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# One "Click" to Access Push–Triazole–Pull Fluorophores Incorporating a Pyrimidine Moiety: Structure–Photophysical Properties Relationships

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Using copper-catalysed Huisgen 1,3-dipolar cycloaddition, we describe the synthesis of new A-π-D compounds containing a pyrimidine moiety as π-acceptor (A) and various *para*-substituted benzene rings as donors (D). Structure–photophysical properties relationships revealed the triazole ring to be a better π-conjugated linker than the triple bond.

## Introduction

During the last decade, a great deal of effort has been put into the design and synthesis of new push–pull organic dyes[1] due to their non-linear optical (NLO) properties,[2] in particular in optoelectronics,[3] biological imaging,[4] and dye-sensitized solar cells.[5] These push–pull dyes have also attracted attention as fluorophores, and most of them act as fluorescent sensors, as they have an emission response that depends on their environment.[6] Generally, these push–pull chromophores have an A-π-D structure, where A is an acceptor moiety and D is an electron-donating group connected by a π-conjugated linker. They have received much interest due to their high polarizability. Extensive investigations have been carried out into the synthesis of new A-π-D chromophores and the evaluation of their light-emitting properties.

Due to its electron-withdrawing character, the pyrimidine moiety was chosen as the acceptor part incorporated into the compounds reported in this paper. This diazine moiety has already been incorporated as an electron-withdrawing core or end-cap into linear, star- and banana-shaped oligomers that show good light-emitting properties[7,8] and two-photon absorption.[7,9]

To extend the conjugation along the scaffold of the push–pull chromophores, various conjugated linkers have been described, such as ethynyl or vinyl linkers. More recently, and since the independent discoveries of the $Cu^{I}$-catalysed Huisgen 1,3-dipolar cycloaddition (CuAAC: copper-catalysed azide–alkyne cycloaddition) by Sharpless and Meldal ten years ago,[10] triazole rings have been used as components of several fluorogenic probes,[11] as chelating ligands in fluorescent metal sensors,[12] and less frequently as linkers in the conjugated backbone of push–pull fluorophores.[13]

In some cases, push–triazole–pull (PTP) chromophores incorporating 1,2,3-triazole rings as linkers have been reported to show low to moderate fluorescent properties. However, some of them show a switchable fluorescence, being activated by the addition of metal cations.[13b] Others have been developed as dual-fluorescent pH sensors,[13c] and it may be noted that some of them have good quantum yields.[13a] Previously, the synthesis and light-emitting properties of D-π-A-π-D or A-π-D fluorophores with diazine moieties as acceptor (A), ethynyl or vinylene linkers (π), and aromatic rings (D) have been reported in the literature. The main advantages of the ethynyl linker over its vinylene counterpart are the lack of possible (*Z*)/(*E*) isomerism and its higher stability.[14] With the aim of comparing the influence of the backbones of A-π-D fluorophores on their light-emitting properties, and to establish structure–photophysical properties relationships, "click chemistry" has been used to incorporate a triazole linker instead of an ethynyl one to access new PTP backbones.

The aim of this work was to synthesize a wide range of new fluorophores to determine the influence of the different parts (acceptor, π-conjugated linker, and donor) on the optical properties. The use of readily available and cheap non-fluorescent starting materials to synthesize new fluorophores containing a triazole ring as the transmitter of conjugation was an interesting challenge. The light-emitting properties were determined, and the results were compared to theoretical calculations at the DFT6-31G* level. A study of emission solvatochromism was also performed to determine the influence of solvent polarity on the intramolecular charge transfer (ICT).

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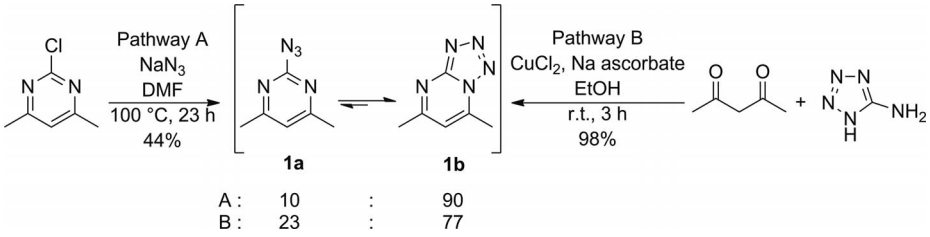


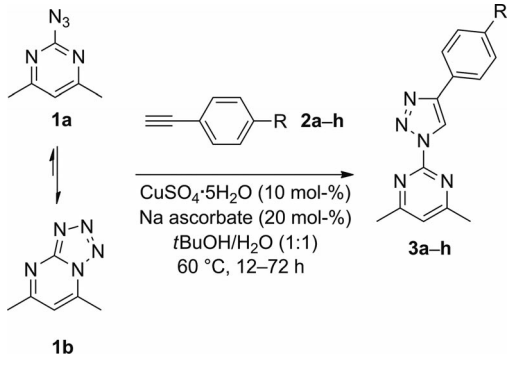

Scheme 1. Synthesis of 2-azido-4,6-dimethylpyrimidine.

## Results and Discussion

Azidopyrimidine starting material **1** was obtained by two pathways A and B (Scheme 1). Pathway A involved nucleophilic aromatic substitution of 2-chloro-4,6-dimethylpyrimidine by $NaN_3$ to give **1** in a moderate 44% yield. Pathway B, involving a cyclodehydration of pentane-2,4-dione with 5-aminotetrazole, gave **1** in an excellent yield of 98%.[15] Although pathway A was discarded due to a lower yield, this nucleophilic substitution has the advantage that it could potentially be applied to a wider range of π-deficient azaheterocycles.

A tautomeric equilibrium between the major tetrazolo form (i.e., **1b**) and 2-azido-4,6-dimethylpyrimidine (**1a**) was observed by $^1H$ NMR spectroscopy in $CDCl_3$ (see Supporting Information). Tetrazole **1b** arises from a spontaneous cyclization between the azido group and the adjacent pyrimidine nitrogen atom (Scheme 1). Such an equilibrium has been described previously in π-deficient heterocycles like pyrimidine that have an azido substituent at C-2.[15,16]

Generally, to induce the copper-catalysed Huisgen 1,3-dipolar cycloaddition, the use of $Cu^I$ salts is necessary. Classical conditions involving the in situ reduction of $Cu^{II}$ salts by sodium ascorbate were used to synthesize 1,4-disubstituted-1,2,3-triazolo derivatives **3a**–**h** (Scheme 2) in good to excellent yields (58–99%, Table 1). This efficient method allowed us to access various chromophores.




Scheme 2. Copper-catalysed azide–alkyne cycloaddition.

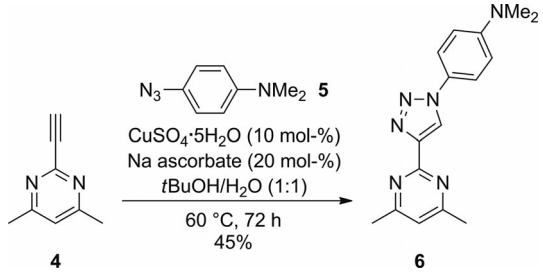
A similar strategy was used to obtain compound **6** (Scheme 3), a regioisomer of **3a**, by carrying out the "click" reaction between 4-azido-*N*,*N*-dimethylaniline[17] (**5**) and 2-ethynyl-4,6-dimethylpyrimidine[18] (**4**).

In order to study the influence of the electron-withdrawing part on the photophysical properties, an analogue of **3a** bearing a 4-cyanophenyl moiety instead of a pyrimidine ring was synthesized. The CuAAC of commercially available 4-ethynyl-*N*,*N*-dimethylaniline (**2a**) and 4-azidobenzonitrile[19] (**7**) gave PTP fluorophore **8** in a low yield (Scheme 4).

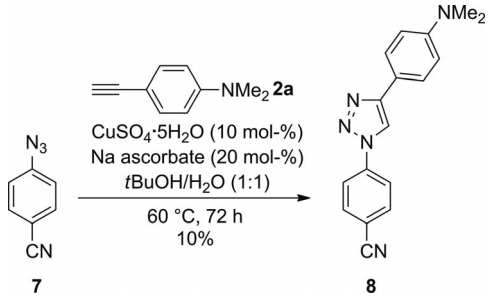
Table 1. Synthesis of push–triazole–pull fluorophores by CuAAC.

| Compound[a] | R | Isolated yield [%] |
|---|---|---|
| **3a** | $NMe_2$ | 79 |
| **3b** | $NPh_2$ | 96 |
| **3c** | $NH_2$ | 58 |
| **3d** | OMe | 99 |
| **3e** | F | 82 |
| **3f** | $CH_3$ | 72 |
| **3g** | H | 89 |
| **3h** | $CF_3$ | 75 |

[a] All reactions were performed on a 0.03 mmol scale with equimolar proportions of azide **1** and alkyne **2**.




Scheme 3. Synthesis of **6**, an isomer of **3a**.




Scheme 4. CuAAC synthesis of cyanobenzene PTP derivative.

The final part of this study consisted of the evaluation of the influence of the π-linker on the photophysical properties. To this end, an ethynyl linker was introduced into the backbone in place of the triazole by a Sonogashira cross-coupling reaction (Scheme 5), which led to **10** in 81% yield.

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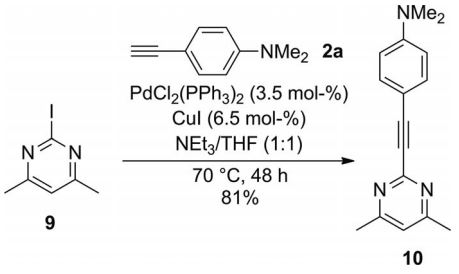


Scheme 5. Sonogashira cross-coupling reaction.

All new compounds were characterized by using a variety of analytical techniques. These materials are perfectly stable in the solid state, and can be stored without special precautions.

## UV/Vis and Photoluminescence (PL) Data

The optical properties of the fluorophores synthesized (**3a**–**h**, **6**, **8**, and **10**) were investigated in $CH_2Cl_2$ at 25 °C by UV/Vis and photoluminescence (PL) spectroscopy. These data are summarized in Table 2. All of the compounds have absorption wavelengths ($\lambda_{abs}$) in the UV region (244–357 nm), and have their emission wavelengths ($\lambda_{em}$) in the UV or green region (345–527 nm). For compounds **3a**–**h**, the fluorescence properties are influenced by the nature of the *para* substituent on the benzene ring.

Table 2. UV/Vis and photoluminescence data.

| Compound[a] | $\lambda_{abs,max}$ [nm] | $\varepsilon$ [$M^{-1}cm^{-1}$] | $\lambda_{em,max}$ [nm] | $\Phi_F$[b] | Stokes shift [$cm^{-1}$] |
|---|---|---|---|---|---|
| **3a** | 289 | 24386 | 486 | 0.47[c] | 14026 |
| **3b** | 333 | 21427 | 476 | 0.45[c] | 9022 |
| **3c** | 267 | 25698 | 476 | 0.30[c] | 16445 |
| **3d** | 254 | 46211 | 389 | 0.01[c] | 13663 |
| **3e** | 244 | 18069 | 345 | <0.01[c] | 11998 |
| **3f** | 250 | 18943 | 364 | <0.01[c] | 12527 |
| **3g** | 246 | 25697 | – | – | – |
| **3h** | 254 | 20753 | – | – | – |
| **6** | 250 | 13893 | 434 | 0.33[c] | 16958 |
| **8** | 285 | 19887 | 527 | 0.36[c] | 16112 |
| **10** | 357 | 42161 | 447 | 0.04[d] | 5640 |

[a] All spectra were recorded in $CH_2Cl_2$ at 25 °C. [b] Quantum yield (±10%) of fluorescence determined by using harmane in 0.1 M $H_2SO_4$ as a standard ($\Phi_F$ = 0.83). [c] Excitation at 300 nm. [d] Excitation at 360 nm.

A comparison of the amino compounds **3a**–**c** reveals that the $\lambda_{abs}$ values are dependent on the substituents on the nitrogen atom. With a dimethylamino group (in compound **3a**), the $\lambda_{abs}$ and $\lambda_{em}$ values and the quantum yield $\Phi_F$ were found to be higher than with an amino group (in compound **3c**). This bathochromic shift is due to the highly electron-donating character of the dimethylamino group. The diphenylamino group (in compound **3b**) resulted in a high $\lambda_{abs}$ (333 nm) and a good quantum yield $\Phi_F$ (0.45). The methoxy group (in compound **3d**), which is a less effective donor than the amino group, gave lower values for $\lambda_{abs}$ (244 nm) and $\lambda_{em}$ (389 nm) and a dramatic decrease of the quantum yield $\Phi_F$ (0.01). An examination of the data for compounds **3e**–**h** reveals similar values for the absorption wavelengths $\lambda_{abs}$ (244–254 nm). Compounds **3g** and **3h**, with a hydrogen atom or an electron-withdrawing $CF_3$ group, are non-emissive, whereas slightly electron-donating groups such as the methyl group (inductive donor effect) in compound **3e** or the fluorine atom (deactivating substituent, mesomeric donor effect) in compound **3f** result in low emission wavelengths $\lambda_{em}$ (345–364 nm) and lower quantum yields $\Phi_F$ (<0.01). Generally, large Stokes shifts were observed. For the first series (compounds **3a**–**h**), the correlations of the maximum absorbance and emission wavelengths with the Hammett reaction constants[20] are represented in Figure 1 and were found to be linear.

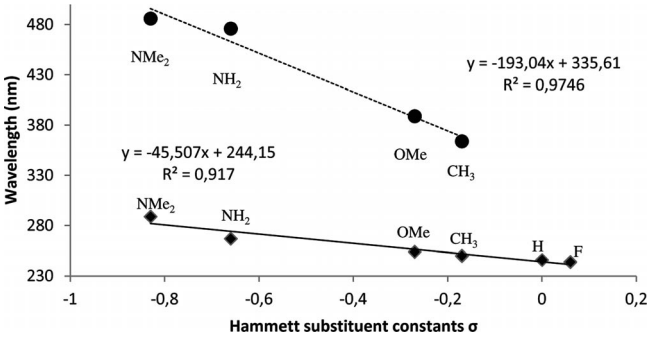


Figure 1. Linear dependences of the maximum absorbance (diamonds) and emission (dots) wavelengths on the Hammett substituent constants for compounds **3a**–**h**.

To evaluate the influence of the structural parts of the scaffold on the light-emitting properties, we compared the data of compounds **3a**, **6**, **8**, and **10**. The backbone of these chromophores differs in the nature of the π-linker between the pyrimidine ring and the *para*-(dimethylamino)phenyl group for **3a**, **6**, and **10**, whereas compounds **3a** and **8** differ in the nature of the electron-withdrawing ring, a pyrimidine for **3a**, and a benzonitrile for **8**.

Triazolo isomers **3a** and **6** show similar photophysical properties in terms of both quantum yields and Stokes shifts. However, hypsochromic shifts were observed in the absorption and emission wavelengths for **6** and compared to its analogue **3a**, which had a higher molar extinction coefficient ($\varepsilon$). Replacement of the triazole ring in **3a** by the ethynyl linker in compound **10** resulted in a higher molar extinction coefficient $\varepsilon$ (42161 vs. 24386), but a dramatic decrease of both quantum yield $\Phi_F$ (0.04 vs. 0.47) and Stokes shift (5640 vs. 14026) was observed. When the pyrimidine ring was replaced by the benzonitrile group, a comparison of the data of compounds **3a** and **8** revealed similar values for the absorption wavelength and quantum yield, and a slightly higher Stokes shift for **8**. Moreover, a significant redshift of the emission wavelength was observed for compound **8**. These results could indicate that compound **8** is a better fluorophore than **3a**, but in spite of this, the much better yields observed in the synthesis of **3a** make this compound attractive for further applications.

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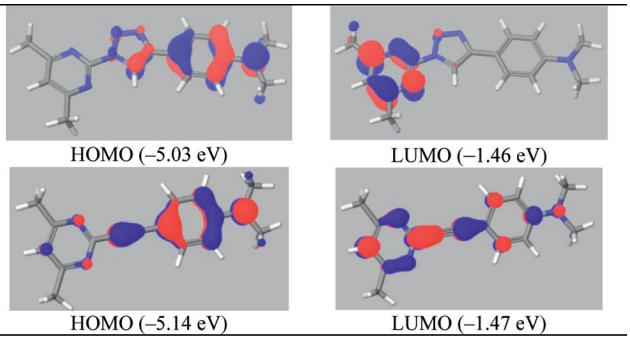
## Molecular Orbital Calculations

To gain insight into the effect of the various substituents on the geometrical and electronic properties of the chromophores, density functional theory (DFT) and time-dependent DFT (TD-DFT) calculations were carried out on the synthesized compounds **3a**–**h**, **6**, and **10** by using the Gaussian 03 and 09 program packages.[21] The geometries of all of the studied systems were optimized by using the B3LYP exchange–correlation hybrid functional together with the 6-31G** basis set. The in vacuo structures were further optimized by applying the self-consistent reaction field (SCRF) under the polarizable continuum model (C-PCM) incorporating dichloromethane as the solvent. The DFT-computed HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) frontier molecular orbitals (FMOs) of chromophores **3a** and **10** are presented in Table 3 (see Supporting Information for compounds **3b**–**h** and **6**). Examination of the computer-modelled structures of the studied systems reveals some common features, such as an absolutely coplanar structure, except for **6**, in which the phenyl ring is slightly out of the plane of the rest of the molecule (dihedral angle 35.9 °). A comparison of the electronic structures reveals that the localization and nature of the HOMO and LUMO are almost the same for all of the individual homologues (see Table 3), the only difference being in the energies of these FMOs, which depend on the structure.[22] The HOMO orbitals of all of the chromophores showed the same character, being localized on the benzene and triazole rings. Changing the nature of the R group connected to the benzene ring had a great influence on the HOMO energy level.

Table 3. HOMO and LUMO levels of chromophores **3a** and **10**.




To shed some light on the optical absorption process, we used TD-DFT to study the vertical excitation in chromophores **3a**–**h**, **6**, and **10**. Singlet vertical excitation energies were determined by using both B3LYP and CAM-B3LYP[23] exchange–correlation functionals. The results of the TD-DFT calculations with the B3LYP functional are reported in Table 4, in which the observed absorption wavelength is compared to the calculated value corresponding to the largest oscillator strength (*f*). In most cases, the calculated and experimental values are well correlated, with a maximum difference of 2.8% for compound **3a**. It is well established that the low percentage of exact orbital exchange in B3LYP can lead to an underestimation of the charge-transfer interactions for extended systems.[24] The use of CAM-B3LYP, which is a Coulomb-attenuated functional, usually provides significantly improved long-range excitation energies.[25] However, it must be noted that the use of the CAM-B3LYP functional gave bad results, probably because our systems are not very extended, so allowing the classic B3LYP functional to still be efficient. Moreover, it can be seen that the HOMO–LUMO gaps are also in good agreement with the observed absorption properties. Increasing the strength of the donor group connected to the benzene ring led to a decrease in the gap, which explains the bathochromic effect. The lower absorption wavelength observed with compound **8** is due to the above-mentioned deconjugation of the (dimethylamino)phenyl moiety. Changing the triazole linker (in compound **3a**) into a triple bond (in compound **10**) slightly increased the HOMO–LUMO gap. However, this fact does not explain the bathochromic shift observed. It must also be pointed out that the UV spectrum of compound **10** showed two absorption bands, probably due to the topology of the triple bond. These two absorption bands were nicely predicted by TD-DFT calculations (Table 4), and are related to different transitions: HOMO–LUMO for the higher (calculated at 370 nm) and mainly (HOMO–1)–LUMO for the lower (calculated at 240 nm). For these reasons, comparisons are not easy to establish, and the above mentioned redshift could be simply explained by the triazole linker's having a better electronic transfer than that of the triple bond. Moreover, the fact that the LUMO of **10** is still slightly located on the phenyl ring, in contrast to the LUMO of **3a**, confirms the better efficiency of the triazole linker, and could explain the significant difference in the quantum yield.

Table 4. HOMO–LUMO gaps and TD-DFT predictions of $\lambda_{abs}$.

| Compound | $\lambda_{abs,max}$ [nm] | $\lambda_{abs,calcd.}$ [nm] | Strongest *f* | R | HOMO–LUMO gap [eV] |
|---|---|---|---|---|---|
| **3a** | 289 | 281.2 | 0.603 | $NMe_2$ | 3.57 |
| **3b** | 333 | 333.2 | 0.566 | $NPh_2$ | 3.51 |
| **3c** | 267 | 267.8 | 0.790 | $NH_2$ | 3.77 |
| **3d** | 254 | 254.9 | 0.706 | OMe | 4.18 |
| **3e** | 244 | 245.5 | 0.704 | F | 4.54 |
| **3f** | 250 | 249.4 | 0.921 | $CH_3$ | 4.47 |
| **3g** | 246 | 245.1 | 0.775 | H | 4.55 |
| **3h** | 254 | 255.7 | 0.326 | $CF_3$ | 4.79 |
| **6** | 250 | 244.6 | 0.617 | $NMe_2$ | 4.11 |
| **10** | 242/357 | 240/370 | 1.183 | $NMe_2$ | 3.67 |

## Solvatochromism

The photophysical properties of regioisomers **3a** and **6** were evaluated in different solvents. The aim of this study was to explore the effect of solvent polarity on the photophysical properties of the fluorophores and to correlate these effects to their structures. The photoluminescence data in aprotic solvents are summarized in Table 5, Figures 2, 3, 4, and 5. When a protic polar solvent such as

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MeOH was used, a complete quenching of the fluorescence was observed with both of the regioisomers. The absorbance spectra showed only a slight dependence on the solvent polarity, which is characteristic of an insignificant intramolecular interaction between the donor and acceptor end-capping fluorophores in the ground state. In contrast, a solvent-polarity-dependent emission was shown by both regioisomers **3a** and **6**. For both of these fluorophores, the maximum emission wavelength was plotted against $E_T(30)$ (the Dimroth–Reichardt polarity parameter; see Supporting

Table 5. Optical properties of **3a** and **6** in different solvents.

| Compound[a] | Solvent | $\lambda_{abs,max}$ [nm] | $\varepsilon$ [$M^{-1}cm^{-1}$] | $\lambda_{em,max}$ [nm][b] | Stokes shift [$cm^{-1}$] |
|---|---|---|---|---|---|
| **3a** | toluene | 305 | 15914 | 432 | 9639 |
| | dioxane | 284 | 26057 | 456 | 13281 |
| | THF | 278 | 1571 | 482 | 14464 |
| | EtOAc | 284 | 15090 | 480 | 14464 |
| | $CHCl_3$ | 289 | 16042 | 469 | 13280 |
| | $CH_2Cl_2$ | 289 | 24386 | 486 | 14026 |
| | DMF | 288 | 19676 | 538 | 16134 |
| | DMSO | 291 | 23177 | 556 | 16379 |
| | MeCN | 288 | 19528 | 544 | 16340 |
| **6** | toluene | 305 | 14659 | 390 | 7146 |
| | dioxane | 301 | 18220 | 421 | 9469 |
| | THF | 305 | 15291 | 428 | 9422 |
| | EtOAc | 300 | 19604 | 428 | 9968 |
| | $CHCl_3$ | 305 | 15807 | 420 | 9146 |
| | $CH_2Cl_2$ | 250, 306 | 13893, 12834 | 434 | 16958, 9638 |
| | DMF | 306 | 18485 | 488 | 12188 |
| | DMSO | 311 | 18809 | 503 | 12274 |
| | MeCN | 301 | 18014 | 496 | 13061 |

[a] All spectra were recorded at 25 °C. [b] Excitation at 300 nm.

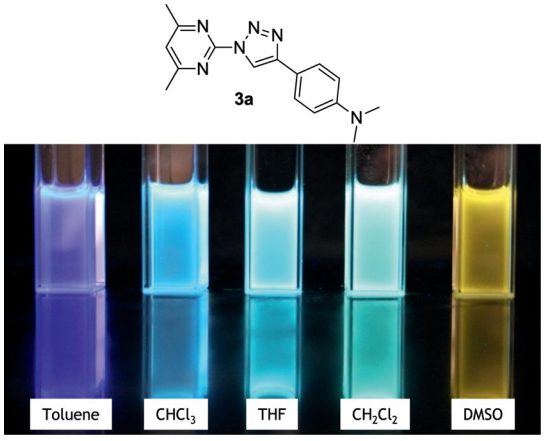


Figure 2. Structure and colour changes of compound **3a** in various solvents.

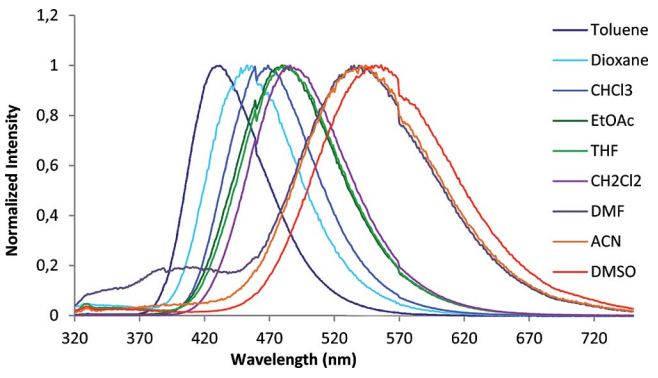


Figure 3. Normalized emission spectra of compound **3a** in various solvents.

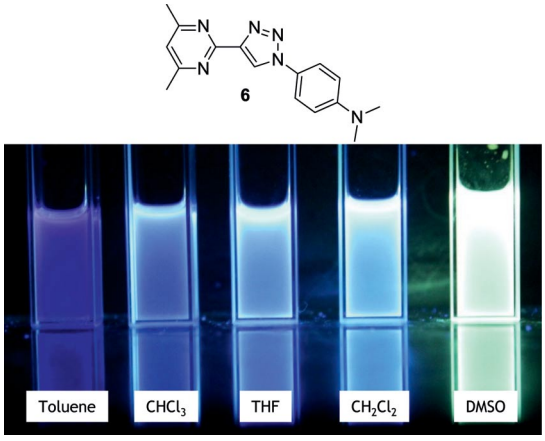


Figure 4. Structure and colour changes of compound **6** in various solvents.

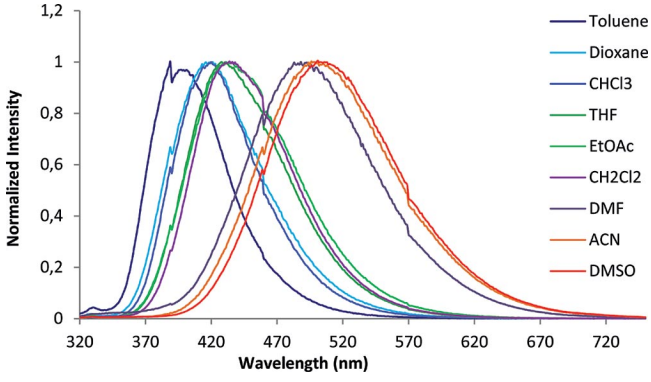


Figure 5. Normalized emission spectra of compound **6** in various solvents.

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Information).[26] Furthermore, broad structureless emission and larger Stokes shifts were observed when the solvent polarity was increased. Thus, a redshift of 124 and 113 nm for **3a** and **6**, respectively, was observed on changing from toluene to DMSO, which is characteristic of internal charge transfer upon excitation.

## Conclusions

By using an efficient click-chemistry strategy, push–triazole–pull chromophores were synthesized in good to excellent yields, and interesting fluorescence properties were observed. The influence of the *para* substituent borne by the phenyl ring was evaluated, and this showed that increasing the strength of the electron-donating group increased the fluorescence properties and induced a bathochromic shift. We also demonstrated that a triazole linker offers better photoluminescence properties than an ethynyl linker. Furthermore, theoretical calculations support our experimental results. The PTPs **3a** and **6** showed strong emission solvatochromism, and redshifted broad structureless bands were obtained in polar aprotic solvents, which is characteristic of intramolecular charge-transfer in excited states.

Further development of new chromophores and evaluation of these N-heterocyclic chelators in ligand–metal interactions are currently underway in our laboratory.

## Experimental Section

**General Remarks:** All chemicals were purchased from commercial sources and used without further purification unless otherwise specified. Analytical thin layer chromatography was performed on silica gel plates (Merck® TLC Silica gel 60 $F_{254}$), and compounds were detected by irradiation with UV light (254 nm). Chromatographic purification of compounds was achieved with silica gel (mesh size 60–80 μm). IR spectra were recorded with a Perkin–Elmer Spectrum 100 FT IR spectrometer. HRMS spectra ($ESI^+$) were recorded with an LC Waters Acquity coupled to a Waters LCT Premier XE instrument. Elemental analyses were performed with a Carlo Erba 1106 apparatus. Measurement accuracy is around ±0.4% on C. Melting points were measured with a Kofler bench. The $^1H$, $^{19}F$, and $^{13}C$ NMR spectra were recorded with a Bruker Avance spectrometer operating at 300, 282, and 75 MHz, respectively. The chemical shifts $\delta$ are reported in parts per million (ppm), and the residual solvent peaks were used as an internal reference [$\delta$ = 7.26 ($^1H$) and 77.16 ($^{13}C$) ppm for $CDCl_3$; $\delta$ = 0.00 ($^{19}F$) ppm for $CFCl_3$]. Data appear in the following order: chemical shift in ppm, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant $J$ in Hz, number of protons.

**2-Azido-4,6-dimethylpyrimidine (1a) and 5,7-Dimethyltetrazolo[1,5-*a*]pyrimidine (1b)**

**Method A:** A solution of 2-chloro-4,6-dimethylpyrimidine (1.06 g, 7.4 mmol) in DMF (48 mL) was treated with $NaN_3$ (1.82 g, 31.3 mmol) at 100 °C for 21 h. The solvent was evaporated under reduced pressure, and the residue was purified by silica gel flash chromatography (EtOAc) to give 2-azido-4,6-dimethylpyrimidine (486 mg, 44%, **1a** and **1b** combined).

**Method B:** $CuCl_2$ (20.1 mg, 0.15 mmol) was dissolved in EtOH (4.5 mL), resulting in a green solution. Sodium ascorbate (26.4 mg, 0.15 mmol) was added, and the mixture was stirred for 5 min to give a colourless, homogeneous mixture. Pentane-2,4-dione (0.15 mL, 1.50 mmol) and 1*H*-tetrazol-5-amine (127.5 mg, 1.50 mmol) were added, and the resulting mixture was stirred at room temperature for 3 h. $NH_4Cl$ (satd. aq.; 15 mL) was added, and the resulting suspension was extracted with EtOAc (5× 30 mL). The organic extracts were dried with $Na_2SO_4$ and concentrated in vacuo to give a mixture of compounds **1a** and **1b** (219 mg, 98%, **1a** and **1b** combined) as a white powder.

**Data for 1a**: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 2.42 (s, 6 H, $CH_3$), 6.76 (s, 1 H, 5-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 23.9 ($CH_3$), 116.2, 161.8, 169.3 ppm.

**Data for 1b**: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 2.75 (s, 3 H, $CH_3$), 2.95 (s, 3 H, $CH_3$), 6.94 (s, 1 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.1, 25.5, 112.8, 144.7, 155.2, 169.1 ppm. HRMS: calcd. for $C_6H_8N_5$ $[M + H]^+$ 150.0780; found 150.0777.

**General Procedure for the [3 + 2] Cycloaddition of Azides and Terminal Alkynes:** Sodium ascorbate (9.3 mg, 0.047 mmol) and $CuSO_4{\cdot}5H_2O$ (5.9 mg, 0.024 mmol) were added to a mixture of 5,7-dimethyltetrazolo[1,5-*a*]pyrimidine (**1**; 35.0 mg, 0.235 mmol) and alkyne **2** (0.235 mmol) in a mixture of $H_2O$/*t*BuOH (1:1, 1 mL). The mixture was stirred at 60 °C for 72 h. Then $NH_3$ (dilute aqueous; 10 mL) was added, and the crude mixture was extracted with EtOAc (3× 10 mL). The organic layer was dried with $MgSO_4$ and filtered, and the solvents were evaporated. The title triazolyl compounds were purified by column chromatography (EtOAc).

**4-[1-(4,6-Dimethylpyrimidin-2-yl)-1*H*-1,2,3-triazol-4-yl]-*N*,*N*-dimethylaniline (3a):** By using the general procedure and starting from **1** (32 mg) and 4-ethynyl-*N*,*N*-dimethylaniline (**2a**; 88 mg), title compound **3a** (27 mg, 79%) was isolated as a yellow powder; m.p. 199–201 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 2.60 (s, 3 H), 2.99 (s, 6 H), 6.78 (d, $J$ = 8.97 Hz, 2 H), 7.05 (s, 1 H), 7.82 (d, $J$ = 8.97 Hz, 2 H), 8.66 (s, 1 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 24.2, 40.6, 112.5, 116.8, 118.3, 119.6, 127.1, 148.5, 150.7, 154.3, 169.6 ppm. IR (neat): $\tilde{\nu}$ = 3167, 2924, 2856, 2810, 1657, 1599, 1534, 1510, 1421, 1345, 1227, 1194 $cm^{-1}$. HRMS: calcd. for $C_{16}H_{19}N_6$ $[M + H]^+$ 295.1676; found 295.1671.

**4-[1-(4,6-Dimethylpyrimidin-2-yl)-1*H*-1,2,3-triazol-4-yl]-*N*,*N*-diphenylaniline (3b):** By using the general procedure and starting from **1** (45 mg) and **2b** (81 mg), title compound **3b** (120 mg, 96%) was isolated as a white powder; m.p. 200–202 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 2.62 (s, 1 H), 7.02–7.16 (m, 9 H), 7.25–7.30 (m, 4 H), 7.82 (d, $J$ = 8.7 Hz, 2 H), 8.74 (s, 1 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 24.2, 117.9, 123.3, 123.7, 124.8, 127.2, 129.5, 147.6, 148.3, 169.8 ppm. IR (neat): $\tilde{\nu}$ = 3166, 2922, 2853, 1599, 1539, 1488, 1470, 1424, 1329, 1269, 1240, 1177 $cm^{-1}$. HRMS: calcd. for $C_{26}H_{23}N_6$ $[M + H]^+$ 419.1984; found 419.1990.

**4-[1-(4,6-Dimethylpyrimidin-2-yl)-1*H*-1,2,3-triazol-4-yl]aniline (3c):** By using the general procedure and starting from **1** (36 mg) and 4-ethynylaniline (**2c**; 28 mg), title compound **3c** (36 mg, 58%) was isolated as a beige powder (58%); m.p. 221–223 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 2.59 (s, 6 H), 6.74 (d, $J$ = 8.7 Hz, 2 H), 7.06 (s, 1 H), 7.73 (d, $J$ = 8.7 Hz, 2 H), 8.66 (s, 1 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 24.1, 112.8, 115.3, 117.1, 119.6, 120.6, 127.4, 146.9, 148.3, 154.2, 169.7 ppm. IR (neat): $\tilde{\nu}$ = 3426, 3347, 3241, 3176, 1640, 1616, 1602, 1534, 1504, 1472, 1421, 1348, 1299, 1226, 1182 $cm^{-1}$. $C_{14}H_{14}N_6$ (266.30): calcd. C 63.14, H 5.30, N 31.56; found C 63.34, H 5.03, N 31.60.

**2-[4-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-1-yl]-4,6-dimethylpyrimidine (3d):** By using the general procedure and starting from **1** (35 mg) and 1-ethynyl-4-methoxybenzene (**2d**; 31 mg), title com-

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pound **3d** (66 mg, 99%) was isolated as a beige powder; m.p. 138–140 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.56 (s, 6 H), 3.80 (s, 3 H), 6.93 (d, $J$ = 8.85 Hz, 2 H), 7.03 (s, 1 H), 7.84 (d, $J$ = 8.85 Hz, 2 H), 8.68 (s, 1 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 24.0, 55.4, 114.2, 117.6, 119.7, 122.8, 127.4, 147.7, 154.0, 159.8, 169.6 ppm. IR (neat): $\tilde{\nu}$ = 3161, 2959, 2928, 2836, 1600, 1534, 1501, 1472, 1441, 1345, 1250, 1176 cm$^{-1}$. HRMS: calcd. for $C_{15}H_{15}N_5O$ $[M + H]^+$ 282.1355; found 282.1337.

**2-[4-(4-Fluorophenyl)-1*H*-1,2,3-triazol-1-yl]-4,6-dimethylpyrimidine (3e):** By using the general procedure and starting from **1** (35 mg) and 1-ethynyl-4-fluorobenzene (**2e**; 28 mg), title compound **3e** (52 mg, 82%) was isolated as a beige powder; m.p. 199–201 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.57 (s, 6 H), 7.06–7.13 (m, 3 H), 7.86–7.91 (m, 2 H), 8.74 (s, 1 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 24.1, 115.7, 116.0, 118.2, 119.9, 126.3, 126.4, 127.8, 127.9, 147.0, 154.0, 161.2, 164.5, 169.7 ppm. $^{19}$F NMR (282 MHz, $CDCl_3$): $\delta$ = –113.6 ppm. IR (neat): $\tilde{\nu}$ = 3167, 3068, 2922, 2853, 1729, 1600, 1498, 1432, 1414, 1343, 1222, 1025 cm$^{-1}$. HRMS: calcd. for $C_{14}H_{13}N_5F$ $[M + H]^+$ 270.1155; found 270.1161.

**4,6-Dimethyl-2-(4-*p*-tolyl-1*H*-1,2,3-triazol-1-yl)pyrimidine (3f):** By using the general procedure and starting from **1** (35 mg) and 1-ethynyl-4-methylbenzene (**2f**; 27 mg), title compound **3f** (45 mg, 72%) was isolated as a beige powder; m.p. 169–171 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.38 (s, 3 H), 2.60 (s, 6 H), 7.07 (s, 1 H), 7.22 (d, $J$ = 7.8 Hz, 2 H), 7.84 (d, $J$ = 7.8 Hz, 2 H), 8.77 (s, 1 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 21.4, 24.1, 118.2, 119.8, 126.1, 127.4, 129.6, 138.5, 148.0, 154.2, 169.7 ppm. IR (neat): $\tilde{\nu}$ = 3163, 2958, 2918, 2851, 1602, 1539, 1474, 1436, 1426, 1347, 1232, 1029 cm$^{-1}$. HRMS: calcd. for $C_{15}H_{16}N_5$ $[M + H]^+$ 266.1406; found 266.1411.

**4,6-Dimethyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)pyrimidine (3g):** By using the general procedure and starting from **1** (32 mg) and ethynylbenzene (**2g**; 88 mg), title compound **3g** (48 mg, 89%) was isolated as a white powder; m.p. 179–181 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.60 (s, 6 H), 7.07 (s, 1 H), 7.35 (m, 1 H), 7.44 (m, 2 H), 7.94 (m, 2 H), 8.81 (s, 1 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 24.1, 118.5, 119.8, 126.1, 128.5, 128.9, 130.1, 147.8, 154.0, 169.7 ppm. IR (neat): $\tilde{\nu}$ = 3176, 3062, 2918, 1600, 1538, 1473, 1429, 1346, 1296, 1234, 1013 cm$^{-1}$. $C_{14}H_{13}N_5$ (251.29): calcd. C 66.92, H 5.21, N 27.87; found C 66.87, H 5.22, N 27.82.

**4,6-Dimethyl-2-{4-[4-(trifluoromethyl)phenyl]-1*H*-1,2,3-triazol-1-yl}pyrimidine (3h):** By using the general procedure and starting from **1** (35 mg) and 1-ethynyl-4-(trifluoromethyl)benzene (**2h**; 40 mg), title compound **3h** (56 mg, 75%) was isolated as a white powder; m.p. 213-215 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.59 (s, 6 H), 7.08 (s, 1 H), 7.66 (d, $J$ = 8.4 Hz, 2 H), 8.04 (d, $J$ = 8.1 Hz, 2 H), 8.88 (s, 1 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 24.1, 119.5, 120.1, 125.8, 125.9, 126.2, 133.6, 146.5, 153.9, 169.9 ppm. $^{19}$F NMR (282 MHz, $CDCl_3$): $\delta$ = –63.1 ppm. IR (neat): $\tilde{\nu}$ = 3170, 3098, 2923, 2852, 1605, 1539, 1471, 1429, 1321, 1298, 1029, 1015 cm$^{-1}$. HRMS: calcd. for $C_{15}H_{13}N_5F_3$ $[M + H]^+$ 320.1123; found 320.1126.

**4-[4-(4,6-Dimethylpyrimidin-2-yl)-1*H*-1,2,3-triazol-1-yl]-*N*,*N*-dimethylaniline (6):** By using the general procedure and starting from 4-azido-*N*,*N*-dimethylaniline (**5**;[13] 39 mg) and 2-ethynyl-4,6-dimethylpyrimidine (**4**;[14] 32 mg), title compound **6** (34 mg, 75%) was isolated as a white powder; m.p. 117–119 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.57 (s, 6 H), 3.03 (s, 6 H), 117–119 (d, $J$ = 9 Hz, 2 H), 6.97 (s, 1 H), 7.63 (d, $J$ = 9 Hz, 2 H), 8.56 (s, 1 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 24.1, 40.5, 112.3, 118.7, 122.0, 122.8, 126.6, 150.7, 158.6, 167.3 ppm. IR (neat): $\tilde{\nu}$ = 3467, 3141, 2922, 2807, 1611, 1589, 1525, 1430, 1363, 1344, 1278, 1168 cm$^{-1}$. HRMS: calcd. for $C_{16}H_{19}N_6$ $[M + H]^+$ 295.1671; found 295.1666.

**4-{4-[4-(Dimethylamino)phenyl]-1*H*-1,2,3-triazol-1-yl}benzonitrile (8):** By using the general procedure and starting from 4-azidobenzonitrile (**7**;[15] 43 mg) and 4-ethynyl-*N*,*N*-dimethylaniline (**2a**; 43 mg), title compound **8** (9 mg, 10%) was isolated as a brown powder; m.p. 239–241 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 3.02 (s, 1 H), 6.80 (d, $J$ = 9 Hz, 2 H), 7.77 (d, $J$ = 8.7 Hz, 2 H), 7.85 (d, $J$ = 8.7 Hz, 2 H), 7.97 (d, $J$ = 8.7 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 40.5, 112.1, 112.5, 115.3, 117.6, 118.0, 120.5, 127.1, 134.0, 140.2, 149.8, 150.9 ppm. IR (neat): $\tilde{\nu}$ = 3111, 2925, 2852, 2230, 1618, 1608, 1570, 1502, 1409, 1354, 1223, 1034 cm$^{-1}$. HRMS: calcd. for $C_{17}H_{16}N_5$ $[M + H]^+$ 290.1346; found 290.1351.

**4-[(4,6-Dimethylpyrimidin-2-yl)ethynyl]-*N*,*N*-dimethylaniline (10):** Triethylamine (5 mL) and THF (5 mL) were added to 2-iodo-4,6-dimethylpyrimidine (**9**; 157.1 mg, 0.671 mmol), 4-ethynyl-*N*,*N*-dimethylaniline (**2a**; 126.7 mg, 0.873 mmol), CuI (10.2 mg, 0.044 mmol) and $PdCl_2(PPh_3)_2$ (16.5 mg, 0.024 mmol) under argon. The resulting mixture was heated at 70 °C for 72 h and then filtered through Celite®. After purification by column chromatography (EtOAc/petroleum ether, 1:1), title compound **10** (137 mg, 81%) was isolated as a beige powder; m.p. 173–175 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.50 (s, 6 H, $CH_3$), 3.00 (s, 6 H, $CH_3$), 6.64 (m, 2 H, HAr), 6.91 (s, 1 H, 5-H), 7.55 (m, 2 H, HAr) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 24.0, 40.1, 87.2, 89.5, 107.7, 111.5, 118.2, 134.1, 150.8, 153.2, 167.0 ppm. IR (neat): $\tilde{\nu}$ = 3092, 2919, 2861, 2807, 2202, 1603, 1576, 1522, 1430, 1358, 1343, 1224, 1180, 1167 cm$^{-1}$. HRMS: calcd. for $C_{16}H_{18}N_3$ $[M + H]^+$ 252.1501; found 252.1502.

**Supporting Information** (see footnote on the first page of this article): General procedures, characterization data, $^1$H and $^{13}$C NMR spectra.

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