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The optical properties, synthesis and characterization of novel 5-aryl-3-benzimidazolyl-1-phenyl-pyrazoline derivatives

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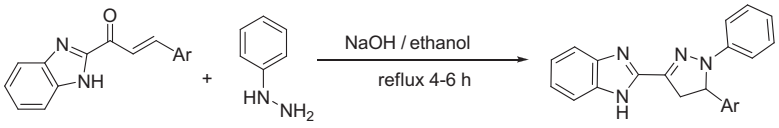
HIGHLIGHTS

- Novel pyrazoline derivatives were prepared and fully characterized.
- UV–vis absorption and fluorescence spectroscopy of all compounds were measured.
- Influence of solvent on UV–vis absorption and fluorescence spectroscopy was examined.

GRAPHICAL ABSTRACT



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ABSTRACT

A series of novel 5-aryl-3-benzimidazolyl-1-phenyl-pyrazoline derivatives were synthesized by the reaction of benzimidazolyl chalcone and phenylhydrazine in 41–72% yields. The compounds were characterized using IR, ^{1}H NMR and HRMS. Absorption and fluorescence spectra were measured in different organic solvent. An intense absorption maxima was noted at ca. 370 nm and emission maxima was noted at ca. 460 nm. The absorption spectra of the pyrazoline derivatives reveal that 5-aryl group attached to the pyrazoline ring hardly influenced the maximum absorption. The fluorescence spectra of these compounds indicated the emission wavelength was red shifted and the fluorescence intensity was decreased with the increase in solvent polarity.

Introduction

Pyrazoline derivatives have attracted increasing attention due to their pharmaceutical applications such as antimicrobial [1–3], antiamoebic [4,5], antinociceptive [6], anticancer [7], antidepressant [8] and anti-inflammatory [9–13], They also have potential applications in conjugated fluorescent dyes emitting blue fluorescence with high fluorescence quantum yield [14,15] and electroluminescence fields [16–18]. Attempts have been made to synthesize and elucidate the effects of substituent on the absorption and fluorescence properties of this class of compounds [19–24].

The design and synthesis of fluorescent small molecules with desirable properties are of considerable current interest in biology research. The advent of sensitive fluorescence detectors has enabled advances in biological imaging and the emergence of the field of single molecule spectroscopy [25,26]. To date there have been relatively few studies of the cellular localization of agents in which small molecule is linked to a fluorophore, such as coumarin [27,28]. Thus, in continuation of our efforts on the synthesis of various biologically and optically active heterocycles [29–34], we would like to synthesize novel small molecules with both potential bioactivity and fluorescent property. Recently, Zhao reported the synthesis and optical properties of 1,3,5-triaryl pyrazoline derivatives and ferrocenyl pyrazoline derivatives [35,36]. In light of few report concerning the fluorescent property of benzoimidazolyl pyrazoline, herein, we would like to report the synthesis, characterization and optical properties of novel 5-aryl-3-benzimidazolyl-1-pyridazinyl-pyrazoline derivatives.

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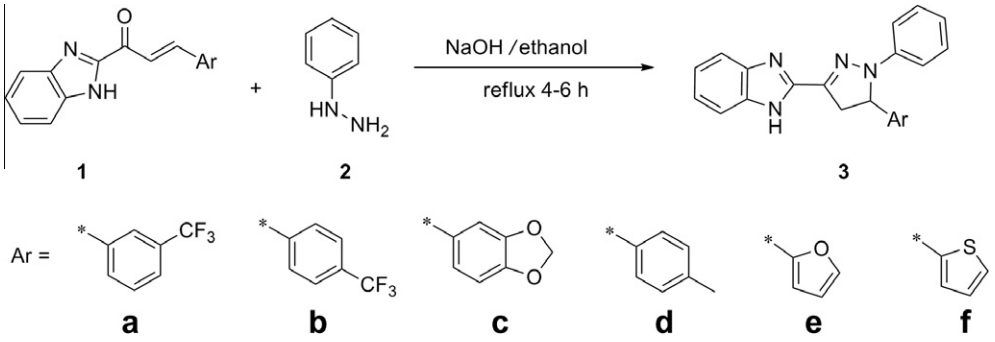

Scheme 1. Synthesis of 5-aryl-3-benzimidazolyl-1-phenyl-pyrazoline derivatives.

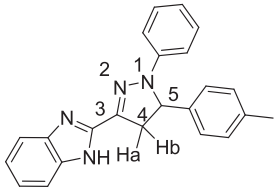

Fig. 1. Structure of compound **3d**.

Materials and methods

General

Thin-layer chromatography (TLC) was conducted on silica gel 60 F_{254} plates (Merck KGaA). ^{1}H NMR spectra were recorded on a Bruker Avance 300 (300 MHz) spectrometer, using $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal standard. IR spectra were recorded with an IR spectrophotometer VERTEX 70 FT-IR (Bruker Optics). HRMS spectra were recorded on a Q-TOF6510 spectrograph (Agilent). UV–vis spectra were recorded on a U-4100 (Hitachi). Fluorescent measurements were recorded on a PerkineElmer LS-55 luminescence spectrophotometer.

*General procedure for the synthesis of compound **3***

To a stirred solution of substituted chalcone (**1**) (1.0 mmol) in ethanol (20 mL) was added phenylhydrazine (**2**) (1.2 mmol) and NaOH (2.0 mmol) and the reaction mixture was refluxed for 3–6 h as shown in Scheme 1. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was cooled to room temperature and the precipitate was filtered, washed with water and ethanol, and then dried to give pure **3**.

Results and discussion

*Synthesis of compound **3***

The synthetic procedures of compounds **3a–f** are shown in Scheme 1. Starting chalcone **1** can be easily prepared by Claisen–Schmidt condensation between 2-acetyl-1*H*-benzo[d]imidazole and aromatic aldehydes in the presence of ethanolic solution of sodium hydroxide according to the literatures [36]. The 3,5-diaryl pyrazoline derivatives **3a–f** were obtained by the reaction of chalcone **1** with phenylhydrazine **2** at reflux condition in 41–72% yields. Comparing the yield of **3a** and **3b** (69% and 72%, respectively), we found that the reaction of **2** and **1a** or **1b** with trifluoromethyl group had higher yield than that of **1c** or **1d** with dioxol or methyl group, respectively, by reason of difference in electron withdrawing.

Structure characterization

The structures of products **3a–f** were characterized by spectroscopic methods (^{1}H NMR, IR, and HRMS). In the ^{1}H NMR spectra

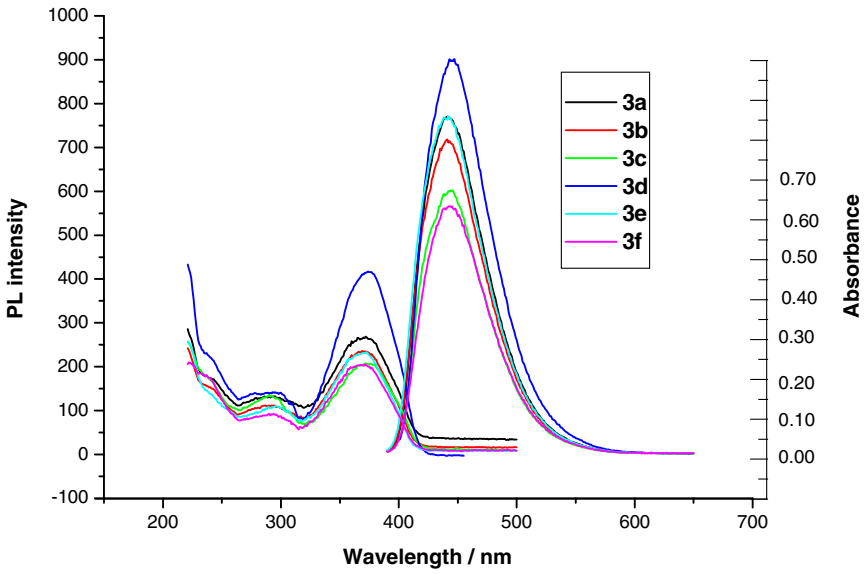

Fig. 2. Absorption and emission spectra of compounds **3a–f** in cyclohexane solution.

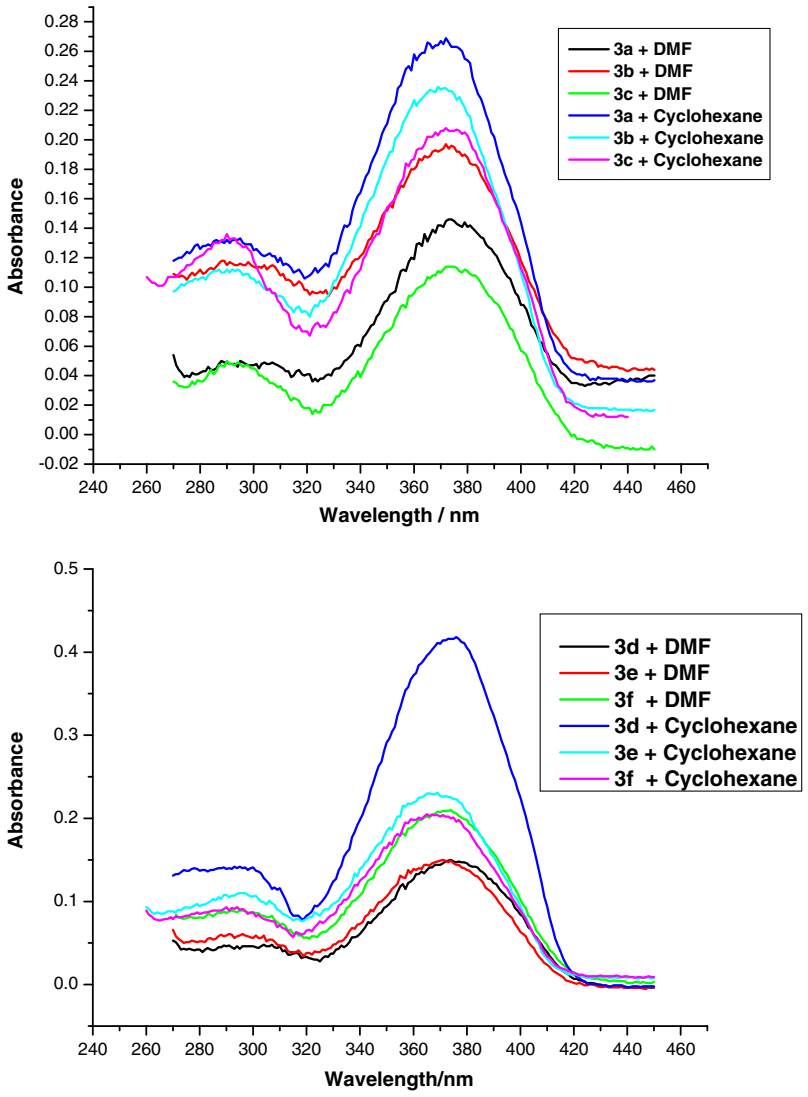

Fig. 3. UV–vis spectra of **3a–f** in different solvents.

($CDCl_3$) of pyrazoline, protons H_A and H_B that are geminal protons at C4 carbon, appear in the region 3.43–3.68 and 3.93–4.12 ppm respectively as doublet of doublets in all compounds. The data indicate that the structure of 5-aryl ring has definite effects on the chemical shift. The chemical shifts of compounds **3a–d** with substituted phenyl group are similar while **3e** and **3f** with furanyl and thiophenyl group change more compared with **3a–d**. The CH proton at C5 also appeares as doublet of doublets in the region of 5.30–5.69 ppm. Similar to the chemical shifts of the CH proton at C4, the group at position 5 also has very strong influence on the chemical shift. Furthermore, different from the CH proton shift at C4, the substituent on the phenyl group also has very strong influence on the chemical shift of the CH proton shift at C5. The IR spectra of all the compounds show C=N stretch at 1591–1595 cm^{-1}, which indicates that the structure of 5-aryl ring has little effects on the absorption. For example, compound **3d** (Fig. 1), obtained as yellow crystals, gave an [M+H]-ion peak at *m/z* 353.1765 in the HRMS, in accordance with the molecular formula $C_{23}H_{21}N_4$. The IR spectra showed the characteristic absorption bands at 1593 (C=N). In the ^1H NMR spectra ($CDCl_3$) of pyrazoline, it revealed a singlet at δ 2.29 (3H, $-CH_3$). Protons H_a and H_b that are geminal protons at C4 carbon, appears at 3.46 and 4.09 ppm as

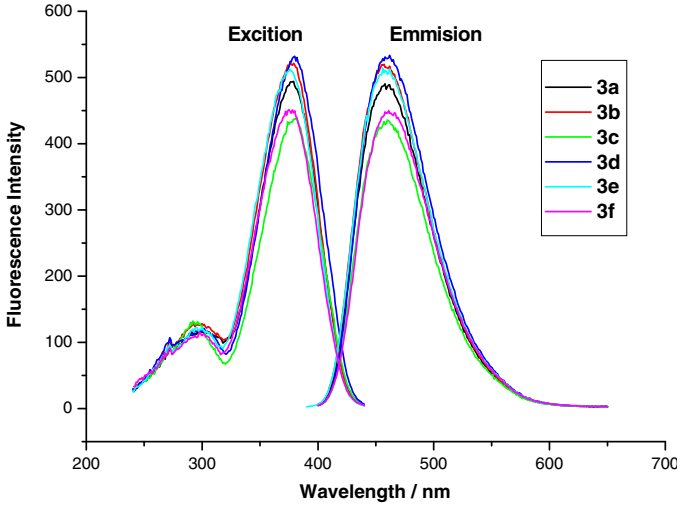

Fig. 4. The flurescence excitation and emission spectra of compounds **3a–f** in dichloromethane.

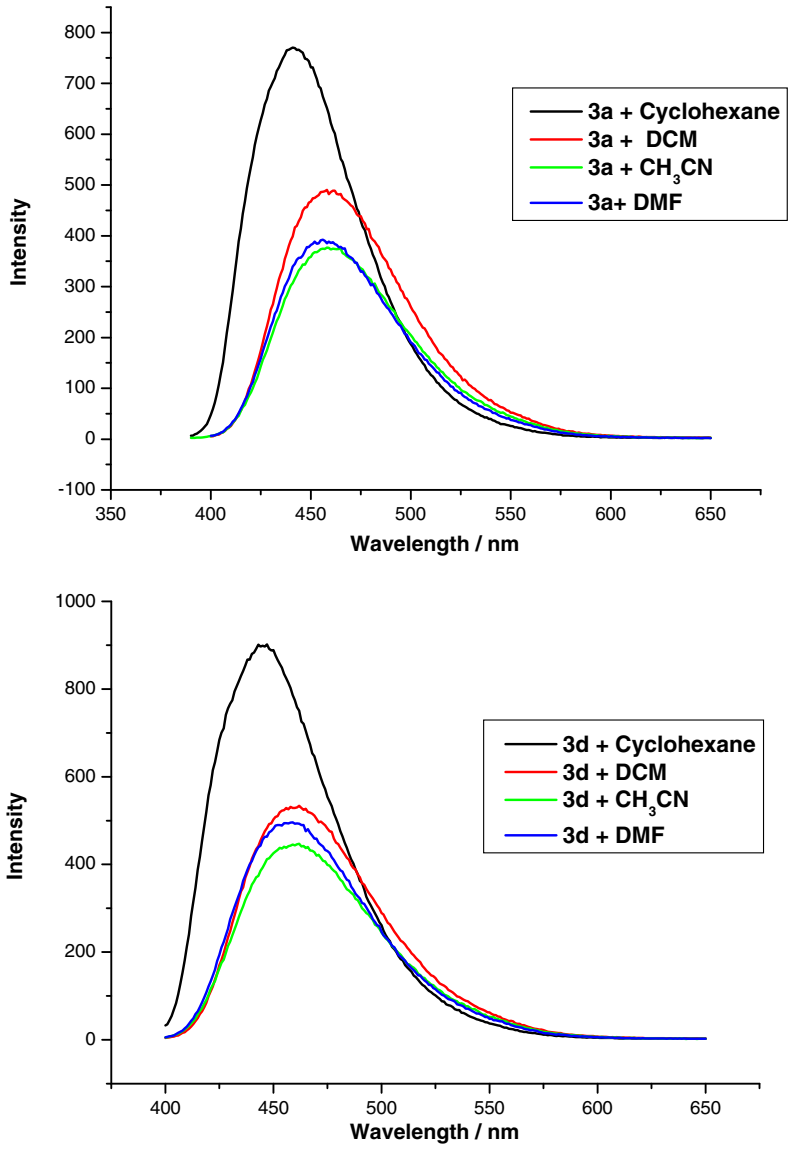

Fig. 5. Emission spectra of compounds **3a** and **3d** in different solution.

Table 1
The optical characteristics of the compounds **3a–f** in cyclohexane and DMF.

	λ_{max} (nm)		λ_{ex} (nm)	F_{max} (nm)		Stokes shift (nm)		Eg (eV)		Φ_F
	CHX	DMF		CHX	DMF	CHX	DMF	CHX	DMF	CHX
3a	372	373	380	441	456	69	83	2.97	2.97	0.11
3b	369	372	380	441	454	72	82	2.97	2.97	0.10
3c	372	374	380	444	459	72	85	2.97	2.97	0.13
3d	372	374	380	447	459	75	85	2.96	2.95	0.12
3e	374	371	380	442	454	68	83	2.98	2.98	0.15
3f	372	374	380	442	456	70	82	2.98	2.95	0.18

doublet of doublets. The CH proton at C5 also appeared as doublet of doublets at 5.36 ppm due to vicinal coupling with two non-equivalent geminal protons of C4 carbon.

*Absorption spectral characteristics of the compounds **3a–f***

For UV–vis absorption measurements, the dye concentration was 1×10^{-6} mol L^{-1}, and the UV–vis absorption spectra of compounds **3a–f** measured in cyclohexane solutions are given in Fig. 2 and Table 1. Several absorption peaks could be observed in the wavelength range from 220 to 420 nm, while almost no absorption was observed beyond 420 nm. The data indicated that, electron-withdrawing groups (CF_3) and electron-donating group (CH_3) attached to 5-aryl group hardly influenced the maximum absorption. Actually, the chromophoric system is composed of the two aryl substituents in the 1- and 3-position and three atoms (N1–N2–C3) out of the five pyrazoline ring. The remaining two carbon atoms (C4 and C5) of the ring are sp^3 hybridized and are not part of the conjugated system. The attached aromatic (Ar) in C5 cannot extend to the π-conjugation system because they are al-

most perpendicular to π-system, although they are strong electron donor [36].

Furthermore, the absorption spectra of the compounds **3a–f** in different solvents with the concentration of 1×10^{-6} mol L^{-1} are presented in Fig. 3. It is observed that the absorption spectra of these compounds change little with increasing solvent polarity, indicating that there is no charge transfer in the ground state.

Fluorescence spectral characteristics

The emission spectra of compounds **3a–f** in dichloromethane solution (1×10^{-6} mol L^{-1}) are presented in Fig. 4 and Table 1. Similar to the absorption spectrum, the emission of pyrazoline compounds had also almost independent on the group at position 5.

The solvent effects on the fluorescence characteristics of compounds **3a** and **3d** were studied, which indicated that the emission wavelengths of the compounds were red shifted and the fluorescence intensity decreased with the increase of solvent polarity (Fig. 5 and Table 1). It is believed that the potential energy surface of the emitting state is different from that of the ground state and a photo-induced ICT takes place in the fluorescence states with increasing solvent polarity. That is to say, the molecule is solvated significantly in the S_1 excited state, resulting in a difference in dipolemoment between the S_1 excited state and the ground state.

Conclusion

In summary, a series of novel 5-aryl-3-benzimidazolyl-1-phenyl-pyrazoline derivatives were synthesized by the reaction of benzimidazolyl chalcone and phenylhydrazine in 41–72% yields. The compounds were characterized using IR, ^{1}H NMR, and HRMS. Absorption and fluorescence spectra were measured in different organic solvent; an intense absorption maxima was noted at ca. 370 nm and emission maxima was noted at ca. 460 nm. The absorption and fluorescence spectra of the pyrazoline derivatives reveal that 5-aryl group attached to the pyrazoline ring hardly influenced the maximum absorption. The fluorescence spectra of these compounds indicated the emission wavelength was red shifted and the fluorescence intensity was decreased with the increase in solvent polarity (Table 1).

Acknowledgments

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.saa.2012.08.036.

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