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Synthesis and photophysical studies of novel 2-[5-(4-diethylaminophenyl)thiophen-2-yl]quinazoline derivatives

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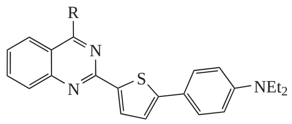
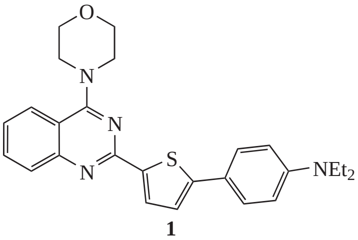
Two novel 2-[5-(4-diethylaminophenyl)thiophen-2-yl]quinazoline derivatives were obtained using Suzuki cross-coupling as the key step. Optical studies have demonstrated that 4-cyanoquinazoline derivative possesses low photoluminescence, whereas its 3*H*-quinazolin-4-one counterpart represents promising photoluminescent molecule.



R = CN, λ_{em} = 471 nm (toluene);
λ_{em} = 539 nm (MeCN)
R = OH, λ_{em} = 490 nm, φ = 71% (toluene);
λ_{em} = 541 nm, φ = 28% (MeCN)

Arylated 2,4-disubstituted quinazolines are prospective photoluminescent and electroluminescent materials. Among them, donor–quinazoline–donor type containing 4-diethylaminophenyl residue are of special interest.[1] On the other hand, thienyl substituted diazines with extended π-conjugated system exhibit electrochemical, optical and electronic structural properties.[2] Arylamino derivatives, in particular *N*,*N*-dialkyl- and *N*,*N*-diphenylanilines, are electron-rich compounds which find use as hole transporting materials and light emitters.[3]

Recently, we reported the functionalization of 2-(thiophen-2-yl)-4-(morpholin-4-yl)quinazoline fluorophore at the 5-position of thiophene ring with aryl and arylethynyl moieties through bromination and subsequent palladium-catalyzed cross-coupling reactions.[4] The thus obtained 2-[5-(4-diethylaminophenyl)thiophen-2-yl]-4-(morpholin-4-yl)quinazoline **1** demonstrated emission of green light upon irradiation and the highest quantum yield. The effect of its protonation has also been studied, and the ability of this molecule to function as colorimetric and luminescent pH sensor has been revealed with significant colour changes and luminescence switching upon the introduction of acid.[4]



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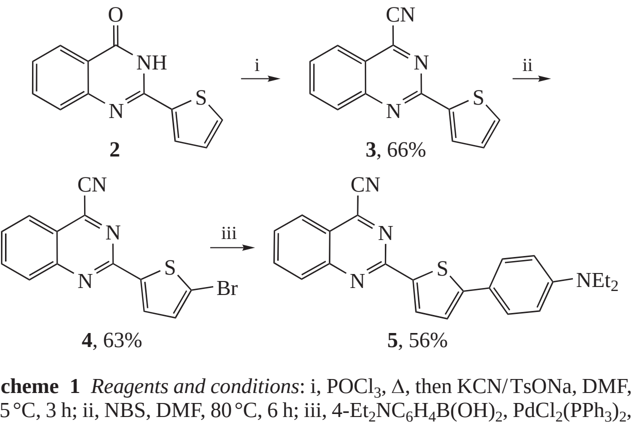
Modification of compound **1** at the 4-position of quinazoline core seems to be useful in tuning the photophysical properties. Incorporation of cyano group instead of morpholino residue or oxo group as a part of 3*H*-quinazolin-4-one can afford quinazoline-based push–pull systems, which was the purpose of this study.

Transformation of 2-(thiophen-2-yl)quinazolin-4-one **2** into 4-chloro derivative[5] followed by replacement of chlorine atom with cyano group afforded derivative **3** (Scheme 1). Application of sodium tosylate as a base for the synthesis of 4-cyano-2-phenylquinazoline was reported previously.[6] Bromination of compound **3** at the thiophene moiety was accomplished by heating with *N*-bromosuccinimide in DMF. It should be noted that 4-morpholino analogue of compound **3** underwent bromination under milder conditions.[4] Bromide **4** was then subjected to the Suzuki cross-coupling with 4-diethylaminophenylboronic acid (see Scheme 1) to give product **5** in reasonable (56%) yield after column chromatography.[†]

^{13}C NMR spectroscopic data for compounds **3**–**5** were consistent with their structures. In the mass spectra of thienylquinazolines, the peaks with 100% relative intensity were observed for molecular ion (compound **3**), $[M-Br]^+$ (compound **4**) and $[M-Me]^+$ (compound **5**). The bands in the range of 2200–2260 cm^{-1} typical of



Scheme 1 *Reagents and conditions*: i, POCl$_3$, Δ, then KCN/TsONa, DMF, 95 °C, 3 h; ii, NBS, DMF, 80 °C, 6 h; iii, 4-Et$_2$NC$_6$H$_4$B(OH)$_2$, PdCl$_2$(PPh$_3$)$_2$, PPh$_3$, K$_2$CO$_3$, PhMe, EtOH, H$_2$O, 85 °C, 7 h.

[†] For the experimental procedures, see Online Supplementary Materials.

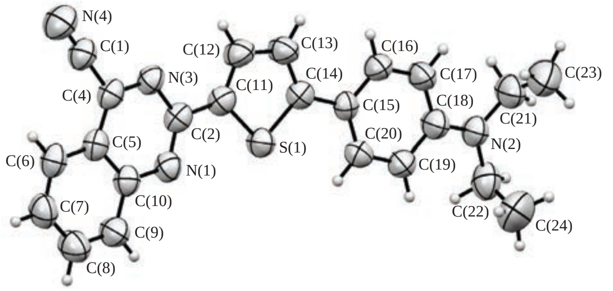
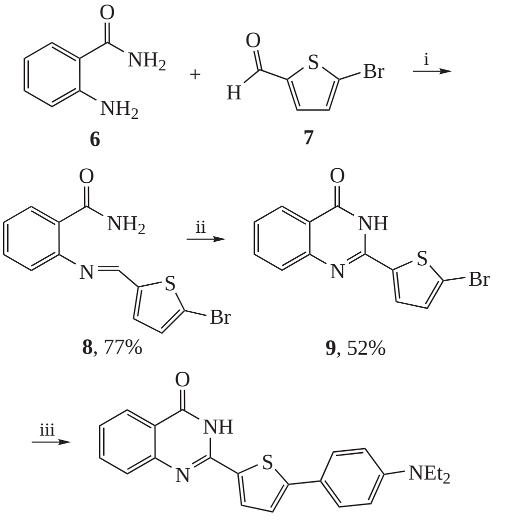


Figure 1 Molecular structure of quinazoline **5** in the thermal ellipsoids of 50% probability. The disordered components are omitted for clarity.

CN group were not observed in the IR spectra of quinazolines **3** and **5**, possibly, because their nitrile group is directly attached to the π-conjugated system (*cf.* ref. 7). The Raman scattering spectra of compounds **3** and **5** demonstrated the low-intensive signals of CN group at 2240 cm^{-1} (see Online Supplementary Materials).

According to the XRD data,‡ compound **5** is crystallized in the centrosymmetric monoclinic space group (Figure 1). Except for the diethylamino moiety, the molecule is planar with maximal deviations of the atoms from the least squared plane 0.15 Å. The diethylamino group shows strong vibrations, its ethyl groups being disordered into two positions with occupancy coefficients 0.7/0.3. In additions to nonspecific intermolecular contacts, in the crystal the shortened contacts CN···HC(7) $[2-x, -1-y, -z]$ 2.658 Å are present. As a result, 'H-bonded' dimers of the molecules are formed with the length of the planar molecular system 27 Å (see Figure S2, Online Supplementary Materials). However, any efficient π–π interactions in the crystal are not observed.

Synthesis of 4-oxo analogue is shown in Scheme 2. 2-(5-Bromothiophen-2-yl)quinazolin-4(3*H*)-one **9**, the key cross-coupling intermediate, was obtained from 2-aminobenzamide **6** and 5-bromothiophene-2-carbaldehyde **7** using previously described technique.[8] Attempted access to compound **9** by bromination of precursor **2** failed. The heating of the latter with *N*-bromosuccinimide in DMF or in AcOH/Ac$_2$O mixture caused bromination at the benzene ring along with the required bromination of the thiophene residue. Cyclization of intermediate azomethine **8** by refluxing in ethanol in the presence of copper(II) chloride led to 5-bromothienyl derivative of quinazoline **9** in high yield. Further Suzuki cross-coupling with 4-diethylaminophenylboronic acid provided the target product **10** in satisfactory (50%) yield after column chromatography (see Scheme 2). Notably, the use of PdCl$_2$(PPh$_3$)$_2$–PPh$_3$ catalyst (see Scheme 1, synthesis of **5**) in the case of **10** was less efficient. The structure of product **10** was confirmed by the ^{1}H, ^{13}C NMR spectroscopy and mass spectrometry data. In the mass spectra of thienylquinazolines, peaks with 100% relative intensity were observed for [M – Br]$^+$ (compound **9**) and [M – Me]$^+$ (compound **10**).



10, 50%

Scheme 2 *Reagents and conditions*: i, EtOH, Δ, 3 h; ii, CuCl$_2$, EtOH, Δ, 5 h; iii, 4-Et$_2$NC$_6$H$_4$B(OH)$_2$, Pd(PPh$_3$)$_4$, K$_2$CO$_3$, THF, 80 °C, 12 h.

Table 1 Optical spectroscopy data for the thienylquinazoline derivatives **1**, **5** and **10**.

Compound	Solvent	λ_{abs}/nm[a]	λ_{em}/nm	φ (%)[b]	Stokes shift $\Delta\nu_{St}$/cm^{-1}
1	toluene	405	476	67	3683
	MeCN	401	544	23	6555
5	toluene	402	471	< 1	3644
	MeCN	397	539	< 1	6636
10	toluene	410	490	71	3982
	MeCN	404	541	28	6268

[a] Both absorption and emission spectra were measured in MeCN and toluene solution at room temperature at $c = 0.1$ μmol ml^{-1}. [b] Fluorescence quantum yield (±10%) determined relative to 3-aminophthalimide in EtOH as a standard[12] ($\varphi = 60\%$), excitation at 400 nm.

Photophysical properties of 2-thienylquinazoline derivatives **5** and **10** were evaluated in two solvents with different dielectric constants, namely toluene ($\varepsilon_r = 2.38$) and acetonitrile ($\varepsilon_r = 36.64$).[11] The spectral data are summarized in Table 1 (for UV-VIS spectra, see Online Supplementary Materials).

Compounds **5** and **10** demonstrate absorption wavelengths (λ_{max}) at 397–410 nm, which are close to that of 4-morholino derivative **1** and do not depend significantly on solvent nature. Quinazoline **5** possesses weak emission in both acetonitrile and toluene solutions, and emission maxima do not differ significantly from those of compound **1** (see Table 1). The maxima of the emission bands of compound **10** are located at 541 nm (in acetonitrile) and 490 nm (in toluene). Both compounds show red shifts of emission bands on increase in solvent polarity from toluene to acetonitrile. The Stokes shifts are rather large thus providing a clear indication of high polarizability of these π-conjugated systems.

It should be noted that the values of Stokes shifts for quinazolines **1**, **5** and **10** grow from 3644–3982 cm^{-1} in toluene to 6268–6636 cm^{-1} in acetonitrile. This may be due to greater stabilization of the polarized molecules **1**, **5**, **10** in the excited state by more polar molecules of a solvent. Fluorescence quantum yield of compound **10** is strongly dependent on the polarity of solvents (28% in MeCN and 71% in toluene, see Table 1) as in the case of compound **1**. Optical properties of compounds **1** and **10** are rather close, however, unlike compound **1**, quinazoline **10**

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‡ *Crystal data for* **5**. The single crystal (red prism, 0.38 × 0.26 × 0.17 mm), C$_{23}$H$_{20}$N$_4$S, was used for X-ray analysis. Analysis was performed at 295(2) K on an Xcalibur3 diffractometer using graphite monochromated MoKα radiation (λ = 71.073 nm) and CCD detector. An empirical absorption correction was applied [μ(MoKα) = 1.554 mm^{-1}]. Crystal is monoclinic, space group $P2_1/c$ with $a = 11.566(4)$, $b = 9.527(6)$ and $c = 18.088(9)$ Å, $\beta = 90.57(4)°$, $V = 1993.1(18)$ Å^3, $Z = 4$. On the angles $3.82 < \theta < 65.95°$, 15626 reflections were collected, among them 3411 unique reflections ($R_{int} = 0.0655$), 1747 reflections with $I > 2\sigma(I)$. Completeness to $\theta = 65.95°$ was 98.20%. The structure was solved by direct method and refined by full-matrix least squares at F^2 using the SHELXTL program package.[9] All non-hydrogen atoms were refined anisotropically, the positions of the hydrogen atoms were calculated using a riding model in isotropic approximation. GOF at F^2 was 1.034; final R values $[I > 2\sigma(I)]$: $R_1 = 0.0481$, $wR_2 = 0.1026$; R values (all reflections): $R_1 = 0.0851$, $wR_2 = 0.1076$; largest diff. peak/hole 0.261/–0.171 e Å^{-3}.

CCDC 1540006 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.

did not reveal colour changes and luminescence switching upon addition of acid. Nevertheless, it is worth noting that the synthetic pathway to compound **10** includes less steps than that to quinazoline **1**, moreover, quinazolinone **10** was found to exhibit an intensive blue fluorescence (φ ~ 71%) when excited with visible light and therefore has potential as a blue fluorophore.

In summary, we have effectively prepared and characterized two novel thienylquinazoline derivatives **5** and **10**. Incorporation of cyano group into compound **1** instead of morpholino residue does not have a significant impact on the position of absorption and emission bands and considerably reduces the luminescence quantum yield. Meanwhile, 3*H*-quinazolin-4-one **10** bearing the same 5-(4-diethylaminophenyl)thiophen-2-yl substituent at the 2-position proved to possess strong photoluminescence. Notably, compound **10** is a close analogue of 2-(5-phenylthien-2-yl)-quinazolin-4-one exhibiting antibacterial activity.[13]

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2018.01.002.

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