Crystal Structure and ESIPT Phenomena of Anionic 2H-Phenanthro[9,10-c]pyrazol-11-ols postprint

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Abstract

Using 4 -methoxy-5-hydroxyisoflavone and 4 ,5-dihydroxy-7-methoxyisoflavone as lead compounds, 6-methoxy-2H-phenanthro[9,10-c]pyrazol-11-ol (1a) and 9-methoxy-2H-phenanthro[9,10-c]pyrazol-6,11-diol (1b) were synthesized via two dehydration processes in EtOH solution. They were characterized by IR, ^{1}H NMR, and ^{13}C NMR spectroscopy. Black prismatic crystals of 1a were grown by the slow solvent evaporation technique from a 40:1 (v/v) CHCl /MeOH mixture, and the structure was determined by single-crystal X-ray diffraction. In the crystal structure, 1a was stabilized by intramolecular (O–H ⋯ N) and intermolecular (N–H ⋯ O, O–H ⋯ O, ⋯ , C–H ⋯) interactions. Furthermore, the fluorescence properties of 1a and 1b in basic and neutral media revealed that they exhibit excited-state intramolecular proton transfer (ESIPT) phenomena.

Full Text

Preamble

Crystal Structure and ESIPT Phenomena of Anionic 2H-Phenanthro[9,10-c]pyrazol-11-ols

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ABSTRACT
Using 4 -methoxy-5-hydroxyisoflavone and 4 ,5-dihydroxy-7-methoxyisoflavone as lead compounds, 6-methoxy-2H-phenanthro[9,10-c]pyrazol-11-ol (1a) and 9-methoxy-2H-phenanthro[9,10-c]pyrazol-6,11-diol (1b) were synthesized via two dehydration processes in ethanol solution. The compounds were characterized

by IR, ^{1}H NMR, and ^{13}C NMR spectroscopy. Black prism crystals of 1a were grown by slow solvent evaporation from a 40:1 (v/v) CHCl /MeOH mixture, and the crystal structure was determined by single-crystal X-ray diffraction. In the crystal structure, 1a was stabilized by intramolecular (O–H · · · N) and intermolecular (N–H · · · O, O–H · · · O, · · · , C–H · · ·) interactions. Furthermore, fluorescence studies of 1a and 1b in basic and neutral media revealed that these compounds exhibit excited-state intramolecular proton transfer (ESIPT) phenomena.

Keywords: isoflavone; photocyclization; crystal structure; fluorescence; ESIPT
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1 INTRODUCTION

Excited-state intramolecular proton transfer (ESIPT) represents a unique photophysical process in the excited state that has been reported for various derivatives, including benzophenones, flavones, anthraquinones, quinolines, quinoxalines, benzazoles, azoles, and salicylidene anilines [1-4]. A notable characteristic of this process is that molecules typically exhibit tautomerism, resulting in significant red-shifts in their emission wavelengths [5, 6]. ESIPT has found diverse applications in laser dyes, photostabilizers, radiation scintillators, luminescent materials, molecular probes, ion sensing, and photo-switching of polymorphs [7-9].

Pyrazole and its derivatives constitute an important class of heterocyclic compounds with wide-ranging applications. These compounds exhibit significant biological and pharmaceutical activities, including anti-inflammatory [12], antitumor [13], anticancer [14], analgesic [15], and anti-fertility effects [16]. Additionally, heterocyclic aromatic compounds (HACs) containing pyrazole rings have attracted attention as matrix materials due to their unique properties and potential applications stemming from their special structures [17, 18]. Building on our previous work [19], this study introduces a hydroxyl group to the 11-position of the 2H-phenanthro[9,10-c]pyrazole skeleton (Fig. 6 [Figure 6: see original paper]). 6-Methoxy-2H-phenanthro[9,10-c]pyrazol-11-ol (1a) and 9-methoxy-2H-phenanthro[9,10-c]pyrazol-6,11-diol (1b) were synthesized via photocyclization and dehydration in 1:1 (v/v) EtOH/H O and characterized by IR, ^{1}H NMR, and ^{13}C NMR spectroscopy. Fortunately, single crystals of 1a were obtained by slow solvent evaporation from a 40:1 (v/v) CHCl /MeOH mixture, enabling determination of its crystal structure. The fluorescence properties of 1a and 1b were subsequently investigated in basic and neutral media.

Fig. 1 [Figure 1: see original paper]. One-pot synthesis of 2H-phenanthro[9,10-c]pyrazol-11-ols from isoflavones

2 EXPERIMENTAL

2.1 Materials and Methods

All reagents were commercially available and used without further purification. 4 -Methoxy-5-hydroxyisoflavone and 4 ,5,7-trihydroxyisoflavone were purchased from Hebei Guogin Pharmaceutical Company. 4 ,5-Dihydroxy-7-methoxyisoflavone was synthesized according to a literature method [20]. Melting points were determined on an X-5 melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AM 400 or AM 600 instruments in DMSO-d . High-resolution mass spectrometry (HRMS) was performed using electron-spray ionization (ESI), and IR spectra were recorded on a Nicollet 170SX FT-IR spectrophotometer using KBr pellets. All irradiation experiments were conducted in a BL-GHX-V photochemical reactor equipped with a 500 W medium-pressure mercury lamp. Reaction progress was monitored by thin-layer chromatography (TLC) using silica gel 60 GF plates. Silica gel (200–300 mesh) was used for column chromatography. Crystal diffraction data were collected on a Bruker Smart-1000 CCD diffractometer.

2.2 Synthesis and Characterization of Compounds 1a and 1b

Based on the literature procedure [19], the preparation of 2H-phenanthro[9,10-c]pyrazol-11-ols is outlined in Fig. 1. 3,4-Diaryl-1H-pyrazoles were synthesized according to a literature method [20]. Hydrazine hydrate (80%, 5 mmol) was added to an ethanol solution (10 mL) of the appropriate 4 -methoxy-5-hydroxyisoflavone or 4 ,5-dihydroxy-7-methoxyisoflavone (1 mmol), and the mixture was refluxed at 80 °C until TLC indicated complete consumption of the isoflavone. The mixture was adjusted to pH 6–7 with 3 M HCl, diluted with 40 mL ethanol and 50 mL redistilled water, placed in 100 mL quartz tubes, deaerated by bubbling argon for 30 min, and irradiated with a medium-pressure mercury lamp (500 W) for 10 hours at 20 °C. Reaction progress was monitored by TLC. The solvent was then removed under reduced pressure, and the residue was purified by column chromatography on silica gel using chloroform-methanol (40:1) to afford the corresponding products 1a and 1b, which were characterized by ^{1}H NMR, ^{13}C NMR, IR, and HRMS.

Data for 1a: Yield 70%, isolated as a pink powder, m.p. 250.2–251.9 °C. ^{1}H NMR (600 MHz, DMSO-d) (ppm): 3.95 (s, 3H), 7.15 (d, J = 7.7 Hz, 1H), 7.28 (d, J = 8.5 Hz, 1H), 7.49 (t, J = 7.9 Hz, 1H), 8.09 (s, 1H), 8.23 (t, J = 7.7 Hz, 2H), 8.48 (s, 1H), 10.95 (s, 1H), 13.15 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d) (ppm): 55.3, 106.5, 111.3, 111.9, 114.8, 115.9, 116.7, 120.8, 124.9, 127.5, 128.1, 130.9, 132.0, 133.0, 153.5, 156.9. IR (KBr) (cm ^{1}): 3468 (w, N–H), 3181 (b, O–H), 3114, 2931, 2567, 1589, 1471, 1419 (s, benzene skeleton C=C), 1359 (w, C–H), 1253, 1211, 1164, 1066, 952, 844, 800, 692, 651. HRMS (ESI) calcd. for C H N O [M+H] 265.0977, found 265.0968.

Data for 1b: Yield 57%, isolated as a pink powder, m.p. 336.5–338.3 °C. ^{1}H NMR (600 MHz, DMSO-d) (ppm): 3.93 (s, 3H), 6.75 (s, 1H), 7.14 (d, J = 8.0

Hz, 1H), 7.47 (s, 1H), 7.91 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 8.38 (s, 1H), 9.60 (s, 1H), 11.01 (s, 1H), 12.95 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d) (ppm): 55.2, 97.1, 100.5, 106.5, 108.7, 114.9, 117.3, 120.1, 124.8, 128.1, 131.7, 133.0, 142.9, 154.7, 155.1, 158.7. IR (KBr) (cm ^{1}): 3466 (w, N–H), 3167 (b, O–H), 3109, 2956, 2567, 1591, 1479, 1423 (s, benzene skeleton C=C), 1354 (w, C–H), 1213, 1161, 1068, 956, 800, 656. HRMS (ESI) calcd. for C H N O [M+H] 281.0926, found 281.0926.

2.3 X-ray Structure Determination

A black prism crystal of compound 1a with approximate dimensions of 0.35 mm × 0.29 mm × 0.12 mm, suitable for X-ray diffraction analysis, was obtained from a CHCl /MeOH system (v/v = 40:1) by slow evaporation at room temperature. Data were collected on a Bruker Smart-1000 CCD diffractometer equipped with graphite-monochromated MoK radiation (= 0.71073 Å) using a - scan mode in the range 2.32 < < 25.09° at 296(2) K. A total of 5442 reflections were collected, of which 2002 were independent (R_int = 0.0225). Of these, 1674 reflections with I > 2 (I) were observed and used in subsequent refinements. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were added at calculated positions and refined using a riding model. The structure was solved by direct methods and refined on F^2 by full-matrix least-squares using the SHELX-97 program [22]. Final refinement converged to R = 0.0646 and wR = 0.1487 (w = 1/[^{2}(F_o^2) + (0.0921P)^2 + 0.2900P], where P = (F_o^2 + 2F_c^2)/3), (Δ/)_max = 0.000, S = 0.986, Δ _max = 0.211 and Δ _min = -0.214 e/Å^3. Compound 1a crystallizes in the monoclinic space group P2 /c with a = 8.8388(17), b = 11.109(2), c = 12.732(2) Å, = 97.012(3)°, V = 1240.8(4) Å^3, Z = 4, F(000) = 552, D_c = 1.415 g · cm ^{3} and = 0.095 mm ^{1}.

2.4 Luminescent Properties

Compounds 1a and 1b were dissolved in ethanol to prepare 1 × 10 M solutions. The fluorescence spectra of 1a were measured under various conditions, including basic and neutral media, with excitation slit = 7.5 nm and emission slit = 2.5 nm. For 1b, both excitation and emission slits were set to 2.5 nm. Visual fluorescence was recorded by photographing the solutions under a UV lamp (_ex = 365 nm).

3 RESULTS AND DISCUSSION

3.1 Single-Crystal Structure Analysis

Fig. 2 [Figure 2: see original paper]. Molecular structure with atomic numbering for 1a. Displacement ellipsoids are plotted at the 50% probability level.

The molecular structure of 1a is illustrated in Fig. 2. The molecule consists of four rings, a methoxy group, and a hydroxy group. The rings include three phenyl rings—A(C(9)-C(14)), B(C(2)-C(5), C(15), C(16)), and C(C(5), C(6),

C(8), C(9), C(14), C(15))—and a pyrazole ring D(C(6)-C(8), N(1), N(2)). The atoms of each ring display an almost coplanar configuration, with mean deviations from their least-squares planes of 0.0014 Å (A and C), 0.0039 Å (B and C), and 0.0028 Å (D and C). Selected bond lengths and bond angles are presented in Table 1 .

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

Bond/Angle	Value
O(2)-C(10)	1.359(3)
N(1)-C(7)	1.319(3)
N(2)-C(8)-C(6)	106.8(2)
N(1)-N(2)-C(8)	110.7(2)
O(2)-C(10)-C(9)	116.1(2)
N(1)-N(2)	1.346(3)
O(1)-C(1)	1.412(3)
C(7)-N(1)-N(2)	106.8(2)
N(1)-C(7)-C(6)	111.5(2)
O(1)-C(2)-C(3)	115.4(2)
O(1)-C(2)	1.372(3)
N(2)-C(8)	1.363(3)
C(2)-O(1)-C(1)	118.5(2)
O(1)-C(2)-C(16)	124.2(2)
N(2)-C(8)-C(9)	130.1(2)

Fig. 3 [Figure 3: see original paper]. Part of the crystal structure of 1a, showing C-H $\cdots$ and $\cdots$ stacking interactions. Symmetry codes: (a) -x, -y, -z; (b) -x, y+1/2, -z+1/2; (c) x, -y+1/2, z+1/2.

Stacking interactions represent a significant research area in supramolecular chemistry and crystal engineering [23-25]. As shown in Fig. 3, two types of stacking interactions exist in the crystal structure of 1a. The first is a $\cdots$ stacking interaction formed between two neighboring molecules arranged in an antiparallel fashion, involving rings A and B of one molecular skeleton and rings B and A of another, with a centroid-to-centroid distance of 3.683 Å. The second type occurs via C-H $\cdots$ stacking interactions. Three distinct C-H $\cdots$ stacking interactions are observed in the crystal structure of 1a, with distances of H(11)b (symmetry code: (b) -x, y+1/2, -z+1/2) to CgB (centroid of ring B), H(12)b (symmetry code: (b) -x, y+1/2, -z+1/2) to CgC (centroid of ring C), and H(4)c (symmetry code: (c) x, -y+1/2, z+1/2) to CgA (centroid of ring A) being 0.3093, 0.2686, and 0.2924 nm, respectively, which fall within the normal range for C-H $\cdots$ stacking [26]. These results demonstrate that both $\cdots$ stacking and C-H $\cdots$ interactions are present in the crystal structure of 1a.

Fig. 4 [Figure 4: see original paper]. Sheet structure of compound 1a formed by intramolecular and intermolecular hydrogen bonds. Symmetry codes: (a) -

x+1, y+1/2, -z+1/2; (b) x+1, -y+1/2, z+1/2.

As shown in Fig. 4, both intramolecular and intermolecular hydrogen bonds exist in 1a. The intramolecular hydrogen bond O(2)-H(2)···N(2) (2.729 Å, 116.7°) forms between the hydroxyl hydrogen atom H(2) and the nitrogen atom N(2) of pyrazole ring D. Molecules are further linked into chains via intermolecular hydrogen bonds. The hydroxyl oxygen atom O(2)a accepts a proton from another molecule to form the intermolecular hydrogen bond N(1)-H(1)···O(2)a (symmetry code: (a) -x+1, y+1/2, -z+1/2) with a bond length of 2.754 Å and bond angle of 138.8°, which connects molecules of the asymmetric unit. Additionally, the hydrogen bond O(2)-H(2)···O(1)b (symmetry code: (b) x+1, -y+1/2, z+1/2) is observed between adjacent molecules with a bond length of 3.205 Å and bond angle of 145.7°. Details of hydrogen bond lengths and angles are given in Table 2 . The combination of ··· stacking, C-H··· interactions, and hydrogen bonding assembles the crystal structure of 1a into a three-dimensional supramolecular network.

Table 2. Hydrogen Bond Lengths (Å) and Bond Angles (°)

D-H···A	d(D-H)	d(H···A)	d(D···A)	Angle
O(2)-H(2)···N(2)	-	-	2.729(3)	116.7
N(1)-H(1)···O(2)a	-	-	2.754(3)	138.8
O(2)-H(2)···O(1)b	-	-	3.205(3)	145.7

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

3.2 Impact of Alkalinity on Fluorescence

Fig. 5 [Figure 5: see original paper]. Excitation spectra (dashed line) and emission spectra (solid line) of 1a and 1b measured in ethanol (solid line 1), 1 × 10 M NaOH ethanol solution (solid line 2), 1 × 10^{3} M NaOH ethanol solution (solid line 3), and 1 × 10^{1} M NaOH ethanol solution (solid line 4); c = 1 × 10 M.

The fluorescence spectra of 1a and 1b demonstrate that their emission maxima undergo a bathochromic shift with increasing basicity (Fig. 5). For 1a, a broad fluorescence band appears at 447 nm upon excitation at approximately 247 nm, with the Stokes shift increasing to 18,114 cm^{1} in 1 × 10^{3} M NaOH ethanol solution. Similarly, the emission spectra of 1b are summarized in Table 4 , showing a Stokes shift increase to 17,277 cm^{1} in 1 × 10^{3} M NaOH ethanol solution (Table 3).

Table 3. Spectroscopic Properties of the Target Products

Compound	Solvent	_ex (nm)	_em (nm)	Stokes shift (cm ^{1})
1a	Ethanol	-	-	-
1a	Ethanol (1×10 M NaOH)	-	-	-
1a	Ethanol (1×10 ^{3} M NaOH)	-	-	18,114
1a	Ethanol (1×10 ^{1} M NaOH)	-	-	-
1b	Ethanol	-	-	-
1b	Ethanol (1×10 M NaOH)	-	-	-
1b	Ethanol (1×10 ^{3} M NaOH)	-	-	17,277
1b	Ethanol (1×10 ^{1} M NaOH)	-	-	-

In 1 × 10 M NaOH ethanol solution, the 11-hydroxyl group of 1a is ionized, resulting in a fluorescence spectrum distinct from that in neutral solution, while the 6-hydroxyl group of 1b is ionized, yielding a fluorescence spectrum similar to the neutral solution. When the basicity is increased to 1 × 10 ^{3} M NaOH ethanol solution, the 11-hydroxyl groups of both 1a and 1b are ionized, and their fluorescence spectra exhibit bathochromic shifts with large Stokes shifts.

Fig. 6. Excited-state intramolecular proton transfer of compounds under basic conditions.

The abnormal increase in Stokes shifts and the molecular structures indicate that excited-state intramolecular proton transfer (ESIPT) occurs in the molecular skeleton. In neutral solution, the compound could not form an intramolecular hydrogen bond such as N–H $\cdots$ O because the proton on the pyrazole ring is tautomeric. Upon addition of NaOH, the tautomeric form becomes stabilized, and the compound exists as the N–H $\cdots$ O tautomer, facilitating formation of anion 3 (Fig. 6). Anion 3 then generates the anionic keto form 5* through an ESIPT process, in which the phenolic hydroxyl proton transfers to the nitrogen atom of the adjacent pyrazole ring. The keto form 5* emits yellowish-green light with a large Stokes shift when returning to the ground state, as shown in Fig. 7 [Figure 7: see original paper]. The resulting keto form 5 then enters the next cycle. Under a UV lamp (_ex = 365 nm), 1a in ethanol solution exhibits blue luminescence, while in basic ethanol solution it displays yellow luminescence (Fig. 7).

Fig. 7. Luminescence of 1a in ethanol (left) and in 1 × 10 ^{3} M NaOH ethanol solution (right), excited with a UV lamp (_ex = 365 nm).

4 CONCLUSION

In summary, 2H-phenanthro[9,10-c]pyrazol-11-ols 1a and 1b were successfully synthesized from isoflavones via two dehydration processes in ethanol. The crystal of 1a forms a three-dimensional structure through intramolecular (O–H $\cdots$ N) and intermolecular (N–H $\cdots$ O, O–H $\cdots$ O, $\cdots$, C–H $\cdots$) interactions. Fluorescence studies in neutral and basic media demonstrated that these anionic 2H-phenanthro[9,10-c]pyrazol-11-ols exhibit ESIPT phenomena.

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Note: Figure translations are in progress. See original paper for figures.