7.0 mL) were added to 50 mL 1,4-dioxane solution. Then 14 g (19.2 mL) triethylamine was added to the mixed solution with stirring at 0 °C for about 6 h. After that, the mixture was heated to room temperature. The pH of the solution was adjusted to 6~7 by adding drops of hydrochloric acid solution (2 mol/L) using micropipette. And the mixed solution was extracted by ethyl acetate; the organic phase was obtained and dried with anhydrous MgSO$_4$. Excessive carbon disulfide and ethyl acetate were removed by rotatory evaporation resulting in yellow precipitate. The yellow precipitate was recrystallized from chloroform and dissolved in 2.5 g acetic anhydride with stirring and reflux for about 4 h, obtaining yellow precipitate which was then filtered off under low pressure to afford the title compound. This compound was recrystallized from ethanol, giving yellow block crystals in 10% yield (calculated from the first material 2-aminobenzoic acid). m.p.: 270~271 °C. ESI-MS: M$^+$ 193.8. Anal. cacld. (%) for C$_8$H$_5$NOS$_2$ ($M_r$ = 194.98): C, 49.21; H, 2.58; N, 7.17; O, 8.19; S, 32.84. Found (%): C, 48.58; H, 2.71; N, 7.10; S, 32.22. $^1$H NMR (400MHz, DMSO-$d_6$), (ppm): 7.40~7.41~7.43 (t, 1H), 7.57 (d, 1H, $J$ = 8Hz), 7.82 (t, 1H, $J$ = 8Hz), 13.8 (s, 1H). $^{13}$C NMR (100MHz, DMSO-$d_6$), (ppm): 119.29, 120.06, 125.88, 126.18, 137.46, 142.52, 184.23, 188.53.

Scheme 1. Synthesis route of compound TDBTO
2.3 X-ray crystallography

The diffraction data were collected on a Bruker SMART Apex CCD diffractometer equipped with a graphite-monochromatic MoKα (λ = 0.71073 Å) radiation using an ω scan mode at 298(2) K. The crystal dimensions are 0.50mm × 0.45mm × 0.13mm. A total of 1990 reflections were measured in the range of 2.4° ≤ θ ≤ 25.24° and 1387 were independent with Rint = 0.0173, of which 1323 were considered as observed (I > 2σ(I)). Lorentz-polarization and empirical absorption corrections were applied to the data. The structure was solved by direct methods with SHELXS-97 and refined by full-matrix least-squares calculations with SHELXL-97 based on F2[17]. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located at the calculated positions. The final refinement including hydrogen atoms converged to R = 0.0361, wR = 0.1032 (w = 1/σ2(Fo)2 + (0.0644P)2 + 0.1172P], where P = (Fo)2 + 2F2/3, S = 1.058, (∆σ)/max = 0.000, (∆ρ)/max = 0.313 and (∆ρ)/min = −0.388 eÅ³.

3 RESULTS AND DISCUSSION

3.1 X-ray crystallography

TDBTO was studied by X-ray crystallographic analysis first. The molecular structure is shown in Fig. 1. The selected bond lengths and bond angles are listed in Tables 1 and 2, respectively.

### Table 1. Selected Bond Lengths (Å) and Bond Angles (°)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Dist.</th>
<th>Bond</th>
<th>Dist.</th>
</tr>
</thead>
<tbody>
<tr>
<td>S(1)–C(8)</td>
<td>1.742(2)</td>
<td>N(1)–C(8)</td>
<td>1.342(2)</td>
</tr>
<tr>
<td>S(1)–C(1)</td>
<td>1.768(2)</td>
<td>N(1)–C(7)</td>
<td>1.386(2)</td>
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<tr>
<td>S(2)–C(8)</td>
<td>1.641(2)</td>
<td>C(1)–C(2)</td>
<td>1.458(3)</td>
</tr>
<tr>
<td>O(1)–C(1)</td>
<td>1.217(2)</td>
<td></td>
<td></td>
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</table>

<table>
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<tr>
<th>Angle</th>
<th>(°)</th>
<th>Angle</th>
<th>(°)</th>
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<tr>
<td>C(8)–S(1)–C(1)</td>
<td>106.55(9)</td>
<td>C(2)–C(1)–S(1)</td>
<td>119.4(2)</td>
</tr>
<tr>
<td>C(8)–N(1)–C(7)</td>
<td>129.3(2)</td>
<td>N(1)–C(8)–S(2)</td>
<td>123.5(2)</td>
</tr>
<tr>
<td>O(1)–C(1)–C(2)</td>
<td>123.9(2)</td>
<td>N(1)–C(8)–S(1)</td>
<td>119.1(2)</td>
</tr>
<tr>
<td>O(1)–C(1)–S(1)</td>
<td>116.7(2)</td>
<td>S(2)–C(8)–S(1)</td>
<td>117.4(2)</td>
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</tbody>
</table>

### Table 2. Hydrogen-bonding Geometry (Å and °)

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<tr>
<th>Donor–H···acceptor</th>
<th>D–H</th>
<th>H···A</th>
<th>D···A</th>
<th>D–H···A</th>
</tr>
</thead>
<tbody>
<tr>
<td>N(1)–H(1A)···O(1)i</td>
<td>0.86</td>
<td>2.13</td>
<td>2.923(2)</td>
<td>152.9</td>
</tr>
<tr>
<td>C(6)–H(6A)···O(1)i</td>
<td>0.93</td>
<td>2.58</td>
<td>3.284(2)</td>
<td>130.1</td>
</tr>
</tbody>
</table>

Symmetry code: (i) x−1, y, z

Fig. 1. ORTEP drawing (50% probability ellipsoids) for TDBTO

Fig. 2. Hydrogen-bonds and π–π interactions (dotted lines) in TDBT (Symmetry codes: (i): 2–x, 1−y, −z, (ii): 2–x, −y, −z)
TDBTO adopts a planar structure in the solid state. All non-hydrogen atoms are located at the least-squares plane with the mean deviation from the plane of 0.0172 Å. The sum of the C(8)–N(1)–C(7) (129.2°), C(8)–N(1)–H(1A) (115.4°) and C(7)–N(1)–H(1A) (115.4°) bond angles is 360°, indicating N(1) is of sp² hybridization. The molecule features long S(1)–C(8) (1.7422(19) Å) and S(1)–C(1) (1.768(2) Å) bonds and short S(2)–C(8) (1.6407(19) Å) bond, which all fall in the single and double bonds (1.82 and 1.56 Å, respectively). And the bond length of N(1)–C(8) (1.342 Å) is remarkably shorter than that of N(1)–C(7) (1.386 Å), suggesting S(2)–C(8) features a double bond and is conjugated with N(1)–C(8).

In the crystal, the title compound is connected by strong and short N(1)–H(1A)···O(1)i (i: x–1, y, z) intermolecular hydrogen bonds. The quite exotic features of the packing of the molecules are revealed by analyzing the molecular arrangement in the crystal lattice. As can be seen from Fig. 2, it contains short C–H···O interaction. Molecules are linked through C(6)–H···O (C···O, 3.284 Å, 133.1°) contacts involving benzene CH and carbonyl oxygen. There also exist face-to-face π-π stacking interaction between the benzene ring and the thiazin ring of an adjacent benzothiazin unit, with the Cg1···Cg2i, Cg1···Cg2ii spacing and centroid separation to be 3.857(2) and 3.603(2) Å respectively, vertical displacement of cg: 3.453 and 3.437 Å, respectively. Cg1: S(1)–C(1)–C(2)–C(7)–N(1)–C(8), Cg: C(2)–C(3)–C(4)–C(5)–C(6)–C(7)). N–H···O hydrogen bonds along with weak C–H···O hydrogen bonding[19] interaction and π-π stacking interactions directly self-assemble supramolecular architectures to form a 3D structure.

3.2 Photoinduced proton transfer reaction

The UV-Vis and fluorescence spectra of TDBTO (1.0 × 10⁻⁵ M) were recorded in ethanol solution upon irradiation with 365 nm UV light. It can be seen from Fig. 3 that before irradiation, there exist strong π-π* transition around 320 nm and n-π* transition around 370 nm. After enough irradiation, the n-π* transition disappears and the π-π* transition intensity decreases a little, which demonstrates that TDBTO has experienced a structure variation so that only π-π* transition is found. Interestingly, it is observed that after UV irradiation the title compound TDBTO becomes fluorescent. With increasing the irradiation time, the fluorescence intensity increases as it can be seen from the fluorescence spectra of TDBTO in ethanol solvent with different irradiation time (Fig. 4). Similar phenomena are also observed in other solvents like acetonitrile. After irradiation of TDBTO for 60 mins. in ethanol solvent, the fluorescence intensity kept constant. The
disappearance of 370 nm band in the absorption spectrum when increasing the irradiation time demonstrates that TDBTO has experienced a photo reaction in the ground state, leading to such a tautomer which becomes more rigidity and/or weakens the excited intramolecular photoinduced electron transfer so that it can be fluorescent. Lapinski L. reported that 2,4-dithiouracil, a close analogue of the title compound, experiences the double-proton-transfer reaction to cause 2,4-pyrimidinedithiol form. Herein it can be resumed that TDBTO experiences a similar photo reaction, as shown in Scheme 2, that is to say, TDBTO also transforms the initial thione into thiol form by UV light. Fluorescence of such analogues of thiocarbonyls is very weak according to the photophysical photochemistry, attributable to the lowest excited state probably to be \(n-\pi^*\)[18]. There exists fluorescence emission in the thiol form of TDBTO, and the lowest excited state is changed to be \(\pi-\pi^*\).

When standing the TDBTO solution after irradiation with UV light in dark for 24 h, it will recrystallize in a thione form. The result of dark investigation also shows that irradiation on TDBTO only changes its tautomer form. Hence, standing in dark favors the thione tautomeric form while standing at UV light shifts the tautomeric equilibrium into the formation of thiol form.

Strong evidence for this proton transfer reaction is characterized by infrared spectra, as shown in Fig. 5. A significant feature of the spectrum after irradiation of TDBTO is the appearance of absorption at 2361 cm\(^{-1}\), indicating the presence of thiol form of the compound. A frequency around 2361 cm\(^{-1}\) and a weak IR intensity characterize the band due to SH stretching vibration\[^9\]. Therefore, irradiation would induce TDBTO proton transfer from thione to thiol form.

4 CONCLUSION

A new thiazin derivative, 2-thioxo-1,2-dihydrobenzo[d][1,3]thiazin-4-one (TDBTO), was synthesized and determined by single-crystal X-ray diffraction. The proton transfer reaction of the molecule occurs when irradiated by UV light (\(\lambda = 365 \text{ nm}\)), transforming the initial thione into thiol form which was characterized by UV absorption spectra, fluorescence spectra and infrared spectra. The knowledge of its photochemical property will help understand the interactions of such molecule in various chemical and biological environments.

REFERENCES