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Crystal structure and properties of new benzimidazopyrido[2,3-*b*]indole-6-carbonitriles

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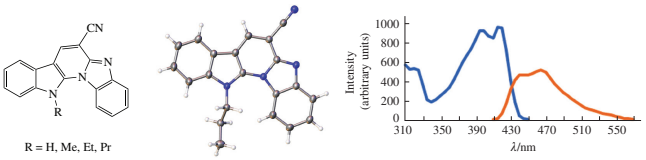
The structure of representatives of a new heterocyclic system, 12*H*-benzimidazo[1′,2′:1,6]pyrido[2,3-*b*]indole-6-carbonitriles, potential bioactive compounds, is elucidated by X-ray diffraction. The compounds exhibit luminescence in the blue region of the spectrum with quantum yields close to unity, which makes them promising phosphors for application in modern emitting devices.



Keywords: indole, benzimidazole, 12*H*-benzimidazo[1′,2′:1,6]pyrido[2,3-*b*]indole-6-carbonitriles, X-ray diffraction analysis, luminescence, luminophore.

The indole system occupies a special place among other heterocyclic systems, as it is the basis in such vital natural compounds as hormones, alkaloids, proteins, phytoalexins, neurotransmitters and plant pigments. Indole derivatives are widely used in medicine as antiviral drugs (arbidol), antiemetics (tropisetron), non-steroidal anti-inflammatory drugs (indomethacin), antihypertensive drugs (dimecarbine), antitumor drugs (sunitinib), drugs that improve blood circulation and brain metabolism (vinpocetine), as well as antidepressants (pirlindol, metrolindol). In addition, among indole derivatives, drugs with antiglaucoma activity and alpha-glycosidase inhibitors have been found;[1] plant protection products, electronic materials and dyes have been created based on indole-containing substances.[2–5]

Previously, much attention was paid to compounds with pyrido[1,2-*a*]benzimidazole scaffold (Figure 1), which showed antitumor (NSC 699944),[6] antiviral,[7] antimicrobial,[8] antifungal (D11-2040)[9] and antimalarial activities (TDR86919).[10]

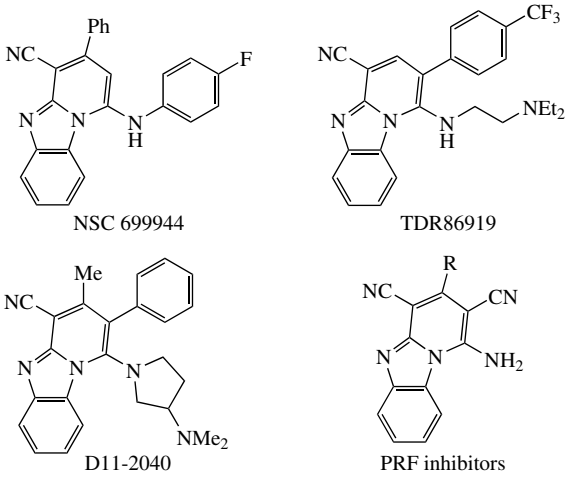
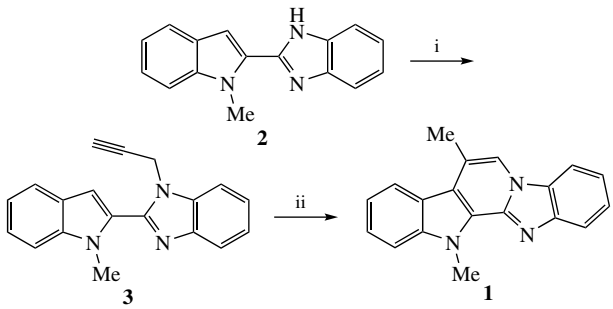


Figure 1 Biologically relevant pyrido[1,2-*a*]benzimidazoles.

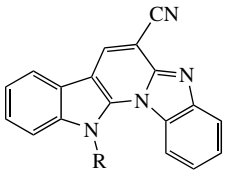
Preparations based on cyanopyridobenzimidazole exhibited inhibitory activity of the cellular function of the protein perforin (PRF) as a potential drug target.[11] The luminescent properties of pyridobenzimidazole scaffold are well known.[12]

However, compounds containing polyfused system of benzimidazolepyridoindole are little known. Only one work[13] reports the synthesis of 7,12-dimethyl-12*H*-benzo[4′,5′]imidazo-[1′,2′:1,2]pyrido[3,4-*b*]indole **1** (Scheme 1). Compound **1** was prepared from benzimidazolindole **2** by propargylation and subsequent heterocyclization of the propargyl intermediate **3**.

Recently, we patented[14] compounds with a similar heterocyclic system, namely, 12*H*-benz[4′,5′]imidazo[1′,2′:1,6]pyrido[2,3-*b*]-indole-6-carbonitriles **4**. The structure of compounds **4a–d** was confirmed by IR, ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry. Their IR spectra contained absorption bands of C=C and C=N bonds in the regions of 1455–1566 cm^{-1}, nitrile groups gave absorption bands in the regions of 2215–2222 cm^{-1}. The ^{1}H NMR spectra showed signals of aliphatic protons in the region of 0.62–2.62 ppm, signals of protons of the N–CH_2 group in the region of 4.42–5.51 ppm, signals of aromatic protons in the region of 7.36–8.99 ppm, and signals of the CH=CCN group



Scheme 1 *Reagents and conditions*: i, HC≡CCH_2Br, K_2CO_3, DMF, room temperature, 14 h; ii, CuI, MeCN, reflux.



4a–d

a R = H **c** R = Et
b R = Me **d** R = Pr

in the region of 9.09–9.50 ppm. Spectral data of ^{13}C NMR and mass spectrometry also correspond to the structure **4**.

In this study, we characterized representative homologue **4b**, and for the final confirmation of the structure we performed X-ray diffraction analysis of compound **4d** (Figure 2).† As follows from the data obtained, the molecule of **4d** is almost flat. The torsion angle between the terminal carbocyclic fragments is 5.43°. Short intermolecular distances between pairwise oppositely located flat structures of polycondensed heterocycle **4d** (Figure 3) indicate the presence of π–π staking (plane [N(8) C(9) C(17) C(18) C(19) C(20)] to plane [C(6) C(7) C(2) C(3) C(4) C(5)] centroid distance is 3.4312(11) Å, centroid–centroid distance is 3.722 Å and shift distance is 1.204 Å).

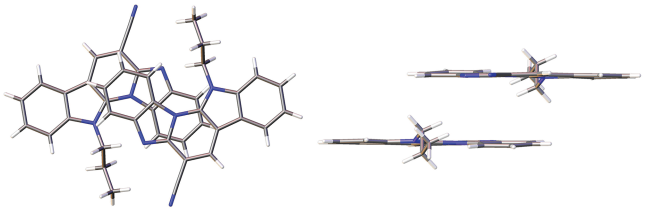


Figure 3 Side and top views of the crystal packing of **4d**.

The benzimidazolepyridoindolecarbonitriles **4** synthesized exhibited high luminescent activity and were patented as effective luminophores.[14] Spectral parameters recorded for solutions in acetonitrile and DMSO are collected in Table 1. The UV–VIS absorption and fluorescence spectra of compound **4c** in acetonitrile are shown in Figure 4. The electronic absorption and photoluminescence spectra of compound **4d** in acetonitrile, as well as the spectra of **4c**,**d** in DMSO, have the similar appearance as in Figure 4.

In order to identify correlations between structure and luminescent properties, we synthesized non-cyclic

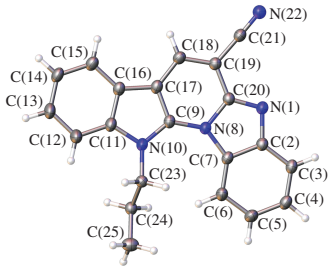


Figure 2 Molecular structure of compound **4d** according to X-ray diffraction data with the atom numbering used in the crystallographic analysis.

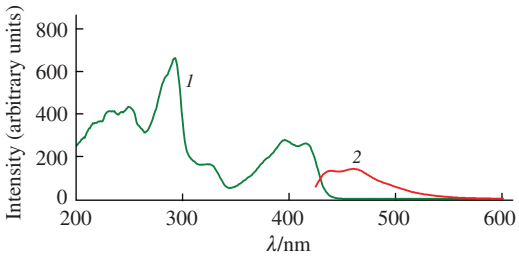


Figure 4 (*1*) Electronic absorption and (*2*) photoluminescence spectra of compound **4c** in acetonitrile, 298 K (2.1×10^{-6} M).

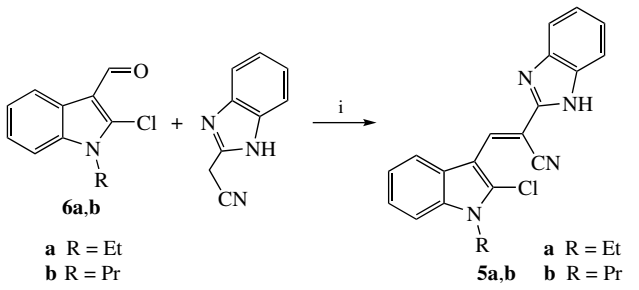
Table 1 Optical data of compounds **4c**,**d** and **5a**,**b** in MeCN and DMSO.

Compound	MeCN			DMSO		
	λ_{max}/nm	ε/dm^3 mol^{-1} cm^{-1}	λ^{fl}_{max}/nm	λ_{max}/nm	ε/dm^3 mol^{-1} cm^{-1}	λ^{fl}_{max}/nm
4c	292	1.96×10^5	439; 460	296	1.48×10^5	442; 464
	397	5.07×10^4		400	3.68×10^4	
	417	4.75×10^4		419	3.64×10^4	
	φ = 0.97[a]; λ^{ex} = 417 nm			φ = 0.99; λ^{ex} = 419 nm		
4d	293	1.85×10^5	440; 462	296	2.26×10^5	440; 464
	397	4.88×10^4		400	4.09×10^4	
	417	4.65×10^4		419	3.95×10^4	
	φ = 0.90; λ^{ex} = 417 nm			φ = 0.94; λ^{ex} = 419 nm		
5a	267	3.60×10^4		270	2.12×10^4	
	386	3.36×10^4		390	1.92×10^4	
	φ = 0.031; λ^{ex} = 385 nm			φ = 0.055; λ^{ex} = 390 nm		
5b	280–294	2.15×10^4	442	282–296	2.88×10^4	446
	386	2.92×10^4		390	3.17×10^4	
	φ = 0.079; λ^{ex} = 385 nm			φ = 0.16; λ^{ex} = 390 nm		

[a] Fluorescence quantum yields were determined using the Parker–Rice method[19] with a solution of anthracene as a standard luminophore.

† *Crystal data for* **4d**. $C_{21}H_{16}N_4$ (M_r = 324.38 g mol^{-1}), triclinic, space group $P\bar{1}$ (no. 2), a = 8.2387(2), b = 9.5255(2) and c = 10.6889(2) Å, α = 106.482(2)°, β = 103.048(2)°, γ = 91.366(2)°, V = 780.13(3) Å^3, Z = 2, T = 100.00(10) K, μ(CuKα) = 0.664 mm^{-1}, d_{calc} = 1.381 g cm^{-3}, 16359 reflections measured (8.894° ⩽ 2θ ⩽ 152.036°), 3239 unique (R_{int} = 0.0273, R_{sigma} = 0.0162) which were used in all calculations. The final R_1 was 0.0445 [$I > 2\sigma(I)$] and wR_2 was 0.1248 (all data). The X-ray diffraction data set was recorded on an Agilent SuperNova diffractometer using a microfocus X-ray radiation source with copper anode and Atlas S2 two-dimensional CCD detector. The reflections were collected, unit cell parameters determined and refined using the specialized CrysAlisPro software suite (Rigaku Oxford Diffraction, 2015).[15] The structures were solved using the ShelXT program (Sheldrick, 2015)[16] and refined with the ShelXL program (Sheldrick, 2015).[17] Molecular graphics and presentation of structures for the publication were performed with the Olex2 ver. 1.5 software suite.[18]

CCDC 2189189 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.



Scheme 2 *Reagents and conditions*: i, Pr^{i}OH, reflux, 1.5–2 h.

2-(benzimidazol-2-yl)-3-(3-indolyl)acrylonitriles **5a**,**b** with the same structural fragments and a fairly long range of π-conjugations (Scheme 2). The starting 1-alkyl-2-chloro-1*H*-indole-3-carbaldehydes **6a**,**b** were prepared as reported.[20] Compounds **5a**,**b** were obtained by boiling indole carbaldehydes **6a**,**b** with benzimidazolylacetonitrile in isopropanol for 1–2 h. The IR spectra of compounds **5a**,**b** contain absorption bands for NH bond vibrations in the region of 2961–2982 cm^{-1}, nitrile groups in the region of 2215 cm^{-1}, C=C and C=N bonds in the region of 1469–1595 cm^{-1}. In the ^{1}H NMR spectra of acrylonitriles **5a**,**b**, in contrast to the spectra of cyclized derivatives **4**, the signal for NH proton is manifested while the signals of aromatic protons and CH=CCN groups are shifted downfield.

The studies on photochemical activity did not reveal significant luminescent properties of compounds **5a**,**b** (see Table 1), probably due to the non-rigidity of their structure, which prevents effective luminescence.

In summary, the structure of the obtained representatives of the new heterocyclic system, 12*H*-benz[4′,5′]imidazo[1′,2′:1,6]-pyrido[2,3-*b*]indole, has been established by IR, NMR spectroscopy, and mass spectrometry data, as well as X-ray diffraction analysis of compound **4d**. Exploring the photochemical properties of the resulting compounds **4** revealed that they luminesce in the blue region of the spectrum with a high quantum yield, which makes it possible to use them as effective luminophores in modern emitting devices.

IR and NMR spectra were recorded at the Center for Collective Use ‘Molecular Spectroscopy’ of the Southern Federal University and the Educational Research Laboratory of Resonance Spectroscopy, Department of Chemistry of Natural and High Molecular Compounds of the Southern Federal University (Rostov-on-Don, Russian Federation).

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2024.02.037.

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