ORGANIC LETTERS

2004
Vol. 6, No. 21
3841−3844

Synthesis and Metalation of Novel Fluorescent Conjugated Macrocycles

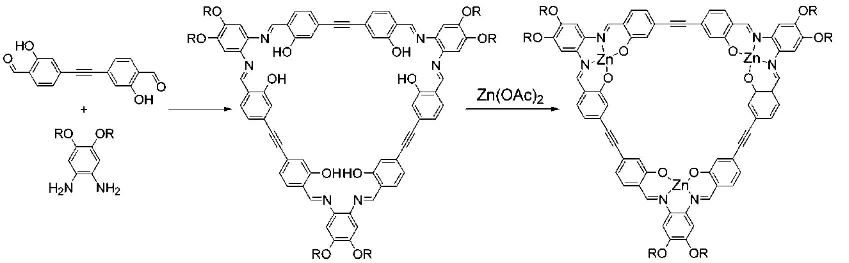
Cecily Ma, Andy Lo, Amir Abdolmaleki, and Mark J. MacLachlan*

Department of Chemistry, University of British Columbia, 2036 Main Mall,
Vancouver, BC, V6T 1Z1, Canada

mmaclach@chem.ubc.ca

Received August 18, 2004

ABSTRACT



Large shape-persistent conjugated macrocycles with tunable pore diameters in the nanometer regime were prepared by a simple, one-pot procedure. These new self-assembled macrocycles contain rings of 48–66 covalently bonded atoms and can bind multiple metal ions, forming soluble luminescent complexes.

Shape-persistent, rigid macrocycles are fascinating targets for creating new materials, including discotic liquid crystals, chemical sensors, catalysts, and fluorescent substances.[1−5] Under certain conditions, conjugated macrocycles may assemble into nanotubes.[6,7] Although many examples of organic macrocycles have been reported, they remain challenging to synthesize, often involving a large number of steps, the use of protecting groups or templates, high dilution and proceeding in low yields.[8,9]

Large macrocycles may be formed by the self-assembly of metal-coordination complexes in solution.[10,11] In these reactions, metals serve to define the structure of the final macrocyclic product and are in its backbone. The incorporation of metals into rigid, conjugated covalently bonded macrocycles may offer opportunities for developing su-

---

(1) (a) Moore, J. S.; Zhang, J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 922−924. (b) Höger, S.; Meckenstock, A.-D.; Pellen, H. *J. Org. Chem.* **1997**, *62*, 4556−4557.

(2) (a) Zhao, D.; Moore, J. S. *Chem. Commun*. **2003**, 807−818. (b) Höger, S. *Chem.*—*Eur. J.* **2004**, *10*, 1320−1329.

(3) (a) Bunz, U. H. F.; Rubin, Y.; Tobe, Y. *Chem. Soc. Rev.* **1999**, *28*, 107−119. (b) Faust, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 2825−2828.

(4) Grave, C.; Schlüter, A. D. *Eur. J. Org. Chem.* **2002**, 3075−3098.

(5) For recent examples of shape-persistent, conjugated macrocycles, see: (a) Yamaguchi, Y.; Kobayashi, S.; Miyamura, S.; Okamoto, Y.; Wakamiya, T.; Matsubara, Y.; Yoshida, Z. *Angew. Chem., Int. Ed.* **2004**, *43*, 366−369. (b) Muller, P.; Usón, I.; Hensel, V.; Schlüter, A. D.; Sheldrick, G. M. *Helv. Chim. Acta* **2001**, *84*, 778−785. (c) Mayor, M.; Didschies, C. *Angew. Chem., Int. Ed.* **2003**, *42*, 3176−3179. (d) Tobe, Y.; Utsumi, N.; Nagano, A.; Naemura, K. *Angew. Chem., Int. Ed.* **1998**, *37*, 1285−1287. (e) Campbell, K.; Tiemstra, N. M.; Prepas-Strobeck, N. S.; McDonald, R.; Ferguson, M. J.; Tykwinski, R. R. *Synlett* **2004**, 182−186. (f) Fischer, M.; Lieser, G.; Rapp, A.; Schnell, I.; Mamdouh, W.; De Feyter, S.; De Schryver, F. C.; Höger, S. *J. Am. Chem. Soc.* **2004**, *126*, 214−222. (g) Höger, S.; Enkelmann, V.; Bonrad, K.; Tschierske, C. *Angew. Chem., Int. Ed.* **2000**, *39*, 2267−2270. (h) Eisler, S.; Tykwinski, R. R. *Angew. Chem., Int. Ed.* **1999**, *38*, 1940−1943.

(6) (a) Zhang, J.; Moore, J. S. *J. Am. Chem. Soc.* **1992**, *114*, 9701−9702. (b) Shetty, A. S.; Zhang, J.; Moore, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 1019−1027. (c) Lahiri, S.; Thompson, J. L.; Moore, J. S. *J. Am. Chem. Soc.* **2000**, *122*, 11315−11319. (d) Höger, S.; Spickermann, J.; Morrison, D. L.; Dziezok, P.; Räder, H. J. *Macromolecules* **1997**, *30*, 3110−3111. (e) Höger, S.; Bonrad, K.; Mourran, A.; Beginn, U.; Möller, M. *J. Am. Chem. Soc.* **2001**, *123*, 5651−5659.

(7) Bong, D. T.; Clark, T. D.; Granja, J. R.; Ghadiri, M. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 988−1011.

(8) Prautzsch, V.; Ibach, S.; Vögtle, F. *J. Inclusion Phenom. Macrocyclic Chem.* **1999**, *33*, 427−458.

(9) Höger, S. *J. Polym. Sci. A* **1999**, *37*, 2685−2698.

(10) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853−908.

(11) For recent examples, see: (a) Jiang, H.; Lin, W. *J. Am. Chem. Soc.* **2004**, *126*, 7426−7427. (b) Lee, S. J.; Luman, C. R.; Castellano, F. N.; Lin, W. *Chem. Commun*. **2003**, 2124−2125. (c) Biradha, K.; Fujita, M. *Adv. Supramol. Chem.* **2000**, *6*, 1−39. (d) Eisenberg, A. H.; Ovchinnikov, M. V.; Mirkin, C. A. *J. Am. Chem. Soc.* **2003**, *125*, 2836−2837. (e) Thuery, P.; Villiers, C.; Jaud, J.; Ephritikhine, M.; Masci, B. *J. Am. Chem. Soc.* **2004**, *126*, 6838−6839. (f) Cutland, A. D.; Halfen, J. A.; Kampf, J. W.; Pecoraro, V. L. *J. Am. Chem. Soc.* **2001**, *123*, 6211−6212. (g) Mukherjee, P. S.; Das, N.; Kryschenko, Y. K.; Arif, A. M.; Stang, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 2464−2473. (h) Sun, S.-S.; Stern, C. L.; Nguyen, S. T.; Hupp, J. T. *J. Am. Chem. Soc.* **2004**, *126*, 6314−6326. (i) Newkome, G. R.; Cho, T. J.; Moorefield, C. N.; Mohapatra, P. P.; Godinez, L. A. *Chem.*—*Eur. J.* **2004**, *10*, 1493−1500.

10.1021/ol0483549 CCC: $27.50

pramolecular materials and sensors triggered by ligand coordination to the metal. Unfortunately, there are few reports of shape-persistent organic macrocycles that bind multiple metal centers.[12]

Schiff-base condensation is a convenient route to small macrocycles.[13] We have previously used this method to synthesize macrocycle **1**, Figure 1.[14] This macrocycle has a very small interior pore and, due to its constrained geometry, is nonplanar even when coordinated to transition metals. As a step to developing large, flat macrocycles that can be assembled into nanotubes, we needed access to larger macrocycles with the metals spaced farther apart. We now report the remarkably efficient preparation of large macrocycles that possess both nanoscopic pores and three N_2O_2 binding sites that can coordinate transition metals. These macrocycles represent a new class of giant, soluble, metal-containing macrocycles.

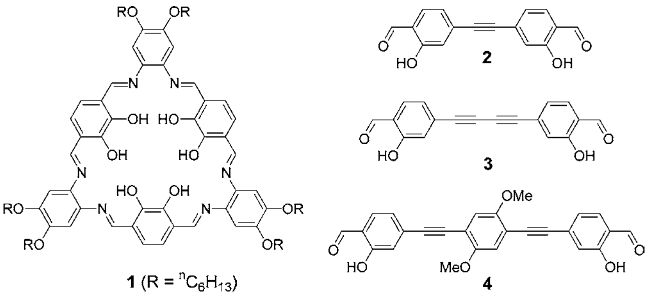
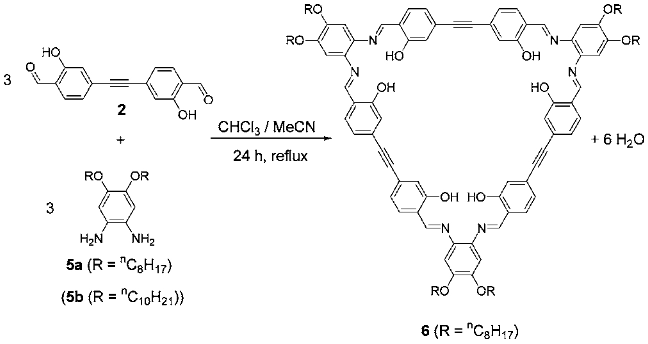


Figure 1. Structures of macrocycle **1** and precursors **2**−**4**.

Compounds **2** and **4** (Figure 1) were synthesized via Pd-catalyzed Sonogashira−Hagihara cross-coupling of 4-ethynylsalicylaldehyde with 4-bromosalicylaldehyde and 1,4-diiodo-2,5-dimethoxybenzene, respectively.[15] Compound **3** was prepared by oxidative coupling of 4-ethynylsalicylaldehyde.

Scheme 1. Synthesis of Conjugated Macrocycle **6**



The reaction of compound **2** with diamine **5a** afforded a red powder **6** in 68% yield (Scheme 1). The ^{1}H NMR spectrum of compound **6** revealed the presence of a single imine (δ 8.58) and a strongly hydrogen-bonded OH resonance (δ 13.27), consistent with D_{3h} symmetry for the macrocycle. MALDI-TOF mass spectrometry showed the molecular ion at $m/z = 1785$, supporting the structure of compound **6**. A Raman spectrum of compound **6** showed the C≡C stretching mode at 2208 cm^{-1}. A single imine stretching mode was observed at 1607 cm^{-1} in the IR spectrum.

To generalize and test the [3 + 3] Schiff-base condensation route to giant macrocyclic proligands, we reacted the longer bis(salicylaldehydes) **3** and **4** with diamines **5b** and **5a** (chosen for reasons of solubility), yielding macrocycles **7** and **8**, respectively. Remarkably, these macrocycles were obtained in 62 and 40% yield, respectively.

This one-pot, template-free, selective synthesis of these expanded macrocycles seems surprising, given the inherent flexibility of the precursor bis(salicylaldehydes) **2**−**4**. Whereas in the preparation of macrocycle **1**, the diformyldihydroxybenzene precursor has a fixed geometry, there is nearly free rotation around the benzene−alkyne bond in **2**−**4**. The reaction was not conducted under dilute conditions, with removal of water, or in the presence of a template. ^{1}H NMR spectroscopy of the supernatant solution from the preparation of **6** showed only **6** and a fragment formed by the condensation of **2** and **5a** in 1:2 ratio,[16] without formation of oligomeric or polymeric materials. The reversibility of the imine condensation reaction allows the reaction to reach the thermodynamically favored [3 + 3] macrocyclic condensation product.

Semiempirical calculations of their flat conformations indicate that macrocycles **6** and **7** have edge lengths (from the center of the salen pockets) of ca. 13.3 and 15.5 Å, respectively. Macrocycle **8**, a covalently bound ring with 66 atoms, has an interior diameter of >15 Å, and the salen pockets are arranged in an equilateral triangle separated by ca. 20.0 Å. The incorporation of phenyleneethynylene spacers into the backbone of the macrocycles has enabled the facile preparation of large, flat macrocycles with tunable diameters.

---

[12] (a) Henz, O.; Lentz, D.; Schäfer, A.; Franke, P.; Schlüter, A. D. *Chem.*—*Eur. J.* **2002**, *8*, 357−365. (b) Li, J.; Ambroise, A.; Yang, S. I.; Diers, J. R.; Seth, J.; Wack, C. R.; Bocian, D. F.; Holten, D.; Linsey, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 8927−8940. (c) Rucareanu, S.; Mongin, O.; Schuwey, A.; Hoyler, N.; Gossauer, A.; Amrein, W.; Hediger, H.-U. *J. Org. Chem.* **2001**, *66*, 4973−4988. (d) Campbell, K.; McDonald, R.; Ferguson, M. J.; Tykwinski, R. R. *Organometallics* **2003**, *22*, 1353−1355. (e) Baxter, P. N. W. *Chem.*—*Eur. J.* **2003**, *9*, 5011−5022. (f) Baxter, P. N. W. *Chem.*—*Eur. J.* **2003**, *9*, 2531−2541.

[13] For recent examples of macrocycles containing Schiff-bases, see: (a) Gawroński, J.; Kołbon, H.; Kwit, M.; Katrusiak, A. *J. Org. Chem.* **2000**, *65*, 5768−5773. (b) Kuhnert, N.; Rossignolo, G. M.; Lopez-Periago, A. *Org. Biomol. Chem.* **2003**, *1*, 1157−1170. (c) Shimakoshi, H.; Kai, T.; Aritome, I.; Hisaeda, Y. *Tetrahedron Lett.* **2002**, *43*, 8261−8264. (d) Kwit, M.; Gawroński, J. *Tetrahedron: Asymmetry* **2003**, *14*, 1303−1308. (e) Gao, J.; Martell, A. E. *Org. Biomol. Chem.* **2003**, *1*, 2795−2800. (f) Zhao, D.; Moore, J. S. *J. Org. Chem.* **2002**, *67*, 3548−3554. (g) Depree, C. V.; Beckmann, U.; Heslop, K.; Brooker, S. *Dalton Trans.* **2003**, 3071−3081. (h) Chadim, M.; Buděšinský, M.; Hodačová, J.; Závada, J.; Junk, P. C. *Tetrahedron: Asymmetry* **2001**, *12*, 127−133. (i) Sessler, J. L.; Veauthier, J. M.; Cho, W.-S.; Lynch, V. M. *Inorg. Chem.* **2004**, *43*, 1220−1228. (j) Akine, S.; Taniguchi, T.; Nabeshima, T. *Tetrahedron Lett.* **2001**, *42*, 8861−8864.

[14] Gallant, A. J.; MacLachlan, M. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 5307−5310.

[15] (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467−4470. (b) Hundertmark, T.; Littke, A. F.; Buchwald, S. L.; Fu, G. C. *Org. Lett.* **2000**, *2*, 1729−1731.

[16] ^{1}H NMR (300 MHz, CDCl$_3$): δ 13.24 (s, 2H, OH), 8.53 (s, 2H, CH═N), 7.35 (d, 2H, CH), 7.16 (d, 2H, CH), 7.10 (dd, 2H, CH), 6.77 (s, 2H, CH), 6.34 (s, 2H, CH), 3.94 (m, 8H, OCH$_2$), 3.85 (s, 4H, NH$_2$), 1.8−0.8 (m, 60H, C$_7$H$_{15}$).

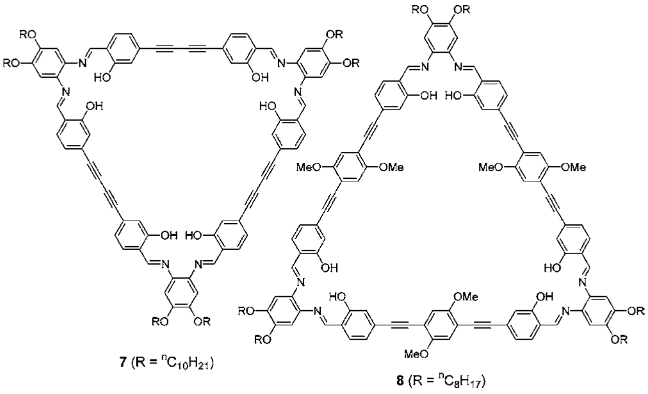


Figure 2. Structures of large macrocycles **7** and **8**.

Metalation of the macrocycles was investigated to demonstrate that these macrocycles can coordinate multiple transition metals in their salen-type pockets. All three metal-free macrocycles **6**−**8** are weakly luminescent in THF ($\Phi = 0.13-0.15\%$). When macrocycle **6** was titrated with Ni^{2+}, the fluorescence intensity decreased, Figure 3a. A large positive deviation from linearity in the Stern−Volmer analysis indicates that the quenching is static, likely due to a metal−ligand charge-transfer band near 550 nm that facilitates energy transfer through a nonradiative pathway.[17] In addition, the quenching is essentially complete when 3 equiv of Ni(II) are added, giving the stoichiometry of the final product. On the other hand, upon titration with Zn^{2+}, macrocycle **6** undergoes a significant increase in fluorescence, Figure 3b. This enhanced fluorescence is attributed to the Zn^{2+} binding to the salen-type ligands, where it deprotonates the phenol and rigidifies the macrocycle. The changes that occurred in the UV−visible spectra arise from the coordination of Zn^{2+} ions to the N_2O_2 binding sites.

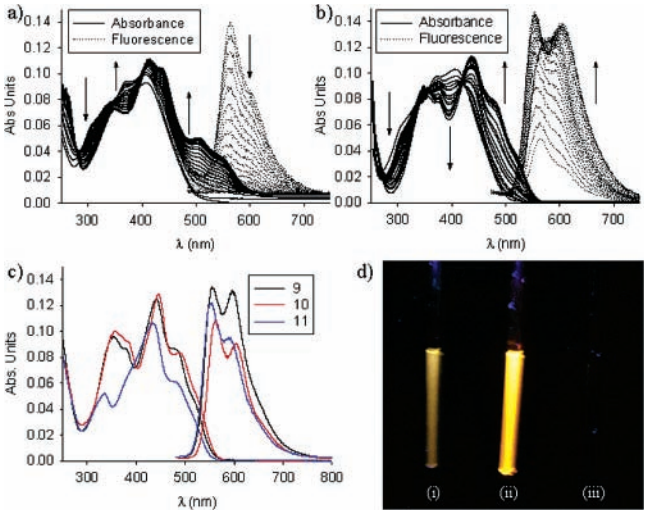
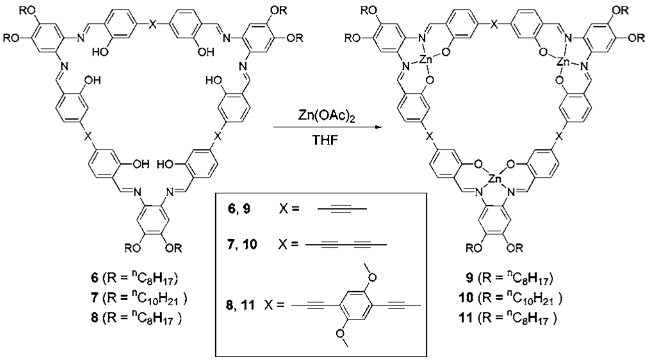


Figure 3. (a) UV−visible and fluorescence spectra of macrocycle **6** upon titration with $Ni(OAc)_2$ (THF). (b) UV−visible and fluorescence spectra of macrocycle **6** upon titration with $Zn(OAc)_2$ (THF). (c) UV−visible and emission spectra for macrocycles **9**−**11**. (d) Photograph of fluorescence from macrocycle **6** (i) with no metal, (ii) with zinc acetate, and (iii) with nickel acetate. Solvent: THF, 5×10^{-5} M; $\lambda_{exc} = 365$ nm.

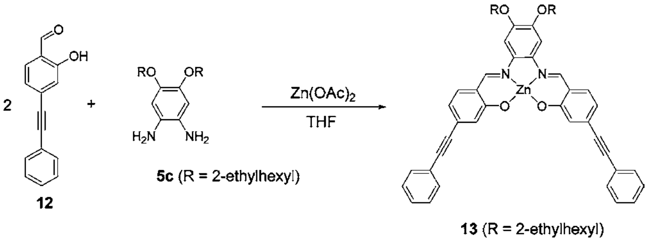
When macrocycle **6** was reacted with 3 equiv of $Zn(OAc)_2{\cdot}2H_2O$ in THF, a new product **9** was obtained, Scheme 2. MALDI-TOF MS of the red product confirmed the incorporation of 3 Zn(II) ions into the complex. In addition, the Raman spectrum of **9** showed a single C≡C stretching mode at 2196 cm^{-1}. The UV−visible spectrum of the complex shows a bathochromic shift relative to macrocycle **6**, consistent with enhanced conjugation in the ligand. Moreover, metallomacrocycle **9** is luminescent in THF ($\Phi = 0.86\%$) with peaks at 558 and 596 nm. Macrocycles **7** and **8** were reacted with excess $Zn(OAc)_2$ to produce the trimetalated macrocycles **10** and **11**, respectively. These macrocycles are also weakly luminescent in solution, Figure 3c. Figure 3d compares the fluorescence of macrocycle **5** upon reaction with 3 equiv of $Zn(OAc)_2$ (i.e., **9**) and $Ni(OAc)_2$.

Scheme 2. Synthesis of Metallomacrocycles **9**−**11**



It is noteworthy that the fluorescence spectra of **9**−**11** are nearly identical. This suggests that the luminescence is localized to the metal complexes and that there is little electronic coupling of the metal complexes through the

Scheme 3. Synthesis of Model Compound **13**



---

[17] Murphy, C. B.; Zhang, Y.; Troxler, T.; Ferry, V.; Martin, J. J.; Jones, W. E., Jr. *J. Phys. Chem. B* **2004**, *108*, 1537−1543.

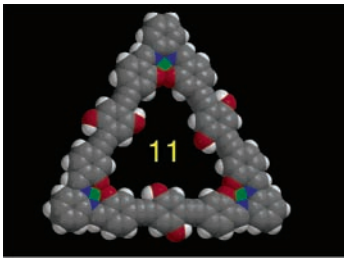


Figure 4. Minimum energy structure of trimetallic macrocycle **11** as determined by semiempirical (PM3) methods using M = Ni(II) and with peripheral alkoxy chains and methyl groups omitted.

organic backbone. Model compound **13** (prepared from 5-(phenylethynyl)salicylaldehyde **12** as shown in Scheme 3) is also fluorescent, with peaks at 537 and 567 nm (Φ = 0.96%). This represents a blueshift of ca. 20 nm from metallomacrocycle **9**, indicating that the bridging groups do have some effect on the fluorescence of the macrocycles. This is also relevant to our studies of conjugated poly(salphenyleneethynylenes) since macrocycle **11** is a cyclic analogue of these polymers.[18]

In summary, we report a simple, general approach to building new, large, shape-persistent conjugated macrocycles with tunable pore diameters in the nanometer regime. These macrocycles can bind multiple metals, forming soluble, luminescent complexes. A space-filling diagram of metallomacrocycle **11** (Figure 4) shows that there is significant space on the inside of these macrocycles. As well, in the case of M = Ni^{2+}, these macrocycles are flat and ready for supramolecular assembly. We are investigating the supramolecular chemistry and coordination chemistry of these and related macrocycles.

Acknowledgment. We thank NSERC, CFI, and UBC for funding and Prof. M. Blades for Raman spectra. C.M. thanks NSERC for a PGSA scholarship.

Supporting Information Available: Experimental procedures and spectroscopic data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0483549

---

[18] Leung, A. C. W.; Chong, J. H.; Patrick, B. O.; MacLachlan, M. J. *Macromolecules* **2003**, *36*, 5051−5054.