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# Halogen–Arene Interactions Assist in Self-Assembly of Dyes**

*Ulrich Mayerhöffer and Frank Würthner**

Halogens are omnipresent in chemistry as they possess high reactivity as well as intriguing electronic properties reflected in their dual electron-withdrawing and electron-donating character. These specific properties also make halogens interesting binding sites in supramolecular chemistry.[1] In recent years, interactions between halogen anions and electron-deficient aromatic π systems have been a topic of particular interest.[2] Likewise the "ambipolar" character of halogen substituents towards electrophiles and nucleophiles through defined and highly directed electrostatic interactions has been increasingly applied in the design of supramolecular arrangements, most importantly in the solid state.[3] In this regard, halogen bonds between the region of positive electrostatic potential of covalently bonded halogen atoms and electron-rich atoms that act as Lewis bases are of particular interest because of their similarity to the commonly observed hydrogen bonds.[4] These studies were mainly focused on electrostatic interactions and considerably less attention has been paid on the contribution of polarizability of halogens and their interaction with π systems.[5] Halogenated solvents, however, were invariably proven to be ideal for the dissolution of aromatic compounds with extended π systems.[6] This special solvation behavior of halogenated solvents compared to nonhalogenated ones cannot be explained in terms of solvent polarity, and thus has to be ascribed to the higher polarizability of such solvents, thus resulting in a favorable interaction of the polarizable halogen atoms with aromatic π surfaces.[6c] Another interesting example of such interactions is the formation of π complexes in the course of electrophilic aromatic bromination reactions.[7] It is, therefore, expected that such dispersive interactions of halogen atoms would play an active role in supramolecular assemblies as well.

Herein we report on the self-assembly of halogenated squaraine dyes, a process shown to be driven by such dispersive halogen interactions. We have investigated the thermodynamic parameters of the aggregation process of such squaraines in organic solvents by concentration- and temperature-dependent UV/Vis/NIR absorption as well as NMR experiments, and elucidated the aggregate structures in solution. To study the aggregation behavior of acceptor-substituted squaraines in less polar solvents such as toluene, we chose a series of 4-methylquinolinium-based acceptor-substituted squaraines which feature dodecyl chains as lipophilic anchors at the nitrogen atoms of the quinolinium groups (Figure 1). The synthesis and NIR fluorescence properties of these squaraines have been recently published.[8]

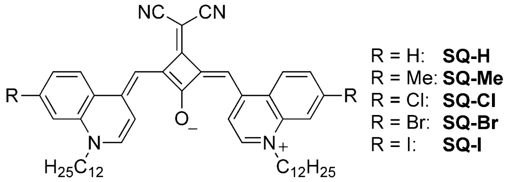

***Figure 1.*** Structures of the squaraine dyes **SQ-H**, **SQ-Me**, **SQ-Cl**, **SQ-Br**, and **SQ-I**.

Within this series, the substitution of a hydrogen atom at the donor moiety by different halogen atoms (Cl, Br, I), on one hand, and by a methyl group, on the other hand, allows the elucidation of halogen effects on the aggregation properties of these dyes.

The absorption spectra of monomers of these squaraines in dichloromethane show the expected characteristic features, namely an intense main band in the long-wavelength region with a maximum at $\lambda = 870$ nm for both **SQ-H** and **SQ-Me**, $\lambda = 885$ nm for **SQ-Cl**, $\lambda = 891$ nm for **SQ-Br**, and $\lambda = 900$ nm for **SQ-I** (see Figures S1–S5 in the Supporting Information).[8] By changing the solvent to the less polar solvent toluene, a bathochromic shift of the main absorption band is observed with concomitant band narrowing and more pronounced vibronic progressions for the whole series of dyes, thus leading to absorption maxima at $\lambda = 903$ (**SQ-H**, **SQ-Me**), 915 (**SQ-Cl**), 923 (**SQ-Br**), and 928 nm (**SQ-I**). These spectral changes upon solvent variation can be ascribed to a decrease of the dipole moment upon optical excitation (negative solvatochromism)[6c] and a stiffening of the chromophore in the less polar solvent. Other than these solvent effects, no differences in the band shape were observed for **SQ-H** and **SQ-Me** upon concentration or temperature variation, for concentrations up to $10^{-3}$ M in toluene, thus demonstrating the lack of aggregation of these nonhalogenated squaraines under the investigated conditions (see the Supporting Information). In contrast, the halogenated squaraines **SQ-Cl**, **SQ-Br**, and **SQ-I** show a second hypsochromically shifted absorption band in toluene upon increasing the concentration (e.g., **SQ-Br**; Figure 2). The spectra for **SQ-Cl** and **SQ-I** are displayed in Figures S6 and S8, respectively, in the Supporting Information. As the spectra in Figure 2a reveal, with increasing concentration the intensity of the monomer band of **SQ-Br** decreases, whilst a hypsochromic aggregate band at $\lambda = 808$ nm evolves. The transformation from monomeric species

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[*] U. Mayerhöffer, Prof. Dr. F. Würthner
Universität Würzburg, Institut für Organische Chemie and
Center for Nanosystems Chemistry
Am Hubland, 97074 Würzburg (Germany)
E-mail: wuerthner@chemie.uni-wuerzburg.de

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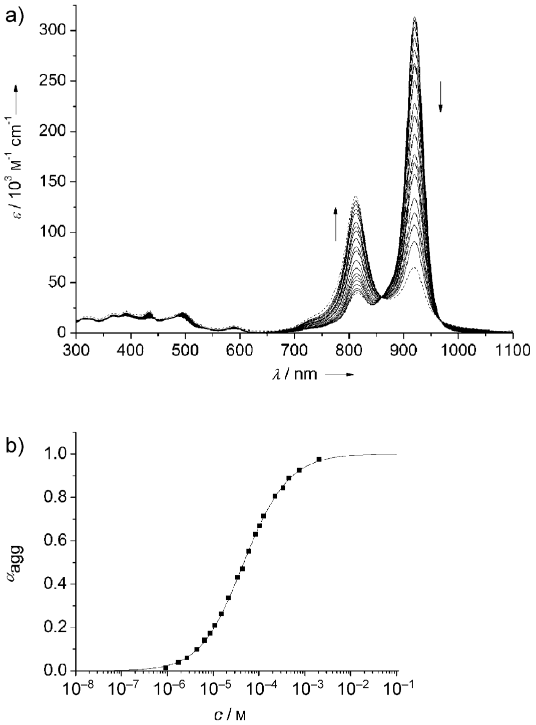

**Figure 2.** a) Concentration-dependent UV/Vis/NIR absorption spectra of squaraine **SQ-Br** in toluene from $10^{-6}$ M to $10^{-3}$ M; the arrows indicate spectral changes with increasing concentration. b) Plot of aggregate fractions, $\alpha_{\mathrm{agg}}$, versus concentration and fit of the data according to the isodesmic model.[9b]

to aggregated species is characterized by two well-defined isosbestic points at $\lambda = 968$ and 860 nm. Additional isosbestic points can also be found for the squaraine absorption bands at lower wavelengths. The observed clear isosbestic points suggest an equilibrium between two defined species, a monomeric species with absorption at $\lambda = 923$ nm and an aggregated species with absorption at $\lambda = 813$ nm for **SQ-Br**. This hypsochromic shift of $\Delta\lambda = 110$ nm points to a sandwich-type, face-to-face ordered aggregate (*H*-aggregate).[6a,b] Since very similar hypsochromic shifts of $\Delta\lambda = 107$ nm for **SQ-Cl** and $\Delta\lambda = 110$ nm for **SQ-I** are observed, we can assume quite similar aggregate structures for these halogenated squaraine dyes.

For the formation of dye aggregates by self-assembly, different pathways have been proposed in literature.[9] Although several models, including cooperative and anticooperative ones, are taken into account for the aggregation process of the present series of squaraines, only the isodesmic model describes the observed equilibria in satisfying accuracy.[9b] This model, also known as the equal-*K* model, is based on the assumption that each monomer addition to the growing aggregate is governed and described by one single equilibrium constant, $K_{\mathrm{e}}$. Considering the structural nature of squaraine aggregates (*H*-type as revealed by strong hypsochromic shift), the assumption of such an isodesmic growth is reasonable since squaraines are, as a result of their rigid molecular structure,[8] planar compounds with two equal π faces. Thus, for the formation of the initial dimer in solution neither a major driving force will be required to bring the molecules into a favorable conformation, nor the remaining free π faces would be altered to discriminate a further growth of the aggregate as required for a cooperative or anticooperative mechanism. Figure 2b shows the plot of the aggregate fractions $\alpha_{\mathrm{agg}}$ for **SQ-Br** as a function of concentration along with the corresponding fit according to the isodesmic model (for more details and plots for **SQ-Cl** and **SQ-I** see the Supporting Information). From these plots the equilibrium constants of the isodesmic aggregation processes at 293 K were determined to be $K_{\mathrm{e}} = 8.5\times10^{3}\,\mathrm{M}^{-1}$ for **SQ-Cl**, $K_{\mathrm{e}} = 1.25\times10^{4}\,\mathrm{M}^{-1}$ for **SQ-Br**, and $K_{\mathrm{e}} = 1.27\times10^{4}\,\mathrm{M}^{-1}$ for **SQ-I**. These values suggest a slight increase of the aggregation constant from **SQ-Cl** to **SQ-I**. However, the absolute values are quite identical, thus supporting the assumption made above that the aggregates of these squaraines are of similar structure and they possess similarly strong intermolecular interactions.

The aggregation of the halogenated squaraine dyes was studied by temperature-dependent UV/Vis/NIR absorption experiments to assess the thermodynamic parameters for their aggregation processes. The temperature-dependent spectra in the range between 273 K and 373 K observed for the halogenated squaraines **SQ-Cl**, **SQ-Br**, and **SQ-I** are shown in the Supporting Information (Figures S9–S17). A similar spectral signature as in the concentration-dependent studies is observed, namely the transformation from the respective aggregated species at low temperatures to monomeric species at high temperatures, thus revealing the reversibility of the aggregation process.

In their recent work, Meijer and co-workers introduced a method for the analysis of such temperature-dependent data to enable a sensitive differentiation between different aggregation mechanisms.[10] To apply this procedure to our systems, temperature-dependent UV/Vis/NIR absorption experiments were performed for each of the squaraine dyes **SQ-Cl**, **SQ-Br**, and **SQ-I** at three different concentrations and the data were analyzed according to this method (for details see the Supporting Information). The degree of aggregation, $\alpha_{\mathrm{agg}}$, was fitted according to the isodesmic model following known literature procedures.[10] The $\alpha_{\mathrm{agg}}$ value is therein estimated according to Equation (1) where the melting temperature, $T_{\mathrm{m}}$, is the temperature at which $\alpha_{\mathrm{agg}} = 0.5$, $R$ is the universal gas constant, and $\Delta H$ is the molar enthalpy release related to the formation of noncovalent intermolecular interactions.

$$\alpha_{\mathrm{agg}} \cong \frac{1}{1+\exp\left[-0.908\Delta H\frac{T-T_{\mathrm{m}}}{RT_{\mathrm{m}}^{2}}\right]} \qquad (1)$$

The degree of aggregation, $\alpha_{\mathrm{agg}}$, can additionally be used in Equation (2) to obtain the average degree of polymerization, $DP_{\mathrm{N}}$, and the equilibrium constant $K_{\mathrm{e}}$ as a function of temperature for the given concentration $c_{\mathrm{T}}$.

$$DP_{\mathrm{N}} = \frac{1}{\sqrt{1-\alpha(T)}} = \frac{1}{2}+\frac{1}{2}\sqrt{4K_{\mathrm{e}}(T)c_{\mathrm{T}}+1} \qquad (2)$$

The calculated values for $K_{\mathrm{e}}$ then allow the determination of the thermodynamic parameters describing the self-assembly process of the respective squaraine by applying the van't Hoff relation (see Table S1 in the Supporting Information).

A characteristic feature of the isodesmic process is that small-sized dye aggregates are formed and only grow to extended structures at high concentration.[9] For the aggregates studied herein, $DP_N$ values above three are only observed at concentrations higher than $7\times10^{-4}$ M (see Table S1 in the Supporting Information). The values obtained for the enthalpy release $\Delta H$ (**SQ-Cl**: $-31.0\,\mathrm{kJ\,mol^{-1}}$, **SQ-Br**: $-32.3\,\mathrm{kJ\,mol^{-1}}$, **SQ-I**: $-34.8\,\mathrm{kJ\,mol^{-1}}$) as well as for the change in entropy $\Delta S$ (**SQ-Cl**: $-38.4\,\mathrm{J\,mol^{-1}\,K^{-1}}$, **SQ-Br**: $-38.0\,\mathrm{J\,mol^{-1}\,K^{-1}}$, **SQ-I**: $-44.4\,\mathrm{J\,mol^{-1}\,K^{-1}}$) upon aggregation are all within the same range and rather temperature independent. The similarity of the values for the squaraines **SQ-Cl**, **SQ-Br**, and **SQ-I** confirm that the aggregation processes of these squaraines are very similar. The calculated values for the different equilibrium constants obtained for temperature-dependent measurements are somewhat lower than those obtained from the concentration-dependent studies. However, they are still in the range of $10^3\,\mathrm{M^{-1}}$ to $10^4\,\mathrm{M^{-1}}$, and again the highest $K_e$ values are found for the iodinated squaraine **SQ-I**, thus suggesting that the latter is the strongest aggregating dye in the present series.

Besides tracking the aggregation process by UV/Vis/NIR spectroscopy, it can be monitored by NMR spectroscopy since the aggregation of chromophores also induces a change in the electronic environment. The $^1$H NMR spectra of **SQ-I** in [D$_8$]toluene exhibit sharp and defined signals in the decisive aromatic region within a concentration range from $c=1\times10^{-3}$ M to $c=2\times10^{-6}$ M (see Figure S18 in the Supporting Information). Fortunately, over the whole concentration range the characteristic proton signals (highlighted in color in Figure S18) are not overlapped by the solvent signals, and thus allow the analysis of their chemical shift upon aggregation. An upfield shift upon increasing concentration, as observed for proton H4 (blue) at around 7.8 ppm, indicates an aggregation-induced shielding, whilst a downfield shift as observed for the other highlighted proton signals at around $\delta=9.0$, 6.2, and 2.8 ppm indicate a deshielding effect by the aggregate structure. The analysis of the obtained data according to the isodesmic model afforded aggregation constants of $K_e=9.5\times10^3\,\mathrm{M^{-1}}$ to $K_e=1.1\times10^4\,\mathrm{M^{-1}}$ (Figure 3), which are in accordance with the values obtained from the UV/Vis/NIR absorption experiments.

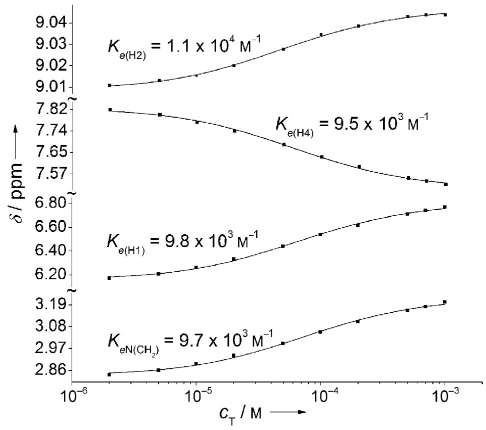

***Figure 3.*** Fit of the respective chemical shifts of the protons H1, H2, H4, and NCH$_2$ according to the isodesmic model.

Such sharp signals in the $^1$H NMR spectra are rarely observed for aromatic π stacks, and thus offer an ideal opportunity for the elucidation of the aggregate structure by 2D-NMR experiments. As **SQ-I** showed the highest aggregation constant and also provided the best solubility within the studied dye series, 2D-NMR measurements were performed exemplarily for this dye (for details see the Supporting Information). In both ROESY and NOESY experiments clear cross-peaks of H2 with H3′ and H4′, respectively, are observed (Figure 4a). As these protons are spatially separated from each other in the molecular structure, the observed cross-peaks can only arise from intermolecular interactions to neighboring dyes, thus indicating that those protons are in close proximity within the formed aggregate. Further proof for this assumption is obtained from ROESY data in CDCl$_3$,

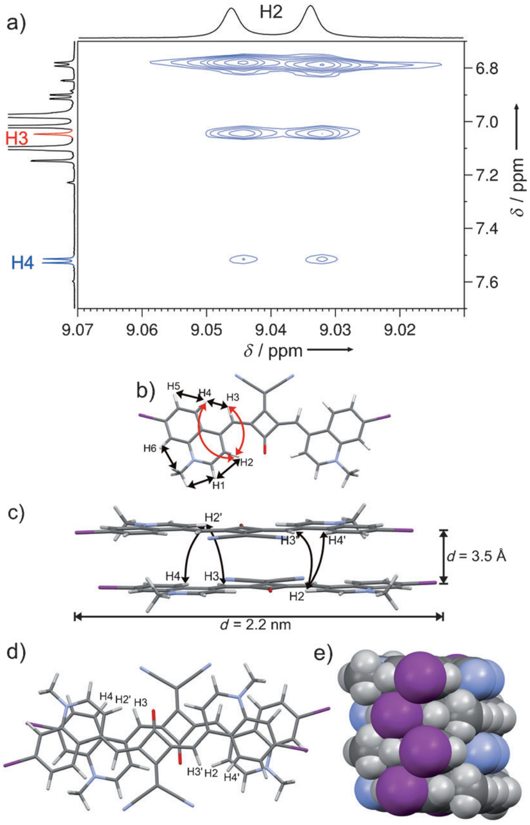

***Figure 4.*** a) ROESY spectrum of **SQ-I** showing the significant NOE cross-peaks ($c=3\times10^{-3}$ M; [D$_8$]toluene; 600 MHz). b) Calculated molecular structure of **SQ-I** by MM$^+$ and AM1 methods. The cross-peaks, resulting from intramolecular contacts, as observed in the ROESY experiments and which are also observed for monomeric dyes in CDCl$_3$ are indicated by black arrows. Those cross-peaks derived from intermolecular contacts, observed only for aggregated dyes in [D$_8$]toluene, are marked with red arrows. c) Side view of the modeled dimer aggregate of **SQ-I**. The arrows indicate the observed intermolecular ROESY and NOESY cross-peaks. d) Top view of a modeled dimer aggregate of **SQ-I**. e) Illustration of the proposed π-stacked *H*-aggregate structure of **SQ-I**. All geometry optimizations were performed at the MM+ and AM1 levels using HyperChem v8.0.

where the dyes are monomerically dissolved and no cross-peaks between the crucial protons are detectable. Molecular modeling studies for squaraine dimers suggest an antiparallel packing motif where the proton H2 of one chromophore is in close vicinity to H3′ and H4′ of the neighboring molecule in accordance with the 2D-NMR data (Figure 4 c,d). This arrangement leads to the formation of one-dimensional π stacks with alternating oriented squaraine chromophores, as illustrated in Figure 4 e. It is noteworthy that such an antiparallel π-stacking motif has been also observed in crystal structures of similar acceptor-substituted squaraines[11] as well as merocyanines,[12] and was attributed to dipole–dipole interactions.[13]

In view of the observed significance of halogen substituents for the aggregation of the present acceptor-substituted squaraine dyes, the question arises as to which noncovalent interactions are responsible for the observed difference in aggregation behavior of nonhalogenated **SQ-H** and **SQ-Me**, on one hand, and **SQ-Cl**, **SQ-Br**, and **SQ-I**, on the other hand. The aggregate structure deduced from 2D-NMR experiments and molecular modeling shows that the halogen atoms point out of the π stack, thus suggesting that sterics might play a role. However, the van der Waals radius of iodine (198 pm) is identical with that of the methyl group (200 pm).[14] Therefore, sterics cannot explain the observed differences in this series of dyes. Electrostatic interactions can also be ruled out as the major driving force for the aggregation because the contact between the halogen atoms at their nucleophilic equators and the neighboring electron-rich squaraines does not comply with the requirements of halogen bonding.[15] Therefore, we conclude that the interaction is governed by halogen–halogen and halogen–arene interactions that are largely of a dispersive nature. The importance of C–Cl/C–Br···π-interactions has recently been pointed out as an important contribution to protein–ligand binding affinity,[16] whilst the significant contributions of related sulfur–arene interactions are well accepted owing to the ubiquitous appearance of sulfur-π-contacts in proteins.[17] Accordingly, we attribute the halogen-mediated increase in the interaction strength between squaraine dyes to a gain in dispersive interaction energy,[5] which is in agreement with the high polarizabilities of iodine ($5.4\times10^{-24}\,\text{cm}^3$), bromine ($3.1\times10^{-24}\,\text{cm}^3$), and chlorine ($2.2\times10^{-24}\,\text{cm}^3$) and compare well with the polarizability of sulfur ($2.9\times10^{-24}\,\text{cm}^3$).

In summary, the studied dyes **SQ-Cl**, **SQ-Br**, and **SQ-I** were found to form *H*-aggregates driven by π–π stacking, dipole–dipole, and dispersive halogen interactions. This aggregation process thus appears to us to be the first quantitatively studied example for the existence of dispersive halogen interactions in supramolecular chemistry and complements previously investigated examples for electrostatically driven halogen bonding and halogen anion–π interactions.

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**Keywords:** dyes/pigments · halogens · self-assembly · stacking interactions · supramolecular chemistry

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[15] In most common cases of halogen bonding, halogen atoms function as electron-deficient sites (similar to hydrogen atoms in hydrogen bonding) when they form a contact to a Lewis base such as nitrogen, and is positioned on the opposite site of the

carbon–halogen bond, that is, the so-called σ hole of the halogen is responsible for such interactions. In a second case halogens interact as electron donors orthogonal to the carbon–halogen bond with electrophilic partners such as protons. For further discussion, see references [3] and [4]. Clearly both cases do not apply to the situation given for our squaraine aggregates.

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