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COMMUNICATION

Squaraine [2]catenanes: synthesis, structure and molecular dynamics†‡

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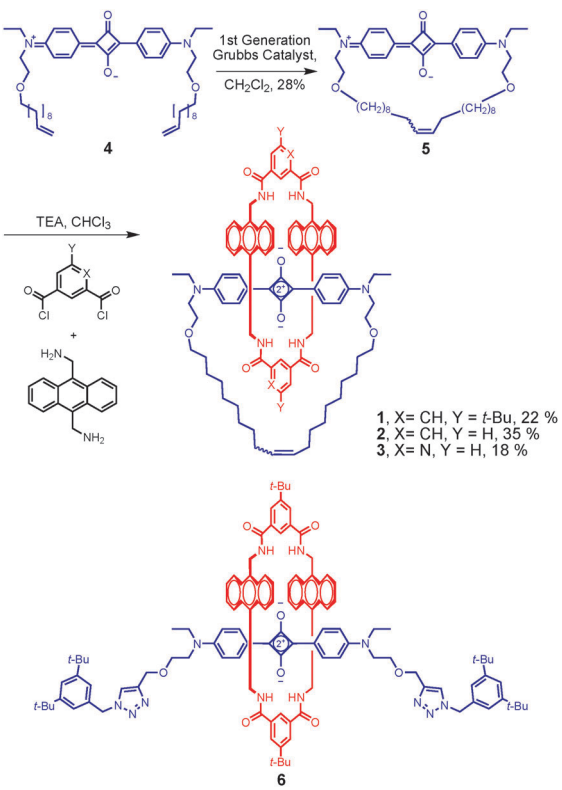
Three squaraine [2]catenanes are synthesized and found to have bright, deep-red fluorescence and high chemical stability. The interlocked molecules undergo two large-amplitude dynamic processes, twisting of the squaraine macrocycle and skipping over the partner tetralactam.

In 2005 we reported that highly fluorescent squaraine dyes can be permanently encapsulated inside tetralactam macrocycles to make interlocked [2]rotaxane molecules.[1] These compounds exhibit a range of favorable chemical and photophysical properties that make them attractive candidates as high performance fluorescence imaging probes,[2] chemiluminescent dyes,[3] photosensitizers,[4] and chemosensors.[5] Structural modifications of the rotaxane building blocks have lead to rationalizable changes in molecular dynamics,[6] chemical reactivity,[7] and photophysical properties.[8,9] Utilizing this expanding knowledge base we are beginning to design next-generation molecules with different interlocked topologies and here we report compounds **1–3** as the first examples of highly fluorescent and extremely stable squaraine [2]catenanes.[10] In addition to the synthetic methods and optical properties, we describe a solid-state catenane structure and characterize the solution-state molecular dynamics.

The [2]catenane synthesis starts with the bisalkene squaraine **4** which was converted into squaraine macrocycle **5** in 28% yield under ring closing metathesis conditions (Scheme 1).[11] Consistent with literature precedence, the macrocycle alkene unit in **5** is a 25 : 75 mixture of *cis* : *trans* isomers. Conversion of this squaraine macrocycle into squaraine catenanes **1–3** was achieved in the yield range of 18–35% by conducting Leigh-type clipping reactions using the appropriate diacid chloride and 9,10-bis(aminomethyl)anthracene.[12] Listed in Table 1 are the standard photophysical properties for compounds **1–5**. The two unencapsulated dyes **4** and **5** exhibit typical squaraine absorption and emission maxima. The large red-shifts upon conversion to catenanes **1–3** are very similar qto the optical changes previously observed with analogous squaraine rotaxanes having anthracene-containing tetralactam macrocycles.[8] The insensitivity of the squaraine optical properties to interlocked topology is notable and suggests that we can confidently design increasingly complicated mechanically-linked molecular architectures with predictable photophysics.

Another attractive feature with squaraine encapsulation is enhanced chemical stability. The electrophilic cores of squaraine dyes are readily attacked by strong nucleophiles and previously we have shown that squaraine rotaxanes such as **6** exhibit high levels of steric protection from thiols in weakly polar solvents such as chloroform.[1,13] However, the rotaxane protection effect is much weaker in more polar organic solvents that disrupt non-covalent association of encapsulated squaraine dye with the surrounding tetralactam



Scheme 1 Synthesis of squaraine [2]catenanes **1–3** and chemical structure of squaraine rotaxane **6**.

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‡ Electronic supplementary information (ESI) available: Synthesis and spectral data and summary of X-ray analysis. CCDC 813692. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1cc10946d

Table 1 Absorption and emission values in $CHCl_3$ (5.0 μM)

Compound	λ_{abs} (nm)	λ_{em} (nm)	$\log_{10}\varepsilon$	Φ_f[a]
1	663	699	5.08	0.42
2	663	699	5.14	0.43
3	667	700	5.16	0.42
4	632	650	5.18	0.51
5	633	652	5.22	0.51

[a] Fluorescence quantum yields determined using 4,4-[bis-(*N*,*N*-dimethylamino)phenyl]squaraine as a standard (Φ_f) 0.70 in $CHCl_3$, error limit (±5%).

and expose the reactive squaraine core.[8a] This solvent enhanced reactivity is reflected by the plot in Fig. 1 showing a rapid decrease in squaraine absorption band for rotaxane **6** due to attack by excess 2-mercaptoethanol in DMF. In contrast, the plot for catenane **1** under identical conditions shows a half-life that is approximately 100-fold longer, indicating a substantially higher degree of steric protection. Apparently, it is much harder for the encapsulated squaraine in catenane **1** to be displaced from the surrounding tetralactam by the DMF solvent. We conclude that squaraine catenanes retain the impressive deep-red fluorescent properties of squaraine rotaxanes but exhibit significantly enhanced resistance to nucleophilic attack in polar organic solvents.[14]

Catenane **3**, with its novel tetralactam macrocycle containing two bridging pyridine 2,4-dicarboxamide units, is relatively insoluble and was readily obtained as single crystals. Analysis by X-ray diffraction was possible even though the compound exists as a mixture of four stereoisomers—in addition to the squaraine macrocycle alkene stereochemistry, the tetralactam component in **3** can have planar or axial symmetry depending on the relative positions of the two pyridyl nitrogen atoms. Shown in Fig. 2 is the solid-state molecular structure with a *trans* alkene geometry and the tetralactam having planar symmetry because the two pyridyl nitrogens have a *syn* relationship. The structure shows no major distortions from expected bond angles and bond distances. The squaraine chromophore is essentially planar which agrees with the unperturbed absorption data in Table 1.[15] As discussed below, there is hindered rotation about the two aniline C–N bonds at each end of the squaraine chromophore, such that the macrocycle can be twisted to adopt either *syn* or *anti* conformations with essentially identical energies (Fig. 3A). The catenane chemical structure that is drawn in Scheme 1 depicts the squaraine macrocycle in a *syn* conformation with respect to these two C–N bonds, but the X-ray crystal

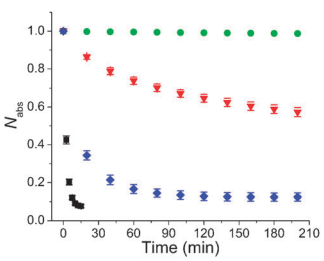

Fig. 1 Normalized changes in squaraine (5.0 μM) absorption for: **6** in DMF (●), mixtures of 2-mercaptoethanol (50 μM) with either **1** (▼), **6** (♦), or **5** (■) in DMF. All samples at room temperature and in the dark.

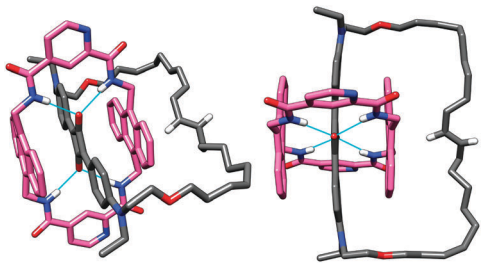

Fig. 2 X-Ray crystal structure of squaraine [2]catenane **3**. For clarity, only amide and alkene hydrogens are shown and intramolecular hydrogen bonds are indicated as light blue lines.

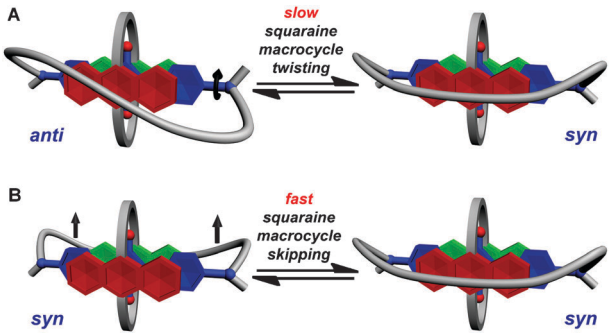

Fig. 3 Squaraine [2]catenane molecular dynamics showing; (A) slow squaraine macrocycle twisting between *syn* and *anti* conformations, and (B) fast squaraine macrocycle skipping over the tetralactam.

structure shows that the *anti* macrocycle conformation is preferred in the solid state, a bias that is attributed to crystal packing forces. This *anti* conformation constrains the alkene unit in the squaraine macrocycle to be directly over the face of the adjacent anthracene unit in the partner tetralactam component. The tetralactam adopts a flattened macrocyclic chair conformation that is very similar to that observed with analogous squaraine rotaxanes.[8a] The catenane and rotaxane co-conformations are also similar in that both anthracene units in the tetralactam encapsulate the C_4O_2 core of the squaraine chromophore. The distance between the centers of the two anthracene units in catenane **3** is 6.95 Å and each amide residue in the tetralactam is hydrogen bonded to a squaraine oxygen atom with NH–O distances of 2.10–2.16 Å.[7]

Compared to squaraine catenane **3**, catenanes **1** and **2** are more soluble and thus they were chosen for detailed study by variable temperature NMR. Both molecular systems exhibit similar temperature dependent changes in spectral patterns, suggesting that they undergo the same dynamic processes. The large anisotropic shielding of the squaraine chemical shifts indicates that the solid-state structure is firmly maintained in solution with the tetralactam encapsulating the squaraine chromophore. This helps explain why the catenane exhibits such high steric protection of the electrophilic squaraine core (Fig. 1). Further inspection of the NMR spectra indicates that the catenanes undergo two large-amplitude dynamic motions due to conformational exchange.[16] One motion, with a relatively low activation energy, is skipping of the hydrocarbon chain of the squaraine macrocycle over a bridging isophthalamide unit in the partner tetralactam component. (Fig. 3B). At room temperature, the process is sufficiently rapid to produce a

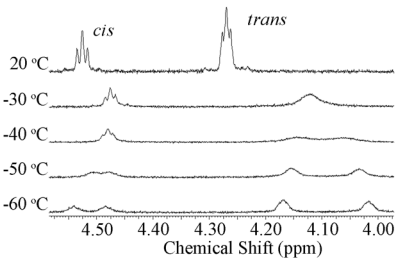

Fig. 4 Partial ^{1}H NMR spectra (500 MHz) of catenane **2** in CD_2Cl_2 showing the squaraine macrocycle *cis* and *trans* alkene signals. The spectra indicate two-site exchange of equally populated *syn* and anti conformations.

single set of exchange-averaged signals for the tetralactam's two anthracene units.§ In other words, NMR cannot distinguish the anthracene unit inside the tetralactam from the anthracene that is outside. Even at low temperatures it is not apparent that squaraine macrocycle skipping becomes slow relative to the NMR time scale. For example, the four sets of tetralactam benzylic protons remain chemical shift equivalent at −90 °C. The second, large-amplitude motion is twisting of the squaraine macrocycle due to hindered rotation about the squaraine aniline C–N bonds which exhibit partial double bond order due to strong delocalization with the squaraine chromophore (Fig. 3A). In this case, the activation barrier is sufficiently high that signal coalescence is observed at around −40 °C and slow exchange spectra are obtained at lower temperatures. The key evidence that unambiguously identifies this dynamic process is the two-site exchange phenomena exhibited by the squaraine macrocycle alkene signals (Fig. 4). Measurements of the coalescence temperatures and limiting chemical shifts for these signals (see ESI) allowed determination of the free energy of activation to be 11.6 ± 0.3 and 11.4 ± 0.2 kcal mol^{-1} for **1** and **2**, respectively. Thus, the dynamic process is independent of the size of the group at the 5-position of the two isophthalamide units in the tetralactam, suggesting that this motion does not involve the tetralactam.¶ Moreover, the energy barrier is quite similar to the value of 13 kcal mol^{-1} for squaraine aniline C–N bond rotation in a related squaraine rotaxane system.[17] Additional broadening of some catenane signals is observed at −90 °C (see ESI), and most likely this is due to slowing of low energy dynamic processes such as squaraine macrocycle skipping and tetralactam macrocyclic chair/boat flips.[6,18]

In summary, squaraine catenanes **1–3** are the first examples of a new class of interlocked squaraine-derived molecular architecture. The catenane topology exhibits unique dynamic processes as summarized in Fig. 3. Recently, we reported that squaraine rotaxanes with anthracene-containing tetralactam macrocycles can be converted by simple photooxidation into endoperoxide derivatives that undergo a chemiluminescent cycloreversion reaction.[3] Preliminary studies indicate that squaraine catenanes exhibit the same phenomenon and work is ongoing to determine how the chemiluminescence intensity is altered by the changes in structural topology. This study was supported by the NSF and the University of Notre Dame.

Notes and references

§ The co-conformational exchange in Fig. 3B can also be acheived by tetralactam circumrotation, but this is a less favored pathway because it must break four hydrogen bonds. For further discussion, see ref. 16 and 18.

¶ The Leigh group has reported that energy barriers for tetralactam circumrotation in [2]catenanes are quite sensitive to tetralactam molecular structure and solvent. For tetralactams with isophthalamide units, the steric bulk at the 5-position has a large influence on circumrotation rates. For further discussion, see ref. 18.

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