# Regioselective Synthesis of 1,2- vs 1,3-Squaraines

**Elisabetta Ronchi,[†] Riccardo Ruffo,[†] Silvia Rizzato,[‡] Alberto Albinati,[‡]
Luca Beverina,*,[†] and Giorgio A. Pagani[†]**

*Department of Materials Science and INSTM, University of Milano-Bicocca,
Via Cozzi 53, I-20125, Milano, Italy, and Department of Structural Chemistry,
University of Milano, Via Venezian 21, 20133 Milano, Italy*

luca.beverina@mater.unimib.it

ABSTRACT
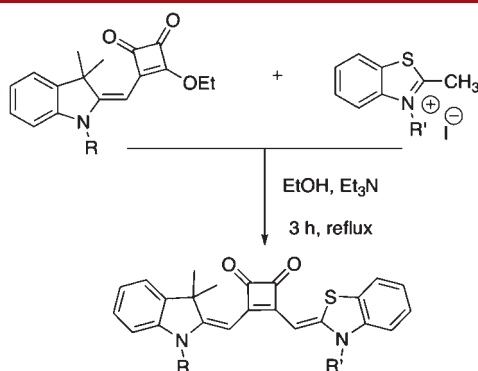
Squaraines have been known for many decades as very stable and versatile vis−NIR absorbing dyes. They have found applications for example as sensitizers in organic photovoltaics and photodetectors. The most common squaraine structure is the 1,3-regioisomer. Their 1,2-regioisomers are seldom mentioned and unanimously regarded as side products. A facile direct synthesis of 1,2-squaraines, highlighting the role played by reaction conditions and electronic factors, is described. The first electrochemical characterization of these dyes is also shown.

Squaraines (squarylium dyes) are the condensation product of two electron rich derivatives (activated arenes, anhydrobases) and squaric acid.[1] Although alternative syntheses are possible,[2] symmetric squaraines have almost unanimously been prepared by direct condensation of the reactants under azeotropic removal of the formed water.[3] Mostly, the reaction is regioselective and the major products correspond to the 1,3-isomers. These products are, from the electronic point of view, reminiscent of cyanines, with which they share most of the photophysical properties (i.e., a sharp and intense absorption band, NIR fluorescence, nonlinear optical behavior).[4] Scheme 1 shows, as a representative example,

the condensation of 2 equiv of the anhydrobase generated *in situ* by reaction of **1a** with a suitable base (quinoline, imidazole, triethylamine) with squaric acid to give the 1,3-squaraine **2**[5] (the major product) and the corresponding 1,2-regioisomer **3** (the side product). Symmetric diarylcyclobutendiones (that is 1,2-squaraines in the case of a conjugated substituent) have been selectively prepared by the Friedel−Kraft reaction of squaryl chloride and 2 equiv of a suitable arene.[6]

Nonsymmetric derivatives can be prepared by the sequential Stille−Liebeskind/Srogl reactions of 3-chloro-4-arylthiocyclobutene with suitable precursors.[7] The direct

[†] Department of Materials Science and INSTM, University of Milano-Bicocca.

[‡] Department of Structural Chemistry, University of Milano.

(1) Beverina, L.; Salice, P. *Eur. J. Org. Chem.* **2010**, *7*, 1207–1225.

(2) Law, K.; Bailey, F. *J. Org. Chem.* **1992**, *57*, 3278–3286.

(3) Keil, D.; Hartmann, H. *Dyes Pigm.* **2001**, *49*, 161–179.

(4) Sreejith, S.; Carol, P.; Chithra, P.; Ajayaghosh, A. *J. Mater. Chem.* **2008**, *18*, 264–274.

(5) Santos, P. F.; Reis, L. V.; Almeida, P.; Serrano, J. P.; Oliveira, A. S.; Vieira Ferreira, L. F. *J. Photochem. Photobiol., A* **2004**, *163*, 267–269.

(6) Ried, W.; Vogl, M. *Liebigs Ann. Chem.* **1977**, 101–105. The first 1,2-squaraine was prepared by acid hydrolysis of 1,2-diphenyl-3,3,4,4-tetrafluorocyclobuten by Blomquist (Blomquist, A. T.; La Lancette, E. A. *J. Am. Chem. Soc.* **1961**, *83*, 1387–1391).

(7) Aguilar-Aguilar, A.; Peña-Cabrera, E. *Org. Lett.* **2007**, *9*, 4163–4166.

Scheme 1
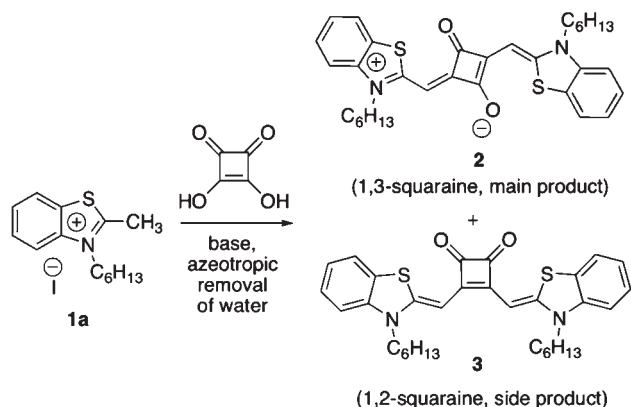
reaction of an activated arene (dimethylaniline) and butyl squarate in humid BuOH gives the 1,2-squaraines only in traces amounts.[8] Treibs and Jacobs obtained 1,2-squaraines by reaction of activated arene and squaric acid in acetic anhydride. In this case the squaric acid is readily converted in the corresponding acetate, which in turn behaves like squaryl chloride.[9] The literature does not report any useful direct synthesis of 1,2-squaraines from squaric acid or esters. Moreover no detailed characterization of their properties with respect to the most common 1,3-derivatives is available.

Our interest in this class of compounds was prompted by the remarkable performances that standard 1,3-squaraines show as active materials in photoconducting devices.[10] Also, the lack of complete condensation regioselectivity in the reaction between an activated molecule and squaric acid has important consequences in the synthesis of polysquaraines.[11] The formation of the 1,2-regioisomer corresponds in this case to the formation of 1,2-diketonic defects that are incorporated in the growing polymer chain.[12] A better understanding of the factors influencing the 1,2- versus 1,3- condensation pathways could provide guidelines for the synthesis of fully regioregular polysquaraines.

To explore the potentially appealing chemical and photophysical properties of 1,2-squaraines, we repeated the only literature procedure describing (but without a complete characterization) the direct formation of **3** as a byproduct in the synthesis of **6a**.[13] We

reacted ethyl squarate and **1a** in ethanol in the presence of a stoichiometric amount of triethylamine. The reaction gave **6a**, along with a strongly red colored byproduct that was isolated by chromatography and crystallized by the orthogonal solvents method to obtain single crystals. The diffraction analysis confirmed the proposed structure for derivative **3** (see Figure 1).

This first experiment shows that 1,2-squaraines share with their 1,3-regioisomers a strong coloration. They also possess a very remarkable stability and complete redox reversibility (vide infra). All these properties make them suitable as sensitizers in organic photovoltaic and photodetecting devices.[14] In particular, 1,2-squaraines could be highly interesting for green-operating photodetectors as they show a strong absorption close to the technologically relevant wavelength of 550 nm.[15] The 1,3-squaraines do not efficiently absorb in this region.

Scheme 2
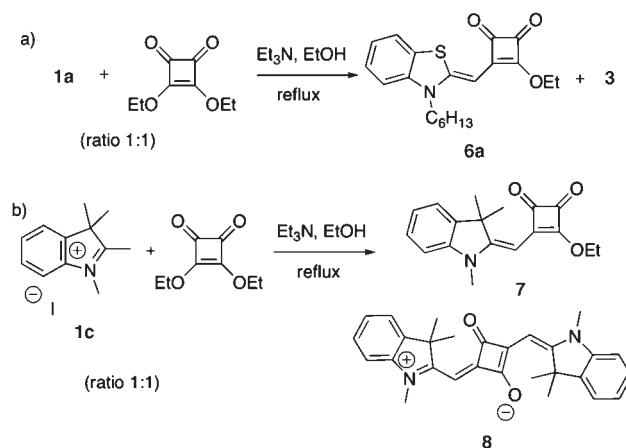
In this paper, we focus on the improvement of a regioselective synthesis of 1,2-squaraines. In order to do this, we first studied, as a reprehensive case, the syntheses under a variety of different conditions of two symmetric squaraines, the benzothiazole derivative **2** and the dimethylindolenine derivative **8**,[16] along with their corresponding 1,2-regioisomers (Schemes 1 and 2b).

The first important observation to start with is that **3** was first obtained while preparing **6a**.[13] Derivative **3** could be formed by the reaction of a second equivalent of **1a** either with **6a** or with the corresponding emisquaraine **6b** obtained by in situ hydrolysis of **6a**. We tested the two possible reaction pathways by reacting **1a** independently with **6a** in anhydrous ethanol and with the emisquaraine **6b** in absolute ethanol. In the first case

(8) Law, K.-Y.; Court Bailey, F. *Can. J. Chem.* **1986**, *64*, 2267–2273.

(9) Treibs, A.; Jacob, K. *Liebigs Ann. Chem.* **1966**, *699*, 153–167.

(10) (a) Bagnis, D.; Beverina, L.; Huang, H.; Silvestri, F.; Zheng, Y.; Pagani, G. A.; Marks, T. J.; Facchetti, A. *J. Am. Chem. Soc.* **2010**, *132*, 4074–4075. (b) Wei, G.; Wang, S.; Sun, K.; Thompson, M. E.; Forrest, S. R. *Adv. Energy Mater.* **2011**, *1*, 184–187.

(11) Eldo, J.; Ajayaghosh, A. *Chem. Mater.* **2002**, *14*, 410–418.

(12) Chenthamarakshan, C. R.; Eldo, J.; Ajayaghosh, A. *Macromolecules* **1999**, *32*, 5846–5851.

(13) (a) Sprenger, H. E.; Ziegenbein, W. *Angew. Chem., Int. Ed.* **1967**, *6*, 553–4. (b) Sprenger, H. E.; Ziegenbein, W. *Angew. Chem., Int. Ed.* **1967**, *7*, 530–535.

(14) Binda, M.; Agostinelli, T.; Caironi, M.; Natali, D.; Sampietro, M.; Beverina, L.; Ruffo, R.; Silvestri, F. *Org. Electron.* **2009**, *10*, 1314–1319.

(15) Binda, M.; Natali, D.; Sampietro, M.; Agostinelli, T; Beverina, L. *Nucl. Instrum. Meth. A* **2010**, *624*, 443–448.

(16) Treibs, A.; Jacob, K. *Liebigs Ann. Chem.* **1968**, *712*, 123–137.

we exclusively obtained the 1,2-regioisomer **3**. In the second case we obtained mainly the 1,3-regioisomer **2** with small amounts of **3** (not isolated, only seen on TLC) (Scheme 3).
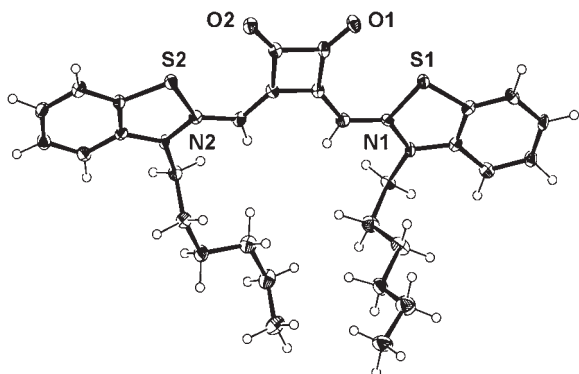
Figure 1. A view of the ORTEP diagram of structure of **3** (disordered THF solvent molecules have been omitted for clarity). Thermal ellipsoids are drawn at 50% probability.

The anhydrobase of **1a** is thus able to react directly with emisquarate **6a**, and this reaction is 1,2-regioselective. Conversely, the reaction with the emisquaraine follows a 1,3-condensation pathway.

Scheme 3

sq = squaraine
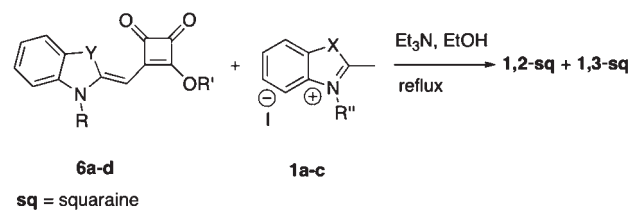
|	Y	R	R'	X	R''	products[c]
6a	S	n-C$_6$H$_{13}$	Et	**1a**	S	n-C$_6$H$_{13}$	**3**
6b	S	n-C$_6$H$_{13}$	H	**1a**	S	n-C$_6$H$_{13}$	**2 + 3**
6a	S	n-C$_6$H$_{13}$	Et	**1a**	S	n-C$_6$H$_{13}$	**2 + 3**[a]
6c	C(Me)$_2$	n-C$_6$H$_{13}$	Et	**1a**	S	n-C$_6$H$_{13}$	**1,2-sq**
6a	S	n-C$_6$H$_{13}$	Et	**1b**	C(Me)$_2$	n-C$_6$H$_{13}$	no reaction
6c	C(Me)$_2$	n-C$_6$H$_{13}$	Et	**1c**	C(Me)$_2$	CH$_3$	**1,3-sq**[b]

[a]Refluxing pyridine as the solvent. [b]Microwave heating (100 °C, 3 bar), the anhydrobase was generated *ex situ*. [c]Yields are reported in the Supporting Information.

The presence of small amounts of **3** can be ascribed to the reaction of **1a** with the little **6a** formed by *in situ* esterification of the emisquaraine **6b** with the solvent of the reaction (Scheme 3).

On going from the very reactive benzothiazole anhydrobases[17] to the corresponding more stable dimethylindolenine derivatives (**1b**, **1c**), we observed a different behavior. The reaction of 1 equiv of **1c** with ethyl

squarate mainly gave the corresponding emisquarate **7** along with a little of the 1,3-squaraine **8**, exactly the opposite of what we observed for the benzothiazole derivatives (Scheme 2b).

Scheme 4
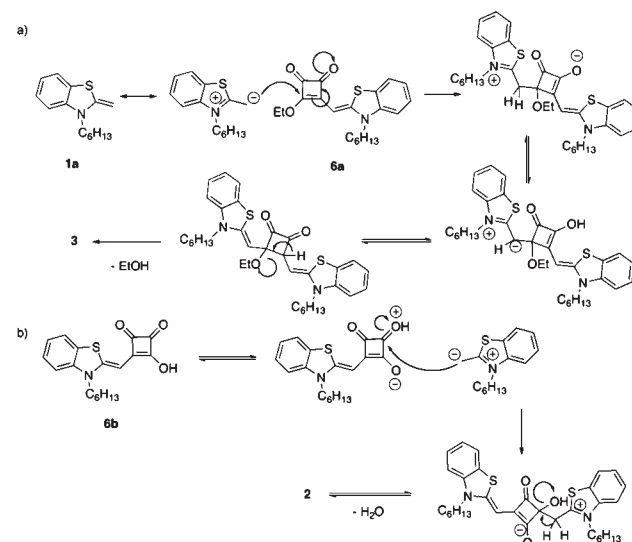
Scheme 4 shows the tentative mechanism for the 1,2 and 1,3 condensation pathways. When **1a** reacts with **6a**, the first step involves a 1,4-conjugated addition at the squarate double bond. It follows a 1,5-proton shift between the benzothiazole methylene and the enolate. Finally a thermally promoted elimination of ethanol gives exclusively **2**. The attack involves the carbonyl α to the benzothiazole methylene because the other carbonyl is in direct conjugation with benzothiazole and thus more electron-rich (and less electrophilic) (Scheme 4a).

Conversely, when **1a** reacts with **6b**, the nucleophilic attack involves the carbonyl β to the benzothiazole methylene. We speculate that this is the consequence of the high acidity of squaric acid and emisquaraines.[18] **6b** is partially dissociated in alcoholic solution. The carbonyl in the α position is conjugated with the enolate and thus electron-rich. Conversely, the catalytic protonation of the carbonyl in the β position makes the nucleophilic attack of **6a** particularly easy. Thermally driven elimination of water gives exclusively the 1,3-squaraine **3**. This mechanism is also supported by Law's observation that the reaction of dimethylindolenine with butylsquarate is acid catalyzed.[8] Therefore, the formation of a 1,2-squaraine requires a very reactive electron-rich precursor, as in this case there is no need of catalytic protonation to enhance the reaction site electrophilicity. This is the reason why we could not prepare a symmetric 1,2-squaraine out of a dimethylindolenine anhydrobase. **1c** is not reactive enough to

(17) Denes, V. I.; Farcasan, M.; Ciurdaru, G. *Chem. Ber.* **1964**, *97*, 1246–1251 and references therein.

(18) West, R.; Powell, D. L. *J. Am. Chem. Soc.* **1963**, *85*, 2577–2579.

directly react with **7**. The formation of small amounts of **8** is the consequence of the slow hydrolysis of **7** in ethanol solution (Scheme 3).
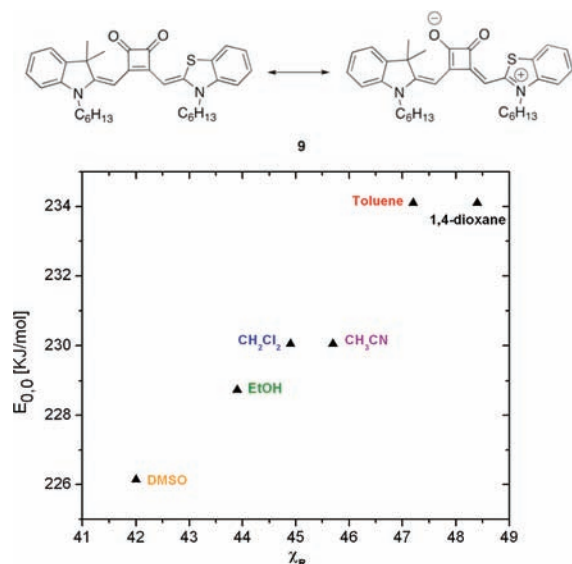

Figure 2. Transition energies of **9** in six solvents plotted against Brooker's χ_R values in the same solvents.

One important consequence of our proposed mechanism is that the nonsymmetric 1,2-squaraine **9** bearing both a dimethylindolenine and a benzothiazole side group could only be prepared by the reaction of **6c** with **1a**. In fact, the reaction of **6a** with **1b** only gave the starting materials (Scheme 3). In short, the amount of the 1,2-regioisomer in a 1,3-squaraine synthesis depends on both the reaction conditions and nature of the reactants. First, only a very reactive species is able to efficiently react with the emisquarate to give the 1,2-squaraine. Second, the amount of emisquarate present in solution depends both on the nature of the alcohol employed (primary, secondary,..) and on the reaction time and temperature. Thus, in the case of poorly reactive arenes and anhydrobases, the amount of 1,2-regioisomer will be low in any case, while, in the case of highly reactive electron rich molecules, the condensation regioselectivity can only be controlled by reducing the parasite esterification of the emisquaraine intermediate. From the standpoint of the photophysical properties, we already discussed how 1,3-squaraines are reminiscent of cyanines. In the case of 1,2-squaraines, the allowed canonic representations show a delocalization of the nitrogen lone pair over the carbonyl of the squarate core, thus giving a merocyanine structure. This is confirmed by the data shown in Figure 2 and Table S1 of the Supporting Information. The transition energies for the absorption spectra of the

representative derivative **9** in different solvents are linearly correlated with the corresponding Brooker's χ_R values.[19]

We tested the electrochemical properties of **9**. Figure 3 shows its CV plot in a 0.1 M solution of tetrabutylammonium hexafluorophosphate in CH_2Cl_2. The plot shows two completely reversible oxidations ($V_{1/2}(1) = 0.13$ V, $E_{1/2}(2) = 0.48$ V versus Fc^+/Fc redox couple) associated with the oxidation of the electron rich benzothiazole and dimethylindolenine side groups respectively. These data place the HOMO level for **9** at -5.3 eV, significantly below that of the 1,3-squaraines we so far employed in OPV devices.[10a] This is considered beneficial for the increase of the open circuit voltage.
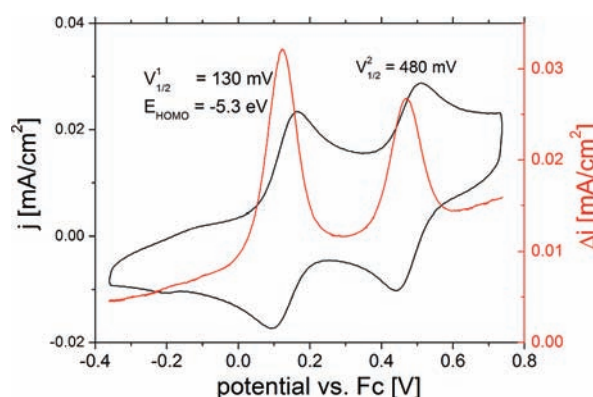
Figure 3. Cyclic voltammetry (black) and differential pulse voltammetry (red) for derivative **9** in 0.1 M TBAMPF$_6$ in CH_2Cl_2 with respect to the Fc/Fc^+ redox couple. The working, counter and pseudoreference electrodes were a Glassy Carbon (GC) disk, a Pt flag, and a Ag/AgCl wire, respectively.

In conclusion, we identified the main electronic factors and reaction conditions leading to the formation of 1,2-squaraines. We proposed a mechanism for the 1,2 vs 1,3 condensation regiochemistry and we successfully exploited these findings in the facile synthesis of symmetric and nonsymmetric 1,2-squaraines. We also demonstrated that such compounds behave like redox reversible merocyanines holding promise as new sensitizers in organic photoconducting devices.

Supporting Information Available. Synthetic protocols, absorption and emission spectra for **2** and **9**, cyclic voltammetry plot for **2**, crystal data and refinement parameters (Table S3), and crystallographic information files (CIF) for **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

(19) The detailed photophysical characterization of the compound will be published elsewhere.