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Revisit of a series of ICT fluorophores: skeletal characterization, structural modification, and spectroscopic behavior

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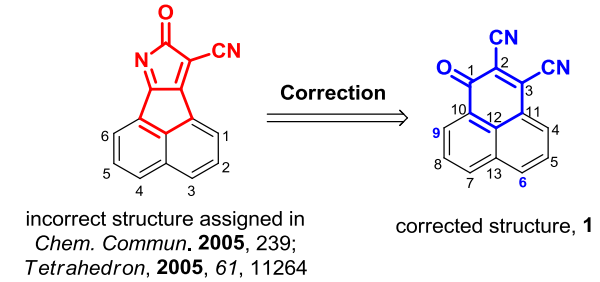
ABSTRACT

We have revisited the synthesis of a series of ICT fluorophores, which were reported to have a core structure of 8-oxo-8*H*-acenaphtho[1,2-*b*]pyrrol-9-carbonitrile. However, based on the 2D NMR and X-ray diffraction analysis, their core structure was corrected as 1-oxo-1*H*-phenalene-2,3-dicarbonitrile (**1**). Compound **1** shows a highly electron-deficient nature and can easily undergo oxidative S_NAr^H reaction on the naphthyl ring to produce a series of novel ICT fluorophores. The regioselectivity of this substitution reaction was studied by introduction of representative nucleophiles. Moreover, due to the strong rigidity and efficient ICT nature, the obtained fluorescent dyes display very good spectroscopic properties even in an aqueous environment.

1. Introduction

A series of novel fluorophores were synthesized in 2005 and were reported to have a core structure of 8-oxo-8*H*-acenaphtho[1,2-*b*]pyrrol-9-carbonitrile (Scheme 1, left).[1] It was reported that this core structure could undergo oxidative S_NAr^H (nucleophilic substitutions of aromatic hydrogen) reactions[2] with different nucleophiles (on C_3 or C_6) to produce a variety of acenaphtho-heterocyclic derivatives.[3] These compounds have good rigidity and strong ICT (intramolecular charge transfer) nature that afford them with good spectroscopic properties.[1,3] Furthermore, they have been widely employed in the development of fluorescent sensors,[4] antitumor agents,[5] DNA intercalators,[6] and protein inhibitors.[7]

However, we recently discovered that the original core structure was mistakenly assigned based on some conflicts between the assigned structure and its NMR data: (a) two carbon signals on ^{13}C NMR spectra (at 113.29 and 113.48 ppm) cannot be correctly assigned; and (b) the coupling between H_9 and carbonyl carbon (C_1) is conflicted with the original structure. The precise backbone was then corrected as 1-oxo-1*H*-phenalene-2,3-dicarbonitrile (**1**, Scheme 1, right) based on detailed structural analysis with two-dimensional (2D) NMR (Fig. S1).[8] As a result, we conclude that the reported structures of all its derivatives are incorrect. In addition, it is necessary to perform a detailed structural analysis of the S_NAr^H products in order to determine the regioselectivity of the substitution reactions. Therefore, several typical nucleophiles were selected in the S_NAr^H reaction of **1** and the structures of the final



Scheme 1. Comparison of the corrected structure **1** with the mistakenly assigned structure in literature.

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products were carefully elucidated. Several of these products have shown very good spectroscopic properties even in water solution.

2. Results and discussion

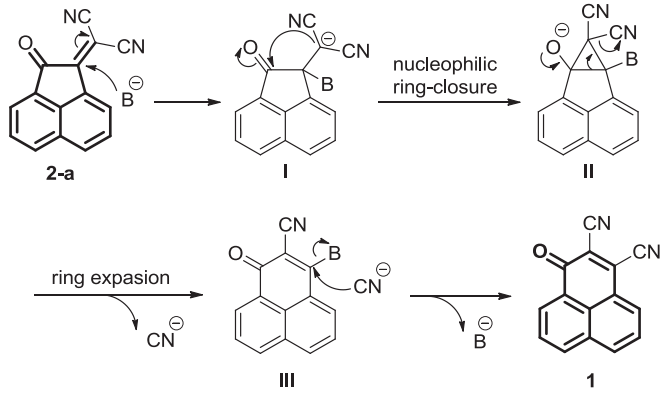
2.1. Preparation of 1

Compound **1** was synthesized very efficiently via a convenient two-step procedure. The starting material acenaphthoquinone undergoes Knoevenagel condensation with malononitrile to yield **2-a**, which was then isomerized under basic condition to produce **1** in good yield. Different bases were screened for the isomerization reaction. We found that although a stronger base could accelerate the isomerization process, it would lead to more impurities (Table 1). Considering these, K_2CO_3 was used as the base in our work because it provided the relative fast and clean reaction. Compound **2-a** is a common precursor for the synthesis of spiro-acenaphthylene compounds.[9,10] However, when treated with base, it undergoes isomerization to produce **1**. A base-catalyzed ring-expansion mechanism is proposed as shown in Scheme 2. Firstly, the base adds to the electron-deficient double bond of **2-a**, following a nucleophilic ring-closure of **I** to give **II** and a ring-expansion reaction to form **III**. Finally the nucleophilic substitution with cyanide ion produces **1**, 1-oxo-1*H*-phenalene-2,3-dicarbonitrile.

Table 1
Isomerization from **2-a** to **1** catalyzed by different bases

Inorganic base	Time	Yield[d] (%)	Organic base	Time (h)	Yield[d] (%)
Cs_2CO_3[a]	15 min	80	DIEA[a]	1.0	81%
K_2CO_3[a]	2.0 h	88	DMAP[a]	1.0	92%
K_3PO_4[a]	2.5 h	90	DABCO[b]	5–6	58%
NaAc[b]	5–6 h	93	Pyridine[c]	48	47%

[a] Compound **2-a** (2.17 mmol), base (10 mol %).
[b] Compound **2-a** (1.09 mmol), base (10 mol %).
[c] Compound **2-a** (2.17 mmol), base (30 mol %).
[d] Isolated yield.



Scheme 2. Proposed base-catalyzed ring-expansion reaction from **2-a** to **1**.

2.2. Oxidative S_NAr^H reaction of 1

Due to the strong electron-withdrawing groups on **1**, its naphthalene ring shows a highly electron-deficient nature and oxidative S_NAr^H reactions can precede smoothly under very mild conditions. Several nucleophiles, such as thiols, hydroxide, and amines, were used for the structural modification of **1** (Scheme 3). The regioselectivity of oxidative S_NAr^H reactions on **1** were also studied by using 2D NMR and X-ray diffraction.

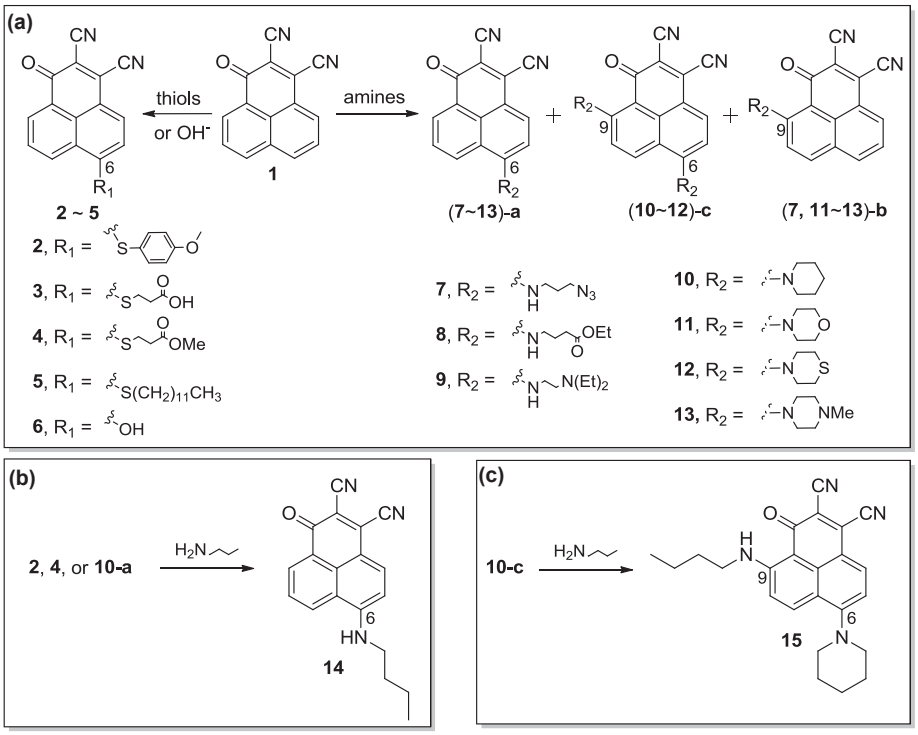
When **1** was reacted with *p*-methoxybenzenethiol, only a single regioisomer **2** was produced in an isolated yield of 60%. Its crystal structure (Fig. 1, left) shows the backbone of 1-oxo-1*H*-phenalene-2,3-dicarbonitrile that is consistent with 2D NMR analysis result of **1**.[8] Additionally, the thiophenol moiety is linked to C_6. This result is consistent with our previous report that the C_6 (numbered as C_3 in the original report[3]) is the most favorable position for a nucleophilic attack.

However, the oxidative S_NAr^H reaction of **1** with mercaptopropionic acid was very slow and less efficient. After refluxing in CH_3CN for 2 days, only a small fraction of **1** was converted to the product as a single regioisomer, **3**, in a yield of ~9% (Scheme 3). We hypothesize the sluggish reactivity is resulted from the acidic nature of mercaptopropionic acid, which are unfavorable for the oxidative S_NAr^H reaction.[12] To confirm this, MeOH was used as the solvent to promote the S_NAr^H reaction. Upon being refluxed for 2 days, most starting materials **1** was consumed, and esterified product **4** was produced with a yield of 48% together with product **3** (~9%). The structure of **3** was characterized by HRMS and 2D NMR, including $^1H-^{13}C$ HMBC, $^1H-^1H$ COSY, and $^1H-^{13}C$ HSQC,[11] which support the backbone skeleton as a 1-oxo-1*H*-phenalene-2,3-dicarbonitrile. Moreover, the coupling signal at (3.68 ppm, 152.1 ppm) in its $^1H-^{13}C$ HMBC spectra (Fig. S2) was assigned as the correlation between H_{14} and C_6, indicating the thiol group is attached to C_6. For compound **4**, in addition to the MS and NMR analyses, we obtained its crystal structure (Fig. 1 right), from which we can clearly observe the thiol group is also on C_6. Both of their (**3** and **4**) regioselectivity results are consistent with that of compound **2**.

Hydroxide was also employed as a nucleophile for the S_NAr^H reaction of **1**. It was very fast and a bright fluorescent compound **6** was produced, which was characterized by 2D NMR analyses (Fig. S5). The regioselectivity result shows the substitution takes place at the C_6 exclusively. In its ^{13}C NMR spectra, C_1 and C_6 show the chemical shifts of 178.31 and 186.12 ppm, respectively, indicating that **6** offers two major resonance structures (Fig. S5, inset).

When amino compounds were employed as nucleophiles, the oxidative S_NAr^H reactions of **1** were much faster and more efficient in comparison with thiol-based nucleophiles. Usually they could finish within a few hours, albeit more isomers were generated. For example, secondary amine can produce three possible products during this substitution reactions, 6-substituted (**10-a**–**13-a**), 9-substituted (**11-b**–**13-b**) or 6,9-disubstituted (**10-c**–**12-c**) of **1** (Scheme 3).[3] However, when ~1.0 equiv of amines were used, the 6-substituted product is obviously the major product. For example, the reaction between **1** and piperidine (1.0:1.1) was finished within 2 h in CH_3CN at room temperature, affording **10-a** with a reasonable yield and trace amount of **10-b**, **10-c** as side-products. When excess amount of piperidine used, more **10-b** and **10-c** were produced.[3]

The 2D NMR analysis was carried out again to confirm the structure of **10-a**. Here, we take **10-a** as an example to show the structural elucidation by 2D NMR. In the $^1H-^{13}C$ HMBC spectra (Fig. S6), the long-range ^1H, ^{13}C coupling correlation of H_9 (8.74 ppm) to C_1 (177.8 ppm) is clearly observed, confirming the 1-oxo-1*H*-phenalene backbone. H_8 and then H_7 can be assigned based on $^1H-^1H$ COSY spectra (Fig. S7), which is also supported by the similar dd splitting pattern of H_7 with H_9 (0.9 Hz). Additional $^1H-^{13}C$ HMBC correlations of both H_8 (7.84 ppm) and H_5 (7.13 ppm) to C_{13} (125.5 ppm), as well as H_8 to C_{10} (129.7 ppm) and H_5 to C_{11} (115.3 ppm), respectively, are consistent with the naphthalene ring skeleton. The last proton resonance (at 8.13 ppm) in ^1H NMR spectra can be assigned as H_4. Based on $^1H-^{13}C$ HSQC spectra (Fig. S8), C_4, C_5, C_7, C_8, and C_9 can be assigned, and C_6 assigned based on its correlations to H_4 and H_7 at (8.13 ppm, 160.9 ppm) and (8.48 ppm, 160.9 ppm) in $^1H-^{13}C$ HMBC spectra. The corrected assignments of H_4, H_7, and H_9 are confirmed by their simultaneously correlations with C_{12} at (8.13, 129.3 ppm), (8.48, 129.3 ppm), and (8.74, 129.3 ppm). The long-range ^1H, ^{13}C coupling correlation of aliphatic proton H_{14} (3.67 ppm) to quaternary carbon



Scheme 3. (a) S_NAr^H reactions of **1** with different nucleophiles. (b) and (c) Substitution reaction with primary amine.

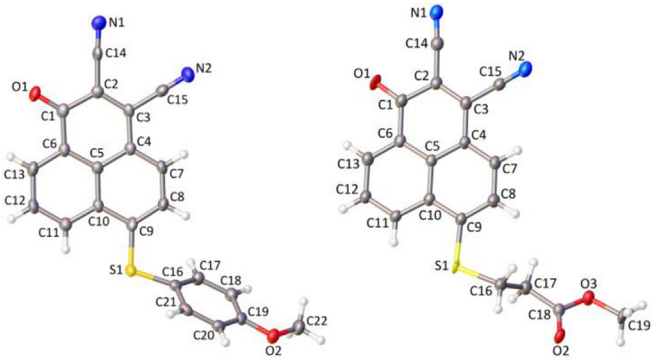


Fig. 1. Crystal structures of **2** (left) and **4** (right). Displacement ellipsoids are shown at the 60% probability level.[11]

C_6 (160.9 ppm) confirms the piperidinyl substitution on C_6. In addition, the $^1H-^1H$ NOESY spectra (Fig. S9) have further confirmed the regiochemistry of this substitution. Two coupling signals at (3.67 ppm, 7.13 ppm) and (3.67 ppm, 8.48 ppm) are observed that ascribe to the correlations of H_{14} with H_5 and H_7, respectively. These two coupling signals indicate that H_{14} is closed to H_5 and H_7, supporting the regiochemistry of the piperidinyl substitution.

When primary amines were used, oxidative S_NAr^H reactions with **1** mainly gave 6-substituted products (**7-a**–**9-a**). Meanwhile 9-substituted product can be also produced in low yield, but no 6,9-disubstituted products. For example, 3-azidopropan-1-amine can produce two isomers by oxidative S_NAr^H reaction with **1**. As shown in Scheme 3, the amino group was modified either on C_6 or C_9 to generate the products **7-a** or **7-b**. The $^1H-^{13}C$ HMBC and $^1H-^1H$ NOESY spectra can help to confirm the modification position of these two products.[11] The $^1H-^{13}C$ HMBC of **7-a** shows a coupling signal at (3.63, 156.7 ppm), which is assigned as the correlation between aliphatic proton H_{14} and quaternary carbon C_6 (Fig. 2a). There are also two coupling signals at (9.52, 108.9 ppm) and (9.52, 122.9 ppm) that ascribe to the correlations of (H_N, C_5) and (H_N, C_{13}). All these results confirm that the amino group was modified on C_6 of compound **7-a**. The $^1H-^1H$ NOESY spectra can also support this results, in which, the correlations between H_{14} and H_5, and H_N with H_7, are confirmed by the coupling signals at (3.63, 6.97 ppm) and (9.52, 8.87 ppm). For compound **7-b**, the coupling from aliphatic H_{14} (3.79 ppm) to quaternary carbon C_9 (158.3 ppm) in $^1H-^{13}C$ HMBC spectra reveals the amino substitution on C_9 (Fig. 2b). Moreover, there is no proton at C_9 as shown in the ^1H NMR and $^1H-^{13}C$ HMBC spectra of **7-b**. In the $^1H-^1H$ NOESY spectra of **7-b** (Fig. S15), H_{14} shows a correlation with H_8 at (3.79 ppm, 7.35 ppm) that also demonstrate the amino substitution on C_9 in **7-b**.

Based on the substitution study of compounds **2**–**13**, we can conclude that C_6 is the most electrophilic carbon thus more favorable for S_NAr^H reaction, and C_9 is probably the second favorable one. In addition, the substituents such as thiol groups (**2**, **4**) and secondary amino group (**10-a**,**c**) on **1** can be easily replaced by primary amine, for example, *n*-butyl amine, to give **14** or 6,9-disubstituted product with different amino groups (**15**), as reported previously.[3]

2.3. Spectroscopic properties study

The S_NAr^H reaction resulted in a series of new ICT fluorophores that show blue, purple or orange colors in acetonitrile with maximum absorption peaks longer than 500 nm, approaching to 600 nm (Table 2). Among these, **4**, **6**, and **7-a** display maximum emission peaks of 584, 563, and 595 nm, with yellow, green, and orange fluorescence, respectively (Fig. 3 and inset pictures). The spectroscopic data of selected dyes are listed in Table 2. Compounds **4**, **6**, and **7-a** all show high fluorescence quantum yields in acetonitrile, demonstrating the strong ICT nature. Compound **6** has an excellent fluorescent quantum yield even in an aqueous environment, which can potentially be used in bioimaging applications.

In comparison, **7-b** is almost non-fluorescent, likely because its electron-donating group is located on the *ortho*-position of its electron-withdrawing groups that offer **7-b** a much less efficient ICT nature than its isomer **7-a**. The fluorescence of **10-a** strongly

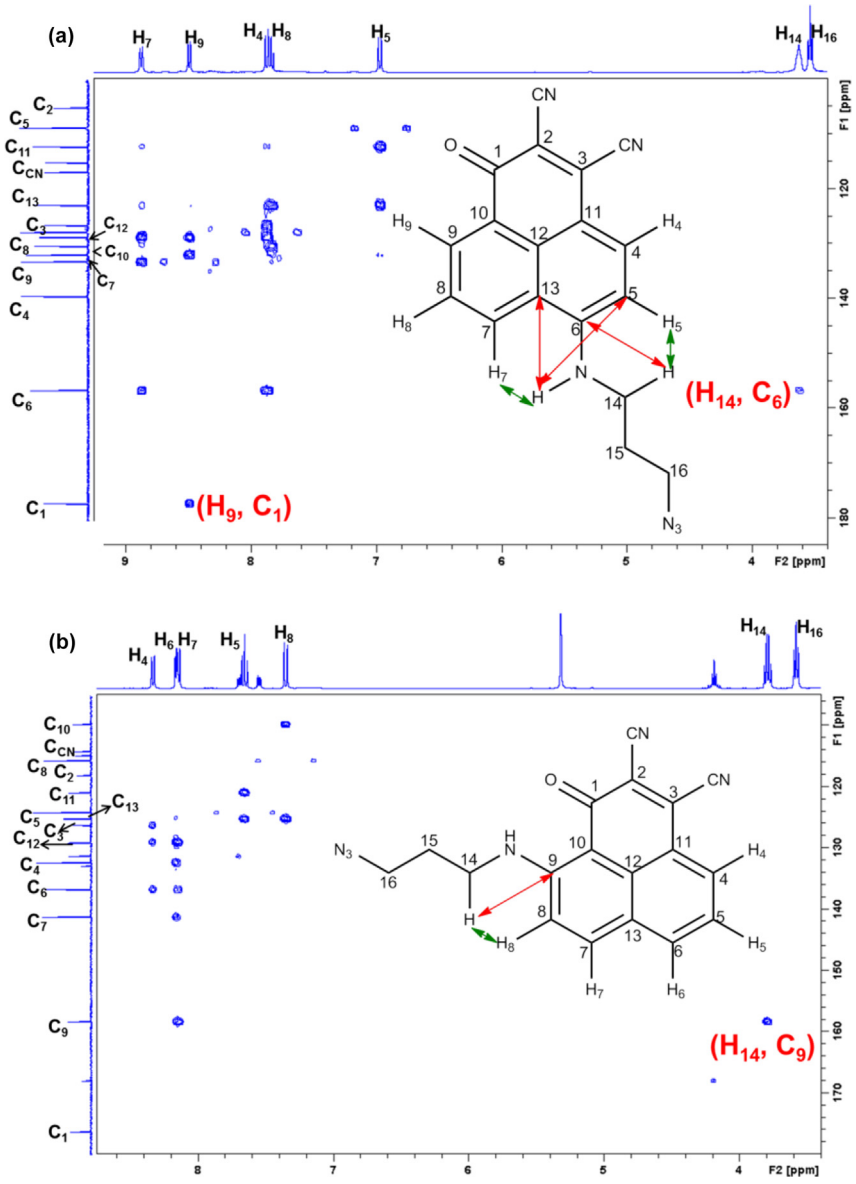


Fig. 2. Partial 400 MHz $^{1}H-^{13}C$ HMBC spectra of **7-a** (a) and **7-b** (b). Red arrows in inset structures highlight the correlations between H_{14} and C_6 or C_9. Green arrows show the correlations between protons observed by $^{1}H-^{1}H$ NOESY spectra.

Table 2
Spectroscopic data of selected dyes in acetonitrile

Dyes	λ_{ab} (nm)	λ_{em} (nm)	$\Delta\lambda$ (nm)	log ε	Φ^{a}
4	511	584	73	4.31	0.35
6	533	563	30	3.67	0.82
7-a	574	595	21	4.74	0.70
7-b	533	565	32	4.17	0.02
10-a[b]	549	607	58	3.53	0.38

[a] Determined by comparison with rhodamine B in ethanol (Φ=0.49).[14]
[b] Determined in toluene.

depends on the nature of solvent. In acetonitrile, it is almost non-fluorescent, presumably due to the efficient radiationless deactivation in the excited states.[13] However, in toluene **10-a** shows a pink color and a quantum yield of 0.38, with emission of orange fluorescence (Fig. S16).

3. Conclusion

Based on 2D NMR and X-ray diffraction study, we have presented detailed characterization on a core structure, 1-oxo-1*H*-phenalene-2,3-dicarbonitrile (**1**), whose skeleton was mistakenly assigned in the previous report.[1,3] With an electron-deficient aromatic ring, **1** can smoothly undergo oxidative S_NAr^H reactions to produce a series of novel ICT fluorophores. The regioselectivity study shows that C_6 is the most electrophilic carbon thus more favorable for S_NAr^H reaction, and C_9 is probably the second favorable one. In addition, the produced ICT fluorophores, for example, **4**, **6**, and **7-a**, display very good spectroscopic properties. Therefore, the core structure of **1** can be adopted as a precursor for the development of novel ICT fluorescent dyes.

4. Experimental

4.1. General information

Chemicals used in the synthesis were purchased from Aldrich and Acros without further purification. NMR spectra were run in acetone-d_6, $CDCl_3$, CD_2Cl_2 or DMSO-d_6 on a Bruker AVANCE-IIIHD spectrometer. All chemical shifts are reported as parts per million (ppm) w.r.t. TMS and referenced by residual solvent resonances. All

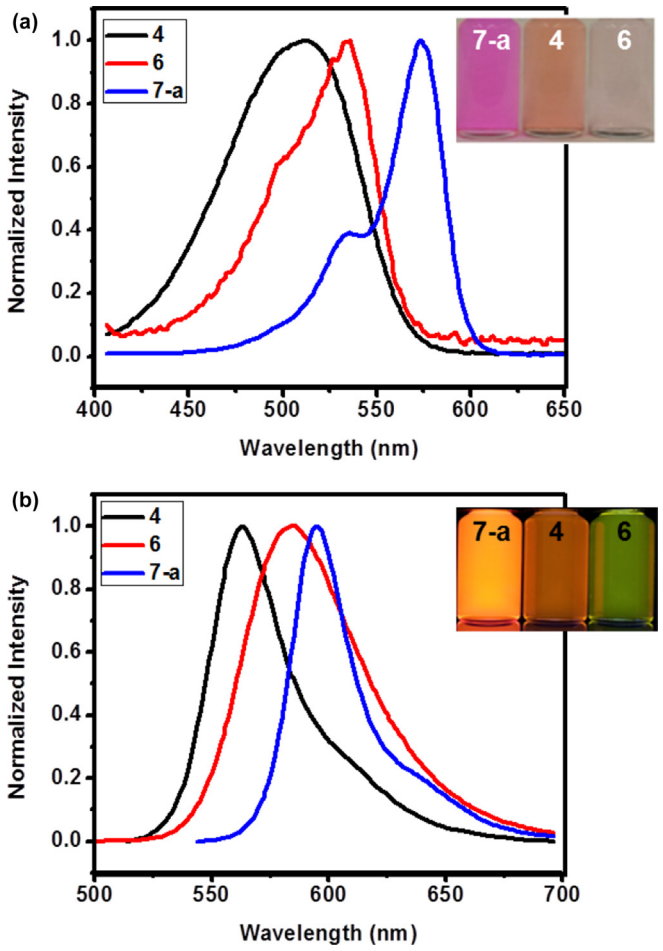


Fig. 3. Normalized absorption (a) and emission (b) spectra of selected dyes (25 μM) in acetonitrile. Inset pictures show dyes **7-a**, **4**, and **6** in acetonitrile under sunlight (inset a) or UV light (inset b).

HMBC experiments were run with a delay that was optimized to long-range $^{1}H-^{13}C$ coupling of 10 Hz. Mass spectra were recorded using Micromass Q-TOF I mass spectrometer. Fluorescence quantum yields were determined in acetonitrile, toluene or water using rhodamine B in ethanol (Φ=0.49) as the standard.[14] The path length was 1 cm with a cell volume of 3.0 mL. X-ray intensity data were collected using a Bruker SMART APEX diffractometer (Mo Kα radiation, l=0.71073 Å).[15] The raw area detector data frames were reduced and corrected for absorption effects with the SAINT+ and SADABS programs.[15] Final unit cell parameters were determined by least-squares refinement of 7220 reflections from the data set. Direct methods structure solution, difference Fourier calculations and full-matrix least-squares refinement against F^2 were performed with SHELXS/L[16] as implemented in OLEX2.[17]

4.2. Synthesis

Synthesis of ***1***: **2-a** was synthesized by the previously reported method.[1] Compound **2-a** (2.17 mmol, 500 mg) was suspended in anhydrous CH_3CN (40 mL). Under stirring, the mixture was heated to refluxed temperature and then added the base. After complete consumption of **2-a** monitored by TLC, the solvent was removed to afford crude product **1**, which was purified by column chromatography on silica gel eluted with DCM/hexane (1:1 to 5:1, v/v) to give **1** as a yellow solid (see Table 1 for yields).

General protocol for the synthesis of ***2–13***: **1** was suspended in anhydrous CH_3CN or MeOH and stirred at room temperature for 5 min. The nucleophiles (1.1 equiv for amines, 5.0 equiv for thiols) were then added in portions and the resultant solution was continued to stir at room (for amines) or refluxed (for thiols) temperature for several hours (for amines) or days (for thiols). After removal of solvents by evaporation under reduced pressure, the crude products were purified by silica gel chromatography with DCM/MeOH as eluent. Compound **6** was synthesized by the previously reported method.[3]

NMR data for typical compounds:

4.2.1. Compound ***1***. HRMS [**1**] calculated 230.0480, observed 230.0484. ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H (ppm) 8.76 (dd, 1H, J=7.2, 0.8 Hz), 8.46 (dd, 1H, J=8.0, 0.8 Hz), 8.42 (d, 1H, J=7.2 Hz), 8.39 (d, 1H, J=8.4 Hz), 7.97 (dd, 1H, J=8.0, 7.6 Hz) 7.86 (t, 1H, J=7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C (ppm) 178.03 (C_1), 138.33 (C_7), 138.03 (C_6), 134.81 (C_4), 133.79 (C_9), 132.65 (C_{13}), 132.22 (C_3), 129.24 (C_8), 128.29 (C_{10}), 127.94 (C_5), 127.31 (C_{12}), 123.01 (C_{11}), 120.50 (C_2), 113.48 (C_{CN}), 113.29 (C_{CN}).

4.2.2. Compound ***2***. Compound **2** was prepared in refluxed CH_3CN for 24 h and purified by silica gel chromatography with DCM as eluent. Yield: 60%. HRMS [**2**] calculated 368.0613, observed 368.0619. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 8.87 (d, 1H, J=8.3 Hz), 8.82 (d, 1H, J=7.4 Hz), 8.02 (d, 1H, J=8.2 Hz), 7.96 (t, 1H, J=7.9 Hz), 7.58 (d, 2H, J=8.6 Hz) 7.11 (d, 2H, J=8.6 Hz), 7.01 (d, 1H, J=8.1 Hz), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C (ppm) 176.5, 160.9, 154.3, 136.6, 132.9, 132.6, 131.5, 130.0, 128.2, 127.7, 127.5, 126.1, 122.2, 118.5, 116.5, 115.3, 112.2, 111.8, 54.6.

4.2.3. Compounds ***3*** *and* ***4***. Compounds **3** and **4** were prepared in refluxed CH_3OH for 2 days and purified with DCM/MeOH (50:2, v/v, for **3**) and DCM (for **4**) as eluent. Yields: 9% for **3** and 48% for **4**. HRMS [**3**] calculated 334.0412, observed 334.0421. ^{1}H NMR (400 MHz, acetone-d_6): δ_H (ppm) 8.84 (d, 1H, J=7.6 Hz), 8.72 (d, 1H, J=7.6 Hz), 8.29 (d, 1H, J=8.2 Hz), 8.09 (t, 1H, J=7.6 Hz), 7.94 (d, 1H, J=8.2 Hz) 3.68 (t, 2H, J=6.9 Hz), 2.96 (t, 1H, J=7.1 Hz); ^{13}C NMR (100 MHz, acetone-d_6): δ_C (ppm) 178.3 (C_1), 172.4 (C_{16}), 152.1 (C_6), 134.7 (C_4), 133.9 (C_{10}) 133.8 (C_9), 133.3 (C_7), 132.2 (C_3), 130.9 (C_{13}), 129.6 (C_8), 127.9 (C_{12}), 123.7 (C_5), 120.5 (C_{11}), 118.1 (C_{CN}), 114.5 (C_{CN}), 114.1 (C_2), 33.1 (C_{14}), 27.5 (C_{15}). HRMS [**4**] calculated 348.0569, observed 348.0571. ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H (ppm) 8.79 (d, 1H, J=8.3 Hz), 8.77 (d, 1H, J=7.5 Hz), 8.23 (d, 1H, J=8.1 Hz), 7.93 (t, 1H, J=7.8 Hz), 7.60 (d, 1H, J=8.1 Hz), 3.73 (s, 3H), 3.54 (t, 2H, J=7.2 Hz), 2.87 (t, 2H, J=7.2 Hz); ^{13}C NMR (100 MHz, CD_2Cl_2): δ_C (ppm) 177.9, 171.6, 151.9, 134.1, 134.0, 133.2, 130.6, 129.1, 128.9, 127.6, 122.7, 120.0, 117.6, 113.8, 113.4, 52.4, 33.1, 27.4.

4.2.4. Compounds ***7-a*** *and* ***7-b***. Compounds **7-a** and **7-b** were prepared in CH_3CN at room temperature for 12 h and purified by silica gel chromatography with DCM/MeOH (50:1, v/v, for **7-a**) and DCM (for **7-b**) as eluent. Yields: 36% for **7-a** and 7% for **7-b**. HRMS $[\mathbf{7\text{-}a}+H]^+$ and $[\mathbf{7\text{-}b}+H]^+$: calculated 329.1151, observed 329.1151. Compound **7-a**: ^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 9.52 (s, 1H), 8.87 (dd, 1H, J=7.6, 0.6 Hz), 8.49 (dd, 1H, J=7.6, 0.6 Hz), 7.87 (d, 1H, J=9.2 Hz), 7.84 (t, 1H, J=7.8 Hz), 6.97 (d, 1H, J=9.2 Hz), 3.63 (m, 2H), 3.53 (t, 2H, J=6.7 Hz), 1.99 (q, 2H, J=6.8 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ_C (ppm) 177.3 (C_1), 156.7 (C_6), 139.6 (C_4), 133.3 (C_9), 132.0 (C_7), 130.4 (C_{10}), 128.8 (C_{12}), 127.9 (C_8), 126.6 (C_3), 123.0 (C_{13}), 116.9 (C_{CN}), 115.2 (C_{CN}), 112.3 (C_{11}), 108.9 (C_5), 105.2 (C_2), 49.2 (C_{16}), 42.0 (C_{14}), 28.2 (C_{15}). Compound **7-b**: ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H (ppm) 12.70 (s, 1H), 8.33 (dd, 1H, J=7.8, 1.0 Hz), 8.16 (dd, 1H, J=7.6, 1.0 Hz), 8.15 (d, 1H, J=9.4 Hz), 7.66 (t, 1H, J=7.7 Hz), 7.35 (d, 1H, J=9.4 Hz), 3.79 (quartet, 2H, J=6.8 Hz), 3.58 (t, 2H, J=6.4 Hz), 2.13 (quintet, 2H, J=6.7, 6.5 Hz); ^{13}C NMR (100 MHz, CD_2Cl_2), δ_C (ppm): 176.3 (C_1), 158.3 (C_9), 141.2 (C_7), 136.7 (C_6), 132.3 (C_4), 129.0 (C_{12}), 126.2 (C_3), 125.2 (C_{13}), 124.1 (C_5), 120.9 (C_{11}), 118.1 (C_2), 115.7

(C_8), 114.8 (C_{CN}), 114.2 (C_{CN}), 109.8 (C_{10}), 49.1 (C_{16}), 41.0 (C_{14}), 28.9 (C_{15}).

*4.2.5. Compound **10-a**.* Compound **10-a** was prepared in CH_3CN at room temperature for 2 h and purified by silica gel chromatography with DCM/MeOH (100:1, v/v) as eluent. Yield: 42%. HRMS [**10-a**] calculated 314.1293, observed 314.1296. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H (ppm) 8.74 (dd, 1H, J=7.6, 0.9 Hz), 8.48 (dd, 1H, J=7.6, 0.9 Hz), 8.13 (d, 1H, J=8.6 Hz), 7.84 (t, 1H, J=8.4 Hz), 7.13 (d, 1H, J=8.4 Hz), 3.67 (t, 4H, J=5.5 Hz), 1.96 (m, 4H), 1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C (ppm) 177.8 (C_1), 160.9 (C_6), 136.4 (C_4), 134.0 (C_7), 133.4 (C_9), 129.7 (C_{10}), 129.3 (C_{12}), 126.8 (C_8), 125.5 (C_{13}), 115.3 (C_{11}), 114.6 (C_5), 114.3 (C_{CN}), 113.5 (C_3), 112.0 (C_{CN}), 108.6 (C_2), 54.9 (C_{14}), 26.1 (C_{15}), 24.1 (C_{16}).

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Supplementary data

^{1}H–^{13}C HMBC, ^{1}H–^{1}H COSY, ^{1}H–^{13}C HSQC, ^{1}H–^{1}H NOESY spectra and single crystal data of compounds. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2014.06.032.

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