Journal of Fluorescence (2024) 34:579–586
https://doi.org/10.1007/s10895-023-03304-1

RESEARCH

One-pot Synthesis and Photophysical Studies of A-cycloamino-substituted 5-aryl-2,2'-bipyridines

Mallikarjuna R. Guda[1] · Maria I. Valieva[1,2] · Dmitry S. Kopchuk[1,2] · Rammohan Aluru[1] · Albert F. Khasanov[1] · Olga S. Taniya[1] · Alexander S. Novikov[3,4] · Grigory V. Zyryanov[1,2] · Brindaban C. Ranu[1,5]

Received: 27 April 2023 / Accepted: 5 June 2023 / Published online: 16 June 2023

Abstract

A series of α-cycloamine substituted 2,2’-bipyridines **3ae’-3ce’** was obtained via the one-pot approach based on *ipso*-substitution of a cyano-group in 1,2,4-triazines, followed by *aza*-Diels–Alder reaction in good yields. Photophysical properties, including fluorosolvatochromism, were studied for **3ae’-3ce’** and were compared with *α*-unsubstituted 2,2’-bipyridines. In addition, dipole moments differences in ground and excited states were calculated by both Lippert-Mataga equation and DFT studies and were compared to each other. The correlation between the size of cycloamine unit and the dipole moments differences value (based on Lippert-Mataga equation) was observed. In addition charge transfer indices (D_{CT}, Λ, H and t) were calculated to demonstrate influence of molecular structure on the intramolecular charge transfer degree.

Keywords 2,2’-bipyridines · Cycloamines · Fluorosolvatochromism · Lippert-Mataga equation · CT-indices · DFT studies

Introduction

Fragments of cyclic amines (cycloamines) play a versatile role as units of heterocyclic compounds. They act as pharmacophore units in many drugs [1], with cycloamine units might play a key role in the biological activity of the targeted compounds. For example, the presence of piperidine derivatives significantly enhanced hTRPV1 antagonistic activities [2], piperazine derivatives can be used as pharmacophores for cholinesterase inhibitors [3], while due to azepan moiety it is possible to provide urokinase inhibition activity, as well as antimetastasis activity [4]. Morpholine and thiomorpholine are important pharmacophore units as well [5–8]. Many cycloamine containing heterocycles have found an application as pesticides, herbicides, antifungal agents, etc. [9–13]. Some of pyrrolidine and morpholine containing quinoline derivatives form a quinoline-DNA complex using calf thymus DNA [14]. 4,7-Dipyrrolidinyl-1,10-phenanthroline can be used as a ligand for *N* -arylation in an aqueous medium, unlike pyrrolidine-free 1,10-phenanthroline derivatives [15]. Cyclic amines have found great application in the synthesis of luminescent molecules, especially in donor–acceptor ones [16–18]. Introducing of cycloamines into 2,2’-bipyridine resulted in amine structure dependent solvatochromism, solid state fluorescence and halochromic fluorescence switching due to the donor–acceptor nature of the molecule [19]. It was also possible to obtain luminescent tests for formaldehyde, which can be found in living cells, animals and brain tissues [20]. In addition, modification of d-luciferin with a fragment of azetidine, azepan and thiomorpholine yielded higher photon flux compare to original d-luciferin [21].

Among the existing preparation methods for obtaining cycloamine containing heterocycles, a Pd-catalyzed Buchwald-Hartwig amination is an outstanding one [22, 23]. It is a

✉ Albert F. Khasanov
a.f.khasanov@ya.ru

[1] Institute of Chemical Engineering, Ural Federal University, 19 Mira St., Ekaterinburg 620002, Russia

[2] Postovsky Institute of Organic Synthesis, Ural Branch of the Russian Academy of Sciences, 22 S. Kovalevskaya St. / 20 St., Ekaterinburg 620137, Russia

[3] Institute of Chemistry, St. Petersburg State University, 7/9 Universitetskaya nab., St. Petersburg 199034, Russia

[4] Joint Research Institute of Chemistry, Faculty of Physics, Mathematics and Natural Sciences, Peoples’ Friendship University of Russia (RUDN University), 6 Miklukho-Maklaya St., Moscow 117198, Russia

[5] School of Chemical Sciences, Indian Association for the Cultivation of Science, Jadavpur, Kolkata 700032, India

versatile and efficient amination tool, however, requiring pre-functionalization of a heterocycle with a halogen atom. In addition, there are many examples of nucleophilic substitution reactions of various leaving groups [24–28]. Particularly, construction of bipyridines bearing an amine residue at α-position *via* cross-coupling reactions [29], as well as direct functionalization of 2,2'-bipyridine [30] or its N-oxide [31] by amine residues. It is worth noting the group of Professor Belskaya, who proposed one-pot approach for the insertion of various cycloamines at the C(5) position in 1,2,3-triazoles during its construction [32].

In addition, the approach based on preparation of 2,2'-bipyridines *via* their 1,2,4-triazine analogs [33–35], consisting of the nucleophilic substitution of hydrogen or easily leaving groups in 1,2,4-triazine followed by transformation of the triazine ring into the pyridine one, has to be mentioned. As part of this strategy, 2,2'-bipyridines containing carborane [36], alcohols [37], anilines [38], etc. at the α-position were previously obtained. It is necessary to note the single example of the preparation of α-pyrrolidine-2,2’-bipyridine derivative described by our research group [39]. In this case, the *aza*-Diels–Alder reaction was realized in pressure flask under increased pressure and temperature conditions, since it could not be carried out under milder conditions. In this work, we used this approach to obtain a series of 5-aryl-2,2'-bipyridines containing various cyclic amines residues at the C6 position of pyridine, and studied their photophysical properties.

Experimental

General Information

Unless otherwise indicated, all common reagents and solvents were used from commercial suppliers (Sigma-Aldrich, Acros Organics or Alfa Aesar) without further purification. All workup and purification procedures were carried out using analytical-grade solvents. ^{1}H NMR and ^{13}C NMR spectra were recorded at room temperature at 400 and 100 MHz, respectively, on a Bruker DRX-400 spectrometer using $CDCl_3$ or DMSO-d_6 as the solvent. ^{13}C NMR DEPT 135 spectra were recorded at room temperature at 151 MHz on Bruker AVANCE NEO spectrometer using $CDCl_3$ as the solvent Hydrogen chemical shifts were referenced to the hydrogen resonance of the corresponding solvent (DMSO-d_6, $\delta = 2.50$ ppm or $CDCl_3$, $\delta = 7.26$ ppm). Carbon chemical shifts were referenced to the carbon resonances of the solvent ($CDCl_3$, $\delta = 77.16$ ppm). Peaks were labeled as singlet (s), doublet (d), triplet (t), doublet of doublets (dd), doublet of doublets of doublets (ddd), and multiplet (m). Mass spectra were recorded on a MicrOTOF-Q II (Bruker Daltonics), electrospray as a method of ionization. Elemental analysis was performed on a PerkinElmer PE 2400 elemental analyzer. Melting points were obtained with Stuart SMP10 apparatus and are uncorrected. UV–vis absorption spectra were recorded on a Shimadzu UV-1800 spectrophotometer, and emission spectra were measured on a Horiba FluoroMax-4 by using quartz cells with a 1 cm path length at room temperature. Absolute quantum yields of the luminescence of target compounds in solution were measured by using the integrating sphere Quanta-φ of the Horiba FluoroMax 4 at room temperature. The quantum chemical calculations were carried out at the B3LYP/6-31G* level of theory with the help of the Gaussian-09 [40] program package. No symmetry restrictions were applied during the geometry optimization procedure. The hole-electron analysis was carried out in Multiwfn program (version 3.7) [41]. The Cartesian atomic coordinates for all optimized model structures are presented in the attached xyz-files.

Synthesis and Characterization

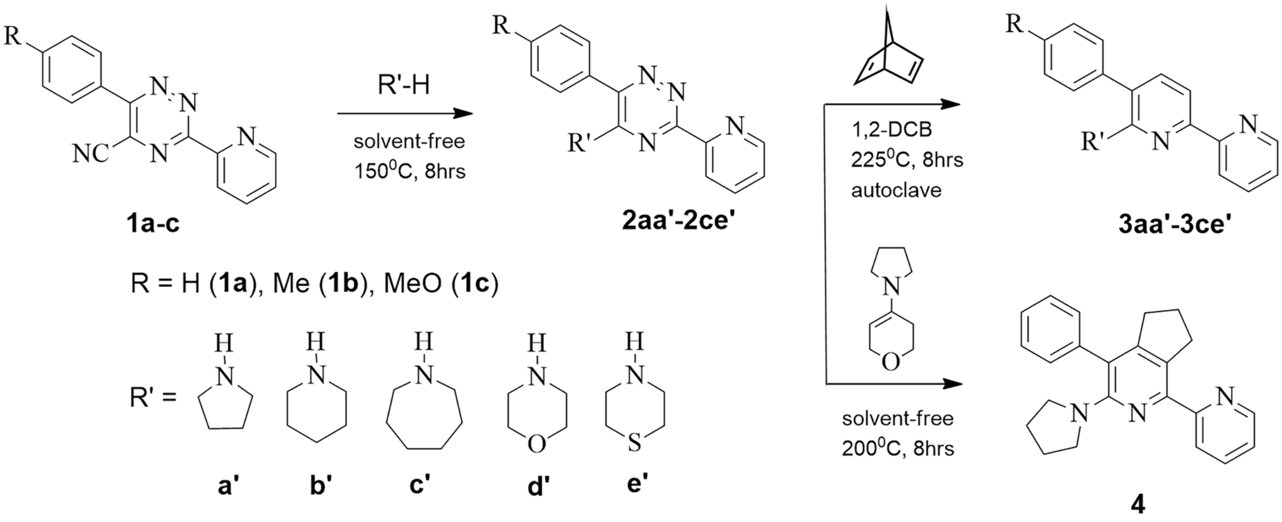
5-Cyano-6-aryl-3-(pyridine-2-yl)-1,2,4-triazines were prepared according to the literature [42].

Typical Procedure for the Synthesis of Corresponding Cycloamine-containing 2,2′-bipyridines 3aa′-3ce′

A mixture of a corresponding 5-cyano-1,2,4-triazine **1a-c** (0.5 mmol, 1 eq.) and a corresponding cycloamine (0.5 mmol, 1 eq.) was mixed in a pressure flask at 150 ℃ under argon for 8 h. Then 2,5-norbornadien (4 eq.) and 1,2-dichlorobenzene (10 mL) were introduced. The reaction mixture was mixed at 225 ℃ under argon for 8 h. Then extra portion of 2,5-norbornadien (4 eq.) was introduced and the reaction mixture was mixed at 225 ℃ under argon for another 8 h. The solvent was removed under reduced pressure, and a solid was triturated by acetonitrile. The resulted precipitate was filtrated and recrystallized from acetonitrile.

Synthesis of 4-phenyl-1-(pyridin-2-yl)-3-(pyrrolidin-1-yl)-6,7-dihydro-5*H*-cyclopenta[*c*]pyridine 4

A mixture of 5-cyano-6-phenyl-1,2,4-triazine **1a** (130 mg, 0.5 mmol, 1 eq.) and pyrrolidine (0.5 mmol, 0.04 mL, 1 eq.) was mixed in a pressure flask at 150 ℃ under argon for 8 h. Then 1-morpholinecyclopentene (0.4 ml, 5 eq.) was introduced and the reaction mixture was stirred at 200 ℃ for 2 h. After that extra portion of 1-morpholinecyclopentene (0.4 ml, 5 eq.) was introduced and the reaction mixture was stirred at 200 ℃ for another 2 h. The reaction mixture was triturated by acetonitrile (4 mL) and the precipitate was filtrated. The product was recrystallized from acetonitrile.



Scheme 1 One-pot synthesis of 2,2'-bipyridines **3aa'-3ae'** and **4**

Results and Discussion

5-Cyano-6-aryl-3-(pyridine-2-yl)-1,2,4-triazines were used as starting compounds **1a-c** obtained by the described procedure [42]. Interaction of **1a-c** with cyclic amines was realized *via ipso*-substitution of the cyano group and performed under solvent-free conditions at 150 ℃ in a pressure flask (Scheme 1). The resulted 1,2,4-triazines **2aa'-2ce'** were used on the next step without isolation and purification with the one-pot approach. The target 2,2'-bipyridines **3aa'-3ce'** were formed as a result of the *aza*-Diels–Alder reaction using 2,5-norbornadiene as a dienophile at 225 ℃ in a 1,2-dichlorobenzene under argon atmosphere (Scheme 1). It is worth noting the possibility of using of 1-morpholinecyclopentene as a dienophile at this step under solvent-free conditions at 200 ℃ to obtain product **4**. Overall yields for this one-pot two-step approach were in range of 60–75% for **3aa'-3ce'** and 62% for **4.**

The structures of the target compounds were confirmed by ^{1}H and ^{13}C NMR spectroscopy, mass spectrometry and elemental analysis.

Photophysical Studies

The photophysical properties of the obtained fluorophores **3aa'-3ce'** were studied (Fig. 1, Table 1). UV/Vis absorption spectra contained two absorption bands with maxima in the ranges of 250–273 nm and 338–360 nm, which can be attributed to the corresponding π-π* and n-π* transitions. The maxima of the longest wavelength absorption bands changed in the range of 12–15 nm with a change in the size and nature of the cycloamine unit, however, no relationship was observed in this case. In addition, no differences were observed between morpholine and thiomorpholine containing fluorophores, while shifts in absorption maxima were detected in case of pyrrolidine, piperidine and

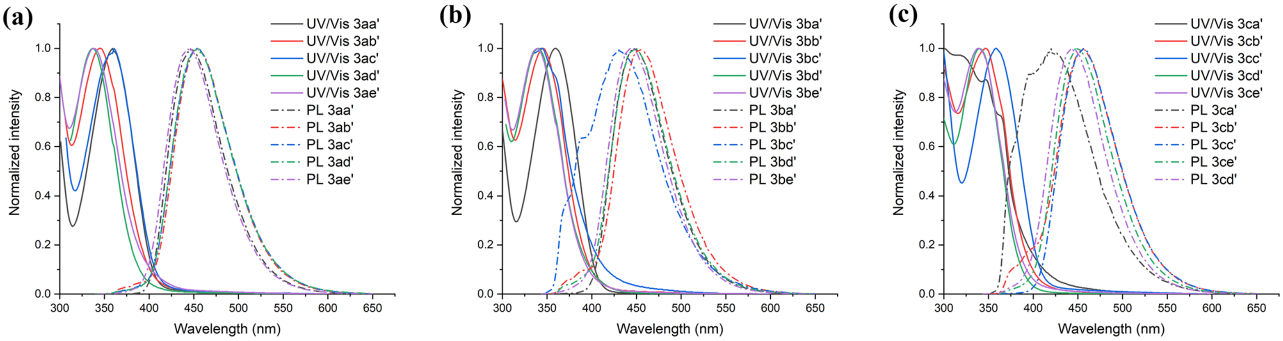
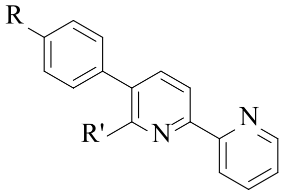


Fig. 1 Normalized UV/Vis absorption and normalized fluorescence emission of **3aa'-3ae'** (**a**), **3ba'-3be'** (**b**) and **3ca'-3ce'** (**c**) in MeCN at rt (C = 10^{-5} M)

Table 1 Photophysical properties of 2,2'-bipyridines **3aa'-3ce'** and **4** in MeCN



Compound	R’	λ_{max}^{abs}	λ_{max}^{EM}	ε_M, $M^{-1}\times cm^{-1}$	Stokes Shift, cm^{-1} (nm)	*Φ*, %
R = H						
[43]	H	298	357	-	5546 (59)	3.2
3aa’	Pyrrolidine-1-yl	273, 357	446	62,700	5590 (89)	30.1
3ab’	Piperidine-1-yl	256, 344	454	56,700	7043 (110)	86.1
3ac’	Azepane-1-yl	260, 358	454	46,700	5674 (92)	50.2
3ad’	Morpholine-1-yl	260, 338	448	49,600	7264 (110)	57.2
3ae’	Thiomorpholine-1-yl	253, 338	446	65,900	7164 (108)	57.3
4	Pyrrolidine-1-yl	259, 360	450	42,100	5556 (90)	41.9
R = Me						
[43]	H	302	360	-	5335 (58)	17.0
3ba’	Pyrrolidine-1-yl	261, 360	398sh, 448	38,300	5456 (88)	40.9
3bb’	Piperidine-1-yl	259, 346	454	30,400	6875 (108)	42.6
3bc’	Azepane-1-yl	250, 345	432	30,500	5837 (87)	39.4
3bd’	Morpholine-1-yl	256, 340	448	42,500	7090 (108)	52.0
3be’	Thiomorpholine-1-yl	257, 339	446	50,100	7077 (107)	41.2
R = MeO						
[43]	H	309	399	-	7300 (90)	89.0
3ca’	Pyrrolidine-1-yl	321sh, 347	397sh, 420	35,600	5065 (73)	41.5
3cb’	Piperidine-1-yl	263, 347	456	35,600	6889 (109)	47.4
3 cc’	Azepane-1-yl	272, 359	456	55,800	5848 (97)	44.9
3 cd’	Morpholine-1-yl	255, 339	449	39,700	7227 (110)	56.0
3ce’	Thiomorpholine-1-yl	254, 339	444	49,300	6976 (105)	63.1

a UV/Vis absorption spectra were measured at rt in range from 250 to 600 nm

b Fluorescence emission spectra were measured at rt (excitation at the maximum of the absorption)

c Absolute quantum yields were measured using the Integrating Sphere of the Horiba-Fluoromax-4 at rt

azepane containing ones. As expected, the introduction of the methyl or methoxy groups into the phenylene fragment did not lead to significant changes in absorption spectra. It is necessary to note the bathochromic shift of absorption maxima for 2,2'-bipyridines **3aa'-3ce'** in comparison with α-unsubstituted 2,2'-bipyridines, i.e., without a cycloamine unit [43]. In this case, the difference was up to 59 nm, and the reason could be attributed to the contribution of the lone pair of electrons of the nitrogen atom of the cycloamine fragment to the n-π* transition.

Introduction of cycloamine units influenced significantly on the fluorescence of **3aa'-3ce'**. In most cases, the spectra were represented by one intense and wide emission band in the range of 350–600 nm with a maxima varying in the range of 432–456 nm (Fig. 1, Table 1), which are 45–97 nm redshifted than the fluorescence maxima for similar α-unsubstituted 2,2'-bipyridines [43]. No relationship was observed between the size and nature of the cycloamine unit and fluorescence; there was only a moderate change in the emission maxima in the range of 8–36 nm. In addition, the introduction of cycloamine fragments increased the Stokes shift values. It is worth noting a significant increase in the luminescence quantum yields values upon the introduction of cycloamine fragments in the series 5-phenyl- and 5-tolyl-2,2'-bipyridines, especially when comparing 5-phenyl-6-(azepan-1-yl)-2,2'-bipyridine **3a,b'** (86.1%) with 5-phenyl-2,2'-bipyridine (3.2%, [43]). In the case of 4-methoxyphenyl derivatives, the quantum yields of compounds **3ca'-3ce '** were lower than for 4-methoxyphenyl-2,2'-bipyridine (89.0%, [43]).

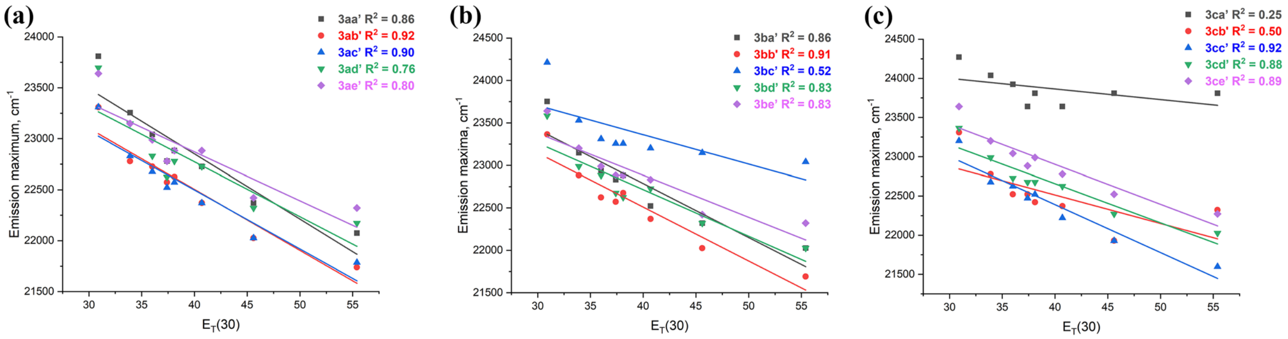


Fig. 2 The variation of the fluorescence emission maximum with the empirical solvent polarity parameter E_T (30) for **3aa'-3ae'** (**a**), **3ba'-3be'** (**b**) and **3ca'-3ce'** (**c**) in cyclohexane, toluene, 1,4-dioxane, ethyl acetate, THF, DCM, MeCN and MeOH

Fluorosolvatochromism

Compounds **3aa'-3ce'** are representatives of D-A push–pull fluorophores since they consist of a cycloamine donor (D) fragment and the 2,2'-bipyridine acceptor (A) one. Therefore, they should exhibit intramolecular charge separation (or intermolecular charge transfer, ICT) during photoexcitation with appearance of long-wavelength emission band. To confirm this, absorption and fluorescence spectra were obtained for the fluorophores **3aa'-3ce'** in solvents of different polarity (Table S1). The UV/Vis spectra, as expected, showed only minor changes with peaks varying within a few nanometers for all **3aa'-3ce'** fluorophores. The fluorescence spectra turned out to be more dependent on the solvent polarity, and the expected bathochromic shift of the emission maxima was observed with increasing solvent polarity. The correlation between emission maxima and solvent polarity and the Dimroth/Reichardt [44, 45] and Kosover [46, 47] scales (based on the empirical parameters Z and E $_T$ (30), respectively) turned out to be linear (Fig. 2, Tables S2-S4) for all fluorophores except **3ca'** and **3cb'** ($R^2 = 0.25$ and 0.50, respectively). In these cases, the emission maxima in the most polar methanol turned out to be blue-shifted due to proticity of methanol.

Moreover, the differences in dipole moments in the ground and excited states (Δμ) for fluorophores **3aa'-3ce'** were calculated by Lippert-Mataga equation [48–50] (Eqs. 1–3) and corresponding plots (Fig. 3).

$$\nu_A - \nu_F = \frac{2}{hc}\left(\frac{\varepsilon - 1}{2\varepsilon + 1} - \frac{n^2 - 1}{2n^2 + 1}\right)\frac{\left(\mu_E - \mu_G\right)^2}{a^3} \tag{1}$$

Equation (1). Lippert-Mataga equation, where ν_A and ν_F are the wavenumbers (cm^{-1}) of the absorption and emission, respectively; h is Planck's constant; c is the speed of light in vacuum; a is the radius of the cavity in which the fluorophore resides (Onsager radius [51]), μ_E and μ_G are the excited and ground state dipole moment, respectively.

$$a^3 = V_{vdW}\frac{3}{4\pi} \tag{2}$$

Equation (2). Onsager radius [51], where V_{vdW} – van der Waals volume.

$$V_{vdW} = \sum(all\ atom\ contributions) - 5.92N_B - 14.7R_A - 3.8R_{NA} \tag{3}$$

Equation (3). Theoretical calculations of van der Waals volume, where, N_B is the number of bonds, R_A is the number

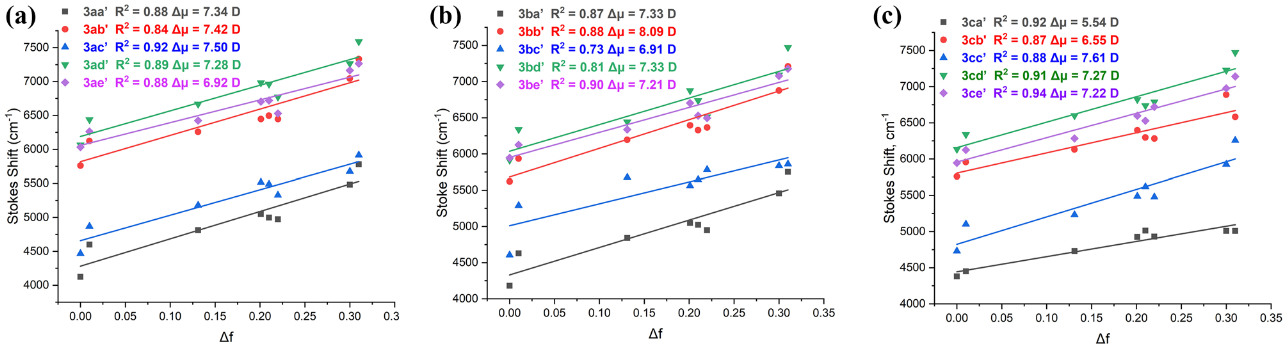


Fig. 3 Lippert-Mataga plot for **3aa'-3ce'** in cyclohexane, toluene, 1,4-dioxane, ethyl acetate, THF, DCM, MeCN and MeOH

of aromatic rings, and R_{NA} is the number of non-aromatic rings.

For all the fluorophores, Δμ values were less 10D that could be explained by weak cycloamine donor unit and, therefore, weak charge separation in excited state. However, an unexpected correlation was determined for fluorophores **3aa'-3ac'**, **3ba'-3bc'** and **3ca'-3 cc'**, that is the larger cycloamine unit, the greater Δμ value (Table 2) with the single exception – compound **3bc'** with the Δμ value of 6.91 D. This correlation was not obvious due to the presence of σ-orbital overlapping only between CH_2-units that had to have no influence on charge separation state. For compounds with morpholine and thiomorpholine units (**3ad'-3ae'**, **3bd'-3be'** and **3 cd'-3ce'**), this correlation was not discovered due to the role of heteroatom (O or S). Comparison of Δμ values calculated by Lippert-Mataga equation with the ones calculated by B3LYP/6-31G* level of theory with the help of Gaussian-09 (Table S5) reveals differences in Δμ values (Table 2). Moreover, no clear correlation between the size of cycloamine unit and Δμ value was observed according to DFT calculations. These differences could be explained by the role of the solvents in Lippert-Mataga equation that was not included in DFT calculations.

DFT Studies and Charge Transfer Indices

As a next step, HOMO–LUMO spatial distributions, energy gap values ΔE, as well as oscillator strength for all **3ae'-3ce'** fluorophores were calculated by B3LYP/6-31G* level of theory with the help of Gaussian-09 (Table 2, Figs. S1-S3). The HOMO-orbitals were distributed mainly on the cycloamine unit, central pyridine and the aromatic substituent, while the LUMO-orbitals distributed only along the 2,2'-bipyridine domain. The lowest ΔE correspond to morpholine- and thiomorpholine-containing molecules **3ad'**, **3ae'**, **3bd'**, **3be'**, **3 cd'** and **3ce'** associated with the most energetically favorable conjugated structures. Meanwhile, the largest values of the oscillator strength correspond to S_0-S_1 π-π* transitions of morpholine-containing compounds **3ad'**, **3bd'** and **3 cd'**, which also confirms the high degree of charge transfer (Table 2).

To gain a deeper understanding of the influence of molecular structure on the intramolecular charge transfer degree, additional calculations of charge transfer indices (CT-indices) have been carried out. These D_{CT}, Λ, H and t indices were initially proposed by Le Bahers et al. [52] and adapted by Lu and Chen [41]. Based on their work, the respective indices (D_{CT}, Λ, H and t) have been calculated for all fluorophores (Eqs. S1-S9, ESI) and are presented in Table 2. Thus, the analysis of CT-indices made it possible to predict a significant overlap between the centroids of the positive donor cycloamine fragment and the negative acceptor 2,2'-bipyridine domain of the D-A fluorophores. Based on the combination of high D_{CT} values close to H values, the lowest Λ index and $t > 0$, it was possible to obtain a series of the most promising compounds with intramolecular charge transfer: **3 cd'**, **3ce'**, **3bd'**, **3be'**, **3ad'** and **3ae'**, which correlates with the experimental values of the Stokes shift and dipole moment difference calculated by the Lippert-Mataga mathematical model. Therefore, DFT calculations and the values of CT indices allowed not only to compile a series, but to arrange it according to the significance of CT fluorophores: **3 cd > 3bd > 3ad > 3ce > 3be > 3ae**.

Table 2 Summary of dipole moment differences (Δμ), energy gap values (ΔE), CT-indices and oscillator strength for the molecules **3aa'-3ce'**

Compound	Δμ, D (LM)	Δμ, D (DFT)	ΔE, eV	D_{CT}, Å	Λ, a.u	H, Å	t, Å	$S_0 \rightarrow S_1$	$S_0 \rightarrow S_2$
3aa'	7.34	2.33	3.94	2.193	0.59	2.927	-0.039	0.2404	0.0051
3ab'	7.42	2.54	4.02	2.304	0.57	2.969	0.052	0.2263	0.0267
3ac'	7.50	2.60	3.99	2.390	0.56	2.886	0.174	0.1922	0.0173
3ad'	7.22	2.51	3.86	2.534	0.53	2.961	0.530	0.1677	0.0194
3ae'	6.91	1.59	3.89	2.753	0.51	3.036	0.784	0.1524	0.1600
3ba'	7.33	2.62	3.91	2.354	0.59	2.948	0.102	0.2712	0.0061
3bb'	8.09	2.75	4.01	2.352	0.58	3.029	0.068	0.2677	0.0470
3bc'	6.91	2.72	3.99	2.479	0.57	2.911	0.270	0.2161	0.0232
3bd'	7.33	2.58	3.85	2.561	0.54	2.999	0.546	0.1969	0.0245
3be'	7.21	1.91	3.89	2.742	0.52	3.069	0.780	0.1807	0.1988
3ca '	5.54	2.97	3.89	2.679	0.59	3.003	0.285	0.3042	0.0276
3cb'	6.55	3.11	3.95	2.769	0.59	3.125	0.238	0.3237	0.0719
3 cc'	7.61	3.08	3.96	2.771	0.57	2.955	0.459	0.2410	0.0447
3 cd'	7.27	2.65	3.83	2.802	0.55	3.030	0.666	0.2345	0.1039
3ce'	7.22	2.24	3.87	2.914	0.54	3.087	0.845	0.2205	0.2172

Conclusion

In summary, a series of α-cycloamine substituted 2,2'-bipyridines **3ae'-3ce'** has been obtained *via* the one-pot approach based on *ipso*-substitution of a cyano-group in 1,2,4-triazines, followed by *aza*-Diels–Alder reaction in good yields. Studies of photophysical properties demonstrated positive influence of cycloamine unit both on absorption and emission maxima, as well as luminescence quantum yields compare to α-unsubstituted 2,2'-bipyridines. Fluorophores **3ae'-3ce'** demonstrated red-shifted emission (fluorosolvatochromism) with increasing of solvent polarity. Dipole moments differences in ground and excited states were calculated by both Lippert-Mataga equation and DFT studies, and are in range of 6.55–8.09 D and 1.91–3.11 D, respectively. An unexpected correlation was determined for fluorophores **3aa'-3ac'**, **3ba'-3bc'** and **3ca'-3 cc'**, that is the larger cycloamine unit, the greater Lippert-Mataga Δμ value with the single exception (**3bc'**). In addition, CT-indices (D_{CT}, Λ, H and t) were calculated. Thus, these data confirm charge-separation in fluorophores **3ae'-3ce'**, while the method of their synthesis could find a potential application in design and construction of functional materials.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10895-023-03304-1.

Author Contributions All authors contributed to the study conception and design. Material preparation, data collection and photophysical studies were performed by M.R.Guda, M.I.Valieva, R.Aluru, A.F.Khasanov, quantum chemical calculations were performed by A.S.Novikov. Data interpretation was performed by A.F.Khasanov, D.S.Kopchuk, O.S.Taniya. Writing—original draft preparation was performed by A.F.Khasanov. Writing—review and editing were performed by D.S.Kopchuk and G.V.Zyryanov. Supervising by B.C.Ranu. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding This work was supported by the Russian Science Foundation grant # 19–73-10144-P (synthesis and primar photophysical studies), by the Russian Science Foundation grant # 21–13-00304 (fluorosolvatochromic studies), and by the RUDN University Strategic Academic Leadership Program (quantum chemical calculations).

Data Availability All relevant data are presented in the manuscript and the supplementary file.

Declarations

Ethics Approval Not applicable.

Conflicts of Interest Authors declare no conflicts of interest.

References

1. Vitaku E, Smith DT, Njardarson JT (2014) Analysis of the structural diversity, substitution patterns, and frequency of nitrogen heterocycles among U.S. FDA Approved Pharmaceuticals. J Med Chem 57:10257–10274. https://doi.org/10.1021/jm501100b
2. Kim MS, Ryu H, Kang DW et al (2012) 2-(3-Fluoro-4-methylsulfonylaminophenyl)propanamides as Potent Transient Receptor Potential Vanilloid 1 (TRPV1) Antagonists: Structure-Activity Relationships of 2-Amino Derivatives in the *N*-(6-Trifluoromethylpyridin-3-ylmethyl) C-Region. J Med Chem 55:8392–8408. https://doi.org/10.1021/jm300780p
3. Mohamed T, Yeung JCK, Rao PPN (2011) Development of 2-substituted-N-(naphth-1-ylmethyl) and N-benzhydrylpyrimidin-4-amines as dual cholinesterase and Aβ-aggregation inhibitors: Synthesis and biological evaluation. Bioorg Med Chem Lett 21:5881–5887. https://doi.org/10.1016/j.bmcl.2011.07.091
4. Buckley BJ, Aboelela A, Majed H et al (2021) Systematic evaluation of structure–property relationships and pharmacokinetics in 6-(hetero)aryl-substituted matched pair analogs of amiloride and 5-(N, N-hexamethylene)amiloride. Bioorg Med Chem 37:116116. https://doi.org/10.1016/j.bmc.2021.116116
5. Zhang F, Bhat S, Gabelli SB et al (2013) Pyridinylquinazolines selectively inhibit human methionine aminopeptidase-1 in Cells. J Med Chem 56:3996–4016. https://doi.org/10.1021/jm400227z
6. Kumari A, Singh RK (2020) Morpholine as ubiquitous pharmacophore in medicinal chemistry: Deep insight into the structure-activity relationship (SAR). Bioorg Chem 96:103578. https://doi.org/10.1016/j.bioorg.2020.103578
7. Kireev D, Chrétien J, Raevsky O (1995) Molecular modeling and quantitative structure-activity studies of anti-HIV-1 2-heteroarylquinoline-4-amines. Eur J Med Chem 30:395–402. https://doi.org/10.1016/0223-5234(96)88249-3
8. Motoyama M, Doan T, Hibner-Kulicka P et al (2021) Synthesis and structure-photophysics evaluation of 2- *N* -Amino-quinazolines: Small molecule fluorophores for solution and solid state. Chem Asian J 16:2087–2099. https://doi.org/10.1002/asia.202100534
9. Urch CJ, Salmon R, Lewis T et al (1996) Bicyclic amines as insecticides. WO 1996037494 A
10. Goeghova M, Zambach W, Muehlebach M et al (2009) Spiroheterocyclic pyrrolidine dione derivatives useful as pesticides. WO 2009049851 A1
11. Duke SO, Cantrell CL, Meepagala KM et al (2010) Natural toxins for use in pest management. Toxins (Basel) 2:1943–1962. https://doi.org/10.3390/toxins2081943
12. Meng L, Zhao H, Zhao S et al (2019) Inhibition of yeast-to-hypha transition and virulence of *Candida albicans* by 2-alkylaminoquinoline derivatives. Antimicrob Agents Chemother 63. https://doi.org/10.1128/AAC.01891-18
13. Fokas D, Coffen DL, Ryan WJ (1999) Spiro[pyrrolidine-2,3'-oxindole] compounds and methods of use
14. Bonacorso HG, Rodrigues MB, Iglesias BA et al (2018) New 2-(aryl/heteroaryl)-6-(morpholin-4-yl/pyrrolidin-1-yl)-(4-trifluoromethyl)quinolines: synthesis *via* Buchwald-Hartwig amination, photophysics, and biomolecular binding properties. New J Chem 42:10024–10035. https://doi.org/10.1039/C8NJ01120F
15. Engel-Andreasen J, Shimpukade B, Ulven T (2013) Selective copper catalysed aromatic N-arylation in water. Green Chem 15:336–340. https://doi.org/10.1039/C2GC36589H
16. Vabre R, Legraverend M, Piguel S (2014) Synthesis and evaluation of spectroscopic properties of newly synthesized push–pull 6-amino-8-styryl purines. Dyes Pigm 105:145–151. https://doi.org/10.1016/j.dyepig.2014.01.025
17. Toche RB, Chavan SN (2014) Synthesis and study the effect of donor-acceptor substituent on fluorescence behavior of thieno[3,2-c]pyridine derivatives. J Fluoresc 24:285–293. https://doi.org/10.1007/s10895-013-1313-8
18. Pigulski B, Męcik P, Cichos J, Szafert S (2017) Use of stable amine-capped polyynes in the regioselective synthesis of

push-pull thiophenes. J Org Chem 82:1487–1498. https://doi.org/10.1021/acs.joc.6b02685

19. Nagarasu P, Kundu A, Pitchaimani J et al (2020) Structure controlled solvatochromism and halochromic fluorescence switching of 2,2′-bipyridine based donor–acceptor derivatives. New J Chem 44:14421–14428. https://doi.org/10.1039/D0NJ02560G
20. Chen J, Shao C, Wang X et al (2020) Imaging of formaldehyde fluxes in epileptic brains with a two-photon fluorescence probe. Chem Commun 56:3871–3874. https://doi.org/10.1039/D0CC00676A
21. Sharma DK, Adams ST, Liebmann KL, Miller SC (2017) Rapid access to a broad range of 6′-substituted firefly luciferin analogues reveals surprising emitters and inhibitors. Org Lett 19:5836–5839. https://doi.org/10.1021/acs.orglett.7b02806
22. Heravi MM, Kheilkordi Z, Zadsirjan V et al (2018) Buchwald-Hartwig reaction: An overview. J Organomet Chem 861:17–104. https://doi.org/10.1016/j.jorganchem.2018.02.023
23. Dorel R, Grugel CP, Haydl AM (2019) The Buchwald-Hartwig amination after 25 years. Angew Chem Int Ed 58:17118–17129. https://doi.org/10.1002/anie.201904795
24. Wang D, Zhang E, Xu T et al (2015) Sequential C-C, C–O, and C–N bond-forming reaction of methyl (–)-3-dehydroshikimate, malononitrile, and bromoalkanes: simple synthesis of 2-(alkylamino)-3-cyanobenzofurans from a biomass-derived substrate. Synlett 27:287–293. https://doi.org/10.1055/s-0035-1560582
25. Thomas S, Roberts S, Pasumansky L et al (2003) Aminoborohydrides 15. The first mild and efficient method for generating 2-(dialkylamino)-pyridines from 2-fluoropyridine. Org Lett 5:3867–3870. https://doi.org/10.1021/ol035430j
26. Lee M, Rucil T, Hesek D et al (2015) Regioselective control of the S_NAr amination of 5-substituted-2,4-dichloropyrimidines using tertiary amine nucleophiles. J Org Chem 80:7757–7763. https://doi.org/10.1021/acs.joc.5b01044
27. Khazir J, Mir BA, Chashoo G et al (2020) Synthesis and anticancer activity of N-9- and N-7- substituted 1,2,3 triazole analogues of 2,6-di-substituted purine. Med Chem Res 29:33–45. https://doi.org/10.1007/s00044-019-02456-9
28. Pang JH, Kaga A, Chiba S (2018) Nucleophilic amination of methoxypyridines by a sodium hydride–iodide composite. Chem Commun 54:10324–10327. https://doi.org/10.1039/C8CC05979A
29. Zhao X, Webster CE (2015) Novel metal complex catalysts and uses thereof
30. Pang JH, Kaga A, Roediger S et al (2019) Revisiting the Chichibabin reaction: C2 amination of pyridines with a NaH−iodide composite. Asian J Org Chem 8:1058–1060. https://doi.org/10.1002/ajoc.201900094
31. Smith AJ, Kalkman ED, Gilbert ZW, Tonks IA (2016) $ZnCl_2$ capture promotes ethylene polymerization by a salicylaldiminato Ni complex bearing a pendent 2,2′-bipyridine group. Organometallics 35:2429–2432. https://doi.org/10.1021/acs.organomet.6b00485
32. Gavlik KD, Sukhorukova ES, Shafran YM et al (2017) 2-Aryl-5-amino-1,2,3-triazoles: New effective blue-emitting fluorophores. Dyes Pigm 136:229–242. https://doi.org/10.1016/j.dyepig.2016.08.015
33. Prokhorov AM, Kozhevnikov DN (2012) Reactions of triazines and tetrazines with dienophiles (Review). Chem Heterocycl Compd (N Y) 48:1153–1176. https://doi.org/10.1007/s10593-012-1117-9
34. Pabst GR, Sauer J (1999) The new and simple 'LEGO' system: Its application to the synthesis of 4-stannyl-, 4-bromo- and branched oligopyridines. Tetrahedron 55:5067–5088. https://doi.org/10.1016/S0040-4020(99)00179-9
35. Foster RAA, Willis MC (2013) Tandem inverse-electron-demand hetero-/retro-Diels–Alder reactions for aromatic nitrogen heterocycle synthesis. Chem Soc Rev 42:63–76. https://doi.org/10.1039/C2CS35316D
36. Kozhevnikov DN, Kozhevnikov VN, Prokhorov AM et al (2006) Consecutive nucleophilic substitution and aza Diels-Alder reaction—an efficient strategy to functionalized 2,2′-bipyridines. Tetrahedron Lett 47:869–872. https://doi.org/10.1016/j.tetlet.2005.12.006
37. Savchuk MI, Khasanov AF, Kopchuk DS et al (2019) New Push-Pull fluorophores on the basis of 6-Alkoxy-2,2'-Bipyridines: Rational synthetic approach and photophysical properties. Chem Heterocycl Compd (N Y) 55:554–559. https://doi.org/10.1007/s10593-019-02495-5
38. Kopchuk DS, Krinochkin AP, Starnovskaya ES et al (2018) 6-Arylamino-2,2′-bipyridine "push-pull" fluorophores: solvent-free synthesis and photophysical studies. ChemistrySelect 3:4141–4146. https://doi.org/10.1002/slct.201800220
39. Savchuk MI, Starnovskaya ES, Shtaitz YK et al (2018) Synthesis of 5-Phenyl-2,2'-bipyridines 6-Substituted with Donor Groups by aza-Diels–Alder Reactions of 5-R-1,2,4-Triazines under High Pressure Conditions. Russ J Gen Chem 88:2213–2215. https://doi.org/10.1134/S1070363218100316
40. Frisch MJ, Trucks GW, Schlegel HB et al (2010) Gaussian 09, Revision C.01, Gaussian, Inc., Wallingford, CT
41. Lu T, Chen F (2012) Multiwfn: A multifunctional wavefunction analyzer. J Comput Chem 33:580–592. https://doi.org/10.1002/jcc.22885
42. Kozhevnikov VN, Kozhevnikov DN, Nikitina TV et al (2003) 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 68:2882–2888. https://doi.org/10.1021/jo0267955
43. Kozhevnikov VN, Shabunina OV, Kopchuk DS et al (2008) Facile synthesis of 6-aryl-3-pyridyl-1,2,4-triazines as a key step toward highly fluorescent 5-substituted bipyridines and their Zn(II) and Ru(II) complexes. Tetrahedron 64:8963–8973. https://doi.org/10.1016/j.tet.2008.06.040
44. Reichardt C (2006) Solvents and solvent effects in organic chemistry, 3rd, updated and enlarged edition, 3rd edn. WILEY-VCH Verlag GmbH & Co, KGaA
45. Reichardt C (1994) Solvatochromic dyes as solvent polarity indicators. Chem Rev 94:2319–2358. https://doi.org/10.1021/cr00032a005
46. Kosower EM (1958) The effect of solvent on spectra. I. A new empirical measure of solvent polarity: Z-values. J Am Chem Soc 80:3253–3260. https://doi.org/10.1021/ja01546a020
47. Kosower EM (1968) Introduction to physical organic chemistry hardcover. John Wiley & Sons
48. Lakowicz JR (2006) Principles of Fluorescence Spectroscopy, 3rd edn. Springer, US, Boston, MA
49. Mataga N, Kaifu Y, Koizumi M (1956) Solvent effects upon fluorescence spectra and the dipolemoments of excited molecules. Bull Chem Soc Jpn 29:465–470. https://doi.org/10.1246/bcsj.29.465
50. Lippert E (1957) Spektroskopische bestimmung des dipolmomentes aromatischer verbindungen im ersten angeregten singulettzustand. Electro chem 61:962–975
51. Zhao YH, Abraham MH, Zissimos AM (2003) Fast calculation of van der Waals volume as a sum of atomic and bond contributions and its application to drug compounds. J Org Chem 68:7368–7373. https://doi.org/10.1021/jo034808o
52. Le Bahers T, Adamo C, Ciofini I (2011) A qualitative index of spatial extent in charge-transfer excitations. J Chem Theory Comput 7:2498–2506. https://doi.org/10.1021/ct200308m