published by Ural Federal University
eISSN 2411-1414
chimicatechnoacta.ru

ARTICLE
2025, vol. 12(2), No. 122010
DOI: 10.15826/chimtech.2025.12.2.10

4,5-Diaryl-3-hydroxy-2,2’-bipyridine-6-carbonitriles as prospective luminophores

Evgeny D. Ladin [ab], Yaroslav K. Shtaitz [ab], Vladimir V. Chernyshov [c], Ilia A. Eliseev [c], Maria I. Valieva [ab], Yulia M. Sayfutdinova [a], Svetlana E. Vatolina [a], Ksenia D. Krasnoperova [a], Youcef Ballou [a], Dmitry S. Kopchuk [ab]*, Grigory V. Zyryanov [ab]

a: Ural Federal University, Ekaterinburg 620009, Russia
b: Institute of Organic Synthesis, Ural Branch of the Russian Academy of Sciences, Ekaterinburg 620219, Russia
c: Medicinal Biotechnology Department, Sirius University of Science and Technology, Sirius Federal Territory 354340, Russia
* Corresponding author: d.s.kopchuk@urfu.ru

Abstract

The derivatives of 3-hydroxy-2,2'-bipyridines are of interest due to their photophysical properties. They are also efficient and selective probes for Cu^{2+} and Zn^{2+} cations. We synthesized a series of 4,5-diaryl-3-hydroxy-2,2'-bipyridine-6-carbonitriles and studied their photophysical properties both in acetonitrile solutions and in powders. The compounds have high fluorescence quantum yield values in powder (up to 92.9%) and low values in acetonitrile solutions. Also, in acetonitrile solutions these compounds exhibit the large Stokes shift values, up to 241 nm, which is important for biovisualization applications. The photophysical properties of several compounds in different solvents were studied. It was demonstrated that the addition of Zn^{2+} cations to solutions of these compounds in THF results in a significant hypsochromic shift of the emission maximum simultaneously with a significant increase in the emission intensity. This shows that these compounds are potential probes for Zn^{2+} cations.

Key findings

- Photophysical properties of a series of 6-cyano-4,5-diaryl-3-hydroxy-2,2'-bipyridines were studied.
- In solution these compounds exhibit a large Stokes shift value, up to 241 nm.
- In powders these compounds exhibit intense fluorescence with absolute quantum yield values of up to 92.9%.
- Addition of Zn^{2+} cations to solutions of these compounds in THF results in a significant hypochromic shift of the emission maximum simultaneously with a significant increase in emission intensity.

Accompanying information

Article history
Received: 27.01.25
Revised: 22.02.25
Accepted: 03.03.25
Available online: 10.03.25

Keywords
3-hydroxy-2,2'-bipyridines; 4-aryl-2-aminooxazoles; 5-cyano-1,2,4-triazines; inverse electron demand Diels-Alder reaction; luminescence; Stokes shift

Funding
The authors are grateful to the Ministry of Science and Higher Education of the Russian Federation (Ref. # 124020200072-0) http://www.minobrnauki.gov.ru.

Supplementary information
Transparent peer review: READ
Supplementary materials: READ

Sustainable Development Goals
7 AFFORDABLE AND CLEAN ENERGY

1. Introduction

The derivatives of 3-hydroxy-2,2'-bipyridines, in particular, [2,2'-bipyridin]-3,3'-diols, are of interest due to their photophysical properties [1, 2]. Due to excited-state intramolecular proton transfer (ESIPT), these substances have a large Stokes shift as well as relatively high fluorescence quantum yields both in solution and in solid form [3, 4]. This leads to their possible applications as lasing dyes [5], for the creation of fluorescent materials [6] and OLED devices [4]. In addition, these compounds are selective fluorescent probes for Zn^{2+} and Cu^{2+} cations [3, 7, 8] as well as for some biological analytes [9]. In general, there is a large number of works on the photophysical and sensory properties of [2,2'-bipyridin]-3,3'-diols [2–10].

However, the photophysical properties of 2,2'-bipyridine derivatives containing only one hydroxy group at the C3 position have been much less studied. In particular, the photophysical properties of unsubstituted 3-hydroxy-2,2'-bipyridine were studied in comparison with 3,3'-dihydroxy-

2,2'-bipyridine [1] as well as with analogous 3'-hydroxy-2,2':6',2''-terpyridines [11], which are also selective fluorescent sensors for Zn^{2+} cations. Besides, we have recently studied the photophysical properties of two compounds from the series of 4,5-diaryl-3-hydroxy-2,2'-bipyridine-6-carbonitriles [12].

The key methods for the synthesis of 3-hydroxy-2,2'-bipyridine derivatives are cross-coupling reactions [13, 14], various homocoupling reactions [15–17], ring expansion reactions of 2-acylfurans with ammonia [18], and the reaction of 2,2'-furil with ammonia [19].

In addition, it is worth to mention our previously discovered unexpected method for the synthesis of substituted 3-hydroxy-2,2'-bipyridine-6-carbonitriles *via* a inverse electron demand Diels-Alder reaction between the corresponding readily available 5-cyano-1,2,4-triazines [20] and 2-amino-4-aryloxazoles as dienophiles [21–23]. This approach is convenient for the synthesis of functionalized 2,2'-bipyridines allowing tuning the photophysical properties of the compounds. Therefore, we synthesized a series of 4,5-diaryl-3-hydroxy-2,2'-bipyridine-6-carbonitriles and investigated the photophysical properties of these compounds.

2. Experimental part

All reagents were purchased from commercial sources and used without further purification. Silica gel 60 (Kieselgel 60, 230–400 mesh) was used for the column chromatography. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 spectrometer (400 and 101 MHz, respectively), 298 K, digital resolution ±0.01 ppm, using TMS as internal standard. Elemental analyses were performed on a PE 2400 II CHN-analyzer (Perkin Elmer). Mass spectra were recorded on a MicrOTOF-Q II mass spectrometer (Bruker Daltonics) with electrospray ionization. FT-IR spectra were recorded on a Bruker Alpha-ATR (Zn/Se) spectrometer in KBr tablets. UV-vis absorption spectra were recorded on a Shimadzu UV-1800 Spectrophotometer using quartz cells with 1 cm path length at room temperature. Emission and excitation spectra were measured on a Horiba FluoroMax-4 using quartz cells with 1 cm path length at room temperature.

The compounds **1a,c** [20], **2b,c** [24] **3a,b** [21], **3e** [12] and **3i** [23] were synthesized as described in the literature. The compounds **2d** [24], **3c,d**, **3f-h** [21] were synthesized according to the procedure proposed for similar compounds.

2.1. *4*-(3,4-Dimethoxyphenyl)oxazol-2-amine (2d)

Yield 242 mg (1.10 mmol, 47%). ^1H NMR ($CDCl_3$, δ, ppm): 3.92 (*s*, 3H, OCH_3), 3.96 (*s*, 3H, OCH_3), 4.95 (*br. s*, 2H, NH_2), 6.89–6.91 (*m*, 1H, $C_6H_3(OCH_3)_2$), 7.19–7.22 (*m*, 2H, $C_6H_3(OCH_3)_2$), 7.41 (*s*, 1H, H-5(Oxazole)). ESI-MS, *m/z*: found 221.09, calculated 221.09 $(M+H)^+$.

General method for the synthesis of compounds **3a–i**.

A mixture of the corresponding 1,2,4-triazine-5-carbonitrile **1** (0.40 mmol) and 4-aryloxazol-2-amine **2** (0.44 mmol) was stirred at 150 °C for 8 h under argon atmosphere. The reaction mixture was cooled to room temperature. The products were separated by column chromatography: (CH_2Cl_2 – ethyl acetate, 9:1) as eluent, R_f = 0.7. Analytical samples were obtained by recrystallization from methanol.

2.2. 3-Hydroxy-5-(4-methoxyphenyl)-4-phenyl-[2,2'-bipyridine]-6-carbonitrile (3c)

Yield 72 mg (0.19 mmol, 48%). ^1H NMR ($CDCl_3$, δ, ppm): 3.80 (*s*, 3H, OCH_3), 6.81–6.84 (*m*, 2H, $C_6\underline{H}_4OCH_3$), 7.12–7.16 (*m*, 2H, $C_6\underline{H}_4OCH_3$), 7.16–7.19 (*m*, 2H, Ph), 7.26–7.33 (*m*, 3H, Ph), 7.45–7.49 (*m*, 1H, H-5'(Py)), 8.02–8.06 (*m*, 1H, H-4'(Py)), 8.49–8.51 (*m*, 1H, H-6'(Py)), 8.74–8.77 (*m*, 1H, H-3'(Py)), 15.66 (*br. s*, 1H, OH). ^{13}C NMR ($CDCl_3$, δ, ppm): 55.2, 113.7 (2C), 117.9, 121.6, 123.5, 124.1, 126.6, 127.8, 128.0 (2C), 130.3 (2C), 131.5 (2C), 133.2, 137.1, 138.2, 138.6, 142.9, 145.0, 156.7, 157.0, 159.7. IR (KBr): $\bar{\nu}$ = 2923, 2834, 2223 cm^{-1}. ESI-MS, m/z: found 380.14, calculated 380.14 $(M+H)^+$. Found, %: C 75.79, H 4.62, N 10.99. $C_{24}H_{17}N_3O_2$. Calculated, %: C 75.98, H 4.52, N 11.08.

2.3. 3-Hydroxy-4,5-bis(4-methoxyphenyl)-[2,2'-bipyridine]-6-carbonitrile (3d)

Yield 70 mg (0.17 mmol, 43%). ^1H NMR ($CDCl_3$, δ, ppm): 3.81 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 6.82–6.86 (*m*, 4H, $C_6\underline{H}_4OCH_3$), 7.08–7.11 (*m*, 2H, $C_6\underline{H}_4OCH_3$), 7.12–7.16 (*m*, 2H, $C_6\underline{H}_4OCH_3$), 7.45–7.49 (*m*, 1H, H-5'(Py)), 8.01–8.06 (*m*, 1H, H-4'(Py)), 8.49–8.52 (*m*, 1H, H-6'(Py)), 8.73–8.76 (*m*, 1H, H-3'(Py)), 15.65 (*br. s*, 1H, OH). ^{13}C NMR ($CDCl_3$, δ, ppm): 54.1, 54.2, 112.5 (2C), 112.8 (2C), 116.9, 120.6, 122.5, 123.0, 124.1, 125.9, 130.5 (2C), 130.6 (2C), 136.0, 136.9, 137.5, 141.9,0143.9, 155.7, 156.1, 158.1, 158.6. IR (KBr): $\bar{\nu}$ = 2954, 2923, 2853, 2230 cm^{-1}. ESI-MS, *m/z*: found 410.15, calculated 410.15 $(M+H)^+$. Found, %: C 73.23, H 4.53, N 10.17. $C_{25}H_{19}N_3O_3$. Calculated, %: C 73.34, H 4.68, N 10.26.

2.4. (3,4-Dimethoxyphenyl)-3-hydroxy-5-phenyl-[2,2'-bipyridine]-6-carbonitrile (3f)

Yield 57 mg (0.14 mmol, 35%). ^1H NMR ($CDCl_3$, δ, ppm): 3.60 (*s*, 3H, OCH_3), 3.86 (*s*, 3H, OCH_3), 6.52–6.55 (*m*, 1H, H-2($C_6\underline{H}_3(OCH_3)_2$)), 6.78–6.82 (*m*, 1H, H-5($C_6\underline{H}_3(OCH_3)_2$)), 6.83–6.87 (*m*, 1H, H-6($C_6\underline{H}_3(OCH_3)_2$)), 7.18–7.23 (*m*, 2H, Ph), 7.28–7.33 (*m*, 3H, Ph), 7.44–7.49 (*m*, 1H, H-5'(Py)), 8.00–8.05 (*m*, 1H, H-4'(Py)), 8.49–8.53 (*m*, 1H, H-6'(Py)), 8.72–8.76 (*m*, 1H, H-3'(Py)), 15.71 (br. s, 1H, OH). ^{13}C NMR ($CDCl_3$, δ, ppm): 54.7, 54.8, 109.6, 112.9, 116.6, 120.7, 122.3 (2C), 123.1, 124.0, 127.3 (2C), 127.5, 129.0 (2C), 133.9, 136.3, 136.8, 137.6, 142.0, 144.0, 147.4, 147.6, 155.6, 156.1. IR (KBr): $\bar{\nu}$ = 2961, 2831, 2230 cm^{-1}. ESI-MS, m/z: found 410.15, calculated 410.15 $(M+H)^+$. Found, %: C 73.17, H 4.61, N 10.34. $C_{25}H_{19}N_3O_3$. Calculated, %: C 73.34, H 4.68, N 10.26.

DOI: 10.15826/chimtech.2025.12.2.10

2.5. 3-Hydroxy-4,5-diphenyl-[2,2'-bipyridine]-6-carbonitrile (3g)

Yield 69 mg (0.20 mmol, 50%). ^{1}H NMR (CDCl$_3$, δ, ppm): 7.12–7.15 (*m*, 2H, Ph), 7.17–7.21 (*m*, 2H, Ph), 7.23–7.30 (*m*, 6H, Ph), 7.44–7.48 (*m*, 1H, H-5'(Py)), 8.00–8.05 (*m*, 1H, H-4'(Py)), 8.48–8.50 (*m*, 1H, H-6'(Py)), 8.73–8.76 (*m*, 1H, H-3'(Py)), 15.69 (*br. s*, 1H, OH). ^{13}C NMR (CDCl$_3$ + DMSO-*d*$_6$, δ, ppm): 116.6, 120.6, 122.1, 123.4, 126.8, 126.9 (2C), 127.2 (2C), 127.5, 129.0 (2C), 129.2 (2C), 132.0, 133.6, 136.4, 137.2, 137.8, 142.1, 144.0, 155.4, 156.0. ESI-MS, m/z: found 350.13, calculated 350.13 (M+H)$^+$. Found, %: C 79.03, H 4.46, N 12.09. $C_{23}H_{15}N_3O$. Calculated, %: C 79.07, H 4.33, N 12.03.

2.6. 4-(3,4-Dimethoxyphenyl)-3-hydroxy-5-(4-methoxyphenyl)-[2,2'-bipyridine]-6-carbonitrile (3h)

Yield 54 mg (0.12 mmol, 31%). ^{1}H NMR (CDCl$_3$, δ, ppm): 3.65 (*s*, 3H, OCH$_3$), 3.79 (*s*, 3H, OCH$_3$), 3.87 (*s*, 3H, OCH$_3$), 6.56–6.58 (*m*, 1H, H-2($C_6\underline{H}_3(OCH_3)_2$)), 6.80–6.85 (*m*, 4H, $C_6\underline{H}_3(OCH_3)_2$ + $C_6\underline{H}_4OCH_3$), 7.11–7.15 (*m*, 2H, $C_6\underline{H}_4OCH_3$), 7.43-7.47 (*m*, 1H, H-5'(Py)), 7.99-8.04 (*m*, 1H, H-4'(Py)), 8.49-8.52 (*m*, 1H, H-6'(Py)), 8.71–8.75 (*m*, 1H, H-3'(Py)), 15.66 (*br. s*, 1H, OH). ^{13}C NMR (CDCl$_3$, δ, ppm): 54.2, 54.8, 54.7, 109.7, 112.9 (3C), 116.9, 120.7, 122.3, 122.6, 123.1, 126.0, 128.7, 130.4 (2C), 136.1, 136.8, 137.6, 141.9, 144.0, 147.4, 147.6, 155.7, 156.0, 158.7. IR (KBr): $\bar{\nu}$ = 2931, 2231 cm^{-1}. ESI-MS, m/z: found 440.16, calculated 440.16 (M+H)+. Found, %: C 71.30, H 4.85, N 9.42. $C_{26}H_{21}N_3O_4$. Calculated, %: C 71.06, H 4.80, N 9.56.

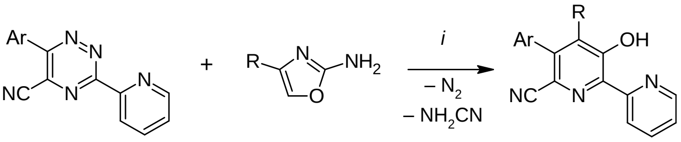
3. Results and discussions

3.1. Synthesis

To synthesize the 4,5-diaryl-3-hydroxy-2,2'-bipyridine-6-carbonitriles, we used our previously described procedure *via* the inverse electron demand Diels-Alder reaction of 6-aryl-5-cyano-3-(pyridin-2-yl)-1,2,4-triazines **1a-c** with 4-(het)aryl-2-aminooxazoles **2a–e** under solvent-free conditions [21]. The products **3a–i** were obtained in yields of 31-55% (Scheme 1). The presence of electron-donating substituents such as (di)methoxyphenyl in the structure of 2-aminoxazoles **2** did not lead to significant changes in the reaction. The structure of the products was confirmed by the data of ^{1}H and ^{13}C NMR spectroscopy, mass spectrome-try and elemental analysis. In particular, the presence of a broadened singlet of the OH group proton at 15.7 ppm can be noted in the ^{1}H NMR spectra.

3.2. Photophysical studies

The photophysical properties of the fluorophores **3a–i** were measured both in a dilute solution of acetonitrile (*C* = 10^{-5} M) and in solid form (powder). Acetonitrile was chosen as an aprotic solvent with an average value of orientational polarizability (Δ*f* = 0.3). The results of the photophysical studies are presented below (Table 1). The non-normalized absorption and emission spectra of the compounds **3a–i** in acetonitrile and in solid state are shown in Figures 1–3 for comparison.



1a-c **2a-e** **3a-i**

Starting compounds		Ar	R	Product	Yield, %
1a	**2a**	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	**3a**	52 [21]
1b	**2a**	Ph	4-ClC$_6$H$_4$	**3b**	55 [21]
1c	**2b**	4-MeOC$_6$H$_4$	Ph	**3c**	48
1c	**2c**	4-MeOC$_6$H$_4$	4-MeOC$_6$H$_4$	**3d**	43
1b	**2c**	Ph	4-MeOC$_6$H$_4$	**3e**	48 [12]
1b	**2d**	Ph	3,4-(MeO)$_2$C$_6$H$_3$	**3f**	35
1b	**2b**	Ph	Ph	**3g**	50
1a	**2d**	4-MeOC$_6$H$_4$	3,4-(MeO)$_2$C$_6$H$_3$	**3h**	31
1b	**2e**	Ph	3-thienyl	**3i**	51 [23]

Scheme 1 Synthesis of 3-hydroxy-2,2'-bipyridines. Reagents and conditions: *i*) neat, 150 °C, 8h, inert atmosphere.

Table 1 The photophysical properties of compounds **3a-i** in CH$_3$CN solution (*C* = 1·10^{-5} M) and in solid form (powder).

	λ_{abs}^{max}, nm [a]	λ_{em}^{max}, nm [b]	ε_M, 10^4 M^{-1}·cm^{-1} [d]	Stokes shift, cm^{-1} (nm)	Φ_f, % [c]	$\lambda_{em\ solid}^{max}$, nm [e]	$\Phi_{f\ solid}$, % [f]
3a	257, 335	561	1.08	12025 (226)	1.7	508	92.2
3b	254, 336	560	0.94	11905 (224)	2.0	510	47.2
3c	261, 337	564	1.76	11943 (227)	<0.1	508	26.9
3d	266, 335	576	1.36	12490 (241)	<0.1	494	43.9
3e	261, 335	574	1.28	12429 (239)	<0.1	500	49.9
3f	281, 334	572	1.86	12458 (238)	<0.1	508	56.9
3g	253, 335	562	1.67	12057 (227)	4.7	486	23.1
3h	290, 335	575	1.99	12459 (240)	<0.1	499	6.1
3i	258, 338	567	1.88	11949 (229)	<0.1	511	92.9

[a] Absorption spectra were measured at r.t. in MeCN in range from 230 to 450 nm;
[b] Emission spectra were measured at r.t. in MeCN (excited at the wavelength of the long-wavelength absorption maximum);
[c] Absolute quantum yields were measured using the Integrating Sphere of the Horiba-Fluoromax-4 at r.t. in MeCN [26];
[d] Extinction coefficient at the long wavelength absorption maximum;
[e] Emission spectra were measured at r.t. in powder (excited at 350 nm);
[f] Absolute quantum yields were measured using the Integrating Sphere of the Horiba-Fluoromax-4 at r.t. in powder [26].

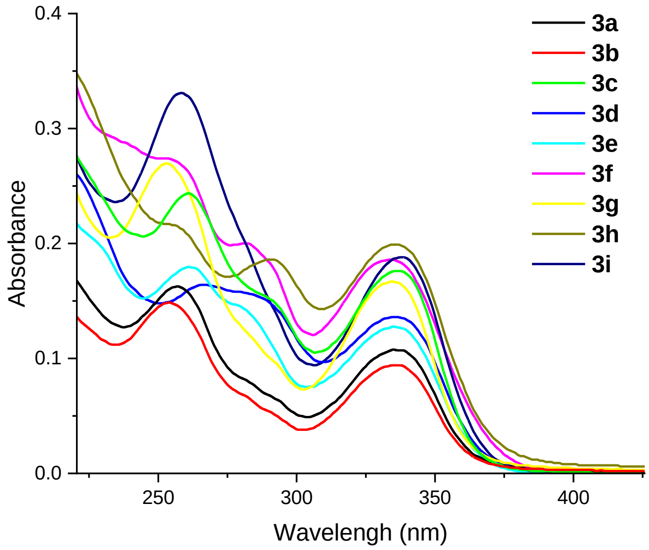


Figure 1 Absorption spectra of **3a-3i** in CH$_3$CN (C = 1·10^{-5} M) at room temperature.

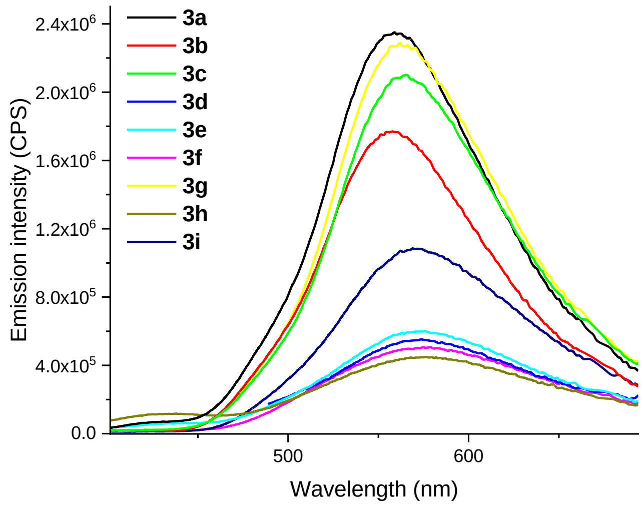


Figure 2 Emission spectra of **3a-3i** in CH$_3$CN (C = 1·10^{-5} M) at room temperature (excited at the wavelength of the long-wavelength absorption maximum).

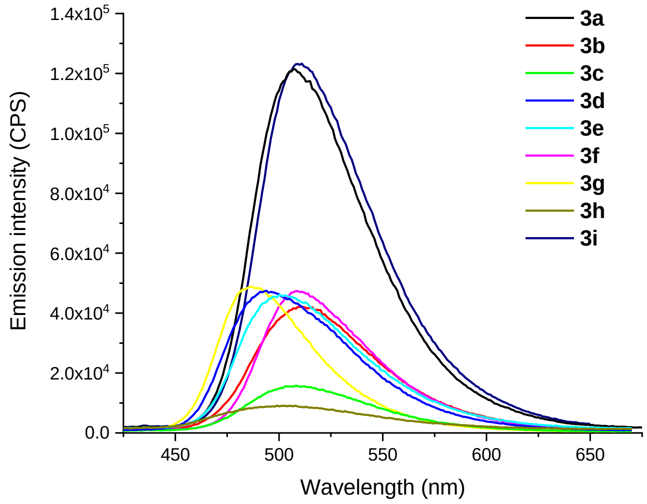


Figure 3 Emission spectra of compounds **3a–i** in powders (excited at 350 nm).

All absorption spectra are similar and contain two major broad absorption bands in the near UV region with λ_{max} ~ 260-290 nm and λ_{max} ~ 335 nm.

The emission spectra of all compounds are unstructured and contain one emission band with maxima in the range from 560 to 575 nm. At the same time, all compounds have an unusually large Stokes shift value, which lies in the range from 224 to 240 nm.

The high value of Stokes shift indicates a large structural difference between the excited and ground states. This structural difference is consistent with the ESIPT process. This process is characteristic of compounds containing an intramolecular hydrogen bond between a hydrogen bond donor (e.g., OH) and a hydrogen bond acceptor (e.g., =N–), which include 3-hydroxy-2,2'-bipyridine derivatives [1–5]. Upon photoexcitation, the electronic charge of the molecules can be redistributed, leading to an increase in the acidity of the hydrogen bond donor group and an increase in the basicity of the hydrogen bond acceptor. As a result, extremely rapid proton transfer from donor to acceptor occurs. In the case of 3-hydroxy-2,2'-bipyridines, the enolic form in the excited state is converted to the keto form in the excited state. Further radiative decay of the excited state leads to the ground electronic state of the keto form, and the reverse proton transfer brings the molecule back to the ground state in the enolic form [4, 10, 27].

It should be noted that the presence of a strong intramolecular hydrogen bond OH···N$_{Py}$ was detected in the crystalline structure of **3** according to the X-ray diffraction data [21, 25]. This is also consistent with a significant downfield shift of the signal from the OH group proton in the ^{1}H NMR spectra (δ ≈ 15.7 ppm).

High values of Stokes shift are attractive for the practical applications of fluorophores. A high Stokes shift value helps to minimise self-quenching and internal filter effects, which is particularly useful in biovisualisation as it helps to reduce the signal-to-noise ratio [28].

All fluorophores **3a–i** have low values of fluorescence quantum yield in acetonitrile solution (up to 4.7 % for compound **3g**).

Most of compounds **3** possess intense fluorescence in the solid state. The powder emission spectra of the fluorophores **3a–i** are represented by one emission band with maxima in the range from 486 to 511 nm (λ_{ex} = 350 nm). The quantum yield of fluorescence in powders ranges from 6.1% (**3h**) to 92.9% (**3i**).

A significant increase in the emission intensity during the transition from dilute acetonitrile solutions to powders indicates that the substances may exhibit aggregation-induced emission (AIE) behavior. The main proposed mechanisms for the increase of the emission during aggregation are the restriction of the intramolecular rotation (RIR). Free rotation of aromatic rings of compounds in dilute solution leads to non-radiative dissipation of excitation energy, which results in quenching of fluorescence. When aggregates are formed, emission is resumed by blocking non-

DOI: 10.15826/chimtech.2025.12.2.10

radiative energy dissipation. Meanwhile, the twisted molecular conformation of AIEgens can eliminate their intermolecular π–π-stacking interactions to avoid excitation energy loss [29–31].

We studied the photophysical properties of the compounds **3b** and **3g** in solvents with different orientation polarization values (from *n*-heptane to MeCN, Table S1-S2 and Figure S1–S2). For compounds **3b** and **3g**, a slight positive solvatochromic shift of 28–29 nm was detected when going from *n*-heptane to MeCN. This low value of the solvatochromic shift usually indicates the absence of intramolecular charge transfer during photoexcitation [32]. In order to prove this mathematically, we plotted the Stokes shift in cm^{-1} as a function of the solvent orientation polarization according to the Lippert-Mataga equation [32]. The difference in the dipole moments of the ground and excited states (Δμ) for both compounds was 6.7 D (Figure S3), indicating that the degree of ICT upon photoexcitation is insignificant ($\Delta\mu < 10$ D) [32].

We found a correlation between the nature of the substituent R (Scheme 1) and the position of the emission maxima of compounds **3** in acetonitrile solution. Thus, it was found that compounds **3d-f, h** containing donor substituents such as 3,4-dimethoxyphenyl and 4-methoxyphenyl have slightly longer wavelength emission maxima in acetonitrile solution compared to compounds **3a–c, g** containing phenyl and 4-chlorophenyl substituents (572–576 nm vs. 560–564 nm).

3.3. Luminescence in the presence of zinc cations

Zn^{2+} cation is the second most abundant transition metal ion in the human body. It plays an important role in a number of biological processes, in particular, in the regulation of enzymes, neural signal transmission, and gene expression [34, 35]. Therefore, the development of fluorescent sensors for this metal cations is an important task. It was previously shown that 3-hydroxy-2,2'-bipyridine derivatives are effective and selective fluorescent probes for Zn^{2+} [3, 8, 11]. Upon interaction with Zn^{2+} cations, these compounds show a significant increase in fluorescence intensity concurrently with a considerable decrease in Stokes shift.

Based on this, we decided to study the luminescent properties of solutions of the compounds **3b** and **3g** in the presence of Zn^{2+} cation. Zinc perchlorate was used for the experiments. In particular, it was found that the addition of 1 eq. Zn^{2+} to solutions of compounds **3b** and **3g** in THF leads to both a significant increase in luminescence intensity and a large hypsochromic shift of the emission maxima (≈ 130 nm) (Figure 4, 5).

Such a significant change in the photophysical characteristics of solutions of the compounds **3b** and **3g** when zinc perchlorate is added to them can be explained by the formation of complexes of these compounds with Zn^{2+} cations.

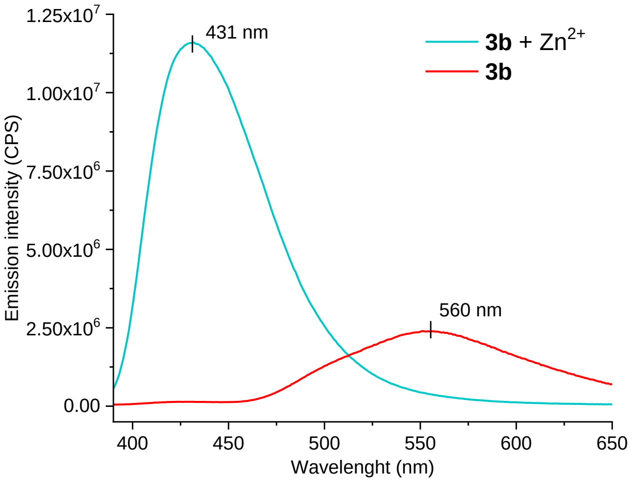


Figure 4 Emission spectra of compounds **3b** in THF ($C = 1\cdot10^{-5}$ M) before and after the addition of Zn^{2+} (1 eq.), excited at 340 nm.

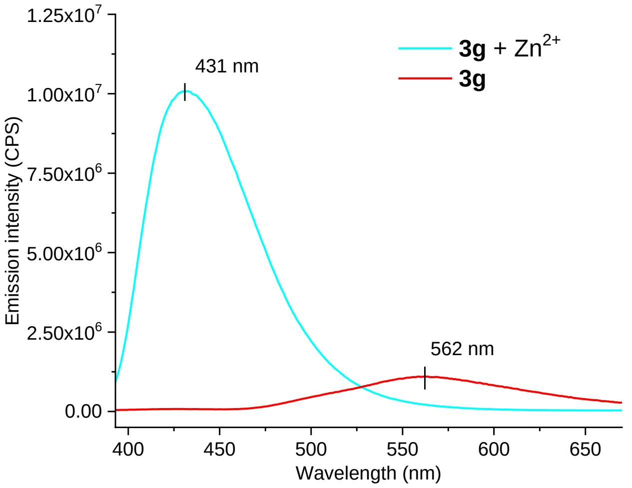


Figure 5 Emission spectra of compounds **3g** in THF ($C = 1\cdot10^{-5}$ M) before and after the addition of Zn^{2+} (1 eq.), excited at 339 nm.

Based on the literature data, it can be assumed that N,N'-coordination of zinc ions by bipyridine ligands occurs [33]. The coordination of Zn^{2+} cation with ligand changes the conformation of bipyridine core from *trans* to *cis*, which prohibits formation of intramolecular hydrogen bonding $OH\cdots N_{Py}$, making the ESIPT process impossible. Consequently, longer-wavelength emission from the keto-form becomes impossible, emission proceeds only from the enol-form, and the emission maximum undergoes a hypsochromic shift. We hypothesize that the increase in intensity upon binding of zinc cation to ligands **3b** and **3g** was due to the formation of a novel effective fluorophores.

Also, we studied the fluorescence response of compounds **3b** and **3g** to the presence of Zn^{2+} cations in acetonitrile solution (Figure S4-S5). In contrast to THF solutions, only a hypsochromic shift of the emission maximum was observed upon addition of zinc cations to acetonitrile solutions of compounds **3b** and **3g**. The change of fluorescence intensity in this case is insignificant.

These properties indicate the possibility of application of compounds **3b** and **3g** as luminescent probes for Zn^{2+}.

4. Limitations

The study showed that the acetonitrile solutions of compounds **3** exhibit low quantum yield of fluorescence. However, in solutions in the presence of Zn^{2+} cations, as well as in powder form, these substances exhibit intense fluorescence.

5. Conclusions

In conclusion, we studied the photophysical properties of 4,5-diaryl-3-hydroxy-2,2'-bipyridine-6-carbonitriles **3a–i**, which we synthesized *via* the inverse electron demand Diels-Alder reaction of 6-aryl-5-cyano-3-(pyridin-2-yl)-1,2,4-triazines with 2-amino-4-(het)aryloxazoles. In particular, these compounds exhibit an unusually large Stokes shift (up to 241 nm), which can be explained by the ESIPT process, and relatively low fluorescence quantum yields of up to 4.7% in acetonitrile solutions. In contrast, in powders these compounds show very intense fluorescence ($\Phi_{f\,\text{solid}}$ up to 92.9%). The effect of adding Zn^{2+} cations on fluorescence was studied for solutions of two compounds. Specifically, the addition of Zn^{2+} cations resulted in both a significant hypsochromic shift of the emission maximum (≈130 nm) and a significant increase in fluorescence intensity.

Supplementary materials

This manuscript contains supplementary materials, which are available on the corresponding online page.

Acknowledgments

This work was performed using the equipment of the Joint Use Center "Spectroscopy and Analysis of Organic Compounds" of the I. Ya. Postovsky Institute of Organic Synthesis of the Ural Branch of the Russian Academy of Sciences.

Author contributions

Conceptualization: G.V.Z., D.S.K.
Data curation: E.D.L., Y.K.S.., V.V.C.
Formal Analysis: E.D.L., Y.K.S., M.I.V.
Funding acquisition: G.V.Z.
Investigation: E.D.L., Y.K.S., M.I.V., Y.M.S., S.E.V., K.D.K., I.A.E.
Methodology: D.S.K., G.V.Z., M.I.V., V.V.C.
Project administration: G.V.Z.
Resources: D.S.K., V.V.C.
Software: G.V.Z.
Supervision: G.V.Z., V.V.C., D.S.K.
Validation: M.I.V.
Visualization: M.I.V., Y.M.S.
Writing – original draft: E.D.L., Y.K.S., D.S.K.
Writing – review & editing: E.D.L, D.S.K., V.V.C., I.A.E., Y.K.S.

Conflict of interest

The authors declare no conflict of interest.

Additional information

Author IDs:
Evgeny D. Ladin, Scopus ID 57413114000;
Yaroslav K. Shtaitz, Scopus ID 57201778255;
Vladimir V. Chernyshov, Scopus ID 57207573772
Ilia A. Eliseev, Scopus ID 58045215800
Maria I. Valieva, Scopus ID 57204922642;
Yulia M. Sayfutdinova, Scopus ID 59308210300;
Svetlana E. Vatolina, Scopus ID 58887855900;
Ksenia D. Krasnoperova, Scopus ID 58750182800;
Dmitry S. Kopchuk, Scopus ID 14123383900;
Grigory V. Zyryanov, Scopus ID 6701496404.

Websites:
Ural Federal University, https://urfu.ru/en/;
Institute of Organic Synthesis, UB RAS, https://iosuran.ru/;
Sirius University of Science and Technology, https://siriusuniversity.ru/eng/.

References

1. Kaczmarek U, Balicki R, Lipkowski J, Borowicz P, Grabowska A. Structure and Photophysics of Deazabipyridyls. Excited Internally Hydrogen-Bonded Systems with One Proton Transfer Reaction Site. J Chem Soc Perkin Trans. 1994;7:1603–1610. doi:10.1039/p29940001603
2. Borowicz P, Grabowska A, Leś A, Kaczmarek Ł, Zagrodzki B. New Phototautomerizing Systems: Non-Symmetric Derivatives of [2,2′-Bipyridyl]-3,3′-Diol. Chem Phys Lett. 1998;291(3–4):351–359. doi:10.1016/S0009-2614(98)00565-X
3. Ulrich G, Nastasi F, Retailleau P, Puntoriero F, Ziessel R, Campagna S. Luminescent Excited-State Intramolecular Proton-Transfer (ESIPT) Dyes Based on 4-Alkyne-Functionalized [2,2′-Bipyridine]-3,3′-diol Dyes. Chem A Eur J 2008;14(14):4381–4392. doi:10.1002/chem.200701803
4. Trannoy V, Léaustic A, Gadan S, Guillot R, Allain C, Clavier G, Mazerat S, Geffroy B, Yu PA. Highly Efficient Solution and Solid State ESIPT Fluorophore and Its OLED Application. New J Chem. 2021;45(6):3014–3021. doi:10.1039/D0NJ05600F
5. Sepioł J, Bulska H, Grabowska A. The Dihydroxy Derivative of 2,2'-Bipyridyl as a New Proton-Transfer Lasing Dye. Chem Phys Lett. 1987:140(6):607–610. doi:10.1016/0009-2614(87)80496-7
6. Rurack K, Hoffmann K, Al-Soufi W, Resch-Genger U. 2,2‘-Bipyridyl-3,3‘-Diol Incorporated into AlPO4 -5 Crystals and Its Spectroscopic Properties as Related to Aqueous Liquid Media. J Phys Chem B. 2002;106(38):9744–9752. doi:10.1021/jp0259622
7. Reynal A, Etxebarria J, Nieto N, Serres S, Palomares E, Vidal-Ferran A. A Bipyridine-Based "Naked-Eye" Fluorimetric Cu2+ Chemosensor. Eur J Inorg Chem. 2010;2010(9):1360–1365. doi:10.1002/ejic.200900887
8. Mandal S, Ghosh S, Banerjee C, Kuchlyan J, Sarkar N. Unique Photophysical Behavior of 2,2′-Bipyridine-3,3′-Diol in DMSO–Water Binary Mixtures: Potential Application for Fluorescence Sensing of Zn^{2+} Based on the Inhibition of Excited-State Intramolecular Double Proton Transfer. J Phys Chem B. 2013;117(40):12212–12223. doi:10.1021/jp406853r
9. Mandal S, Ghosh S, Aggala HHK, Banerjee C, Rao VG, Sarkar N. Modulation of the Photophysical Properties of 2,2′-Bipyridine-3,3′-Diol inside Bile Salt Aggregates: A Fluorescence-Based Study for the Molecular Recognition of Bile Salts. Langmuir. 2013;29(1):133–143. doi:10.1021/la304319r
10. Zhao X, Zhu L, Li Q, Yin H, Shi Y. The Interplay between ESIPT and TADF for the 2,2′-Bipyridine-3,3′-Diol: A Theoretical Reconsideration. IJMS. 2022;23(22):13969. doi:10.3390/ijms232213969
11. Huang J, Bai X, Li L, Zheng Z, Xu Z, Cui Y, Cao J, Xu L. Transition-Metal-Free Oxidative C(Sp2)–H Hydroxylation of Terpyridines: A HOMO-Raising Strategy for the Construction of a New Super-Stable Terpyridine Chromophores. Chem A Eur J. 2017;23(17):4055–4059. doi:10.1002/chem.201605793
12. Rammohan A, Krinochkin AP, Kopchuk DS, Shtaitz YK, Savchuk MI, Starnovskaya ES, Zyryanov GV, Rusinov VL, Chupakhin ON. Synthesis and Photoluminescent Properties of 4,5-Diaryl-3-Hydroxy- and 3-Methoxypyridine-6-Carbonitriles. Russ J Org Chem. 2022;58(2):180–183. doi:10.1134/S1070428022020038

13. Mongin F, Trécourt F, Mongin O, Quéguiner G. New Syntheses of Orelline and Analogues via Metalation and Cross-Coupling Reactions. Tetrahedron. 2002;58(2):309–314. doi:10.1016/S0040-4020(01)01142-5
14. Huo W, Miki K, Tokunaga D, Mu H, Oe M, Harada H, Ohe K. Dual-Stimuli-Responsive Probes for Detection of Ovarian Cancer Cells and Quantification of Both pH and Enzyme Activity. Bull Chem Soc Japan. 2021;94(8):2068–2075. doi:10.1246/bcsj.20210168
15. Forshaw S, Knighton RC, Reber J, Parker JS, Chmel NP, Wills M. A Strained Alkyne-Containing Bipyridine Reagent; Synthesis, Reactivity and Fluorescence Properties. RSC Adv. 2019;9(62):36154–36161. doi:10.1039/C9RA06866J
16. Yang PS, Tsai MT, Tsai MH, Ong CW. The Regioselective Homocoupling of Meta-Hydroxypyridines with Hypervalent Iodine(III). Chem Asian J. 2015;10(4):849–852. doi:10.1002/asia.201403359
17. Zhang S, Zhang D, Liebeskind LS. Ambient Temperature, Ullmann-like Reductive Coupling of Aryl, Heteroaryl, and Alkenyl Halides. J Org Chem. 1997;62(8):2312–2313. doi:10.1021/jo9700078
18. Chubb RWJ, Bryce MR, Tarbit B. Synthesis of 2-Heteroaryl-3-Hydroxypyridines by Ring Expansion Reactions of 2-Acylfurans with Ammonia. J Chem Soc Perkin Trans 1. 2001;16:1853–1854. doi:10.1039/b105228b
19. Gao L, Delle Piane M, Corno M, Jiang F, Raja R, Pera-Titus M. Synthesis of Amine Derivatives from Furoin and Furil over a Ru/Al2O3 Catalyst. Catal Sci Technol. 2024;14(9):2593–2599. doi:10.1039/D3CY01605F
20. Kozhevnikov VN, Kozhevnikov DN, Nikitina TV, Rusinov VL, Chupakhin ON, Zabel M, König B. A Versatile Strategy for the Synthesis of Functionalized 2,2‘-Bi- and 2,2‘:6‘,2‘ ‘-Terpyridines via Their 1,2,4-Triazine Analogues. J Org Chem. 2003;68(7):2882–2888. doi:10.1021/jo0267955
21. Krinochkin AP, Mallikarjuna RG, Kopchuk DS, Slepukhin PA, Shtaitz YK, Khalymbadzha IA, Kovalev IS, Kim GA, Ganebnykh IN, Zyryanov GV, Chupakhin ON, Charushin VN. 2-Aminooxazoles as Novel Dienophiles in the Inverse Demand Diels–Alder Reaction with 1,2,4-Triazines. Mendeleev Comm. 2021;31(4):542–544. doi:10.1016/j.mencom.2021.07.035
22. Rammohan A, Krinochkin AP, Kopchuk DS, Shtaitz YaK, Kovalev IS, Savchuk MI, Zyryanov GV, Rusinov VL, Chupakhin ON. Conditions for the Synthesis of 4,5-Diaryl-3-Hydroxy-2,2’-Bipyridine-6-Carbonitriles by the Reaction of 1,2,4-Triazine-5-Carbonitriles with 2-Aminooxazoles. Russ J Org Chem. 2022;58(2):175–179. doi:10.1134/S1070428022020026
23. Krinochkin AP, Valieva MI, Starnovskaya ES, Shtaitz YaK, Rybakova SS, Sharafieva ER, Kopchuk DS, Zyryanov GV, Rusinov VL. The Synthetic Approaches to (3-Thienyl)-Containing 2,2’-Bipyridines as Potential Monomers for Electropolymerization. Dokl Chem. 2022;506(1):196–201. doi:10.1134/S0012500822700100
24. Pattanayak BK, Rout DN, Mahapatra GN. Studies on Oxazoles. Part I : Synthesis and Chlorination of Some New 2-Amino-4-Substituted Oxazoles and Their Use as Fungicides. J Indian Chem Soc. 1978;55:264–267. doi:10.5281/ZENODO.6379265
25. Slepukhin PA, Rybakova AV, Gaviko VS, Rammohan A, Shtaitz YaK, Krinochkin AP, Ladin ED, Kopchuk DS, Zyryanov GV, Rusinov VL. Single-Crystal X-Ray Diffraction Study of 4,5-Diaryl-3-Hydroxy-2,2′-Bipyridine-6-Carbonitriles. Russ Chem Bull. 2023;72(12):2825–2836. doi:10.1007/s11172-023-4091-8
26. Porrès L, Holland A, Pålsso, L-O, Monkman AP, Kemp C, Beeby A. Absolute Measurements of Photoluminescence Quantum Yields of Solutions Using an Integrating Sphere. J Fluoresc. 2006;16(2):267–273. doi:10.1007/s10895-005-0054-8
27. Sedgwick AC, Wu L, Han H-H, Bull SD, He X-P, James TD, Sessler JL, Tang BZ, Tian H, Yoon J. Excited-State Intramolecular Proton-Transfer (ESIPT) Based Fluorescence Sensors and Imaging Agents. Chem Soc Rev. 2018;47(23):8842–8880. doi:10.1039/C8CS00185E
28. Liu X, Xu Z, Cole JM. Molecular Design of UV–Vis Absorption and Emission Properties in Organic Fluorophores: Toward Larger Bathochromic Shifts, Enhanced Molar Extinction Coefficients, and Greater Stokes Shifts. J Phys Chem C 2013;117(32):16584–16595. doi:10.1021/jp404170w
29. Rodrigues ACB, Seixas De Melo JS. Aggregation-Induced Emission: From Small Molecules to Polymers—Historical Background, Mechanisms and Photophysics. Top Curr Chem (Z). 2021;379(3):15. doi:10.1007/s41061-021-00327-9
30. Dong L, Peng HQ, Niu LY, Yang QZ. Modulation of Aggregation-Induced Emission by Excitation Energy Transfer: Design and Application. Top Curr Chem (Z). 2021;379(3):18. doi:10.1007/s41061-021-00330-0
31. Gao M, Tang BZ. Fluorescent Sensors Based on Aggregation-Induced Emission: Recent Advances and Perspectives. ACS Sens. 2017;2(10):1382–1399. doi:10.1021/acssensors.7b00551
32. Lakowicz JR (2006) Principles of Fluorescence Spectroscopy. Springer, Springer US, Boston, MA. doi:10.1007/978-0-387-46312-4
33. Zhang SG, Hou C. Aquabis(3′-Hydroxy-2,2′-Bipyridine-3-Olato-κ2 N , N ′)Zinc(II). Acta Crystallogr E Struct Rep Online. 2008;64(9):m1131–m1131. doi:10.1107/S1600536808024495
34. Sensi SL, Paoletti P, Bush AI, Sekler I. Zinc in the Physiology and Pathology of the CNS. Nat Rev Neurosci. 2009;10(11):780–791. doi:10.1038/nrn2734
35. Berg JM, Shi Y. The Galvanization of Biology: A Growing Appreciation for the Roles of Zinc. Sci. 1996;271(5252):1081–1085. doi:10.1126/science.271.5252.1081.