π-Extension of a 4-Ethoxy-1,3-thiazole via Aryl Alkyne Cross Coupling: Synthesis and Exploration of Electronic Structure

Journal:	*Photochemical & Photobiological Sciences*
Manuscript ID	PP-ART-05-2015-000219.R1
Article Type:	Paper
Date Submitted by the Author:	08-Sep-2015

Complete List of Authors:	Habenicht, Stefanie; Friedrich Schiller University Jena, Institute of Organic Chemistry and Macromolecular Chemistry Schramm, Stefan; Friedrich Schiller University Jena, Institute of Organic Chemistry and Macromolecular Chemistry Zhu, Mingming; Friedrich Schiller University Jena, Institute of Organic Chemistry and Macromolecular Chemistry Freund, Robert; Friedrich Schiller University Jena, Institute of Organic Chemistry and Macromolecular Chemistry Langenstück, Teresa; Friedrich Schiller University Jena, Biomolecular Photonics Group, Jena University Hospital Strathausen, Rainer; Friedrich Schiller University Jena, Institute of Organic Chemistry and Macromolecular Chemistry; Friedrich Schiller University Jena, Biomolecular Photonics Group, Jena University Hospital Weiss, Dieter; Friedrich Schiller University Jena, Institute of Organic Chemistry and Macromolecular Chemistry Biskup, Christoph; Friedrich Schiller University Jena, Biomolecular Photonics Group, Jena University Hospital Beckert, Rainer; Friedrich Schiller University Jena, Institute of Organic Chemistry and Macromolecular Chemistry

Journal Name

ARTICLE

π-Extension of a 4-Ethoxy-1,3-thiazole via Aryl Alkyne Cross Coupling: Synthesis and Exploration of Electronic Structure

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Stefanie H. Habenicht[a], Stefan Schramm[a], Mingming Zhu[a], Robert R. A. Freund[a], Teresa Langenstück[b], Rainer Strathausen[a,b], Dieter Weiß[a], Christoph Biskup[b] and Rainer Beckert[a]†

A series of four donor aryl alkynyl substituted thiazole derivatives **3a-d** and three similar aryl donor-acceptor systems **6a-c** have been synthesized. All compounds bear different electron-donating groups in 5-position of the thiazole core. The influence of both electron donor strength and the additional phenylethynyl unit on photophysical properties, i.e. UV/Vis absorption, fluorescence emission and fluorescence lifetime, has been evaluated. Additionally, theoretical calculations have been performed at the CAM-B3LYP/6-31+G(d,p) level and a good agreement with the experimental data has been achieved. The new derivatives synthesized via Palladium catalyzed cross coupling are featured by moderately strong emission between 474 and 538 nm (Φ_F = 0.35 – 0.39) and Stokes' shifts ranging from 0.54 to 0.79 eV (4392 – 6351 cm^{-1}). The smaller chromophores of type **6** exhibit modest to high fluorescence emission (Φ_F = 0.45 – 0.76) between 470 and 529 nm and their Stokes' shifts range from 0.59 to 0.65 eV (4765 – 5251 cm^{-1}).

Introduction

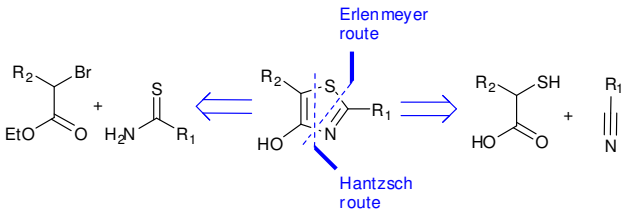
Though 4-hydroxythiazoles have been known for several decades, their (photo)chemical and (photo)physical properties have only been examined in recent years.[1] The heterocyclic core unit of this substance class is the keystone of several natural products, e.g. luciferin which is the compound responsible for the bioluminescence of the firely (*lampyridae)*.[2] Consequently, derivatives based on 4-hydroxythiazole are subject of in-depth scientific investigation in application oriented research involving chromophores/fluorophores and are still subject to research in different groups.[3,4]

Tailor-made derivatives have been used as blue emitting species in polymer backbones,[5] as energy donors along with acceptors based on Ruthenium(II) complexes for FRET applications in polymers,[6] as chromophores/light harvesting ligands in Ruthenium(II) complexes in DSSCs,[7,8] and also as fluoride ion sensor.[3] Very recently, an azide-modified probe for fluorescence and mass spectrometric detection in activity-based protein profiling and functional metabolic profiling based on 4-hydroxy-1,3-thiazole has been reported.[9] Furthermore, recent research indicates that thiazole-based fluorophores, due to their matching excitation and emission characteristics, are potential sensitizers for the highly efficient chemiluminescence of the 2-coumaranones.[10-12]

4-Hydroxy-1,3-thiazoles are usually either synthesized following the Hantzsch or Erlenmyer route both of which are suitable for efficient construction of complex systems (Scheme 1). The Hantzsch synthesis, a cyclizing condensation, involves α-substituted α-bromoacetic esters, aromatic carbothioamides and catalytic amounts of a base whereas the Erlenmeyer route utilizes stochiometric amounts of a base, aromatic carbonitriles, and α-substituted α-mercaptoacetic acid derivatives. Since those α-mercaptoacetic acid derivatives are not as easily accessible as complementary α-bromo derivatives, the Hantzsch route is often favored.

Solubility and photophysical properties can be tailored by varying substituents R^1, R^2 and by etherification of the phenolic hydroxyl group. Modulating the solubility of these compounds is especially important as 4-hydroxy-1,3-thiazoles form strong intermolecular hydrogen bonds and are hardly soluble even in dipolar aprotic solvents such as DMSO and DMF.

As substituents R^1 and R^2, arylic and heteroarylic groups are well established as they expand the conjugated π-system and allow the construction of donor-π-acceptor systems, for



Scheme 1: Synthetic routes towards 4-Hydroy-1,3-thiazoles according to Hantzsch and Erlenmeyer.[13]

[a] *Institute of Organic Chemistry and Macromolecular Chemistry, Friedrich Schiller University, Humboldtstr. 10, 07743 Jena, Germany*
[b] *Biomolecular Photonics Group, Jena University Hospital, Friedrich Schiller University, Nonnenplan 2-4, 07743 Jena, Germany.*
† Corresponding author. Email: c6bera@uni-jena.de

Electronic Supplementary Information (ESI) available: selected calculated torsion angles, Lambert-Beer plots, ^{1}H and ^{13}C NMR spectra. See DOI: 10.1039/x0xx00000x

example with a 2-pyridyl moiety in 2-position (R^1) and a 4-methoxyphenyl unit in 5-position (R^2).[1]

In a recent publication, Buchwald Hartwig amination reactions have been performed with 4-methoxy-1,3-thiazole derivatives in order to synthesize donor-π-acceptor systems with triarylamine donor moieties for use in DSSCs.[8] No further investigations involving cross coupling reactions with 4-hydroxy-1,3-thiazoles have been reported yet. In an attempt to close this synthetic gap, we performed different aryl alkyne cross coupling reactions.

Alkynes, because of their rigidity and conjugated π-system, are not only excellent building blocks for unsaturated molecular scaffolds, but also constitute attractive functional groups that can be transformed in many ways. Because of the unsaturated, high-energy structure of such compounds, the Sonogashira cross-coupling reaction has become one of the most important methods in the formation of carbon-carbon bonds over the past decades and plays an important role in the synthesis of pharmaceuticals, agrochemicals and functional materials. We therefore tested this reaction in order to extend the π-conjugation between terminal aryl moieties and 4-hydroxythiazole type fluorophores.

Photophysical properties of the new compounds have been examined, the influence of the newly introduced phenylethynyl unit on the photophysical behavior has been evaluated and quantum chemical calculations have been performed.

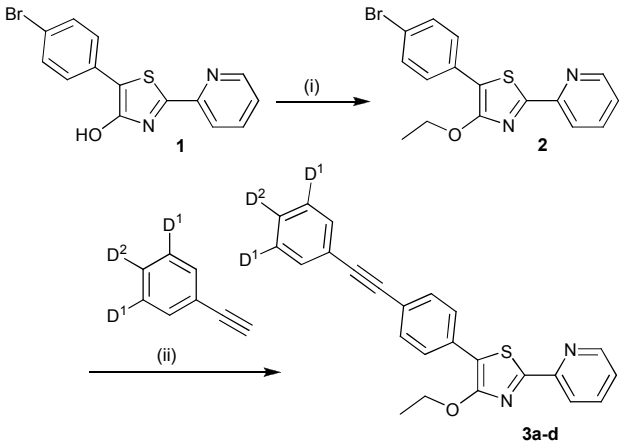
Results and Discussion

Synthesis

Synthesis of the 4-hydroxy-1,3-thiazole **1** was performed as described in the literature[9] and followed by Williamson type etherification in acetone, using K_2CO_3 as a base to yield **2** as cross coupling precursor. Palladium catalyzed Sonogashira cross coupling reactions have then been performed according to literature procedures.[14,15] Phenylacetylene derivatives bearing different electron donating groups (D) were used in the cross coupling reactions. The new π-extended derivatives **3a**-**d** were obtained in moderate to good yields (Scheme 2, Table 1).

Although all of the phenylacetylene derivatives used bear electron donating groups, it appears that cross coupling yields increase with increasing donor strength. **3d** bears two methoxy groups and there is only one in **3c**, but the electronic effect of substituents in *meta* position (**3d**) is only moderate and those in *para* position (**3c**) have a much stronger influence on the π-system. **3b** and **3a**, which involve a *p*-amino and a *p*-dimethylamino group were both obtained in 76% yield which is significantly higher than the yields of **3d** (20%) and **3c** (51%).

A proposed mechanism for this type of cross coupling reaction, employing TBAF as both solvent and base and $Pd(PPh_3)_2Cl_2$ as catalyst, has been published by Liang et al.[15] It is stated that the TBAF used in the reaction is probably responsible for the deprotonation of the acidic acetylene-H which can then form a palladium complex from which the desired product can be



Scheme 2: Synthesis of phenylethynyl derivatives **3a-d**. **3a**: D^1 = H, D^2 = $N(CH_3)_2$; **3b**: D^1 = H, D^2 = NH_2; **3c**: D^1 = H, D^2 = OCH_3; **3d**: D^1 = OCH_3, D^2 = H. (i) EtI, K_2CO_3, acetone, reflux, 93%; (ii) $Pd(PPh_3)_2Cl_2$, TBAF·$3H_2O$, 80 °C, 20-76%.

eliminated. According to the proposed mechanism, 1-ethynyl-4-nitrobenzene should work very well as a cross coupling partner, since the ethynyl-hydrogen is more acidic due to the strong acceptor character of the nitro group. In our study, however, we observed the contrary: reaction of **2** with 1-ethynyl-4-nitrobenzene did not afford the desired product, in fact no conversion of the starting material was observed. We therefore suppose that, in our case, electron rich phenylacetylene derivatives act as efficient nucleophiles in a palladium-catalyzed nucleophilic aromatic substitution reaction in a Sonogashira reaction analogue manner.[16]

Additionally to the cross coupling reactions described above, the substituents present in **3a-c** were placed directly on a phenyl ring in 5-position of the thiazole unit to determine and explain the effect of the additional phenylethynyl unit on the photophysical properties. An analogue to **3d** could not yet be obtained. Synthetic routes to compounds **6a-c** are depicted in Scheme 3. Compound **4** has already been reported[7] and was converted to **5** by alkylation of the phenolic hydroxyl group. Reduction of the nitro group affords **6b** which can then be methylated at the amino nitrogen to obtain **6a**. Synthetic protocols for reduction and methylation were adapted from the literature.[17,18] To obtain **6c**, the 4-hydroxy-1,3-thiazole **9** was synthesized via Hantzsch-cyclization between ethyl 2-bromo-2-(4-methoxyphenyl)acetate **7** and pyridine-2-carbothioamide **8** followed by subsequent alkylation with bromoethane.

Optical Properties

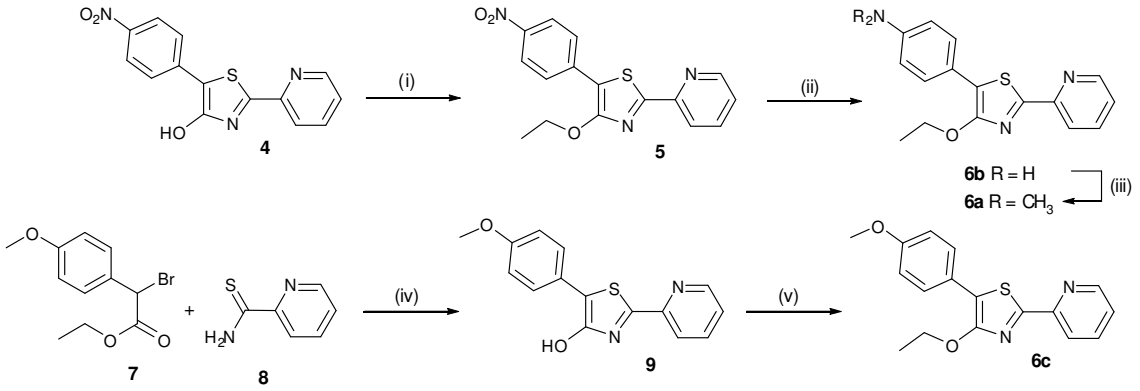
The structures of all new compounds were confirmed by means of NMR, MS (EI and high resolution ESI), UV/Vis and IR

Table 1: Substituent pattern and cross coupling yields for **3a-d**.

Compound	D^1	D^2	Isolated yield (%)
3a	H	$N(CH_3)_2$	76
3b	H	NH_2	76
3c	H	OCH_3	51
3d	OCH_3	H	20

Journal Name

ARTICLE



Scheme 3: Synthesis of **6a-c**. (i) EtI, K_2CO_3, DMSO, r.t., 93%; (ii) Raney-Ni, $N_2H_4 \cdot H_2O$, EtOH, 60 °C, 94%; (iii) 3M H_2SO_4, HCHO (37%), $NaBH_4$, THF, r.t., 80%; (iv) NaOAc, EtOH, reflux, 74%; (v) EtBr, K_2CO_3, acetone, reflux, 32%.

spectroscopy. UV/Vis and fluorescence emission spectra of the dyes are depicted in Figure 1 (**3a-d**) and Figure 2 (**6a-c**) and spectroscopic data are summarized in Table 2 and Table 3.

The UV/Vis absorption and fluorescence emission spectra of **3a-d** and **6a-c** in THF solution were recorded to establish relationships between electron donor strength of the substituents and the additional phenylethynyl unit present in **3a-d** on their photophysical properties. The absorption spectra of **3a-d** display two absorption bands each over a range of 312-401 nm. The bands at shorter wavelength (333, 328, 318 and 312 nm, respectively), correspond to $S_0 \rightarrow S_2$ transitions of compounds **3a-d**. The longer wavelength absorption bands at 401, 399, 393 and 392 nm are consistent with $S_0 \rightarrow S_1$ transitions. Extinction coefficients ε [10^4 M^{-1} cm^{-1}] at λ_{max} of the longer wavelength absorption bands range from 3.73 (**3c**) to 4.76 (**3a**). The absorption spectra of **6a**, **6b** and **6c** (Figure 2) exhibit only one absorption band at 414, 410 and 384 nm, respectively. These bands represent $S_0 \rightarrow S_1$ transitions. Molar extinction coefficients ε [10^4 M^{-1} cm^{-1}] at λ_{max} are 2.13, 2.25 and 2.34 for **6a**, **6b** and **6c**, respectively. We conclude that the additional phenylethynyl unit present in compounds **3a-c** must be responsible for both higher ε values and the second absorption band in these dyes (see Table 2). Furthermore it is worth mentioning that all compounds characterized by UV/Vis spectroscopy clearly follow the Lambert-Beer law in the concentration range between 10^{-5} and 10^{-6} M (Figures S1-S7, ESI), arguing against aggregation in the ground state.

The emission spectra of **3a** and **3b** in THF show single less

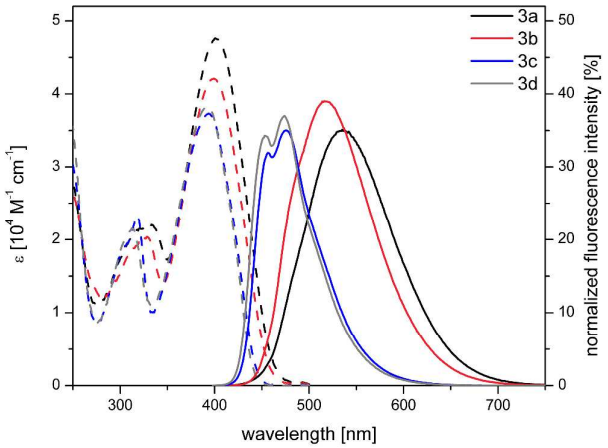


Figure 1: Absorption (dashed) and emission (solid) spectra (10^{-6} M) of **3a-d** in THF. Emission spectra are normalized with regard to quantum yield.

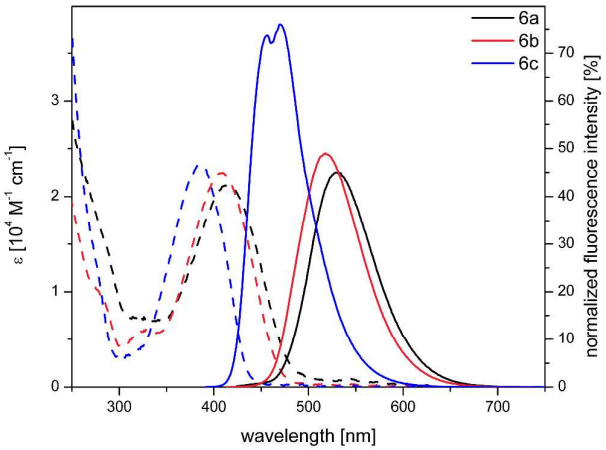


Figure 2: Absorption (dashed) and emission (solid) spectra (10^{-6} M) of **6a-c** in THF. Emission spectra are normalized with regard to quantum yield.

Table 2: Comparison of experimental and computed absorption maxima of **3a-d** and **6a-c** in THF.

compound	λ_{max} [nm]		ε
	measured	calculated	[10^4 M^{-1} cm^{-1}]
3a	401 (333)[a]	382 (311)[a]	4.76
3b	399 (328)[a]	378 (302)[a]	4.21
3c	393 (318)[a]	375 (296)[a]	3.73
3d	392 (312)[a]	373 (291)[a]	3.84
6a	414	383	2.13
6b	410	370	2.25
6c	384	361	2.23

[a]Less intense bands in brackets.

structured bands at 538 and 518 nm, respectively. The emission spectra of both **3c** and **3d** show vibrational progressions (Figure 1, Table 3). Fluorescence quantum yields determined for dyes **3a-d** are very similar and range from 0.35 to 0.39. As for **3a** and **3b**, the emission spectra of **6a** and **6b** in THF show single less structured bands in a similar emission range (529 and 518 nm). The emission spectrum of **6c** in THF again shows two emission maxima, a more intense one at 470 nm and a slightly less intense one at 456 nm. The fluorescence quantum yields determined for **6a**, **6b** and **6c** are 0.45, 0.49 and 0.76 respectively. It is noteworthy that the quantum yield of **6c** is significantly higher than that of its phenylethynyl equivalent **3c**.

Although all molecules contain one sulfur atom each, which can promote intersystem crossing to the triplet manifold *via* spin-orbit-coupling,[19-21] fluorescence quantum yields are rather high for all compounds described. This finding is consistent with previous observations.[9,22]

Stokes' shifts range from 0.54 to 0.79 eV (4392 – 6351 cm^{-1}) for **3a-d** and are increasing with substituent donor strength, thus reflecting more structural reorganization upon photoexcitation.[23] The same trend was observed for **6a-c** with Stokes' shifts ranging from 0.59 to 0.65 eV (4765 – 5251 cm^{-1}; see Table 3).

Fluorescence lifetimes determined for the methoxy aryl alkynyl substituted thiazole derivatives (**3c,d**) were 1.1 ns. The fluorescence decay obtained from the amino aryl alkynyl substituted thiazole derivatives (**3a,b**) had to be approximated with a biexponential decay, indicating that in the excited state two distinguished isomers contribute to the fluorescence decay. The amplitude weighted mean lifetimes were 1.9 ns (**3a**) and 1.4 ns (**3b**). For the aryl substituted thiazoles (**6a-c**) lifetimes ranged from 3.3 to 3.8 ns (see Table 3). Overall, thiazoles with stronger electron donors in 5-position exhibited longer fluorescence lifetimes and the smaller molecules **6a-c** showed longer lifetimes than their cross coupled equivalents **3a-d**. This is most likely caused by a greater number of degrees of freedom in **3a-d**, which are simply caused by a larger number of atoms per molecule, as compared to **6a-c**. Furthermore, all lifetimes are in good agreement with previous measurements for 4-alkoxy-1,3-thiazole derivatives.[5,24]

Electronic Structure Calculations

In order to gain a more detailed insight in the absorption and emission characteristics of the here presented 4-ethoxy-1,3-thiazoles, density functional theory (DFT) and time dependent density functional theory (TD-DFT) calculations have been performed. The effects of solvation (THF) have been addressed for ground and excited state properties by means of a polarizable continuum model.[25]

After an initial systematic conformational search with MMFF,[26] the best geometries were optimized at the CAM-B3LYP/6-31+G(d,p)[27] level of theory as implemented in Gaussian 09.[28] After the ground state optimization and its validation via frequency calculation, the six lowest singlet excited states have been calculated. Fluorescence emission was calculated according to Kasha[29] from the S_1 equilibrium structure.

The predicted ground-state structures are, expectedly, quite planar. Only the aryl or phenylethynyl units, respectively, are twisted with regard to the thiazole core within a range of 13.46° to 22.72° (see Table S1, ESI). For **3a-d**, torsion angles increase slightly with increasing donor strength of the substituents D^1, D^2 (see Scheme 2). For **6a-c**, the angles are quite similar and a distinct trend was not observed. In case of the arylic compounds (**6a-c**) the ethoxy moiety is in plane with the thiazole core. The opposite is the case for the phenylethynyl derivatives (**3a-d**) in which the ethyl group is twisted nearly 90° out of plane. However, this should not influence the absorption or emission characteristics of the compounds as the ethoxy groups are not part of the conjugated π-system.

The frontier orbitals are depicted in Figure 3. The LUMOs of all studied molecules are mainly concentrated around the pyridyl-thiazole subunit, with only sparse localization around the aryl

Table 3: Comparison of experimental and computed fluorescence emission maxima of **3a-d** and **6a-c** in THF.

Compound	λ_{max} [nm]		ν_{St}		Φ_F[b]	τ[c]
	measured	calculated	[eV]	[cm^{-1}]		[ns]
3a	538	524	0.79	6351	0.35	1.94
3b	518	497	0.71	5758	0.39	1.39
3c	475 (457)[a]	480	0.54	4413	0.35	1.10
3d	474 (453)[a]	470	0.55	4392	0.37	1.10
6a	529	536	0.65	5251	0.45	3.81
6b	518	515	0.63	5085	0.49	3.30
6c	470 (456)[a]	478	0.59	4765	0.76	3.30

[a]Less intense bands in brackets. [b]Fluorescence quantum yields are relative to the quantum yield of quinine sulfate in 0.05 M H_2SO_4 (Φ_F = 0.52). [c]Fluorescence lifetimes determined by a monoexponential fit (**3c-6c**) or amplitude weighted mean fluorescence lifetimes determined by a biexponential fit (**3a, 3b**). The individual lifetime components are (**3a**) τ_f = 0.37 ns, τ_s = 2.39 ns, and (**3b**) τ_f = 0.30 ns, τ_s = 1.70 ns, respectively.

Journal Name

ARTICLE

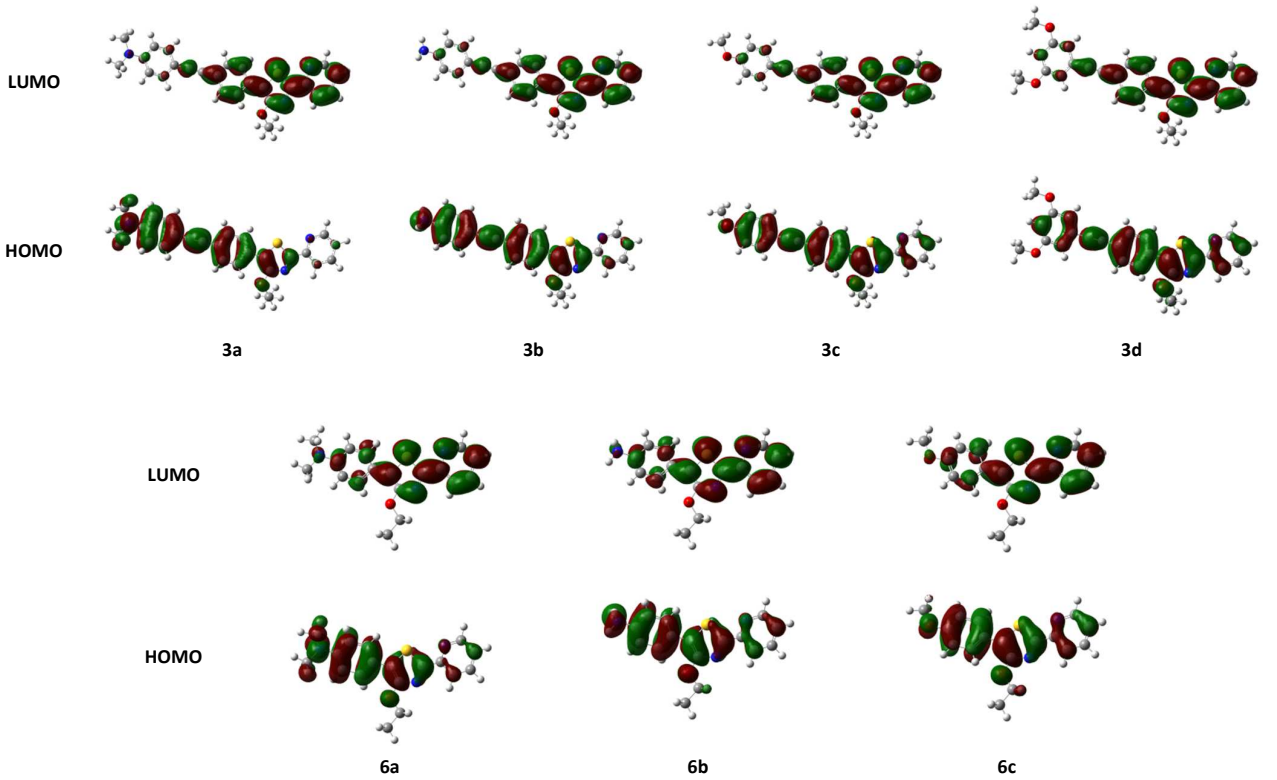


Figure 3: Frontier orbitals of **3a-d** and **6a-c** optimized at the CAM-B3LYP/6-31+G(d,p) level of theory.

or phenylethynyl moieties of the molecules, whereas the HOMOs are mostly concentrated around the arylic subunits in 5-position of the thiazole and around the thiazole core itself. Moreover, the MO constructs suggest a significant overlap of the HOMO and the LUMO wave function for all molecules. This observation nicely corresponds with the high experimental extinction coefficients (especially in **3a-d**) and is also reflected in high theoretical oscillator strengths (see Table 4). Generally, the calculated absorption and emission maxima are in a good to very good agreement with the experimental values. Nonetheless, it must be emphasized that the calculated absorption properties entail a larger error (0.15 – 0.32 eV) than the calculated emission properties (-0.03 – 0.10 eV). Yet the error is mostly within the 0.3 eV margin that is typical for TD-DFT calculations[30,31] and especially for thiazole-based chromophores like firefly oxyluciferin.[32]

The UV/Vis-absorption of the studied molecules mainly consists of transitions from the HOMO to the LUMO. Due to the stronger electron donating properties of their individual substituents, **3a** and **3b** also show a significant share of HOMO-1 to LUMO transitions. This effect does not emerge in the corresponding arylic derivatives **6a,b**. All emission characteristics of the here studied molecules mainly consist of LUMO to HOMO transitions. Looking at the oscillator strengths, it is noteworthy that those of the phenylethynyl derivatives (**3a-d**) are increased by almost a factor of 2 compared to those of the arylic structures (**6a-c**). This finding is in a good agreement with the experimentally determined extinction coefficients.

Experimental

General procedures and spectroscopic methods

Reagents were purchased from commercial sources and were used directly unless otherwise stated. All solvents were of reagent grade and were dried according to common practice and distilled prior to use. Reactions were monitored by TLC, which was carried out on 0.2 mm Merck silica gel plates (60 F_{254}). ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance 250 and 400 spectrometers, chemical shifts (δ) are

Journal Name

ARTICLE

Table 4: Calculated absorption and emission properties to/from the S_1 in THF.

	Transition	Weight [%]	ΔE [eV]	*f*	ΔE_{exp} [eV]
Absorption					
3a	H→L	62	3.25	1.800	0.16
	H-1→L	28			
3b	H→L	74	3.28	1.647	0.17
	H-1→L	18			
3c	H→L	84	3.30	1.571	0.15
3d	H→L	91	3.32	1.501	0.16
6a	H→L	89	3.24	0.916	0.24
6b	H→L	92	3.35	0.833	0.32
6c	H→L	94	3.44	0.802	0.21
Emission					
3a	H←L	80	2.37	-	0.06
3b	H←L	87	2.49	-	0.10
3c	H←L	92	2.58	-	-0.03
3d	H←L	94	2.64	-	0.02
6a	H←L	95	2.31	-	-0.03
6b	H←L	96	2.40	-	0.01
6c	H←L	97	2.60	-	-0.04

Main contributions (> 10%) to the wavefunction; weight, absorption and emission energies (ΔE); oscillator strengths (*f*), error of the calc. to the exp. value (ΔE_{exp}), H = HOMO, L = LUMO.

given relative to signals arising from the solvent. Mass spectra were measured using a Finnigan MAT SSQ 710. Melting points were measured with a Cambridge Instruments Galen III apparatus (Boëtius system) and are uncorrected. UV/Vis spectra were recorded with a PerkinElmer LAMBDA 45 UV/Vis spectrometer, emission spectra were recorded using a JASCO FP-6500 spectrofluorimeter.

Measurements of the fluorescence intensity were carried out on a PerkinElmer LAMBDA 45 UV/Vis spectrometer and JASCO FP-6500 spectrofluorimeter in the perpendicular excitation–emission geometry, while the absorbance at the excitation wavelength used was adjusted to be between 0.04 and 0.05. The calculation of fluorescence quantum yields was done according to the following equation:[33]

$$\Phi = \Phi_r \frac{I}{I_r} \frac{A_r}{A} \frac{n^2}{n_r^2},$$

where Φ is the quantum yield, I is the corrected integrated emission intensity, A is the absorbance at the excitation wavelength and n is the refractive index of the solvent. The subscript r refers to a reference fluorophore of known quantum yield. Here we used quinine sulfate (Φ = 0.52)[34]. All thiazoles were excited as close as possible to their absorption maximum while staying inside the excitation range given in the literature.[35]

For fluorescence lifetime measurements, fluorophores were dissolved in THF, diluted to a final concentration of 10 µM and filled into capillaries. The setup used for the fluorescence lifetime measurements is described in the literature.[36,37] In brief, a Titanium:Sapphire laser (Mira900, Coherent, Dieburg, Germany) pumped by a 5 W frequency-doubled Nd:YVO_4 laser (5W Verdi, Coherent) was used as a pulsed excitation source. The emission wavelength was tuned to 860 nm. A pulse picker (Model 9200, Coherent) reduced the repetition rate of the laser beam to 2 MHz. The second harmonic (430 nm) of the laser beam was generated by a BBO crystal, directed to the scan head of a confocal laser scanning microscope (LSM510, Zeiss, Jena, Germany) and focused by a 40x objective (Plan-Neofluar, Zeiss) into the lumen of the capillaries. The intensity of the laser beam was adjusted with a neutral density filter so that the power in the focal plane was 100 µW. Fluorescence light was collected by the 40x objective and directed via an

optical glass fiber to a combination of a spectrograph (Model 250is, Chromex, Albuquerque, NM, USA) and a streak camera (Model C5680, Hamamatsu Photonics; Herrsching, Germany). Fluorescence decays were analyzed with our own software written in MATLAB (MathWorks, Natick, MA, USA). To determine the fluorescence lifetimes the fluorescence decay in the wavelength range from 450 to 550 nm was evaluated and approximated by a mono- and biexponential function by iterative reconvolution. In most cases (**3c-6c**) a monoexponential fit was sufficient to approximate the data yielding a χ_r^2 value below 1.5. In these cases, a biexponential model did not improve the χ_r^2 value considerably ($\chi_{m,r}^2/\chi_{b,r}^2$<1.1). Only for compounds **3a**, **3b** a biexponential function improved the fit considerably ($\chi_{m,r}^2/\chi_{b,r}^2$>1.5).

Synthesis of the compounds

5-(4-bromophenyl)-4-ethoxy-2-(pyridin-2-yl)thiazole (2). A suspension of **1** (1.00 g, 3.0 mmol) and K_2CO_3 (622 mg, 4.5 mmol) in 50 mL acetone was treated with iodoethane (0.26 mL, 3.3 mmol). The resulting mixture was then heated to reflux until all starting material had been used up (as indicated by TLC, ca. 7 hrs). After cooling to room temperature, the resulting suspension was poured into 150 mL of water and extracted with $CHCl_3$ (3×30 mL). The combined organic extracts were washed with water and saturated NaCl solution and then dried over $MgSO_4$ and concentrated in vacuo. The remaining solid was further purified by column chromatography (silica, heptane/EtOAc 1:1) to yield the ether as a yellow solid (1.01 g, 2.8 mmol, 93%). mp 112 °C. R_f (silica, heptane/EtOAc 1:1): 0.85. ^{1}H-NMR (250 MHz, $CDCl_3$): δ 1.48 (t, *J* = 7.0 Hz, 3H), 4.58 (q, *J* = 7.0 Hz, 2H), 7.30 (dd, *J* = 6.9 Hz, 5.4 Hz, 1H), 7.49 (d, *J* = 8.6 Hz, 2H), 7.67 (d, *J* = 8.6 Hz, 2H), 7.72-7.84 (m, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 8.59 (d, *J* = 4.7 Hz, 1H). ^{13}C-NMR (63 MHz, $CDCl_3$): δ 15.25, 66.43, 113.39, 119.13, 120.33, 124.25, 128.31, 130.82, 131.74, 137.11, 149.25, 150.95, 159.55, 160.42. MS EI *m/z*: 360 ($M^{\bullet+}$, 100%), 332 ($M^{\bullet+}$ - C_2H_4, 42%), 199 ($M^{\bullet+}$ - $C_9H_9N_2O$, 91%), 133 ($M^{\bullet+}$ - C_9H_8BrS, 32%), 120 ($M^{\bullet+}$ - $C_9H_9BrN_2O$, 77%), 105 ($M^{\bullet+}$ - $C_{10}H_8BrOS$, 97%). HRMS (ESI [+], $CHCl_3$ + MeOH): 382.982230000 (calc. 382.982978390 for $C_{16}H_{13}BrN_2OSNa$). UV/Vis (THF): λ_{max} (log ε): 254 nm (3.54), 376 nm (4.32). Fluorescence (THF): λ_{max} (λ_{exc}): 446 nm (376 nm). IR (ATR): ν / cm^{-1} (vibration) = 2970 (−C−H), 2900 (−C−H), 1581 (arom.), 1470 (CH_2/CH_3 deform.), 1435 (CH_2/CH_3 deform.), 1369 (CH_3 deform.), 1342 (−C−N), 1300 (−C−N.), 1211 (−C−O−C), 1072 (−C−O−C), 833 (=C−H deform.), 779 (−C−S), 691 (−C−Br).

General procedure for the cross coupling reactions (3a-d): To a mixture of **2** (250 mg, 0.7 mmol), the respective phenylacetylene derivative (0.7 mmol) and $Pd(PPh_3)_2Cl_2$ (24 mg, 5 mol %) was added TBAF·$3H_2O$ (3g, 9.5 mmol). The heterogeneous mixture was then heated to 80 °C under a nitrogen athmosphere and the resulting solution was stirred at that temperature for 16 hrs. Then water (50 mL) was added and the mixture was extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were washed with water and saturated NaCl solution and dried over $MgSO_4$. After removing the solvent in vacuo, the crude product was further purified by column chromatography.

4-((4-(4-ethoxy-2-(pyridin-2-yl)thiazol-5-yl)phenyl)ethynyl)-N,N-dimethylaniline (3a). The reaction was performed with 4-ethynyl-N,N-dimethylaniline (106 mg, 0.7 mmol). The product is a yellow solid (224 mg, 0.53 mmol, 76%). mp 203 °C. R_f (silica, toluene): 0.29. ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.51 (t, *J* = 7.0 Hz, 3H), 3.00 (s, 6H), 4.60 (q, *J* = 7.0 Hz, 2H), 6.68 (d, *J* = 8.7 Hz, 2H, 7.28-7.34 (m, 1H), 7.43 (d, *J* = 8.8 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.71-7.81 (m, 3H), 8.11 (d, *J* = 7.9 Hz, 1H), 8.59 (d, *J* = 4.7 Hz, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 15.28, 40.24, 66.37, 87.65, 91.44, 111.90, 114.31, 119.0, 122.20, 124.12, 126.53, 131.03, 131.49, 132.72, 136.85, 149.45, 150.04, 151.25, 159.59, 160.62. MS EI *m/z*: 425 ($M^{\bullet+}$, 67%), 397 (($M^{\bullet+}$ - C_2H_4, 4%), 264 ($M^{\bullet+}$ - $C_9H_9N_2O$, 100%), 248 ($M^{\bullet+}$ - $C_{10}H_{13}N_2O$, 32%). HRMS (ESI [+], $CHCl_3$ + MeOH): 448.147750000 (calc. 448.145954690 for $C_{26}H_{23}N_3OSNa$). UV/Vis (THF): λ_{max} (log ε): 333 nm (4.34), 401 nm (4.68). Fluorescence (THF): λ_{max} (λ_{exc}): 538 nm (401 nm). Φ_F = 35% relative to quinine sulfate. IR (ATR): ν / cm^{-1} (vibration) = 3094 (=C−H), 3024 (=C−H), 2203 (−C≡C), 1608 (arom.), 1470 (CH_2/CH_3 deform.), 1369 (CH_3 deform.), 1342 (−C−N), 1072(−C−O−C), 833 (=C−H deform.), 810 (=C−H deform.), 775 (−C−S).

4-((4-(4-ethoxy-2-(pyridin-2-yl)thiazol-5-yl)phenyl)ethynyl)-aniline (3b). The reaction was performed with 4-ethynylaniline (85 mg, 0.7 mmol). The product is a yellow solid (209 mg, 0.53 mmol, 76%). mp 209 °C. R_f (silica, $CHCl_3$/EtOAc 10:1): 0.55. ^{1}H NMR (250 MHz, DMSO-d_6) δ 1.42 (t, *J* = 7.0 Hz, 3H), 4.55 (q, *J* = 7.0 Hz, 2H), 5.58 (s, 2H), 6.56 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 3H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.89-7.99 (m, 1H), 8.05 (d, *J* = 7.9 Hz, 1H), 8.61 (d, *J* = 4.6 Hz, 1H). ^{13}C NMR (63 MHz, DMSO-d_6) δ 15.53, 66.68, 87.08, 92.87, 108.50, 113.44, 114.10, 119.12, 122.19, 125.60, 125.89, 130.78, 131.74, 133.06, 138.17, 150.04, 150.21, 150.34, 159.52, 161.35. MS EI *m/z*: 397 ($M^{\bullet+}$, 77%), 369 (($M^{\bullet+}$ - C_2H_4, 6%), 236 ($M^{\bullet+}$ - $C_9H_9N_2O$, 100%). HRMS (ESI [+], $CHCl_3$ + MeOH): 420.115050000 (calc. 420.114654570 for $C_{24}H_{19}N_3OSNa$). UV/Vis (THF): λ_{max} (log ε): 328 nm (4.31), 399 nm (4.62). Fluorescence (THF): λ_{max} (λ_{exc}): 518 nm (399 nm). Φ_F = 39% relative to quinine sulfate. IR (ATR): ν / cm^{-1} (vibration) = 3391 (−N−H), 3325 (−N−H), 3221 (−N−H), 3040 (=C−H), 2982 (−C−H), 2879 (CH3), 2203 (−C≡C), 1632 (−N−H deform.), 1470 (CH_2/CH_3 deform.), 1342 (−C−N), 1285 (−C−O−C), 1072 (−C−O−C), 822 (=C−H deform.), 775 (−C−S).

4-ethoxy-5-(4-((4-methoxyphenyl)ethynyl)phenyl)-2-(pyridin-2-yl)thiazole (3c). The reaction was performed with 1-ethynyl-4-methoxybenzene (96 mg, 0.7 mmol). The product is a yellow solid (146 mg, 0.35 mmol, 51%). mp 172 °C. R_f (silica, toluene): 0.38. ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.51 (t, *J* = 7.0 Hz, 3H), 3.83 (s, 3H), 4.60 (q, *J* = 7.0 Hz, 2H). 6.89 (d, *J* = 8.7 Hz, 2H), 7.24-7.34 (m, 1H), 7.45-7.55 (m, 4H), 7.73-7.84 (m, 3H), 8.12 (d, *J* = 7.9 Hz, 1H), 8.60 (d, *J* = 4.6 Hz, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 15.27, 55.29, 66.41, 88.29, 90.15, 114.00, 114.18, 115.45, 119.09, 121.59, 124.18, 126.56, 131.52, 131.68, 133.04, 136.98, 149.25, 151.10, 159.61, 159.71, 160.60. MS EI *m/z*: 412 ($M^{\bullet+}$, 100%), 384 (($M^{\bullet+}$ - C_2H_4, 22%), 251 ($M^{\bullet+}$ - $C_9H_9N_2O$, 98%), 236 ($M^{\bullet+}$ - $C_{10}H_{12}N_2O$, 18%), 208 ($M^{\bullet+}$ - $C_{10}H_8N_2OS$, 38%).

HRMS (ESI [+], $CHCl_3$ + MeOH): 435.113040000 (calc. 435.114320200 for $C_{25}H_{20}N_2O_2SNa$). UV/Vis (THF): λ_{max} (log ε): 318 nm (4.37), 393 nm (4.57). Fluorescence (THF): λ_{max} (λ_{exc}): 475 nm (393 nm). Φ_F = 35% relative to quinine sulfate. IR (ATR): ν / cm^{-1} (vibration) = 3062 (=C−H), 2970 (CH_3), 2901 CH_2), 2214 (−C≡C), 1605 (arom.), 1470 (CH_2/CH_3 deform.), 1431 (CH_2/CH_3 deform.), 1373 (CH_3 deform.), 1346 (−C−N), 1246 (−C−O−C), 1076 (−C−O−C), 1026 (−C−O−C), 822 (=C−H deform.), 775 (−C−S).

5-(4-((3,5-dimethoxyphenyl)ethynyl)phenyl)-4-ethoxy-2-(pyridin-2-yl)thiazole (3d). The reaction was performed with 1-ethynyl-3,5-dimethoxybenzene (118 mg, 0.7 mmol). The product is a yellow solid (61 mg, 0.14 mmol, 20%). mp 138 °C. R_f (silica, heptane/EtOAc 1:1): 0.78. ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.51 (t, *J* = 7.0 Hz, 3H), 3.82 (s, 6H), 4.61 (q, *J* = 7.0 Hz, 2H, 6.47 (t, *J* = 2.1 Hz, 1H), 6.71 (d, *J* = 2.2 Hz, 2H), 7.26-7.32 (m, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.79 (t, *J* = 8.4 Hz, 3H), 8.12 (d, *J* = 7.9 Hz, 1H), 8.60 (d, *J* = 4.1 Hz, 1H). ^{13}C NMR (63 MHz, $CDCl_3$) δ 15.27, 55.43, 66.43, 89.16, 90.11, 101.85, 109.33, 114.00, 119.09, 121.00, 124.23, 124.61, 126.56, 131.92, 131.99, 136.97, 149.39, 151.09, 159.80, 160.55, 160.83. MS EI *m/z*: 442 ($M^{\bullet+}$, 82%), 424 (($M^{\bullet+}$ - C_2H_4, 13%), 281 ($M^{\bullet+}$ - $C_9H_9N_2O$, 100%), 265 ($M^{\bullet+}$ - $C_{10}H_{13}N_2O$, 15%), 238 ($M^{\bullet+}$ - $C_{10}H_8N_2OS$, 6%), 223 ($M^{\bullet+}$ - $C_{11}H_{11}N_2OS$, 24%). HRMS (ESI [+], $CHCl_3$ + MeOH): 465.126280000 (calc. 465.124884861 for $C_{26}H_{22}N_2O_3SNa$). UV/Vis (THF): λ_{max} (log ε): 312 nm (4.33), 392 nm (4.58). Fluorescence (THF): λ_{max} (λ_{exc}): 474 nm (392 nm). Φ_F = 37% relative to quinine sulfate. IR (ATR): ν / cm^{-1} (vibration) = 2970 (−C−H), 2931 (−C−H), 2207 (−C≡C), 2110 (−C≡C), 1681 (−C=N), 1581 (arom.), 1469 (CH_2/CH_3 deform.), 1454 (CH_2/CH_3 deform.), 1342 (−C−N), 1203 (−C−O−C), 1153 (−C−O), 1065 (−C−O−C), 1048 (−C−O−C), 829 (=C−H deform.), 775 (−C−S).

4-ethoxy-5-(4-nitrophenyl)-2-(pyridin-2-yl)thiazole (5). A suspension of **4** (978 mg, 3.3 mmol) and K_2CO_3 (677 mg, 4.9 mmol) in 12 mL DMSO was treated with iodoethane (0.29 mL, 3.6 mmol). The resulting mixture was then stirred at r.t. for 12 h and poured into 300 mL of water. The precipitate was then filtered off, taken up in $CHCl_3$ and the organic phase was dried over $MgSO_4$ and concentrated in vacuo. The remaining solid was further purified by column chromatography (silica, $CHCl_3$) to yield the ether as a bright yellow solid (997 mg, 3.0 mmol, 93%). mp 178 °C. R_f (silica, $CHCl_3$): 0.70. ^{1}H-NMR (250 MHz, $CDCl_3$): δ 1.53 (t, *J* = 7.1 Hz, 3H), 4.65 (q, *J* = 7.1 Hz, 2H), 7.35 (ddd, ^3J = 7.5 Hz, 4.9 Hz, ^4J = 1.1 Hz, 1H), 7.81 (td, ^3J = 7.8 Hz, ^4J = 1.7 Hz, 1H), 7.93 (d, *J* = 9.1, 2H), 8.13 (d, *J* = 7.9 Hz, 1H), 8.22 (d, *J* = 9.1 Hz, 2H), 8.61 (d, *J* = 4.8 Hz, 1H). ^{13}C-NMR (63 MHz, $CDCl_3$): δ 15.21, 66.77, 111.78, 119.78, 124.09, 124.81, 126.62, 137.09, 138.77, 145.37, 149.48, 150.58, 161.15, 163.26. MS EI *m/z*: 327 ($M^{\bullet+}$, 100%), 299 ($M^{\bullet+}$ - C_2H_4, 28%), 166 ($M^{\bullet+}$ - $C_9H_9N_2O$, 18%), 120 ($M^{\bullet+}$ - $C_9H_9N_3O_3$, 24%), 105 ($M^{\bullet+}$ - $C_{10}H_8NO_3S$, 36%). HRMS (ESI [+], $CHCl_3$ + MeOH): 350.059290000 (calc. 350.057533590 for $C_{16}H_{13}N_3O_3SNa$). UV/Vis (THF): λ_{max} (log ε): 400 nm (4.58). Fluorescence (THF): λ_{max} (λ_{exc}): 486 nm (400 nm). IR (ATR): ν / cm^{-1} (vibration) = 3071 (=C−H), 2978 (CH3), 2913 (−C−C), 1585 (arom.), 1508 (−NO_2), 1470 (CH_2/CH_3 deform.), 1335 (−C−N), 1300 (−NO_2), 1269 (−C−O−C), 1076 (−C−O−C), 848 (=C−H deform.), 779 (−C−S).

4-(4-ethoxy-2-(pyridin-2-yl)thiazol-5-yl)aniline (6b). A suspension of **5** (944 mg, 2.9 mmol) in 80 mL ethanol was heated to 60 °C under a nitrogen athmosphere. Then N_2H_4 (80 % in H_2O, 2mL) was added. A catalytic amount of freshly prepared Raney-Nickel was added and the now vigorously bubbling mixture was stirred for 1h. The resulting solution was then heated to reflux for 2h in order to remove excess hydrazine. After cooling to room temperature, it was filtered through a 2 cm thick layer of silica, concentrated in vacuo and the remaining solid was purified by column chromatography (silica, $CHCl_3$/EtOAc 7:1) to yield the amine as an orange solid (806 mg, 2.7 mmol, 94%). mp 120 °C. R_f (silica, $CHCl_3$/EtOAc 7:1): 0.45. ^{1}H-NMR (250 MHz, $CDCl_3$): δ 1.47 (t, *J* = 7.0 Hz, 3H), 3.75 (s, 2H), 4.54 (q, *J* = 7.0 Hz, 2H), 6.71 (d, *J* = 8.6 Hz, 2H), 7.20-7.28 (m, 1H), 7.62 (d, *J* = 8.6 Hz, 2H), 7.74 (td, *J* = 7.8 Hz, 1.7 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 8.57 (d, *J* = 4.2 Hz, 1H). ^{13}C-NMR (63 MHz, $CDCl_3$): δ 15.29, 66.18, 115.17, 115.77, 118.77, 122.15, 123.66, 128.25, 136.75, 145.41, 149.34, 151.56, 158.12, 158.39. MS EI *m/z*: 297 ($M^{\bullet+}$, 100%), 268 ($M^{\bullet+}$ - C_2H_5, 21%), 136 ($M^{\bullet+}$ - $C_9H_9N_2O$, 86%), 105 ($M^{\bullet+}$ - $C_{10}H_{10}NOS$, 13%). HRMS (ESI [+], $CHCl_3$ + MeOH): 320.083980000 (calc. 320.083354450 for $C_{16}H_{15}N_3OSNa$). UV/Vis (THF): λ_{max} (log ε): 410 nm (4.35). Fluorescence (THF): λ_{max} (λ_{exc}): 518 nm (410 nm). Φ_F = 49% relative to quinine sulfate. IR (ATR): ν / cm^{-1} (vibration) = 3398 (−N−H), 3318 (−N−H), 3206 (−N−H), 3044 (=C−H), 2974 (−C−H), 2879 (CH_3), 1535 (−N−H deform.), 1469 (CH_2/CH_3 deform.), 1435 (CH_2/CH_3 deform.), 1342 (−C−N), 1281 (−C−N), 1188 (−C−O−C), 1072 (−C−O−C), 825 (=C−H), 775 (−C−S).

4-(4-ethoxy-2-(pyridin-2-yl)thiazol-5-yl)-N,N-dimethylaniline (6a). 6b (341 mg, 1.1 mmol) was dissolved in a mixture of THF (10 mL), 3M H_2SO_4 (5.5 mL) and 37% HCHO (0.6 mL). Then $NaBH_4$ (217 mg, 5.7 mmol) was added portionwise over a period of 15 minutes. After stirring at r.t. for another 10 minutes, saturated K_2CO_3 solution was added and the resulting mixture was extracted with $CHCl_3$ (3*40 mL). The combined organic extracts were washed with water and saturated NaCl solution and dried over $MgSO_4$. After removing the solvent in vacuo, the remaining oil was purified by column chromatography (silica, $CHCl_3$/EtOAc 10:1) to yield the desired compound as an orange solid (300 mg, 0.9 mmol, 80%). mp 92 °C. R_f (silica, $CHCl_3$/EtOAc 10:1): 0.85. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.49 (t, *J* = 7.0 Hz, 3H), 3.00 (s, 6H), 4.55 (q, *J* = 7.0 Hz, 2H), 6.77 (d, *J* = 9.0 Hz, 2H), 7.25 (ddd, *J* = 7.5 Hz, 4.0 Hz, 1.1 Hz, 1H), 7.70-7.78 (m, 3H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.58 (d, *J* = 4.84 Hz, 1.58 Hz, 0.90 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 15.19, 40.34, 66.05, 112.38, 116.06, 118.60, 119.86, 123.43, 127.89, 136.63, 149.21, 149.24, 151.50, 157.81, 157.89. MS EI *m/z*: 325 ($M^{\bullet+}$, 100%), 296 ($M^{\bullet+}$ - C_2H_5, 48%), 164 ($M^{\bullet+}$ - $C_9H_9N_2O$, 100%), 148 ($M^{\bullet+}$ - $C_{10}H_{13}N_2O$, 40%), 120 ($M^{\bullet+}$ - $C_{11}H_{15}N_3O$, 14%), 105 ($M^{\bullet+}$ - $C_{12}H_{14}NOS$, 19%). HRMS (ESI [+], $CHCl_3$ + MeOH): 348.112740000 (calc. 348.114654570 for $C_{18}H_{19}N_3OSNa$). UV/Vis (THF): λ_{max} (log ε): 414 nm (4.33). Fluorescence (THF): λ_{max} (λ_{exc}): 529 nm (414 nm). Φ_F = 45% relative to quinine sulfate. IR (ATR): ν / cm^{-1} (vibration) = 3098

(=C−H), 2990 (−C−H), 2893 (−C−H), 1608 (arom.), 1470 (CH_2/CH_3 deform.), 1435 (CH_2/CH_3 deform.), 1365 (−C−N), 1327 (−C−N), 1230 (−C−N), 1200 (−C−O−C), 1076 (−C−O−C), 826 (=C−H), 775 (−C−S).

5-(4-methoxyphenyl)-2-(pyridin-2-yl)thiazol-4-ol (9). NaOAc (4.55 g, 55.5 mmol, 2.5 eq.) was added to a solution of pyridine-2-carbothioamide **8** (3.05 g, 22.1 mmol, 1 eq.) and ethyl 2-bromo-2-(4-methoxyphenyl)acetate **7** (9.04 g, 33.1 mmol, 1.5 eq) in ethanol (70 mL). The resulting mixture was stirred under reflux for 2 h. The mixture was allowed to cool to room temperature and then poured into 150 mL of water. The crude product was filtered off and washed with water and ethanol, subsequently. It was then taken up in 50 mL of ethanol, heated to reflux and filtered while the solution was still hot. The product was dried in vacuo and the yellow solid (4.62 g, 16.2 mmol, 74%) was used without further purification. mp 261 °C. R_f (silica, heptane/EtOAc 1:1): 0.29. ^{1}H-NMR (250 MHz, DMSO-d_6): δ 3.76 (s, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 7.43 (ddd, ^3J = 6.8 Hz, 4.9 Hz, ^4J = 2.0 Hz, 1H), 7.70 (d, *J* = 8.8 Hz, 2H), 7.87-7.99 (m, 2H), 8.59 (d, *J* = 4.7 Hz, 1H), 11.16 (s, 1H). ^{13}C-NMR (63 MHz, DMSO-d_6): δ 55.60, 110.83, 114.74, 118.63, 124.91, 125.04, 127.93, 138.08, 150.11, 150.74, 158.27, 158.58, 159.36. MS EI m/z: 284 ($M^{\bullet+}$, 75%), 269 ($M^{\bullet+}$ - CH_3, 2%), 151 ($M^{\bullet+}$ - $C_7H_5N_2O$, 86%), 136 ($M^{\bullet+}$ - $C_9H_8O_2$, 20%), 105 ($M^{\bullet+}$ - $C_9H_7O_2S$, 100%), 78 ($M^{\bullet+}$ - $C_{10}H_8NO_2S$, 54%). HRMS (ESI [+], $CHCl_3$ + MeOH): 307.053150000 (calc. 307.051719960 for $C_{15}H_{12}N_2O_2SNa$). UV/Vis (THF): λ_{max} (log ε): 389 nm (4.28). IR (ATR): ν / cm^{-1} (vibration) = 3059 (=C−H), 2978 (−C−H), 2897 (−C−H), 2835 (−O−CH_3), 1481 (CH_2/CH_3 deform.), 1411 (CH_2/CH_3 deform.), 1346 (−C−N), 1288 (−C−N), 1264 (−C−O−C), 1180 (−C−O−C), 1026 (−C−O−C), 822 (=C−H), 775 (−C−S).

4-ethoxy-5-(4-methoxyphenyl)-2-(pyridin-2-yl)thiazole (6c). A suspension of **9** (802 g, 2.8 mmol) and K_2CO_3 (585 mg, 4.2 mmol) and a catalytic amount of NaI in 40 mL acetone was treated with bromoethane (0.23 mL, 3.1 mmol). The resulting mixture was then heated to reflux for 10 h. After cooling to room temperature, the resulting suspension was poured into 150 mL of water and extracted with $CHCl_3$ (3*30 mL). The combined organic extracts were washed with water and saturated NaCl solution and then dried over $MgSO_4$ and concentrated in vacuo. The remaining solid was further purified by column chromatography (silica, CH_2Cl_2) to yield the ether as a yellow solid (286 mg, 0.9 mmol, 32%). mp 81 °C. R_f (silica, CH_2Cl_2): 0.68. ^{1}H-NMR (250 MHz, $CDCl_3$): δ 1.48 (t, *J* = 7.0 Hz, 3H), 3.84 (s, 3H), 4.56 (q, *J* = 6.9 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 7.26 (t, *J* = 6.8 Hz, 1H), 7.63-7.82 (m, 3H), 8.10 (d, *J* = 7.9 Hz, 1H), 8.58 (d, *J* = 4.5 Hz, 1H). ^{13}C-NMR (63 MHz, $CDCl_3$): δ 15.29, 55.31, 66.23, 114.16, 114.78, 118.83, 123.85, 124.45, 128.28, 136.82, 149.37, 151.42, 158.47, 158.51, 159.23. MS EI m/z: 312 ($M^{\bullet+}$, 100%), 284 ($M^{\bullet+}$ - C_2H_4, 23%), 151 ($M^{\bullet+}$ - $C_9H_9N_2O$, 85%), 136 ($M^{\bullet+}$ - $C_{11}H_{12}O_2$, 8%), 105 ($M^{\bullet+}$ - $C_{11}H_{11}O_2S$, 11%). HRMS (ESI [+], $CHCl_3$ + MeOH): 335.082740000 (calc. 335.083020080 for $C_{17}H_{16}N_2O_2SNa$). UV/Vis (THF): λ_{max} (log ε): 384 nm (4.37). Fluorescence (THF): λ_{max} (λ_{exc}): 470 nm (384 nm). Φ_F = 76% relative to quinine sulfate. IR (ATR): ν / cm^{-1} (vibration) = 2982 (−C−H), 2935 (−C−H), 2897 (−C−H), 2832 (−C−H), 21608 (arom.), 1469 (CH_2/CH_3 deform.), 1431 (CH_2/CH_3 deform.), 1369 (CH_3 deform.), 1346 (−C−N), 1288 (−C−N), 1264 (−C−N), 1180 (−C−O−C), 1080 (−C−O−C), 1034 (−C−O−C), 799 (=C−H), 775 (−C−S).

Conclusions

The present work describes the synthesis and optical properties of four new phenylethynyl substituted 4-ethoxy-1,3-thiazole donor-π-acceptor fluorophores and three similar compounds lacking the newly introduced unit. Optical properties of these compounds in THF solution have been investigated and quantum chemical calculations (CAM-B3LYP/6-31+G(d,p) level of theory) were performed in order to explain the experimental results. Structure-property relationships have emerged from a combination of experimental spectroscopic data and DFT/TDDFT calculations. Absorption and emission properties, fluorescence lifetimes and quantum yields correspond nicely with the electronic structure calculations. Future work will evaluate further extension and modification of the fluorophore system and tackle the development of new applications. Work along these lines is currently in progress and will be reported in due course.

Acknowledgement

The authors thank the Bundesministerium für Wirtschaft und Energie (BMWi KF2258002CS2) for financial support. Stefan Schramm gratefully acknowledges the Friedrich-Ebert-Stiftung for financial support. Additionally, we thank Dr. Günther and G. Sentis for measuring the NMR spectra and Mrs. Schönau and Mrs. Heineck for measuring the MS spectra.

Notes and references

1 E. Täuscher, *Beiträge zur Chemie der 4-Hydroxy-1,3-thiazole*, doctoral dissertation, Friedrich-Schiller-Universität Jena, Germany, 2012.

2 P. Naumov, Y. Ozawa, K. Ohkubo, S. Fukuzumi, Structure and Spectroscopy of Oxyluciferin, the Light Emitter of the Firefly Bioluminescence, *J. Am. Chem. Soc.*, 2009, **131**, 11590-11605.

3 L. K. Calderón-Ortiz, E. Täuscher, E. Leite Bastos, H. Görls, D. Weiß, R. Beckert, Hydroxythiazole-Based Fluorescent Probes for Fluoride Ion Detection, *Eur. J. Org. Chem.,* 2012, **13**, 2535-2541.

4 X. Guo, J. Quinn, Z. Chen, H. Usta, y. Zheng, Y. Xia, J. W. Hennek, R. P. Ortiz, T. J. Marks, A. Facchetti, Dialkoxybithiazole: A New Building Block for Head-to-Head Polymer Semiconductors, *J. Am. Chem. Soc.*, 2013, **135**, 1986-1996.

5 R. Menzel, A. Breul, C. Pietsch, J. Schäfer, C. Friebe, E. Täuscher, D. Weiß, B. Dietzek, J. Popp, R. Beckert, U. S. Schubert, Blue-Emitting Polymers Based on 4-Hydroxythiazoles Incorporated in a Methacrylate Backbone, *Macromol. Chem. Phys.*, 2011, **212**, 840-848.

6 B. Happ, J. Schäfer, R. Menzel, M. D. Hager, A. Winter, J. Popp, R. Beckert, B. Dietzek, U. S. Schubert, Synthesis and Resonance Energy Transfer Study on a Random Terpolymer Containing a 2-(Pyridine-2-yl)thiazole Donor-Type Ligand and

a Luminescent $[Ru(bpy)_2(2\text{-(triazol-4-yl)pyridine)}]^{2+}$ Chromophore, *Macromolecules*, 2011, **44**, 6277-6287.

7 R. Menzel, S. Kupfer, R. Mede, D. Weiß, H. Görls, L. González, R. Beckert, Arylamine-Modified Thiazoles as Donor–Acceptor Dyes: Quantum Chemical Evaluation of the Charge-Transfer Process and Testing as Ligands in Ruthenium(II) Complexes, *Eur. J. Org. Chem.*, 2012, **27**, 5231-5247.

8 R. Menzel, D. Ogermann, S. Kupfer, D. Weiß, H. Görls, K. Kleinermanns, L. González, R. Beckert, 4-Methoxy-1,3-thiazole based donor-acceptor dyes: Characterization, X-ray structure, DFT calculations and test as sensitizers for DSSC, *Dyes Pigm.*, 2012, **94**, 512-524.

9 S. Wolfram, H. Würfel, S. H. Habenicht, C. Lembke, P. Richter, E. Birckner, R. Beckert, and G. Pohnert, A small azide-modified thiazole-based reporter molecule for fluorescence and mass spectrometric detection, *Beilstein J. Org. Chem.*, 2014**, 10***,* 2470–2479.

10 S. Schramm, L. F. M. L. Ciscato, P. Oesau, R. Krieg, J. F. Richter, I. Navizet, D. Roca-Sanjuán, Investigations on the synthesis and chemiluminescence of novel 2-coumaranones - II, D. Weiß, R. Beckert, *ARKIVOC*, 2015, **5**, 44-59.

11 S. Schramm, D. Weiß, H. Brandl, R. Beckert, H. Görls, D. Roca-Sanjuán, I. Navizet, Investigations on the synthesis and chemiluminescence of novel 2-coumaranones, *ARKIVOC*, 2013, **3**, 174-188.

12 L. F. M. L. Ciscato, F. H. Bartoloni, A. S. Colavite, D. Weiss, R. Beckert, S. Schramm, Evidence supporting a 1,2-dioxetanone as an intermediate in the benzofuran-2(3*H*)-one chemiluminescence, *Photochem. Photobiol. Sci.*, 2014, **13**, 32-37.

13 C. Roussel, M. Chanon and R. Barone, in *Chemistry of Heterocyclic Compounds: Thiazole and its Derivatives, Part Two*, Editor: J. V. Metzger, John Wiley & Sons, Hoboken, 2009, vol. 34, pp. 369–560.

14 A. Mori, J. Kawashima, T. Shimada, M. Suguro, K. Hirabayashi and Y. Nishihara, Non-Sonogashira-Type Palladium-Catalyzed Coupling Reactions of Terminal Alkynes Assisted by Silver(I) Oxide or Tetrabutylammonium Fluoride, *Org. Lett.*, 2000, **2**, 2935–2937.

15 Y. Liang, Y.-X- Xie and J.-H. Li, Modified Palladium-Catalyzed Sonogashira Cross-Coupling Reactions under Copper-, Amine-, and Solvent-Free Conditions, *J. Org. Chem.*, 2006, **71**, 379–381.

16 K. Sonogashira, Y. Tohda, N. Hagihara, A convenient synthesis of acetylenes: catalytic substitutions of acetylenic hydrogen with bromoalkenes, iodoarenes and bromopyridines, *Tetrahedron Lett.*, 1975, **50**, 4467-4470.

17 A. Vollrath, D. Pretzel, C. Pietsch, I. Perevyazko, S. Schubert, G. M. Pavlov, D. Weiß, R. Beckert and U. S. Schubert, Preparation, Cellular Internalization, and Biocompatibility of Highly Fluorescent PMMA Nanoparticles, *Macromol. Rapid Commun.*, 2012, **32**, 1791-1797.

18 A. Vollrath, D. Pretzel, C. Pietsch, I. Perevyazko, R. Menzel, S. Schubert, G. M. Pavlov, D. Weiß, R. Beckert and U. S. Schubert, Correction: Preparation, Cellular Internalization, and Biocompatibility of Highly Fluorescent PMMA Nanoparticles, *Macromol. Rapid Commun.*, 2013, **34**, 280.

19 D. G. Patel, F. Feng, Y. Y. Ohnishim, K. A. Abboud, S. Hirata, K. S. Schanze, J. R. Reynolds, It Takes More Than an Imine: The Role of the Central Atom on the Electron-Accepting Ability of Benzotriazole and Benzothiadiazole Oligomers, *J. Am. Chem. Soc.*, 2012, **134**, 2599-2612.

20 Z. Zhou, T. S. Corbitt, A. Parthasarathy, Y. Tang, L. K. Ista, K. S. Schanze, D. G. Whitten, "End-Only" Functionalized Oligo(phenylene ethynylene)s: Synthesis, Photophysical and Biocidal Activity, *J. Phys. Chem. Lett.*, 2010, **1**, 3207-3212.

21 J. S. de Melo, L. M. Silva, L. G. Arnaut, R. S. Becker, Singlet and triplet energies of a-oligothiophenes: A spectroscopic, theoretical, and photoacoustic study: Extrapolation to polythiophene, *J. Chem. Phys.*, 1999, **111**, 5427-5433.

22 U.-W. Grummt, D. Weiß, E. Birckner and R. Beckert, Pyridylthiazoles: Highly Luminescent Heterocyclic Compounds, *J. Phys. Chem. A*, 2007, **111**, 1104–1110.

23 S. Haid, M. Marszalek, A. Mishra, M. Wielopolski, J. Teuscher, J. E. Moser, R. Humphry-Baker, S. M. Zakeeruddin, M. Grätzel and P. Bäuerle, Significant Improvement of Dye-Sensitized Solar Cell Performance by Small Structural Modification in π-Conjugated Donor–Acceptor Dyes, *Adv. Func. Mater.*, 2012, **22**, 1291-1302.

24 S. H. Habenicht, M. Siegmann, S. Kupfer, J. Kübel, D. Weiß, D. Cherek, U. Möller, B. Dietzek, S. Gräfe and R. Beckert, And yet they glow: thiazole based push–pull fluorophores containing nitro groups and the influence of regioisomerism, *Methods Appl. Fluoresc.*, 2015, **3**, 025005.

25 J. Tomasi, B. Mennucci, R. Cammi, Quantum Chemical Contiuum Solvation Models, *Chem. Rev.*, 2005, **105**, 2999-3093.

26 T. A. Halgren, Merck molecular force field. I. Basis, form, scope, parameterization, and performance of MMFF94, *J. Comput. Chem.*, 1996, **17**, 490-519.

27 T. Yanai, D. P. Tew, N. C. Handy, A new hybrid exchange–correlation functional using the Coulomb-attenuating method (CAM-B3LYP), *Chem. Phys. Lett.*, 2004, **393**, 51-57.

28 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, M. J. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels,Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox,. *Gaussian 09, Revision A.02*; Gaussian, Inc.: Wallingford, CT, 2009.

29 M. Kasha, Characterization of Electronic Transitions in Complex Molecules, *Discuss. Faraday Soc.*, 1950, **9**, 14-19.

30 D. Jacquemin, E. Perpète, I. Ciofini, C. Adamo, Assessment of the ωB97 family for excited-state calculations, *Theor Chem Acc.*, 2011, **128**, 127-136.

31 D. Jacquemin, V. Wathelet, E. A. Perpète, C. Adamo, *J. Chem. Theory Comput.*, Extensive TD-DFT Benchmark: Singlet-Excited States of Organic Molecules, 2009, **5**, 2420-2435.

32 L. Pinto da Silva, J. C. G. Esteves da Silva, Analysis of the performance of DFT functionals in the study of light emission by oxyluciferin analogs, *Int. J. Quantum Chem.*, 2013, **113**, 45-51.

33 M. Montalti, A. Credi, L. Prodi and M. T. Gandolfi, *Handbook of Photochemistry*, 3rd edition, Taylor & Francis, Boca Raton, 2006.

34 K. Suzuki, A. Kobayashi, S. Kaneko, K. Takehira, T. Yoshihara, H. Ishida, Y. Shiina, S. Oishic and S. Tobita, Reevaluation of absolute luminescence quantum yields of standard solutions using a spectrometer with an integrating sphere and a back-thinned CCD detector, *Phys. Chem. Chem. Phys.*, 2009, **11**, 9850-9860.

35 A. M. Brouwer, Standards for photoluminescence quantum yield measurements in solution (IUPAC Technical Report), *Pure Appl. Chem.*, 2011, **83**, 2213-2228.

36 C. Biskup, T. Zimmer, K. Benndorf, FRET between cardiac Na^+ channel subunits measured with a confocal microscope and a streak camera, *Nat. Biotechnol.*, 2004, **22**, 220-224.

37 B. Hoffmann, T. Zimmer, N. Klöcker, L. Klebauskas, K. König, K. Benndorf, C. Biskup, Prolonged irradiation of enhanced cyan fluorescent protein or Cerulean can invalidate Förster resonance energy transfer measurements, *J. Biomed. Opt.*, 2008, **13**, 031205.

π-Extension of 4-ethoxy-1,3-thiazoles via aryl coupling resulted in twofold increase of molar extinction coefficients and larger Stokes‘ shifts compared to smaller analogs. These easily synthesized compounds are promising candidates for the construction of functional dyes.