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Letter

1,2,4-Triphenylpyrroles: Synthesis, Structure and Luminescence Properties

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Abstract Pyrroles are widely found in natural products and play an important role in biological processes. Certain pyrrole derivatives are fluorescent and may be used as molecular probes or biomarkers in the diagnosis of diseases, such as Alzheimer's or Parkinson's. Herein is reported the synthesis of five new pyrrole derivatives bearing phenyl rings on positions 1, 2, and 4, with electron-donating groups at the periphery. The introduction of more or stronger electron-donating groups red-shifts and increases the efficiency of the fluorescence emission.

Key words triphenylpyrroles, Nef reaction, Paal–Knorr reaction, fluorescence, crystal structure

Heterocyclic compounds, which are often pharmacologically active molecules obtained from either natural or synthetic sources, are receiving considerable attention due to their potential applications in biology and in industry.¹ Among them, pyrrole is a versatile scaffold, the derivatives of which are found in various pharmacophores. Pyrroles are also widely used as intermediates in syntheses of pharmaceuticals, agrochemicals, dyes, photographic chemicals, and perfumes. Pyrroles are backbone components of complex macrocycles, such as porphyrin rings (e.g., heme and vitamin B_{12}) or bile pigments (bilirubin, biliverdin).² Pyrrole derivatives exhibit a wide range of biological properties,³ namely antibacterial,⁴⁻⁷ antifungal, antiviral,⁸ antiinflammatory, anticancer, and antioxidant activities.⁹ This has prompted much recent research on the synthesis of pyrroles,¹ especially from chalcones.^{10,11}

Luminogenic materials are of considerable interest,^{12,13} especially those displaying aggregation-induced emission enhancement (AIEE).¹⁴ The first report on such a material dates from 2001, and it describes a series of silole derivatives that do not luminesce in dilute solutions but are highly



luminescent when aggregated in concentrated solutions or when cast into solid films.¹⁵ We later demonstrated this phenomenon in various families of compounds in which intermolecular hydrogen bonds¹⁶ or weak supramolecular interactions^{17–19} rigidify the crystalline structure. This is different from the observation of solid-state phosphorescence²⁰ or the formation of *J*-aggregates,^{21,22} both of which induce a red-shift of the emission wavelength. In particular, AIEE of pyrrole-based fluorophores and their analogues has been assessed, and their crystal structures have been studied to rationalize the phenomenon.^{23–25}

Here, we wish to report the synthesis, characterization, and photophysical properties of a series of new 1,2,4-triphenylpyrroles. Their syntheses were achieved in moderate yields, and the compounds showed fair quantum yields in dilute solutions. Determination of the crystal structure of one of these pyrroles enabled us to rationalize the quenching observed in concentrated solutions and in the solid state.

The synthetic route encompassed an aldol condensation, a Michael addition, Nef reaction, and a Paal-Knorr reaction (Scheme 1). In the first step, acetophenones were condensed with benzaldehydes to form the corresponding chalcones **1a–c**. The substituents in the 2- and 4-positions of the final products were introduced at this stage. The Michael addition of nitromethane catalyzed by diethylamine (also used as solvent) and 1,8-diazabicyclo[5.4.0]undec-7ene (DBU) afforded intermediates 2a-c in nearly quantitative yields.¹⁰ A Nef reaction transformed the nitro substituent into an aldehyde, yielding the key intermediates **3a-c**. The second step of this reaction was carried out in methanol containing concentrated sulfuric acid, and consequently the major component of the product was obtained as the dimethyl acetal. Because this did not cause a problem in the next step, 3a-c were used, without purification, as mix-



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Scheme 1 Synthetic routes to compounds **4a–e**

tures of the aldehyde and the acetal. In the last step, **3a–c** reacted with aniline or anisidine in a Paal–Knorr reaction, leading to **4a–e** in fair yields.^{26,27}

The new pyrrole derivatives were characterized by NMR spectroscopy and mass spectrometry (see Supporting Information). In the case of **4b**, single crystals suitable for X-ray diffraction were successfully grown from a saturated dichloromethane solution (Figure 1).²⁸ All bond lengths and angles were in the normal ranges.²⁹ The crystal structure showed that due to steric repulsions, the three phenyl rings are not coplanar with the pyrrole ring, reducing conjugation of the backbone.



Figure 1 Molecular structure (a) and unit cell content (b) of **4b**. Thermal ellipsoids are shown at the 50% probability level. Hydrogen atoms are shown with an arbitrary radius (0.30 Å). C, gray; O, red; N, blue; H, white.

The absorption and emission spectra of 1,2,4-triphenylpyrroles **4a–e** were recorded in dichloromethane solution (Figure 2), and the photophysical properties of the compounds are presented in Table 1.

The absorption and emission wavelengths are in the ranges 265–410 nm and 375–515 nm, respectively, depending on the substituents. Electron-donating substituents red-shift the absorption and emission maxima, with a small shift for methoxy groups and a larger one for a dimethylamino group. The influence of the substituents on the



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Figure 2 Absorption and emission spectra of dyes 4a-e at 10^{-5} mol L⁻¹ in dichloromethane (excitation at 300 nm for 4a-d and at 400 nm for 4e)

molar absorptivity is difficult to assess, but it seems to decrease when more-electron-donating groups are present. All the pyrroles studied emit in solution with quantum yields of less than 1% (Table 1 and Figure 2). However, **4e**, which contains a stronger electron-donating dimethylamino groups showed an increased emission efficiency. None of the dyes is luminescent in the solid state, and no AIEE is observed. This is at odds with the results reported for phe-

Table 1 Selected Optical Data Measured in Dichloromethan	e
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Dye	λ_{abs} (nm)	ε (M ⁻¹ cm ⁻¹)	λ _{em} (nm)	φ _f (%)
4a	265	54 000	375	0.15
4b	265	46 000	375	0.11
4c	275	45 000	390	< 0.1
4d	285	18 000	390	< 0.1
4e	410	15 000	515	0.26

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nyl-substituted pyrroles,²⁵ among which 1,2,4-triphenylpyrrole, 1,3,4-triphenylpyrrole, and pentaphenylpyrrole all display AIEE. Presumably, the introduction of substituents onto the phenyl ring disrupts the organization of the dyes in the solid state, promoting emission quenching.

In conclusion, starting from simple building blocks, five new pyrrole derivatives were successfully prepared through Nef and Paal–Knorr reactions. The pyrroles were selectively substituted in the 1-, 2-, and 4-positions with phenyl rings bearing electron-donating substituents. The influence of these groups on the optoelectronic properties of the dyes was studied, and all compounds presented emission properties in dilute solutions. This strategy is valuable for the synthesis of novel molecules with a pyrrole backbone, and for fine-tuning their photophysical properties by functionalization with electron-donating or electron-withdrawing groups for an improved push–pull effect.

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Supporting Information

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- (26) 1,2,4-Triphenylpyrroles 4a-e; General Procedure The appropriate nitro ketone 2a-c (1 equiv) was dissolved in a mixture of MeOH (8 mL) and THF (12 mL) then KOH (1 equiv) was added. The mixture was stirred for 2 h. The solution, cooled in ice, was added dropwise to an ice-cold solution of concd H₂SO₄ (4 mL) in MeOH (10 mL), and the mixture was stirred for ~1 h at rt. Half of the solvent was removed under reduced pressure and the mixture was poured in ice-water. The product was extracted with CH₂Cl₂ and the organic layer was dried (Na₂SO₄) and concentrated to dryness to give compound **3a-c**, which was used in the following step without purification. The appropriate amine (1 equiv) was added to a solution of the acetal 3a-c (1 equiv) in MeOH (5 mL), and the resulting solution was stirred for 24 h at rt. During this time a precipitate formed. H₂O was then added, and the product was extracted with CH₂Cl₂. The organic phase was dried (Na₂SO₄) and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel).
- (27) **1,2,4-Tris(4-methoxyphenyl)-1H-pyrrole** (**4c)**Yellow-brown oil; yield: 23 mg (0.06 mmol, 11%). ¹H NMR (300 MHz, CDCl₃): δ = 7.50 (d, *J* = 8.8 Hz, 2 H), 7.15–7.08 (m, 4 H), 7.07 (d, *J* = 2.0 Hz, 1 H), 6.91 (d, *J* = 8.8 Hz, 2 H), 6.85 (d, *J* = 9.0 Hz, 2 H), 6.77 (d, *J* = 8.9 Hz, 2 H), 6.58 (d, *J* = 2.0 Hz, 1 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.77 (s, 3 H). ¹³C NMR (75 MHz, CDCl₃): δ = 158.4, 158.3, 158.0, 134.7, 133.8, 129.7, 128.3, 127.1, 126.3, 125.6, 124.9, 119.8, 114.3, 113.7, 107.3, 55.6, 55.4, 55.3. ESI(+)–HRMS: *m/z* [M + H]⁺ calcd for C₂₅H₂₄NO₃: 386.1751; found: 386.1743 (–1.99 ppm).
- (28) CCDC 1879235 contains the supplementary crystallographic data for compound **4b**. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.
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