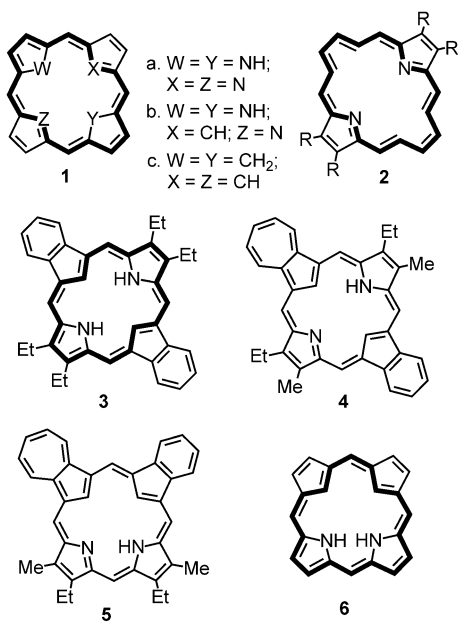
DOI: 10.1002/ange.201206385

Dicarbaporphyrinoids

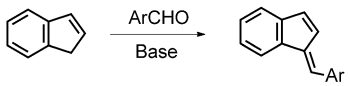
Two-Step Synthesis of Stable Dioxadicarbaporphyrins from Bis(3-indenyl)methane**

Timothy D. Lash, Aaron D. Lammer, and Gregory M. Ferrence*

The origin of the aromatic characteristics of porphyrins (**1a**) and related systems remains the topic of considerable debate.[1–3] Although porphyrins and related macrocycles are often considered to be examples of bridged annulenes,[4–6] some theoretical studies have concluded that the aromatic properties of porphyrinoids are primarily due to the individual pyrrolic rings.[3,7] However, the extent to which the pyrrolic nitrogens contribute to the aromatic properties of porphyrins has been brought into question.[1,2] In particular, dideazaporphyrins **2**, which lack these pyrrole-type nitrogens, have been shown to be strongly diatropic and to possess porphyrin-like electronic absorption spectra.[1,8] In previous studies, we have probed the aromatic properties of porphyrinoids by replacing one or more of the pyrrolic subunits with carbocyclic rings.[5,6] Monocarbaporphyrins related to **1b** have been investigated in detail,[9] but far less is known about dicarbaporphyrinoid systems.[10–16] In principle, these investigations could be extended to quatyrin (**1c**), the theoretically important hydrocarbon analogue of the porphyrins,[5] although severe crowding within the macrocyclic cavity may make this system inaccessible.[17] Syntheses of *opp*-dicarbaporphyrinoids **3**[10] and **4**[11] with two carbocyclic rings interspersed by pyrrolic moieties have been reported, but these porphyrin analogues proved to be rather unstable.[10–12] Nevertheless, dicarbaporphyrin **3** exhibited strongly diatropic characteristics and the UV/Vis spectrum for this species closely resembled the spectra for true porphyrins.[10,13,14] More recently, examples of *adj*-dicarbaporphyrinoid systems have been reported[15,16] including carbaazuliporphyrin **5**.[15] These porphyrinoids proved to be far more stable than **3** and **4** and exhibited significant macrocyclic aromaticity. Unfortunately, to date no examples of *adj*-dicarbaporphyrins **6** with two adjacent cyclopentadiene rings have been synthesized. In our investigations into mono- and dicarbaporphyrins, indene units have usually been used in place of cyclopentadiene moieties because of synthetic considerations.[5,6] For this reason, we set out to target dibenzo-macrocycles related to porphyrinoid **6**.



It is well known that indene reacts with aldehydes under basic conditions to afford fulvenes (Scheme 1).[15] We anticipated that bis(3-indenyl)methane **7**[18] could similarly be used to prepare fulvene derivatives and that this chemistry might be utilized in the synthesis of *adj*-dicarbaporphyrinoids. Owing to the low reactivity of pyrrole aldehydes, this hypothesis was investigated using furan aldehydes. Bis(3-indenyl)methane was reacted with difurylmethane dialdehyde **8** under basic conditions in an attempt to generate the heterodicarbaporphyrinoid **9** (Scheme 2), but no indication of macrocyclic products could be discerned. This result may be due to an unfavorable geometry of the intermediates for macrocyclic ring closure. Therefore, the formation of fulvene products was examined by reacting **7** with 2 equivalents of a series of aromatic aldehydes and KOH in refluxing methanol. When furfural was reacted **7** under these conditions, a fulvene product was generated as a red precipitate.

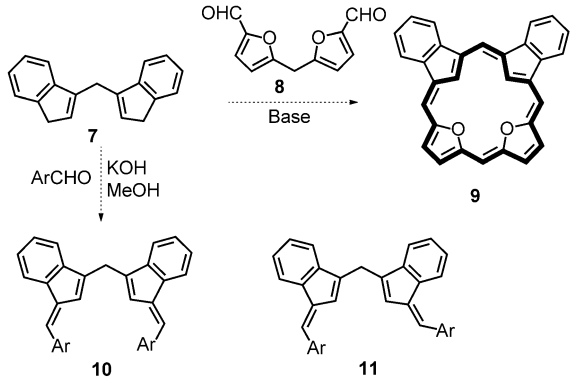


Scheme 1. Synthesis of fulvenes from indene.

[*] Prof. Dr. T. D. Lash, A. D. Lammer, Prof. Dr. G. M. Ferrence
Department of Chemistry, Illinois State University
Normal, IL 61790-4160 (USA)
E-mail: tdlash@ilstu.edu

[**] Part 62 in the series "Conjugated Macrocycles Related to the Porphyrins". This work was supported by the National Science Foundation (NSF) (CHE-0911699 and CHE-1212691) and the Petroleum Research Fund, administered by the American Chemical Society. The authors also thank the Youngstown State University Structure & Chemical Instrumentation Facility's Matthias Zeller for X-ray data collection. The diffractometer was funded by the NSF (0087210), the Ohio Board of Regents (CAP-491), and YSU.

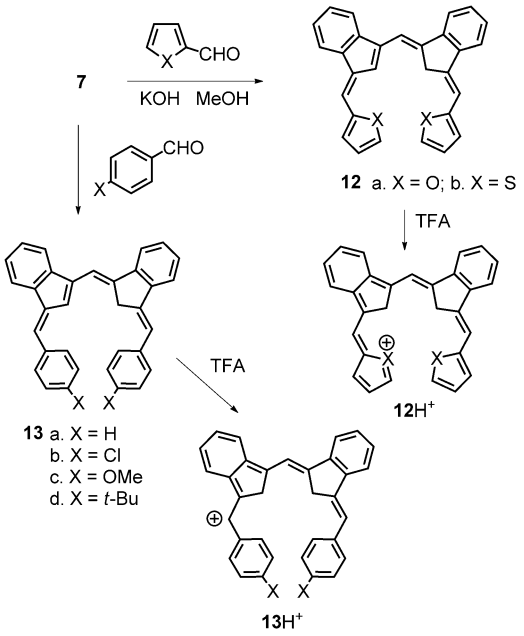
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201206385.



Scheme 2. Proposed syntheses of fulvenes and a porphyrin analogue from bis(3-indenyl)methane.

In small scale reactions using 50 mg of **7**, this product was formed in up to 98% yield, although the yields were lower (73–78%) in larger scale reactions using >1 g of bis-(3-indenyl)methane. Similar results were obtained using thiophene-2-carbaldehyde, benzaldehyde, or 4-substituted benzaldehydes. Initially, it had been anticipated that difulvenes **10** would be formed in these reactions, but the ^{1}H NMR spectra for these products showed that they lacked the expected plane of symmetry. A possible explanation for these results was that the *E*,*Z* isomer **11** had been produced rather than the *E*,*E* isomer **10**. The ^{1}H NMR spectrum for the furfural derivative showed the presence of a broad 2H triplet ($J = 2$ Hz) at 4.11 ppm that was coupled to two 1H resonances at 6.96 and 7.24 ppm. This indicated that a CH=C-CH$_2$-C=CH unit was present within the structure. While this is consistent with structure **11**, detailed analyses using ^{1}H–^{1}H COSY, nOe difference ^{1}H NMR, ^{13}C NMR, and HSQC indicated that the fully conjugated species **12a** was in actual fact the product of this chemistry (Scheme 3). The thiophene product could similarly be attributed to **12b**, whereas the benzaldehyde-derived series were consistent with structures **13a**–**d**. These unusual conjugated species are structurally related to fully conjugated open-chain tetrapyrroles (bilins) and can therefore be considered to be bilin analogues. The structure of the dithiophene bilin analogue **12b** was confirmed by X-ray crystallography, which clearly demonstrated the asymmetry of the two indenyl moieties (Figure 1). There are two crystallographically independent molecules in the asymmetric unit of the structure. The indene containing the apical methylene was identified in both independent molecules. Identification on the basis of difference Fourier location of the hydrogen atoms matched identification of the methylene carbon atoms on the basis of carbon–carbon bond distances.

Bilins **12** and **13** gave orange solutions in dichloromethane, and the UV/Vis spectra showed several broad absorptions between 280 and 450 nm. However, when trifluoroacetic acid (TFA) was added a new species was generated. Addition of TFA to **12a** gave a dark green solution that showed strong absorptions at 450, 623, and 819 nm. The ^{1}H NMR spectrum for **12a** in TFA/CDCl$_3$ showed that the system had gained a plane of symmetry and a 4H singlet was observed at 4.63 ppm. These results indicated



Scheme 3. Synthesis of bilin analogues.

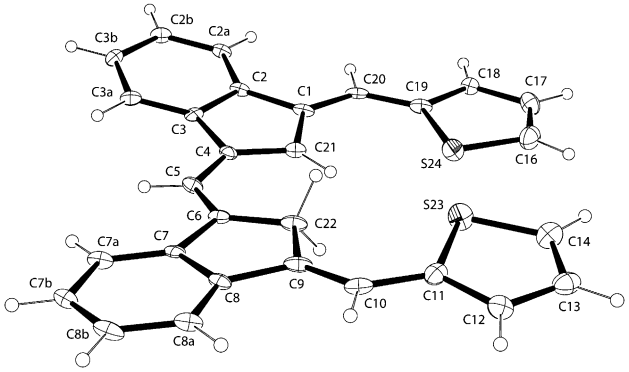
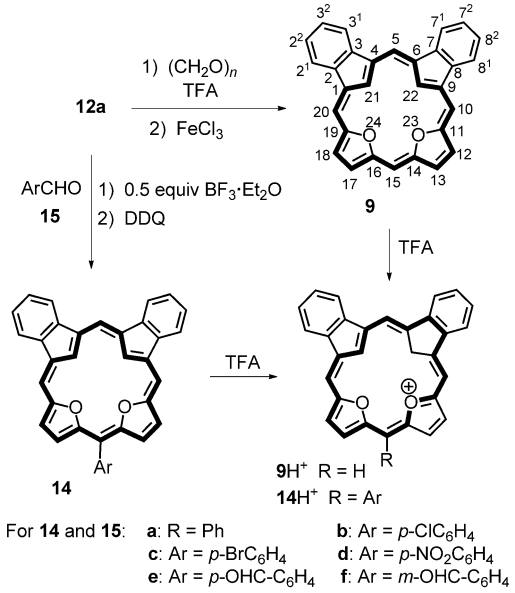


Figure 1. X-ray crystal structure of dithiophene bilin analogue **12b**. Selected bond lengths [Å]: C4–C21 1.388(8), C1–C21 1.457(8), C6–C22 1.466(8), C9–C22 1.487(8). Selected non-bonded separations [Å]: C4···C6 2.487(8), C1···C19 2.501(8), C9···C11 2.492(9), C14···C16 4.57(1), S(23)···S(24) 3.650(3). One of two crystallographically independent molecules is shown for clarity.

that protonation had primarily occurred on an indene unit and that a resonance-delocalized cation, represented by the canonical form **12a**H$^+$, had been generated (Scheme 3). Similar results were obtained for the dithiophene system **12b**. Furthermore, all of the benzaldehyde-derived bilin analogues **13a**–**d** gave rise to the equivalent protonated species **13**H$^+$. These unusual cations are resonance-delocalized carbenium ions that are formed under very mild conditions. The protonated species derived from **13a** and **13b** showed a broad absorption in their UV/Vis spectra at 727 and 729 nm, respectively, but this band was bathochromically shifted to 769 nm for the *tert*-butyl substituted version **13f**. The dimethoxy bilin analogue gave the largest red shift for this series, showing a long wavelength band at 811 nm and its spectra more closely resembled that of **12a** and **12b**. The

cation derived from **12a** was somewhat unstable and, after an hour or so, the ^{1}H NMR spectrum of **12a** in TFA/$CDCl_3$ showed only broad unresolved absorptions. However, protonated bilins **12b**H^+ and **13**H^+ were all reasonably stable and persisted in solution for prolonged periods of time.

The facile protonation and unique properties of bilin analogues **12** and **13** demonstrate that these systems are important in their own right. However, our primary goal was to prepare macrocyclic products from these intermediates. These studies focused on the reactivity of the furfural-derived bilin **12a**, as furans are far more reactive towards electrophilic substitution than thiophenes. When **12a** was reacted with paraformaldehyde in the presence of an acid catalyst, low yields of porphyrinoid product **9** were noted (Scheme 4). The best results were obtained when **12a** was reacted with one



Scheme 4. Synthesis of dioxadicarbaporphyrins.

equivalent of $(CH_2O)_n$ in refluxing 20% TFA/1,2-dichloroethane, followed by oxidation with aqueous ferric chloride. When the oxidation step was not carried out, the conjugated macrocycle could still be isolated, but the product was contaminated with by-products that gave rise to broad absorptions in the ^{1}H NMR spectra. The oxidation appeared to decompose these impurities as well as facilitating the formation of **9**. Even so, the best yields for this reaction were only 5%, and oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) led to complete decomposition. Much better results were obtained when using aromatic aldehydes.

The reaction of **12a** with one equivalent of benzaldehyde in the presence of 0.5 equivalents of $BF_3{\cdot}Et_2O$ in CH_2Cl_2 at room temperature, followed by a brief treatment with DDQ, gave 15-phenyldioxadicarbaporphyrin **14a** in up to 10% yield (Scheme 4). When one equivalent of $BF_3{\cdot}Et_2O$ was used, much lower yields were obtained, but lower concentrations of the catalyst also gave poor results. The quantity of solvent used was also a factor, and for reactions with 100 mg of **12a** the best results were obtained when using 10 mL of CH_2Cl_2. Refluxing the reaction in 1,2-dichloroethane gave poor results, but reactions in refluxing CH_2Cl_2 raised the yield to 39% for the phenyl substituted macrocycle. The substrates 4-chloro- and 4-bromobenzaldehyde (**15b** and **15c**) also gave the best results under these conditions, affording the corresponding aryl substituted porphyrinoids **14b** and **14c** in 26% and 40% yields, respectively. At room temperature, **14b** and **14c** were obtained in only slightly lower yields (23% and 38%, respectively) and these results indicated that electron-withdrawing groups may have a beneficial effect on these reactions. However, 4-nitrobenzaldehyde gave only 12% yield of **14d** under optimized conditions. In this case, the best results were obtained under more dilute conditions (100 mL of CH_2Cl_2 for 100 mg of **12a**) and at room temperature. Reasonable yields of **14e** and **14f** could also be obtained under dilute conditions (15% and 10%, respectively) using dialdehydes **15e** and **15f**. Although linked diporphyrinoids might be formed from dialdehydes **15e** and **15f**, this type of product has not as yet been isolated from these reactions. Nevertheless, the ease of introducing diverse functional groups could potentially allow these dicarbaporphyrinoids to be incorporated into supramolecular systems.

Macrocycles **9** and **14a–f** afforded orange solutions that gave porphyrin-like UV/Vis spectra, each with a Soret band between 436 and 440 nm (Figure 2). For **9**, the Soret band

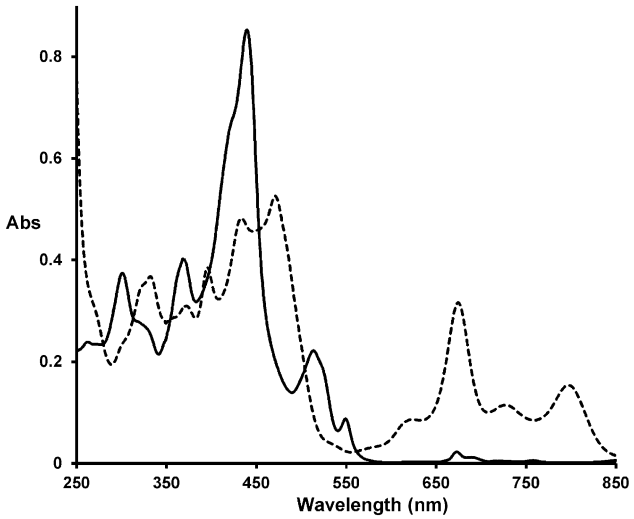


Figure 2. UV/Vis spectra of **14a** in CH_2Cl_2 (——) and 2% TFA-CH_2Cl_2 (cation **14a**H^+; -----).

appeared at 436 nm and Q-type bands appeared at 510 and 547 nm. Moreover, weak absorptions were observed at 668 and 689 nm. Phenyl substituted porphyrinoid **14a** exhibited minor bathochromic shifts, showing these absorptions at 439, 513, 549, 673, and 690 nm (Figure 2). The addition of TFA to solutions of **9** or **14** in CH_2Cl_2 gave the green-colored protonated species **9**H^+ and **14**H^+, respectively, which gave complex UV/Vis spectra showing multiple bands in the Soret region and four absorptions between 600 and 810 nm (Figure 2). The ^{1}H NMR spectra for dioxadicarbaporphyrins

9 and **14** showed that the macrocycles are highly diatropic. Impure samples of **9** in $CDCl_3$ gave resonances for the *meso*-protons downfield at 10.06 (1H), 9.58 (2H), and 9.31 ppm (1H), and the internal CH groups afforded a 2H singlet at −3.60 ppm. However, pure **9** was poorly soluble in organic solvents and the ^{1}H NMR spectrum showed the equivalent resonances at 9.91, 9.40, 9.15, and −4.29 ppm, and these shifts are attributed to aggregation effects. The ^{1}H NMR spectra for aryl substituted porphyrinoids **14** also showed strong diatropic ring currents, and the *meso*-protons for **14a** were observed at 10.05 (1H) and 9.58 ppm (2H), whereas the internal CH groups gave a 2H resonance at −3.61 ppm (Figure 3). The NMR spectra for the cations **9**H$^+$ and **14**H$^+$ in TFA/$CDCl_3$ demonstrated that the protonated species

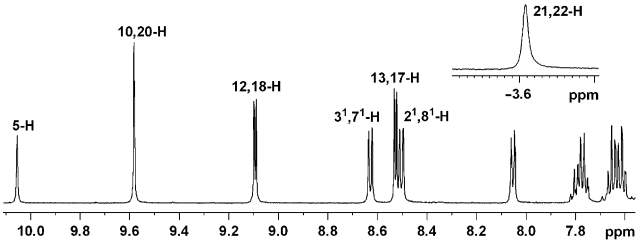


Figure 3. 500 MHz ^{1}H NMR spectrum of phenyl substituted dioxadicarbaporphyrin **14a**. Proton assignment numbering follows the convention used for compound **9** in Scheme 4.

retained a powerful diamagnetic ring current. For **14**H$^+$, the interior CH_2 group gave a singlet at −4.74 ppm, whereas the indene CH group appeared at −2.96 ppm. The *meso*-protons were significantly shifted downfield to give singlets at 10.54 (1H) and 10.62 ppm (2H). ^{13}C NMR spectra for **9** and **14** in $CDCl_3$ confirmed that the macrocycles have a plane of symmetry, but this is lost for the protonated species **9**H$^+$ and **14**H$^+$.

The X-ray crystal structure of **14a** has also been obtained (Figure 4). The solid state structure has the molecule centered on a crystallographic two-fold axis of rotation which contains H5, C5, C15, C15a, C15d, and H15d. The macrocycle is remarkably planar, as evidenced by the 0.0619 Å root-mean-square distance the framework atoms lie from the plane defined by the 24 framework atoms. The largest deviations from the plane are C5 (0.086(7) Å), C15 (−0.094(9) Å), C17 (0.11(1) Å), and C18 (0.090(8) Å), but these deviate by less than 0.06 Å from the aforementioned plane. The structure exhibits framework bond distances consistent with a nearly idealized delocalized π-bonding model with the π-systems for the indenyl benzo-units decoupled from the [18]annulene core, as evidenced by the more single-bond-like C1–C2 (1.476(2) Å), and C3–C4 (1.478(2) Å) bond distances. As would be expected, the phenyl group is canted 77.10(4)° relative to the mean macrocyclic plane.

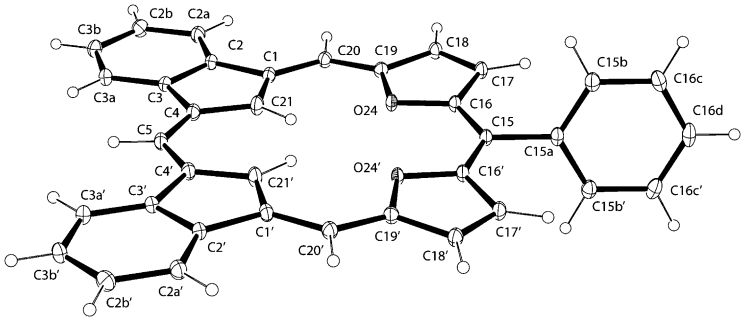


Figure 4. X-ray crystal structure of dicarbaporphyrinoid **14a**. Selected bond lengths [Å]: C1–C2 1.476(2), C3–C4 1.478(2), C4–C5 1.398(2), C4–C21 1.404(2), C21–C1 1.392(2), C15–C16 1.398(2), C16–C17 1.406(2), C17–C18 1.373(2), C18–C19 1.398(2), C19–C20 1.388(2), C20–C1 1.396(2), C16–O24 1.383(2), O24–C19 1.390(2). The molecule is centered on a crystallographic two-fold axis of rotation which contains H5, C5, C15, C15a, C15d, and H15d.

In conclusion, a unique series of bilin analogues has been prepared in excellent yields by reacting aromatic aldehydes with bis(3-indenyl)methane in the presence of potassium hydroxide in refluxing methanol. The furfural-derived bilin analogue condensed with aromatic aldehydes in the presence of $BF_3{\cdot}Et_2O$ to give aryl substituted dioxadicarbaporphyrins in good yields (10–40%). An unsubstituted dibenzodioxadicarbaporphyrin was also obtained by reacting the bilin analogue with paraformaldehyde. The new series of porphyrin analogues are stable compounds and are the first examples of porphyrinoids that incorporate two adjacent indene units. The ease of formation of these conjugated macrocycles will no doubt facilitate detailed investigations into this new class of aromatic bridged annulenes.

Received: August 8, 2012
Published online: September 23, 2012

Keywords: aromaticity · bridged annulenes · carbaporphyrins · fulvenes · indenes

[1] T. D. Lash, S. A. Jones, G. M. Ferrence, *J. Am. Chem. Soc.* **2010**, *132*, 12786 – 12787.
[2] T. D. Lash, *J. Porphyrins Phthalocyanines* **2011**, *15*, 1093 – 1115.
[3] Y. Nakagami, R. Sekine, J.-i. Aihara, *Org. Biomol. Chem.* **2012**, *10*, 5219 – 5229.
[4] E. Vogel, *J. Heterocycl. Chem.* **1996**, *33*, 1461 – 1487.
[5] T. D. Lash, *Synlett* **2000**, 279 – 295.
[6] T. D. Lash, *Eur. J. Org. Chem.* **2007**, 5461 – 5481.
[7] J.-i. Aihara, M. Makino, *Org. Biomol. Chem.* **2010**, *8*, 261 – 266.
[8] See also: E. Pacholska-Dudziak, L. Szterenberg, L. Latos-Grazynski, *Chem. Eur. J.* **2011**, *17*, 3500 – 3511.
[9] a) T. D. Lash, M. J. Hayes, *Angew. Chem.* **1997**, *109*, 868 – 870; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 840 – 842; b) T. D. Lash, M. J. Hayes, J. D. Spence, M. A. Muckey, G. M. Ferrence, L. F. Szczepura, *J. Org. Chem.* **2002**, *67*, 4860 – 4874; c) D. Liu, T. D. Lash, *J. Org. Chem.* **2003**, *68*, 1755 – 1761.
[10] T. D. Lash, J. L. Romanic, M. J. Hayes, J. D. Spence, *Chem. Commun.* **1999**, 819 – 820.
[11] S. R. Graham, D. A. Colby, T. D. Lash, *Angew. Chem.* **2002**, *114*, 1429 – 1432; *Angew. Chem. Int. Ed.* **2002**, *41*, 1371 – 1374.
[12] For examples of resorcinol-derived dicarbaporphyrinoids, see: L. Xu, T. D. Lash, *Tetrahedron Lett.* **2006**, *47*, 8863 – 8866.
[13] Related doubly-N-confused porphyrins are also known; see: a) H. Furuta, H. Maeda, A. Osuka, *J.*

Am. Chem. Soc. **2000**, *122*, 803 – 807; b) H. Maeda, A. Osuka, H. Furuta, *J. Am. Chem. Soc.* **2003**, *125*, 15690 – 15691.

[14] Heterodicarbaporphyrinoids with alternating azulene and furan or thiophene rings have also been reported: a) N. Sprutta, M. Swiderska, L. Latos-Grazynski, *J. Am. Chem. Soc.* **2005**, *127*, 13108 – 13109; b) N. Sprutta, M. Siczek, L. Latos-Grazynski, M. Pawlicki, L. Szterenberg, T. Lis, *J. Org. Chem.* **2007**, *72*, 9501 – 9509.

[15] a) T. D. Lash, D. A. Colby, A. S. Idate, R. N. Davis, *J. Am. Chem. Soc.* **2007**, *129*, 13800 – 13801; b) T. D. Lash, A. D. Lammer, A. S. Idate, D. A. Colby, K. White, *J. Org. Chem.* **2012**, *77*, 2368 – 2381.

[16] Z. Zhang, G. M. Ferrence, T. D. Lash, *Org. Lett.* **2009**, *11*, 101 – 104.

[17] Conjugated macrocycles with the same carbon skeleton as quatyrin have been prepared from calix[4]azulenes; see: a) T. D. Lash, J. A. El-Beck, D. A. Colby, *J. Org. Chem.* **2009**, *74*, 8830 – 8833; b) N. Sprutta, S. Mackowiak, M. Kocik, L. Szterenberg, T. Lis, L. Latos-Grazynski, *Angew. Chem.* **2009**, *121*, 3387 – 3391; *Angew. Chem. Int. Ed.* **2009**, *48*, 3337 – 3341.

[18] H. Li, C. L. Stern, T. J. Marks, *Macromolecules* **2005**, *38*, 9015 – 9027.

