Introduction

Fluorescent organic compounds have been a major focus of research related to materials science and biological interactions over the past decades.1 Ranging from ionic or molecular sensing2 to bioimaging applications3 and, from the organic light-emitting devices,4 bio-macromolecular interactions.5 A plethora of applications has been proposed by exploiting the beneficial properties of such materials that can raise our standard of living. In this field, the fluorogenic heterocyclic compounds display advantageous over hydrocarbon-based fluorophores such as (i) synthetic access methodologies that allow structural diversity, (ii) heteroatoms (B, N, O or S) that make them potential chelating agents for ions, and (iii) better solubility in green solvents. Consequently, various fluorogenic derivatives have been applied in diverse fields, and include coumarins,6 pyrazoles,7 perylene bisimides,8 boron dipyrromethene difluoride (BODIPY),9 cyanines,10 and rhodamines.11

Importantly, for biological and/or optoelectronics applications, ideal fluorescent probes must meet several requirements: the synthetic pathway should be straight (few steps), useful (high yields and low waste generation), and carried out by efficient heating technologies; i.e., microwave (MW) or ultrasound (US). Because a probe for bioimaging is inherently involved in complex biological interactions within the cell, the probe must be as small as possible to reduce its impacts on the biological dynamics and facilitate its diffusion inside the cell organelles.2 Likewise, for most of the photophysical applications, the fluorophore must be able to change its absorption and emission properties with small and simple chemical modifications. Fulfilling the above-mentioned conditions in a single fluorophore is a challenging task and many efforts need to be made in this direction. Recently, pyrazolo[1,5-a]pyrimidines (PPs) have emerged as an attractive alternative due to their small size based on [5,6]-fused N-heterocyclic systems, their efficient synthetic approaches12 and easy functionalization methodologies,13,14 together with their fluorescence properties (high quantum yields in different solvents, and excellent photostability).15 Usually, the PPs receive major attention in biological applications, with the cancer therapeutics field being the most attractive area.16 Very recently, Professor Jian-Feng Ge’s group found that the combination of photophysical properties with biological activities allows the use of these compounds as lipid droplet biomarkers for HeLa cells (cancer cells) and L929 cells.
A family of 7-substituted 2-methylpyrazolo[1,5-a]pyrimidines 4a–g was synthesized by a two-step synthesis sequence starting from the appropriate methyl ketone 1a–g. Compounds 4a–g were synthesized in an overall yield of 67–93% by some variations of protocols previously reported in our lab. For example, we started our work by preparing the precursor β-enaminones 2a–b and 2d–g in high yields (83–97%) via a solvent-free condensation reaction of the respective methyl ketones (1a–b and 1d–g, 1.0 mmol) with an excess of \( N,N \)-dimethylformamide-dimethylacetal (DMF-DMA, 1.5 mmol) under MW irradiation (MWI) at 180 °C for 15 min. However, the β-enaminone–coumarin derivative 2c could only be obtained (in 87% yield) under reflux for 6 h from an equimolar mixture (1 mmol) of 3-acetyl-2H-chromen-2-one (1e) and DMF-DMA in 1,4-dioxane (Scheme 1).26

Subsequently, we examined the solvent-free reaction between an equimolar mixture (0.5 mmol) of the appropriate enamine 2 and 3-methyl-1H-pyrazol-5-amine (3) under MWI at 180 °C.12 Importantly the 7-aryl-3-methylpyrazolo[1,5-a]pyrimidines (4a, 4b, 4d, 4e, and 4g) were obtained in 88–96% yield, while the novel hybrid pyrazolo[1,5-a]pyrimidines-coumarin systems 4c and 4f were obtained (in 80–87% yield) only under reflux for 3 h in acetic acid (1.0 mL). It is likely that the coumarin derivatives (2c, 2g, 4c, and 4f) decomposed under MW conditions at 180 °C (Scheme 1).

### Green chemistry performance

Since fluorophores 4a–g can be recognized as fine chemicals, for practical applications these compounds are required to fulfill some environmental issues related to their production. Therefore, a univariate green metrics analysis based on a common criterion such as reaction mass efficiency (RME) was performed27 (Tables 1 and S1–S7). The RME values found for this family of 7-substituted 2-methylpyrazolo[1,5-a]pyrimidines 4a–g were in the range of 40–53%. The high overall yield and the absence of catalysts explained the good RME performance for the synthesis of 4a–g. Remarkably, the sub-products generated during this synthesis were methanol, dimethylamine and water, useful solvents that can be recovered for use in other chemical processes. To compare the good merits found in these probes, the same calculations were performed for three BODIPY-based fluorophores, a widely used compound in materials science.28

| Compound | Overall yield (%) | RME (%) | Cost per g (USD) |
|----------|------------------|---------|------------------|
| 4a       | 85               | 43      | 2.7              |
| 4b       | 76               | 21      | 1.9              |
| 4c       | 67               | 42      | 6.1              |
| 4d       | 93               | 48      | 1.9              |
| 4e       | 90               | 51      | 1.7              |
| 4f       | 72               | 41      | 95.9             |
| 4g       | 77               | 42      | 65.7             |
| BODIPY-1 (ref. 32) | 19 | 1.3 | 98.0 |
| BODIPY-2 (ref. 33 and 34) | 50 | 17.9 | 35.8 |
| BODIPY-3 (ref. 35) | 38 | 4.4 | 162.6 |

As the starting point we used commercially available raw materials. All calculations were made as the reaction pathway started from 1.0 mmol. Solvent and silica gel used for chromatographic separations were not taken into account.28 For cost per gram calculations, the Sigma-Aldrich prices of the on-line catalog were consulted on August 25, 2020.

### Results and discussion

#### Synthesis

A family of 7-substituted 2-methylpyrazolo[1,5-a]pyrimidines 4a–g was synthesized by a two-step synthesis sequence starting from the appropriate methyl ketone 1a–g. Compounds 4a–g were synthesized in an overall yield of 67–93% by some variations of protocols previously reported in our lab. For
UV-vis and emission spectra

The UV-vis and fluorescence spectra of the 7-substituted 3-methylpyrazolo[1,5-a]pyrimidines 4a–g were measured in different solvents (Fig. 2 and 3 and Table 2). The absorption and emission spectra of these PPs are highly dependent on the nature of the substituent group at position 7. In general, the absorption spectra of 4a–g showed a main band between 340–440 nm that was previously assigned to an intramolecular charge transfer process.\textsuperscript{15,16,37} Notably, with good EDGs such as 4-aniyl 4e, 7-diethylaminocoumarin-3-yl 4f and 4-diphenylaminophenyl 4g, the absorption coefficient (\(\epsilon\)) in THF was as high as 6547, 39 867 and 15 008 M\(^{-1}\) cm\(^{-1}\), respectively. Meanwhile, the presence of EWGs in compounds 4a–c, or neutral groups (NG) such as phenyl in the derivate 4d, decreased the values of \(\epsilon\) as follows: 4a (3320 M\(^{-1}\) cm\(^{-1}\)), 4b (2727 M\(^{-1}\) cm\(^{-1}\)), 4c (7053 M\(^{-1}\) cm\(^{-1}\)), and 4d (3827 M\(^{-1}\) cm\(^{-1}\)) in the same solvent. In particular, coumarin derivatives 4e and 4f displayed the same differences in the absorption spectra as a result of the \(\pi\)-extended conjugation in the coumarin unit. For example, the absorption coefficient of the intramolecular charge transfer (ICT) band at 440 nm for 4f displayed a much higher \(\epsilon\) in THF when compared with that of 4d in the same solvent. A broad absorption band with different shoulders was also observed in compound 4c; this behavior can be attributed to a combination of the ICT phenomenon, as well as the \(\pi\)–\(\pi^*\) and n–\(\pi^*\) transitions of the coumarin and pyrazolo[1,5-a]pyrimidine moieties. In all cases, the absorption maximum wavelengths (\(\lambda_{\text{abs}}\)) were almost unchanged, irrespective of the solvent used, while their molar absorption coefficients tended to show a subtle decrease as the solvent polarity increased.

When PPs 4a–g were excited at their \(\lambda_{\text{abs}}\) in an air-equilibrated solution at 20 °C, they exhibited fluorescence bands at around 474–541 nm (Fig. 3a). For these probes, there was also an important correlation between the fluorescence quantum yield (\(\phi_F\)) and the electronic nature of the substituent at position 7 (Fig. 3b). In a solvent of intermediate polarity (i.e., THF), substituents at position 7, known as EDGs, displayed a much higher \(\phi_F\) values decreased to 0.01 (4a), 0.07 (4b), 0.06 (4c), and 0.06 (4d) in the same solvent. The fact that the \(\phi_F\) values in fluorophores 4f and 4g are remarkably high in solvents of different polarity is a notable virtue that can be useful, for example, in monitoring macromolecules dynamics\textsuperscript{5} or labeling pharmacological targets.\textsuperscript{3} Interestingly, these probes displayed good emission intensities even in polar solvents such as ethanol–water 4 : 1 or THF-water mixtures (Fig. S3†), which is a remarkable property for biological applications.

#### Figures

**Fig. 1** Structural versatility of pyrazolo[1,5-a]pyrimidine-based N-heterocycles.

**Fig. 2** (a) Absorption spectra of compounds 4a–g in THF. (b) Plot of the absorption coefficients of probes 4a–g versus solvent (1 \(\times\) 10\(^{-5}\) M) at 20 °C.

**Fig. 3** (a) Emission spectra of compounds 4a–g in THF. (b) A plot of the quantum yields of probes 4a–g versus solvent (1 \(\times\) 10\(^{-5}\) M) at 20 °C.
Apparent quantum yield for probes in SS. The emission shift of DES interacts with the dipoles of the solvent and thus, the acceptor, which creates a highly dipolar excited state (DES). The charge is transferred from the donor group to the acceptor, resulting in a more polar excited state.

In order to evaluate the solvatochromic features of PPs 4a–g, the relationship between the solvent polarity parameter ($\Delta f$) and the Stokes shift ($\Delta \lambda$), according to the Lippert–Mataga equation, was investigated. From the plots of $\Delta \lambda$ versus $\Delta f$ (Fig. 4), it was found that the slopes of the fitting lines for 4a, 4f and 4g were high, at 10 390, 9381 and 11 015, with acceptable linearity, suggesting that the ICT in these compounds have a larger dipole moment than the ground state due to important charge redistribution. The dipole moment changes ($\Delta \mu$) in those compounds were calculated to be 10.3, 12.8 and 19.0 D. Interestingly, compound 4a with pyridine as an EWG at position 7 displayed a stronger solvatofluorochromic effect than that observed in 4e bearing an EDG in the same position. This behavior can be explained by the π-amphoteric donor/acceptor property in the pyrazolo[1,5-a]pyrimidine core, explicitly a π-excedent-π-deficient fused system. The 7-pyridyl substituent in 4a acts as an EWG and the fused-ring moiety is expected to be a highly polar system based on pyridine, pyrimidine and pyrazole rings. The results indicated that the

### Table 2 Photophysical data of fluorophores 4a–g at 20 °C

| Entry, R–PP | Solvent | $\Delta f$ | Abs, nm ($\epsilon$, M$^{-1}$ cm$^{-1}$) | Em$^b$, nm ($\phi$) | Stokes shift, cm$^{-1}$ |
|------------|---------|-----------|----------------------------------|------------------|----------------------|
| MTBE       | 0.1413  | 363 (1318) | 489 (0.03)                       | 7098             |
| THF        | 0.2010  | 361 (3320) | 493 (0.01)                       | 7417             |
| DCM        | 0.2221  | 363 (2073) | 506 (0.02)                       | 7785             |
| DMF        | 0.2742  | 360 (2927) | 494 (0.02)                       | 7535             |
| ACN        | 0.3055  | 342 (2001) | 500 (0.02)                       | 9240             |
| SS         | —       | —         | 492 (0.22)                       | —                |
| MTBE       | 0.1413  | 341 (2500) | 479 (0.09)                       | 8449             |
| THF        | 0.2010  | 340 (2727) | 481 (0.07)                       | 8622             |
| DCM        | 0.2221  | 343 (2120) | 486 (0.09)                       | 8578             |
| DMF        | 0.2742  | 338 (2213) | 490 (0.05)                       | 9178             |
| ACN        | 0.3055  | 355 (2247) | 487 (0.03)                       | 7635             |
| SS         | —       | —         | 479 (0.63)                       | —                |
| MTBE       | 0.1413  | 340 (6787) | 523 (0.07)                       | 10 291           |
| THF        | 0.2010  | 339 (7053) | 535 (0.06)                       | 10 807           |
| DCM        | 0.2221  | 339 (5233) | 541 (0.01)                       | 11 014           |
| DMF        | 0.2742  | 331 (6953) | 503 (0.05)                       | 10 331           |
| ACN        | 0.3055  | 351 (7267) | 520 (0.04)                       | 10 981           |
| SS         | —       | —         | 520 (0.01)                       | —                |
| MTBE       | 0.1413  | 352 (3520) | 486 (0.13)                       | 7833             |
| THF        | 0.2010  | 345 (3827) | 482 (0.06)                       | 8239             |
| DCM        | 0.2221  | 350 (2849) | 478 (0.16)                       | 7651             |
| DMF        | 0.2742  | 349 (3040) | 490 (0.04)                       | 8245             |
| ACN        | 0.3055  | 345 (3133) | 484 (0.07)                       | 8324             |
| SS         | —       | —         | 475 (0.39)                       | —                |
| MTBE       | 0.1413  | 349 (6127) | 476 (0.36)                       | 7645             |
| THF        | 0.2010  | 349 (6547) | 478 (0.23)                       | 7733             |
| DCM        | 0.2221  | 353 (5128) | 479 (0.40)                       | 7452             |
| DMF        | 0.2742  | 351 (6120) | 478 (0.14)                       | 7570             |
| ACN        | 0.3055  | 345 (8262) | 478 (0.16)                       | 8065             |
| SS         | —       | —         | 488 (0.18)                       | —                |
| MTBE       | 0.1413  | 433 (38 740) | 483 (0.45)                      | 2391             |
| THF        | 0.2010  | 440 (39 867) | 494 (0.23)                      | 2484             |
| DCM        | 0.2221  | 440 (32 867) | 496 (0.31)                      | 2566             |
| DMF        | 0.2742  | 424 (26 027) | 505 (0.43)                      | 3783             |
| ACN        | 0.3055  | 424 (34 033) | 501 (0.31)                      | 3625             |
| SS         | —       | —         | 538 (0.08)                       | —                |
| MTBE       | 0.1413  | 378 (21 667) | 474 (0.68)                      | 5288             |
| THF        | 0.2010  | 387 (15 008) | 476 (0.85)                      | 4831             |
| DCM        | 0.2221  | 385 (20 593) | 488 (0.97)                      | 5415             |
| DMF        | 0.2742  | 384 (17 667) | 510 (0.81)                      | 6366             |
| ACN        | 0.3055  | 379 (18 313) | 512 (0.52)                      | 6854             |
| SS         | —       | —         | 520 (0.13)                       | —                |

Data recorded in different solvents ($1 \times 10^{-3}$ M) and in the solid-state (SS). Relative quantum yield using Prodan as a standard in solution and apparent quantum yield for probes in SS.$^*$

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**Solvatofluorochromism**

Compounds bearing both EDGs and EWGs as substituents, known as push–pull structures, ensure that after light absorption, the charge is transferred from the donor group to the acceptor, which creates a highly dipolar excited state (DES). The DES interacts with the dipoles of the solvent and thus, the emission shifts to longer wavelengths in more polar solvents.$^{1-3}$ Therefore, the solvatofluorochromatic behavior in the emission spectra is a measure of the push–pull properties of a compound. In order to evaluate the solvatochromic features of PPs 4a–g, the relationship between the solvent polarity parameter ($\Delta f$) and the Stokes shift ($\Delta \lambda$), according to the Lippert–Mataga equation, was investigated.$^*$ From the plots of $\Delta \lambda$ versus $\Delta f$ (Fig. 4), it was found that the slopes of the fitting lines for 4a, 4f and 4g were high, at 10 390, 9381 and 11 015, with acceptable linearity, suggesting that the ICT in these compounds have a larger dipole moment than the ground state due to important charge redistribution. The dipole moment changes ($\Delta \mu$) in those compounds were calculated to be 10.3, 12.8 and 19.0 D. Interestingly, compound 4a with pyridine as an EWG at position 7 displayed a stronger solvatofluorochromic effect than that observed in 4e bearing an EDG in the same position. This behavior can be explained by the π-amphoteric donor/acceptor property in the pyrazolo[1,5-a]pyrimidine core, explicitly a π-excedent-π-deficient fused system. The 7-pyridyl substituent in 4a acts as an EWG and the fused-ring moiety is expected to be the EDG (i.e., a A-A-D molecular system based on pyridine, pyrimidine and pyrazole rings). The results indicated that the
yields in solid-state (QY SS) of 0.63, 0.39, 0.22 and 0.18, and
4e

Solid-state excited state (Fig. 6).
substituents, which reduces the charge reorganization in the
properties because of the absence of strong EDG or EWG
properties in the solid-state are highly dependent on
the series (intensity in 4b > 4d > 4e > 4a), since they bear bulky
groups that disfavor both good packing and fluorescence intensity (Fig. 5 and 6).
Likewise, in N-heterocyclic
compounds that lack strong electrostatic interactions due to
aromatic systems, the microcrystalline arrangement allows an intermo-
lar fluorescence quenching due to the antiparallel organi-
zation of the molecules.31,41,42 Likewise, in N-heterocyclic
compounds that lack strong electrostatic interactions due to
the absence of polar functional groups, the van der Waals forces
are mainly responsible for their formation in the solid-state and
apparently, these forces are improved by the presence of simple
aryl groups at the periphery. The supramolecular assembly
can be promoted by the molecular chain formations having aryl
groups or fused heterocyclic moieties in a strategic disposition
of π⋯π stacking and C−H⋯π (or C−H⋯N) interactions.31,41–47
Some haloaryl substituents play a crucial role in molecular
packing and the photophysical properties of their derivatives,
such as the 2,4-dichlorophenyl (2,4-Cl2Ph) group.44,45 In this
context and as expected, probes 4c, 4f and 4g showed lower
emission intensities with respect to those found in the rest of
the series (intensity in 4b > 4d > 4e > 4a), since they bear bulky
groups that disfavor both good packing and fluorescence intensity (Fig. 5 and 6).
Notably, the pyrazolo[1,5-a]pyrimidine core has been widely
studied and various crystal arrangements were reported,12,13,31,46
evincing a molecular packing with parallel12,13 or quasi antipar-
allel12,13 dispositions with respect to each other, which depend
on the nature of the substituents. However, with strong donor
groups at position 7 and without steric effects in other fused
ring positions, an utterly antiparallel molecular organization is
favored (Fig. 6).31 Therefore, the absence of a push−pull structure
in 4b, 4g and 4f, avoids the intermolecular quenching in the solid-state,31,44,45 allowing high-emission intensities with
regard to that observed in derivatives bearing a strong push−
pull arrangement (4a inside of the PP core, 4g and 4f) or bulky
substituent groups (4c, 4g and 4f). Finally, the presence of the
2,4-dichlorophenyl substituent in 4b favors its emission intensity
as a result of the marked dihedral angle between this group
with the heterocyclic core due to the Cl atom at position 2 of this
group.44,45 This effect could reduce the electronic communica-
tion between the two rings45 and result in aggregation-induced
emission (AIE) phenomenon47 (Fig. 5 and 6).
Probes 4a−g stability
The photobleaching characteristics and stability at extreme pH
groups of fluorescent compounds are critical to their application
as fluorescent materials and bio-probes, respectively. Accord-
ingly, the photostability of dyes 4a−g was investigated and
compared with that of prodan (P), coumarin 153 (C-153) and
rhodamine 6G (R6G). After continuous excitation at 365 nm

Fig. 5 Solid-state emission spectra of compounds 4a−g. Photographs
were taken using solid-state samples for each probe under UV light of
365 nm.

Fig. 6 Possible solid-state molecular effects on pyrazolo[1,5-a]
pyrimidines 4.
with a xenon lamp (4.0 mW) at different times, the normalized fluorescence intensities of dyes 4a–g decreased by 89–94%, measured at their maximum wavelength, which is a very good photobleaching performance when compared with those obtained for the commercial probes (Fig. 7a). Likewise, the stability under exposure to extreme pH (pH 2 with H₂SO₄ and pH 12 with KOH and stirring for 1 h at 50 °C; after neutralization, the emission spectra were recorded) was studied and the behavior was followed by the relative fluorescence intensity (Fig. 7b). The results are similar to those found in C-153. Interestingly, acidic conditions have a greater impact on the stability of the pyrazolo[1,5-a]pyrimidine-based probes. These observations can be attributed to the high electronic density in different atoms of the fused-pyrazole and the acid–base interactions could be the beginning of the chemical decomposition.

**Computational calculations**

To have better insight regarding the molecular structures and electronic properties of fluorophores 4a–g, geometry optimization, analytical frequencies, and excited-state energy calculations were performed at the B3LYP level with the Ahlrichs def2-TZVP basis set,[51] as implemented in the ORCA 4.2.0 package.[52,53] For further computational details, please see the attached ESI.[54]

All geometry optimization calculations were performed on the framework of the DFT (Fig. 8). This method has been demonstrated to provide reliable results in this kind of system.[54,55] At the B3LYP level, the ground state of these compounds is a closed-shell singlet (S = 0), in which the electronic structure is characterized by frontier molecular orbitals (FMOs) of antibonding π nature (Fig. 9). We performed the geometry optimizations using an implicit solvation model (as described in the ESI†) to evaluate the stability of each probe as a function of the different solvents considered in the experiments (Tables S11–S17†). For the sake of comparison, Table 3 gives the values obtained in THF for the calculated charges on the nucleophilic carbon and nitrogen atoms (C3 and N4 in Fig. 1 and 8), dihedrals and C7–C8 bond lengths connecting the N-heterocyclic core to 7-aryl groups, the HOMO–LUMO gaps, and polarizabilities. The negative charges in C3 and N4 are comparable, ranging from −0.300 to −0.200, which explains the greater reactivity and regioselectivity of these compounds toward electrophilic species.[56,57]

Importantly, N5 may be subject to alkylation reactions to generate pyrimidinium salts, a key group of compounds in organocatalysis[56] and biochemical applications.[57] While the C7–C8 distances remain virtually unchanged with the different aryl substituents (1.470 ± 0.007 Å), the dihedrals are disturbed to a larger amplitude (from 34° to 64°), causing the resonance breaking between the aryl group and the pyrazolo[1,5-a]pyrimidine core to different extents. The HOMO–LUMO gap also changes as there are variations in the substituents. The calculated gaps are situated in the energy range from 3.3 to 4.3 eV, which is in agreement with the wavelengths of the UV-vis spectra outlined above. The polarizability doubled from 25 Å³ as in 4a up to 53 Å³ as in 4g, which is in accordance with a greater dipole moment in the excited states of the latter, and the fact that the EWGs at position 7 lead to higher solvatochromicisms.

In PPs 4a–g there was a slight decline in the dihedrals, charges, and gaps as the solvent polarity decreased (Tables S11–S17†). Conversely, the polarizability slightly increased with the enhancement of the solvent polarity. As discussed above for the absorption and emission spectra, this behavior reveals that the polarities of the deemed solvents play a minor role in the electronic structure of the studied compounds, as well as in its geometrical arrangement. More interestingly, PPs 4f and 4g showed the opposite behavior, where the polarizability slightly diminished as the solvent polarity increased. In fact, these...
systems have larger polarizabilities due to their EDGs (as well as the smaller charges, dihedrals and HOMO–LUMO gaps, Table 3), which is in line with the greater fluorescence (vide infra). These results can be understood as follows: the smaller the dihedral, the more effective the π-resonance between the heterocyclic moiety and the 7-aryl group, the polarizability increased, and the HOMO–LUMO gap was reduced. Consequently, the respective probes had improved photophysical and electronic properties because of a more favored ICT process.

A deeper analysis of the absorption and emission processes was achieved based on TD-DFT calculations by taking the optimized geometries as a starting point. In this sense, the energies of the five lowest excited singlet states of fluorophores 4a–g in THF were calculated. These energies allowed us to estimate the absorption wavelength of each excited singlet and their respective oscillator strengths via the transition dipole moments. As shown in Table 4 and Fig. S16† compounds with EDGs (4e–g) have greater oscillator strengths and higher absorbances. The highest oscillator strengths of compounds 4a–b and d–g, are associated with the first singlet excited state, whereas for 4c, this strength matches the third singlet excited state. Their transition energies have a mean value of 3.41 ± 0.32 kcal mol⁻¹, in harmony with absorptions in the UV-vis region. The wavelengths linked to the absorption towards the cited excited singlets are well aligned with our experimental results in the same solvent (Table 2). In almost all PPs studied, absorptions are dominated by HOMO → LUMO electronic transitions (Table 4), though in 4c, it is mainly of the HOMO-1 → LUMO type. In PPs 4a–d, the HOMO mainly has the π-character on the PP ring, while the LUMO is largely of π-character on the aryl group (Fig. 9, top). These observations are consistent with the fact that the absorption process is mainly associated with electron transfer from the PP ring to the adjoining aryl group, that is, an ICT to the EWGs and NG. Moreover, since the HOMO and LUMO in 4e–g are largely of π-character on the aryl and PP rings, respectively, the absorption process is reversed (Fig. 9, bottom). Thus, the charge transfer goes from the EDGs to the PP ring. Ultimately, the absorption and fluorescence spectra of PPs 4a–g were predicted (Fig. S16†), including the all-vibrionic transitions, based on the excited singlet of each probe. As expected, the estimated spectral behavior agrees with the experimental data (see ESI† for more details).

Importantly, compound 4f (7-diethylaminocoumarin-3-yl derivative) displayed lower emission intensity and quantum yield as compared to 4g in optical experiments, which was not reflected in the computational estimations. Likewise, the simple coumarin-PP derivative 4c offers both experimental and calculated photophysical results in lower limits (Fig. 4–6, 8 and S16†). These findings are possibly due to the high sensitivity of the coumarin derivatives to the microenvironments (e.g., solvent properties and solid-state aggregation), steric effects (e.g., groups near the D-A junction and irregular packing) and because 4c does not possess strong EDGs on the coumarin ring, such as the diethylamino (Et₂N) group at 4f. In fact, this group offers resonant structures for the two geometries of the 7-Et₂N-coumarin derivatives in the excited state, from (a) a planar emissive ICT excited state, to (b) a nonfluorescent twisted ICT state (TICT), shown in Fig. 10.⁵⁸,⁵⁹

![Fig. 10 Resonant structures of 7-diethylaminocoumarins in the excited state.](Image)

### Table 3 Müliken charges in C3 and N4, C7–C8 bond lengths (Å) and the dihedral angle (°), polarizability (Å³), and HOMO–LUMO gap (eV), of compounds 4a–g in THF

| Probe | Charge N4 | Charge C3 | C7–C8 distance | Dihedral | Polariability | HOMO–LUMO |
|-------|-----------|-----------|----------------|----------|--------------|-----------|
| 4a    | −0.263    | −0.265    | 1.473          | −39.5    | 25.13        | 4.065     |
| 4b    | −0.265    | −0.275    | 1.476          | −63.9    | 29.84        | 3.982     |
| 4c    | −0.264    | −0.272    | 1.468          | −37.4    | 34.11        | 3.584     |
| 4d    | −0.270    | −0.271    | 1.471          | −39.9    | 26.12        | 4.222     |
| 4e    | −0.274    | −0.276    | 1.466          | −35.9    | 29.94        | 4.145     |
| 4f    | −0.272    | −0.296    | 1.463          | −34.6    | 48.56        | 3.299     |
| 4g    | −0.275    | −0.279    | 1.465          | −34.2    | 53.31        | 3.481     |

### Table 4 Dominant electronic transitions to the excited state of interest for 4a–g in THF based on TD-DFT calculations. Energies are in eV and wavelengths (λ) in nm

| Probe | Excited state | Energy | λ_calc/λ_exp | Oscillator strength | Dominant electronic transition |
|-------|---------------|--------|--------------|---------------------|--------------------------------|
| 4a    | 1°A           | 3.31   | 374.3/361    | 0.10                | 95% HOMO → LUMO               |
| 4b    | 1°A           | 3.65   | 340.0/340    | 0.09                | 95% HOMO → LUMO               |
| 4c    | 3°A           | 3.82   | 324.4/339    | 0.19                | 79% HOMO-1 → LUMO             |
| 4d    | 1°A           | 3.53   | 351.7/345    | 0.13                | 94% HOMO → LUMO               |
| 4e    | 1°A           | 3.63   | 342.0/349    | 0.27                | 91% HOMO → LUMO               |
| 4f    | 1°A           | 3.11   | 398.4/440    | 0.88                | 84% HOMO → LUMO               |

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Conclusions

To sum up, we have synthesized a family of fluorescent pyrazolo[1,5-α]pyrimidines 4a-g bearing substituent groups of different electronic natures. The photophysical properties of 4a-g in both solution and solid-state were studied and the experimental results were interpreted by means of TD-DFT calculations. From the synthetic point of view, the RME values calculated for compounds were in the range of 40–53%, a notable performance as compared to a widely used fluorophore such as BODIPY (RME: 1.31–17.9%). Consequently, the simple pyrazolo[1,5-α]pyrimidine derivatives are raw materials with low-cost, which are better eco-friendly alternatives for developing luminescent compounds. The synthesis is mainly MW-assisted and can be done under solvent-free conditions. Regarding the optical properties of 4a-g, these are highly dependent on the substituent nature, in which EDGs such as anisyl, diethylaminocoumarin and triphenylamine improve both ε and φr. Meanwhile, the solvatochromic studies showed the amphoteric behavior of PPs and the Lippert–Mataga equation allowed the calculation of dipole moment changes when going from the ground to the excited state (Δμ) for probes 4a (10.3 D), 4f (12.8 D) and 4g (19.0 D). Remarkable solid-state emission intensities were achieved in some compounds with low capability for the ICT phenomenon (QYss up to 63%). Moreover, these PPs displayed properties comparable with those reported for commercial probes such as Prodan, Coumarin-153 (ref. 60) and Rhodamine 6G,46 and the good photo- and acid-base exposure stability make them attractive alternatives for real applications.

Computational calculations were performed in order to describe the changes in the electronic structure associated with the absorption and emission processes in 4a-g. Geometry optimization calculations on the singlet ground state indicated that the dihedral centered on C7–C8 controls the polarizability and HOMO–LUMO gap of compounds and hence, its respective absorption and fluorescence rates. The smaller the dihedral, the shorter the HOMO–LUMO gap and thus, the ICT phenomena in absorption and emission spectroscopy for the probes are favored. Moreover, the electronic transition analysis of the lowest excited singlet states in probes, revealed that the absorbance experiments at low energy, are governed by a HOMO → LUMO electron transition, while this transition is reversed for emission experiments. The electronic structure analysis based on the FMO nature indicates that EDGs favor large absorption and emission intensities as a result of the ICT process to and from the fused heterocyclic moiety, respectively. When EWGs are used, these intensities remain low, which is in line with the experimental results. Ultimately, both experimental and theoretical results of the coumarin derivatives 4c and 4f provided evidence that the electronic properties of these compounds are governed by different complex phenomena.

Experimental section

General procedures

General procedure for the synthesis of β-enameinomes 2a–g. A 10.0 mL sealable (Teflon screw cap) oven-dried tubular reaction vessel was charged with 1.0 mmol of the respective β-enamnine (2a, 2b, 2d, 2e, or 2g) and 3-methyl-1H-pyrazol-5-amine (3, 49 mg). The resulting mixture was irradiated with MW at 180 °C (200 W) and maintained at this temperature for 2 min in a sealed tube containing a Teflon-coated magnetic stir bar. The resulting reaction mixture was cooled to 55 °C by airflow and the precipitated product formed upon the addition of cold EtOH/H2O (1:1, 1.0 mL) was filtered off, washed and dried to give the corresponding pure product (4a, 4b, 4d, 4e, and 4g) by this protocol previously reported in our lab.13 Importantly, β-enameinone 2c was obtained under reflux for 6 h from an equimolar mixture (1 mmol) of 3-acetyl-2H-chromen-2-one (1c) and DMF-DMA, according the procedure reported by El-Taweel and Eldagdi,65 however, in this case, we used 1,4-dioxane (5.0 mL) as a solvent instead of the xylene used by those authors. Later, the 1,4-dioxane was removed under reduced pressure, yielding the crude product 2c. Finally, all the crude β-enameinones were purified by flash chromatography on silica gel (eluent: CH2Cl2) to afford the pure products 2d–g.

General procedure for the synthesis of pyrazolo[1,5-α]pyrimidines 4a–g. A 10.0 mL sealable (Teflon screw cap) oven-dried tubular reaction vessel was charged with an equimolar mixture (0.5 mmol) of the respective methyl pyridine derivatives and DMF-DMA was removed under reduced pressure, yielding the respective crude β-enameinones (2a, 2b, 2d, 2e, or 2g) and 3-methyl-1H-pyrazol-5-amine (3, 49 mg). The resulting mixture was irradiated with MW at 160 °C (180 W) and maintained at this temperature for 15 min in a sealed tube containing a Teflon-coated magnetic stir bar. The resulting reaction mixture was cooled to 55 °C by airflow and the excess of DMF-DMA was removed under reduced pressure, yielding the respective crude β-enameinones (2a, 2b and 2d–g) via this protocol previously reported in our lab.12 Importantly, β-enameinone 2c was obtained under reflux for 6 h from an equimolar mixture (1 mmol) of 3-acetyl-2H-chromen-2-one (1c) and DMF-DMA, according the procedure reported by El-Taweel and Eldagdi.65 However, in this case, we used 1,4-dioxane (5.0 mL) as a solvent instead of the xylene used by those authors. Later, the 1,4-dioxane was removed under reduced pressure, yielding the crude product 2c. Finally, all the crude β-enameinones were purified by flash chromatography on silica gel (eluent: CH2Cl2) to afford the pure products 2d–g.

Abbreviations

| Abbreviation | Meaning |
|--------------|---------|
| AIE | Aggregation-induced emission |
| BODIPY | 4,4-Difluoro-4-bora-3a,4a diaza-s-indacene |
| DES | Dipolar excited state |
| DMF-DMA | N,N-Dimethylformamide-dimethyacetel |
| EDGs | Electron-donating groups |
| EWGs: | Electron-withdrawing groups |
| ESIPPT | Excited state intramolecular proton transfer |
| FMOs | Frontier molecular orbitals |
| HOMO | Highest occupied molecular orbital |
ICT  Intramolecular charge transfer  
LUMO  Lowest unoccupied molecular orbital  
MWI  Microwave irradiation  
PPs  Pyrazolo[1,5-a]pyrimidines  
QYSS  Quantum yield in solid-state  
RME  Reaction mass efficiency  
TD-DFT  Time-dependent density functional theory  
TICT  Twisted intramolecular charge transfer

**Conflicts of interest**

The authors declare no competing financial interest.

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