A Squaraine-based Near-infrared Dye with Bright Fluorescence and Solvatochromic Property

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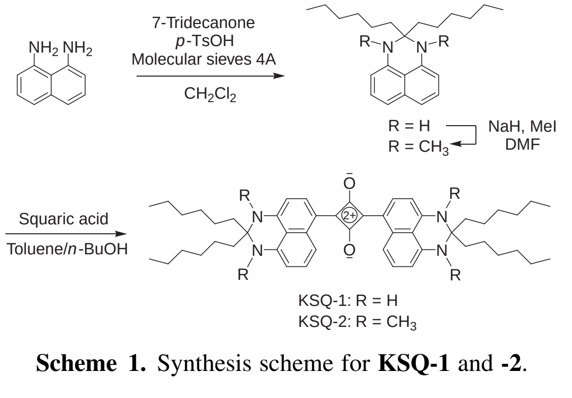
We report a newly synthesized squaraine-based fluorescent dye (**KSQ-2**) with excellent and useful optical characteristics such as a sharp near-infrared (NIR) emission at 751 nm, an extremely high fluorescence quantum yield ($\phi = 0.56$ in cyclohexane), and linear positive solvatochromic properties in the spectral region around 780 nm.

Near-infrared (NIR) fluorescent dyes, which emit light in the NIR region (over 650 nm), have been applied for various devices such as laser dyes, organic light-emitting diodes (OLED), invisible printing inks, probes for photodynamic therapy, and contrast agents for in vivo imaging.[1] Therefore, the development of NIR fluorescent dyes with high performance is required in many fields. Squaraine dyes (1,3-disubstituted squaric acid derivatives) often show their absorption maxima at the far-red and NIR region with high extinction coefficients (around 200,000 $M^{-1}\,cm^{-1}$) and high photostabilities, which are due to the strong electron-accepting ability of squaric acid and their structural rigidity; hence, they have been applied in many fields.[2–4] However, there are relatively few reported squaraine fluorescent dyes, which emit at wavelengths over 700 nm, such as the dialkylanthracene-based squaraines recently published by Basheer et al.[5] Therefore, we decided to investigate the optical properties of these NIR dyes and to develop novel NIR fluorescent dyes based on this investigation.

2,3-Dihydroperimidine-substituted squaraines[6] were chosen by reason of the strong π-electron donating ability of the 2,3-dihydroperimidine unit (Scheme 1). In order to evaluate the influence of N-substitution on the properties of the dye, two different compounds **KSQ-1** (R = H) and **KSQ-2** (R = CH_3) were investigated. The syntheses of the dyes were achieved within three steps with high yields (**KSQ-1**: 44.4%, **KSQ-2**: 29.0%).[7] Absorption and fluorescence maxima of **KSQ-1** in cyclohexane were observed at 802 and 811 nm, respectively. However, the quantum yield was very low ($\phi \leq 0.074$ in any solvents), which implies that the already known dye **KSQ-1**[6] is hardly useful as a fluorescent dye for practical applications. In fact, no reports concerning the use of dihydroperimidine-substituted squaraines as fluorescent dyes have been published. It is assumed that the presence of N–H bonds can favor nonradiative pathways for relaxation from the excited state, such as hydrogen-bond-induced intersystem crossing.[8] On the other hand, **KSQ-2** (N-substituted dye) was found to have a higher extinction coefficient (200,000 $M^{-1}\,cm^{-1}$) and sharp absorption and fluorescence spectra (full width at half maximum height: fwhm 35 nm) in the NIR region ($\lambda_{flu} = 751$ nm), which are even much sharper than those of existing quantum dots (Figure 1).[9] Interestingly, a quantum yield unusually high for NIR fluorophores ($\phi_{cyclohexane} = 0.56$, $\phi_{toluene} = 0.47$) was observed, which is more than eight fold higher compared to that of **KSQ-1** ($\phi_{cyclohexane} = 0.067$) (Table 1). These values (λ_{flu} and ϕ) are also much superior to previously reported NIR fluorescent dyes (squaraine,[5] cyanine,[11] and boron-dipyrromethene[12]). With just a simple alkylation, the already known almost nonemissive dye **KSQ-1**, could be transformed into **KSQ-2** with remarkably improved optical properties. The very recently reported diketopyrrolopyrrole-based NIR fluorescent dyes are the only ones to show comparable optical properties ($\lambda_{flu} = 831$ nm, $\phi = 0.53$ in chloroform).[13]



Scheme 1. Synthesis scheme for **KSQ-1** and **-2**.

Table 1. Optical properties of **KSQ-1** and **-2** in cyclohexane

Dye	λ_{abs}/nm	λ_{flu}/nm	fwhm/nm	$\varepsilon/M^{-1}\cdot cm^{-1}$	ϕ^{a}
KSQ-1	802	811	39	140,000	0.067
KSQ-2	737	751	35	200,000	0.56

[a] ICG ($\phi = 0.11$ in DMSO) was used as a reference standard.[10]

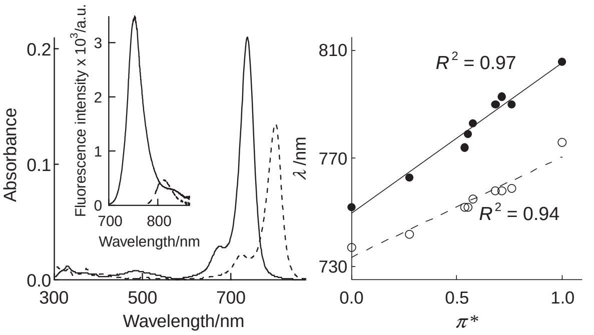


Figure 1. Left: Absorption spectra of **KSQ-1** (1.0×10^{-6} M, dotted line) and **KSQ-2** (1.0×10^{-6} M, solid line) in cyclohexane. Inset: the fluorescence spectra of **KSQ-1** (dotted line, exc.: 802 nm) and **KSQ-2** (solid line, exc.: 737 nm). Right: Plot of the wavelength λ_{abs} or λ_{flu} [nm] of **KSQ-2** versus the solvent polarity parameter π^*. Open and filled circles show absorption and fluorescence data, respectively.

Additionally, distinct behavior toward solvent polarity was

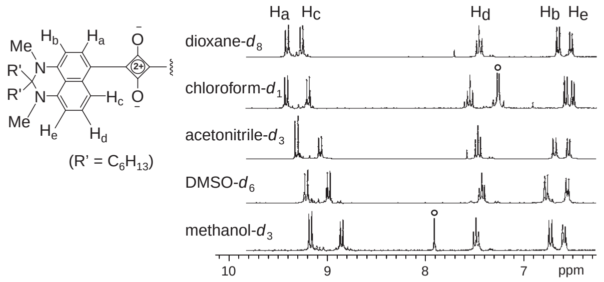


Figure 2. NMR charts of **KSQ-2** (1.35 mM) in various solvents at 25 °C. Chloroform peaks are marked by a circle.

observed in the case of **KSQ-2**, only. The absorption and fluorescence maxima of **KSQ-2** in 9 different solvents were measured and plotted versus the solvent polarity parameter π^*.[7,14] **KSQ-2** exhibited typical positive solvatochromic shifts over a large polarity range ($\lambda_{\mathrm{DMSO}} - \lambda_{\mathrm{cyclohexane}} = 56\,\mathrm{nm}$) with a good linear correlation between the wavelength of maximum absorption or fluorescence and the parameter π^* ($R^2 \geq 0.94$, see Figure 1). Furthermore, **KSQ-2** shows environment polarity-dependent fluorescence intensity changes. The quantum yield of **KSQ-2** increased up to over 70-fold by changing the solvent polarity ($\phi_{\mathrm{cyclohexane}}/\phi_{\mathrm{methanol}} = 70$, $\phi_{\mathrm{toluene}}/\phi_{\mathrm{methanol}} = 60$), while the anthracene-based squaraines do not exhibit any significant solvatochromic shift ($\lambda_{\mathrm{ethanol}} - \lambda_{\mathrm{toluene}} < 10\,\mathrm{nm}$) and no significant polarity-dependent fluorescence change ($\phi_{\mathrm{toluene}}/\phi_{\mathrm{ethanol}} < 6.0$).[5] Hence, the degree of increase of the quantum yield is quite noticeable, and it enables the sensitive detection of polarity changes of the surrounding environment.

NMR measurements of **KSQ-2** in various solvents were performed in order to find some hints to the reasons of the observed solvatochromism and solvent-polarity-induced fluorescence decrease. As shown in Figure 2, only the H_a and H_c protons, which are most closely located to the central C_4O_2 unit, were observed particularly downfield (δ 8.9–9.4). These protons were most strongly influenced and shifted upfield significantly with increasing solvent polarity compared to the other aromatic protons. We suggest that the downfield location of the H_a and H_c signals in nonpolar solvents might be due to an increased ring current deshielding effect caused by the C_4O_2 unit. The observed upfield shifts of H_a and H_c with increasing solvent polarity are likely to be caused by a solvent-induced conformational change and/or a change in the electronic properties of the central C_4O_2 unit due to the presence of the surrounding solvent. A deviation from a planar molecular geometry will result in a decreased ring current deshielding of the H_a and H_c protons and thus, in an upfield shift of the corresponding NMR signals. Furthermore, an increased solvent interaction of the central C_4O_2 unit will further enhance such an effect. In fact, a strong intramolecular charge-transfer (ICT) character was suggested by Bigelow and Freund on the basis of quantum chemical calculations.[15] According to this article, a typical squaraine dye is expected to have an ICT character in both ground and excited states, and the concomitant charge localization induces strong complex solvation. Such finding was confirmed for squaraine dyes by observing positive solvatochromic shifts in VIS spectroscopy.[16,17] In particular in the study by Lapouyade et al.[17] characteristics very similar to those observed for **KSQ-2** (bathochromic shift, larger Stoke's shift, and decreasing quantum yield with increase in solvent polarity) are described. The authors of that article attribute those characteristics to be most probably due to the involvement of a nonemissive decay from a twisted intramolecular charge-transfer (TICT) state. Thus, these theory-based and spectroscopic reports, as well as our own NMR and spectroscopic data, support our suggestion of solvatochromism and fluorescence decrease induced by a conformational change, most probably into a TICT state, resulting in a deviation of **KSQ-2** from a planar structure.

In conclusion, we have successfully synthesized a novel NIR fluorescent dye (**KSQ-2**) based on a known squaraine structure with useful optical characteristics, linear positive solvatofluorochromic properties, and environment-polarity-dependent fluorescence quantum yields.

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