JOC Notes

Social and Antisocial [3 + 3] Schiff Base Macrocycles with Isomeric Backbones

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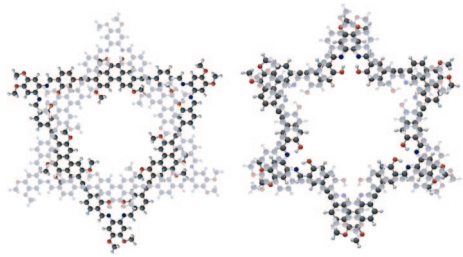

Two new conjugated macrocycles have been prepared in high yield using Schiff base condensation. These are the first Schiff base macrocycles to incorporate phenanthrene, and they contain 66 and 78 atoms, respectively, in their smallest closed ring. Although the backbones of the two macrocycles have nearly the same constitution, one aggregates in chloroform while the other does not. This is rationalized based on the differential overlap of aromatic components in the dimers.

Conjugated, shape-persistent macrocycles are attractive for studies of supramolecular assembly,[1] liquid crystallinity,[2] and nanotube formation.[3] Recent studies from our laboratory and others have shown that imine formation is a synthetically useful route to assemble conjugated macrocycles.[4−7] In particular, we have been targeting macrocycles that have salphen-type N_2O_2 binding sites for further coordination to metals. The size and shape of the macrocycle obtained from the condensation are dictated by the geometry and length of the starting components.[8−10]

In our quest to develop highly luminescent Schiff base macrocycles for sensing applications, we investigated the incorporation of phenanthrene into a Schiff base macrocycle. Previously, phenanthrene has been incorporated into luminescent polymers and materials[11,12] but has seldom been studied as a component of macrocycles.[13,14] Herein, we report the synthesis and characterization of two new macrocycles incorporating phenanthrene. To the best of our knowledge, the new macrocycle **8** with 78 atoms in the smallest closed ring is the largest conjugated macrocycle assembled by Schiff base condensation. This highly efficient synthesis illustrates the utility of Schiff base condensation for making large molecules. Moreover, one of these macrocycles aggregates in solution, while the other does not.

We have previously reported the synthesis of compound **1**, which was found to be a useful precursor in the synthesis of conjugated phenanthrene-containing polymers.[12] Coupling of **1**

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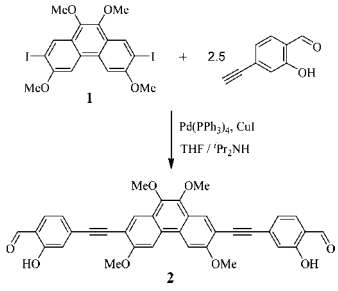
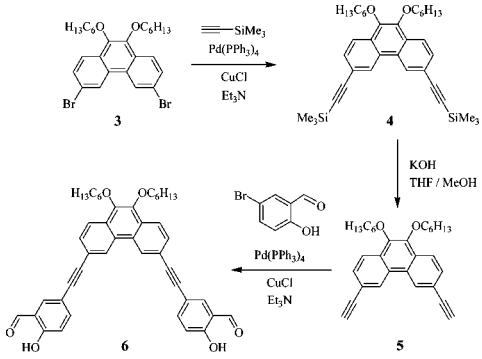
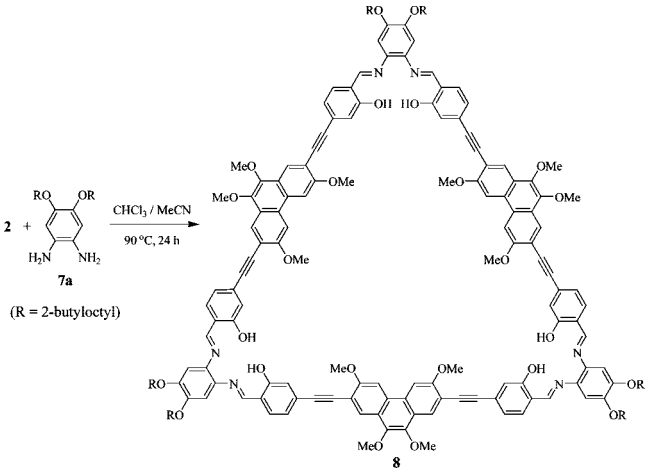
SCHEME 1. Synthesis of Compound 2



SCHEME 2. Synthesis of Compound 6



SCHEME 3. Synthesis of Macrocycle 8



with 4-ethynylsalicylaldehyde afforded compound **2** in 75% yield (Scheme 1). Compound **6** was prepared in three steps (39% overall yield) from dibromodihexyloxyphenanthrene **3** (Scheme 2). Both **2** and **6** have two salicylaldehyde groups bridged by phenanthrene.

Compounds **2** and **6** were reacted with 1,2-dialkoxy-4,5-phenylenediamines **7** to form Schiff base macrocycles. Thus, the reaction of **2** with **7a** afforded dark red macrocycle **8** in 71% yield (Scheme 3). 2-Butyloctyl substituents were selected to ensure the macrocycle was soluble. Similarly, compound **6** was condensed with **7b** to form orange microcrystalline macrocycle **9** in 53% yield (Scheme 4). In this case, hexyloxy substituents were selected on the phenylenediamine since they were deemed sufficient to render the macrocycles soluble, given that the phenanthrene groups also have hexyloxy substituents. The high yields of these macrocycles, which are prepared without a template, are likely attributed to the strong intramolecular hydrogen bonding within the cycles and the preordained geometry of precursors **2** and **6**. NMR spectra of macrocycles

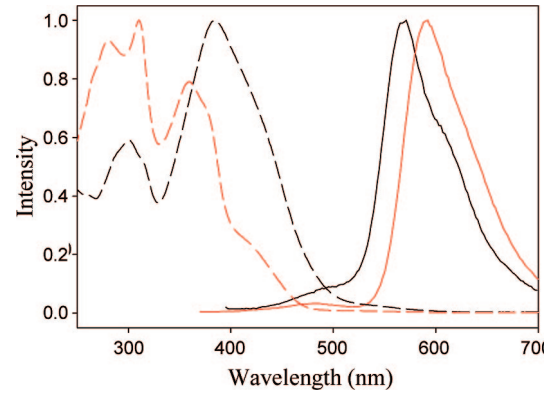
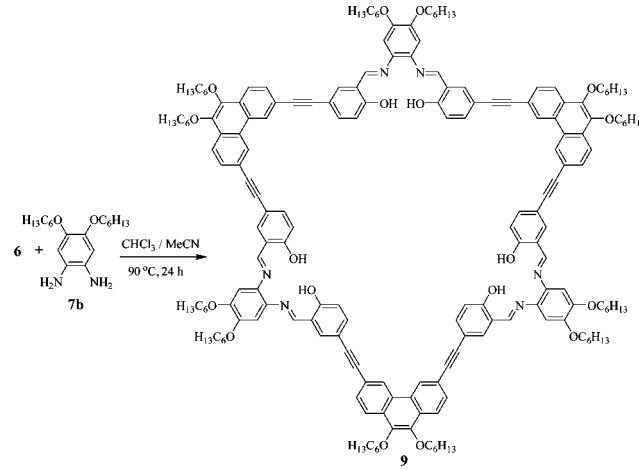


FIGURE 1. Absorption (dashed line) and emission (solid line) spectra of macrocycles **8** (4×10^{-6} M; $\lambda_{exc} = 383$ nm) and **9** (3×10^{-6} M; $\lambda_{exc} = 357$ nm) in CH_2Cl_2 (**8** = black, **9** = red).

SCHEME 4. Synthesis of Macrocycle 9



8 and **9** were consistent with the proposed structures. MALDI-TOF mass spectra verified that the cycles formed were indeed [3 + 3] macrocycles, with the molecular ion as the dominant peak in both cases.

When the alkoxy substituents are ignored, the backbones of triangular macrocycles **8** and **9** are isomeric with 78 and 66 atoms in the smallest closed ring, respectively. In macrocycle **8**, the phenanthrene groups are on the edges with salphen groups forming the corners of a triangle. In macrocycle **9**, the position of the salphen and phenanthrene moieties is interchanged. Macrocycle **8** has a conjugated backbone, and there is alternation of single and double or triple bonds around the ring. In macrocycle **9**, however, the bond alternation is disrupted at each salicylaldimine since the meta-linkage between alkyne and imine prevents a path of alternating single and double bonds. We sought to understand how changing the geometry would affect the electronic and other properties of the macrocycle.

Figure 1 shows the absorption and emission spectra of macrocycles **8** and **9**. Macrocycle **8** has two large absorption bands at 300 and 384 nm, while macrocycle **9** absorbs at 309 and 357 nm. The maximum absorbance for macrocycle **9** is 27 nm blue-shifted from that of macrocycle **8**, a trend that was expected due to the decreased conjugation of macrocycle **9**.

Both macrocycles are weakly luminescent in solution and in the solid state. In solution, macrocycle **8** emits with a maximum at 567 nm (CH_2Cl_2; $\Phi_F = 0.4\%$) and macrocycle **9** emits with a maximum at 588 nm (CH_2Cl_2; $\Phi_F = 1.2\%$).

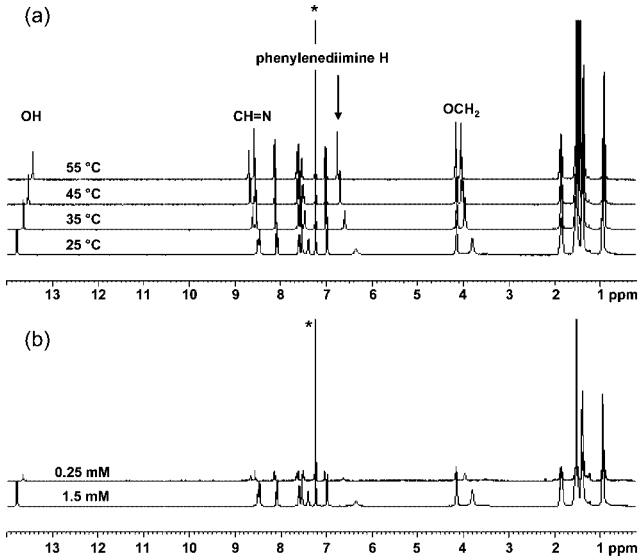


FIGURE 2. (a) Stacked ^{1}H NMR spectra (400 MHz, $CDCl_3$, 1.5 mM) of macrocycle **9** at various temperatures. (b) Stacked ^{1}H NMR spectra (400 MHz, $CDCl_3$, RT) of macrocycle **9** at two different concentrations ($* = CDCl_3$).

Polycyclic aromatic hydrocarbons are well-known to stack as a result of intermolecular $\pi-\pi$ interactions.[15] Macrocycles **8** and **9** both contain many aromatic units that have potential to interact, and we probed their aggregation by variable temperature and variable concentration ^{1}H NMR (VT/VC NMR) spectroscopy.

Initially, solutions of two different concentrations of each macrocycle were prepared, and ^{1}H NMR spectra were obtained at four different temperatures, ranging from 25 to 55 °C at 10 °C intervals. Upon changing the temperature of the samples of macrocycle **8**, the only peak that exhibits a change in chemical shift is the O*H* resonance, which moves upfield from 13.30 to 13.13 ppm over the 30 °C temperature range. This macrocycle also showed no concentration dependence in its chemical shifts. These observations indicate that macrocycle **8** does not aggregate in $CDCl_3$.

On the other hand, VT/VC NMR experiments with macrocycle **9** gave a different result (Figure 2). Hydroxyl resonances shift upfield with increasing temperature and decreasing concentration, while all aromatic resonances shift downfield. The largest shifts (ca. 0.5 to 1.0 ppm) come from the imine proton, the aromatic phenylenediimine proton, and alkoxy OC*H*$_2$. Additionally, the overlapping imine and the phenanthrene proton resonances, found near 8.5 ppm, separate and sharpen with increasing temperature. These initial results clearly indicate that macrocycle **9** aggregates in solution. The monomer to aggregate equilibrium is affected by changes in temperature and concentration.

In an effort to quantify the aggregation of macrocycle **9**, NMR data were collected over a range of concentrations (0.045−2.27 mM) and temperatures (5−55 °C); solubility constraints prohibited data collection at low temperature. The resonances assigned to the imine and phenylenediimine resonances shifted as a function of concentration and temperature. As the total chemical shift change was less than 1 ppm for all resonances, this is more consistent with dimer formation than larger aggregates.[16] Data were fit to a model for dimerization (see Supporting Information) to extract equilibrium constants at each temperature (Table 1).[16] As expected, the association constants decrease as temperature increases, indicative of weaker aggregation at elevated temperatures. Other imine-containing macrocycles have values of K_E at room temperature in the same order of magnitude ($\sim 10^3$ M^{-1}) as for macrocycle **9**.[17]

On the basis of the temperature dependence of the data, the dimerization is clearly enthalpy favored ($\Delta H < 0$) and entropy disfavored ($\Delta S < 0$).[18] This result is consistent with $\pi-\pi$ interactions being primarily involved in the assembly. The negative change in entropy is not unexpected, as aggregation would increase order in solution. Given these results, it is apparent that, at higher temperatures, the chemical shifts are nearly independent of concentration, indicating that elevated temperature effectively deaggregates the macrocycle, and these spectra are most representative of the free macrocycle. Conversely, the most concentrated spectra obtained at the lowest temperature represent, in effect, the macrocycle in a fully aggregated environment.

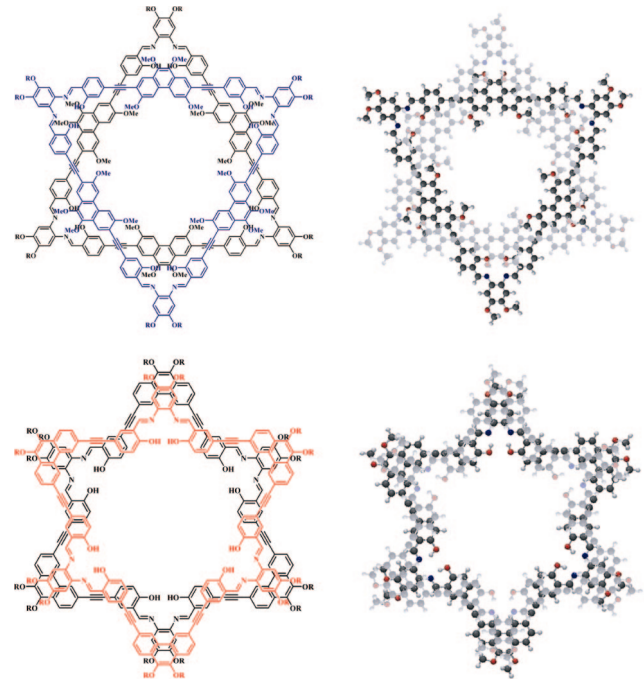


FIGURE 3. Structures of hypothetical planar dimers of macrocycles **8** (top) and **9** (bottom), with ChemDraw representations on the left and Spartan models (not energy minimized) on the right.

TABLE 1. Association Constants K_E for Dimerization of Macrocycle 9 in $CDCl_3$

T (°C, K)	K_E (imine) (M^{-1})	K_E (diimine) (M^{-1})
5, 278	1600 ± 410	5000 ± 1200
15, 288	2700 ± 290	3700 ± 1100
25, 298	1200 ± 380	1000 ± 280
35, 308	580 ± 150	420 ± 120
45, 318	290 ± 90	140 ± 60
55, 328	280 ± 90	150 ± 60

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(18) We determined the thermodynamic parameters from a van't Hoff plot, but this method does not give accurate parameters unless a broad temperature range can be accessed.

Considering that macrocycles **8** and **9** have isomeric backbones, it is surprising that they behave differently in solution. However, Figure 3, which shows hypothetical structures of the dimers, illustrates a possible reason why **8** does not aggregate while **9** does. The macrocycles are rotated in the figure because direct overlap of the aromatic rings would lead to repulsion of the macrocycles rather than attractive forces necessary for aggregation. The dimers depicted in Figure 3 would allow attractive interactions between electron-deficient and electron-rich rings. Dimers of macrocycle **8** lack overlapping aromatic rings, greatly reducing its capacity for π stacking and preventing aggregation. Model dimers of macrocycle **9** have salphen moieties directly aligned with the phenanthrene groups and the protons positioned over the aromatic rings, where they would experience the greatest effects of magnetic anisotropy and exhibit the greatest change in chemical shift in the VT/VC NMR spectra. For example, the phenylenediimine proton is positioned over the center of the phenanthrene rings in the dimer; therefore, the chemical shifts are considerably upfield at lower temperatures and higher concentrations because of the proximity to the ring current. Upon deaggregation, the peaks shift downfield because this proton is no longer in such an electronically shielded environment, which has been confirmed in previous studies.[19,20]

In summary, two giant Schiff base macrocycles with isomeric backbones containing phenanthrene were synthesized and found to be weakly luminescent. One macrocycle (**9**) aggregates in chloroform, while the other (**8**) does not. We attribute this difference to the ability of macrocycle **9** to stack with overlap of salphen groups with phenanthrene moieties, while in macrocycle **8**, fewer $\pi-\pi$ interactions are possible. These macrocycles illustrate the use of Schiff base chemistry as a route to well-defined nanoscale macrocycles.

Experimental Section

Synthesis of Macrocycle 8. Compound **2** (0.145 g, 0.247 mmol) and 1,2-dibutyloctyloxy-4,5-diaminobenzene (**7a**) (0.118 g, 0.247 mmol) were combined in a Schlenk flask in the glovebox. Degassed $CHCl_3$ (15 mL) and MeCN (5 mL) were added to the flask, and the solution was heated to reflux at 90 °C. After heating for 24 h, the solution was cooled and the solid was precipitated by addition of MeCN. The solid was recrystallized from CH_2Cl_2 and MeCN. Yield: 0.180 g, 0.0584 mmol, 71%. Data for **8**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.32 (s, 6H), 8.62 (s, 6H), 8.34 (s, 6H), 7.78 (s, 6H), 7.38 (d, J = 8.0 Hz, 6H), 7.31 (s, 6H), 7.17 (d, J = 8.0 Hz, 6H), 6.81 (s, 6H), 4.13 (s, 18H), 4.08 (s, 18H), 3.93 (d, 12H), 2.0−0.80 (m, 138H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 161.1, 157. 9, 149.8, 142.4, 135.3, 132.1, 129.0, 128.5, 127.9, 124.4, 122.5, 120.8, 119.7, 114.2, 103.0, 94.5, 88.7, 72.5, 61.4, 56.5, 38.4, 32.2, 31.6, 31.3, 30.0, 29.4, 27.2, 23.3, 23.0, 14.4; MALDI-TOF-MS m/z = 3084 ($[M + H]^+$); IR (KBr) ν = 3430, 2952, 2932, 2859, 2204, 1606, 1511, 1457, 1367, 1252, 1207, 1172, 1103, 1015, 813, 696 cm^{-1}; UV−vis (CH_2Cl_2) λ_{max} (ϵ) = 300 (1.3×10^5), 384 (2.2×10^5) nm (L mol^{-1} cm^{-1}); mp >300 °C. Anal. Calcd for $C_{198}H_{234}N_6O_{24}\cdot 2H_2O$: C, 76.27; H, 7.69; N, 2.70. Found: C, 75.94; H, 7.79; N, 3.11.

Synthesis of Macrocycle 9. To a mixture of compound **6** (0.206 g, 0.309 mmol) and 1,2-dihexyloxy-4,5-diaminobenzene (**7b**) (0.096 g, 0.311 mmol) was added 10 mL of each $CHCl_3$ and MeCN. The resulting solution was refluxed at 90 °C for 24 h after which an orange solid precipitated and was filtered. For additional purification, the product was recrystallized in hot $CHCl_3$ and MeCN and washed with petroleum ether. Yield: 0.156 g, 0.0554 mmol, 53%. Data for **9**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.78 (s, 6H), 8.50 (s, 6H), 8.47 (s, 6H), 8.08 (d, J = 8.5 Hz, 6H), 7.60 (d, J = 8.5 Hz, 6H), 7.53 (d, J = 1.3 Hz, 6H), 7.40 (dd, J_1 = 8.6 Hz, J_2 = 1.4 Hz, 6H), 6.98 (d, J = 8.6 Hz, 6H), 6.36 (s, 6H), 4.15 (t, 12H), 3.81 (t, 12H), 1.87−0.94 (m, 132H); ^{13}C NMR (100.7 MHz, $CDCl_3$) δ 161.8, 159.5, 149.1, 143.8, 136.4, 135.7, 134.8, 129.2, 128.1, 126.3, 122.4, 120.8, 119.6, 118.1, 113.8, 90.2, 88.9, 73.6, 69.3, 32.1, 31.9, 30.8, 29.4, 26.2, 26.0, 23.0, 22.9, 14.4, 14.3; MALDI-TOF-MS m/z = 2818.9 ($[M + H]^+$); IR (KBr) ν = 3413, 2958, 2933, 2857, 2204, 1617, 1608, 1503, 1488, 1437, 1352, 1317, 1292, 1263, 1179, 1121, 1062, 828 cm^{-1}; UV−vis (CH_2Cl_2) λ_{max} (ϵ) = 279 (1.9×10^5), 309 (2.0×10^5), 357 (1.5×10^5) nm (L mol^{-1} cm^{-1}); mp >300 °C. Anal. Calcd for $C_{186}H_{210}N_6O_{18}$: C, 79.28; H, 7.51; N, 2.98. Found: C, 79.00; H, 7.67; N, 3.22.

Acknowledgment. We thank NSERC for funding.

Supporting Information Available: Experimental details, characterization, and spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) We cannot eliminate the possibility that the different sizes of the peripheral alkoxy substituents have a role in the stacking. We have not observed significant substituent effects with other macrocycles, but they may be involved here. Efforts are underway to prepare new analogues that will allow better control of the substituents.