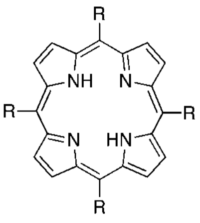
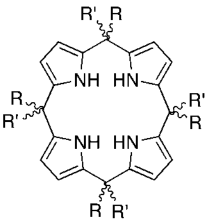
Calixphyrins: Novel Macrocycles at the Intersection between Porphyrins and Calixpyrroles**

Vladimír Král, Jonathan L. Sessler,* Rebecca S. Zimmerman, Daniel Seidel, Vincent Lynch, and Bruno Andrioletti

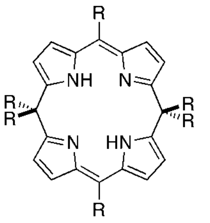
A salient feature of porphyrins (**1**) is full conjugation throughout the macrocyclic skeleton, a property that contributes inter alia to their stability and special aromatic nature.[1] Such conjugation is absent in porphyrinogens (**2**),[2] the tetrapyrrolic precursors from which porphyrins are generally obtained through a net six-electron oxidation process, and in the *meso*-octaalkylated porphyrinogen analogues, the calix[4]pyrroles (**3**).[3, 4] In the case of the latter, the alkyl groups enforce sp^3 hybridization at the linking *meso*-like positions and generally prevent oxidation to the corresponding porphyrins or other intermediate conjugated products. Recently, however, Floriani and co-workers have shown that, through an unusual sequence of organometallic rearrangements, the partial (formal four-electron) oxidation of calix[4]pyrroles could be achieved to produce, among other products, hexaalkylporphodimethenes (**4**).[5] Porphodimethenes[2, 6] are fascinating molecules that lie at the interface between porphyrin and calixpyrrole chemistry. Unfortunately, in spite of Floriani's recent work, these kinds of materials are still not easy to prepare.[2, 6] Herein, we report a simple, rational synthesis of diaryl tetraalkyl porphodimethenes (**5**; Scheme 1), as well as two higher-order homologues, **6** and **7**, that are to the best of our knowledge without precedent in the literature. These molecules, which contain both dialkyl-substituted sp^3-hybridized bridging carbon atoms and *meso*-like dipyrrolylmethene subunits, bear analogy to both the calix[*n*]pyrrole[3, 4, 7] and the porphyrin/expanded porphyrin series of macrocycles.[1, 8] To underscore this analogy, we propose that compounds **5**–**7** be referred to as calix[4]-, calix[6]-, and calix[8]phyrins, respectively, and that the term calix[*n*]phyrin be used in a generic sense to describe this kind of hybrid macrocycle.



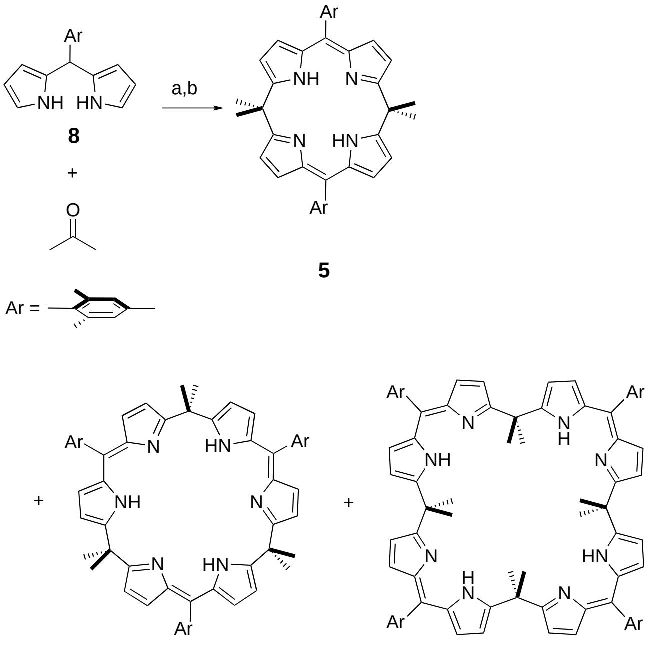
1: R = alkyl, aryl, H



2: R = alkyl, aryl, H; R' = H
3: R = alkyl, aryl; R' = alkyl

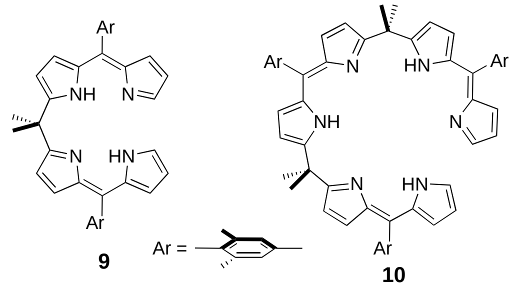


4: R = Et



Scheme 1. Preparation of calix[4]phyrin (**5**) and its higher homologues **6** and **7**. Reagents: a) acid catalyst (TFA, MSA, *p*-TSA, HCl, HBr, or PPA); b) DDQ oxidation.

The synthesis of **5**–**7** is summarized in Scheme 1. Briefly, these compounds are prepared in good yields by the acid-catalysed coupling of mesityldipyrrylmethane (**8**)[9] with acetone at room temperature, followed by 4,5-dichloro-3,6-dioxo-1,2-benzenedinitrile (DDQ) oxidation.[10] In some cases small amounts of the acyclic dimer **9** and trimer **10** were also formed. The reaction proceeds smoothly in a range of solvents and in the presence of various Brønsted acids, including trifluroacetic acid (TFA), methane sulfonic acid (MSA),



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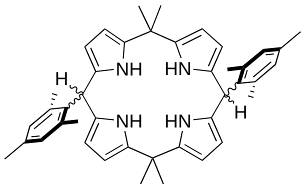
4-methylphenylsulfonic acid (*p*-TSA), HCl, HBr, and polyphosphoric acid (PPA).[11] However, the total and relative yields were strongly dependent on the specific conditions employed. For instance, reaction conditions of acetone as solvent, trifluroacetic acid as catalyst, and 24 h mixing prior to oxidation proved optimal to produce all three calixphyrins; under these conditions calixphyrins **5**–**7** were obtained in 44 %, 23 %, and 9 % yield, respectively, along with the acyclic dimer **9** (2 %) and acyclic trimer **10** (1 %). In contrast, when pure dichloromethane as the solvent and trifluroacetic acid as the catalyst were employed, the calix[4]phyrin **5** was obtained nearly exclusively.

Although unstable, the porphyrinogen-like intermediates that lead to **5**–**7** could be characterized readily using high-resolution mass spectrometry (HR-MS). For the case of **5**, the presumed porphyrinogenlike precursor **11** was isolated under an inert atmosphere and subjected to ^{1}H and ^{13}C NMR analysis. With this critical precursor **11** identified, the course of the subsequent four-electron oxidation step was elucidated. In particular, upon conversion from **11** to **5**, the NH signal shifted significantly (from $\delta = 7.54$ to 13.70) in the ^{1}H NMR spectrum, while the mesityl-bearing *meso*-carbon signal shifted from $\delta = 30$ to 164 in the ^{13}C NMR spectrum. Dramatic color changes were also seen. Whereas calixphyrins **5**–**7** are all orange to red-yellow and have maximal UV/Vis absorbances at 418, 438, and 404 nm, respectively, the mixture of porphyrinogen-like precursors was colorless.



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Compounds **5**–**7** were readily separated from each other and from acyclic and other impurities by column chromatography. They were fully characterized by HR-MS, UV/Vis, and NMR (^{1}H and ^{13}C) spectroscopy, combustion analysis, and, in the case of **5** and **7**, single crystal X-ray diffraction analysis.[12]

The solid state structures of **5** and **7** are shown in Figures 1 and 2, respectively. Inspection reveals that neither system is planar. Indeed, both have marked kinks enforced by their dialkyl-substituted sp^3-hybridized bridging elements. However, both systems also display regions of local planarity corresponding to the dipyrrolymethene links. Thus, as their names imply, they are hybrid molecules that resemble both the aromatic porphyrins and their nonplanar, formally six-electron reduced calixpyrrole analogues. Interestingly, the metal-free form of **5** is far more bent and less planar than the bis-lithium complex of its analogue **4** prepared by Floriani.[5] In this latter case, metal coordination presumably enforces a high degree of local and long-range planarity with the result that surprisingly small pyrrole-methylene-pyrrole dihedral angles of 12.5° are observed.

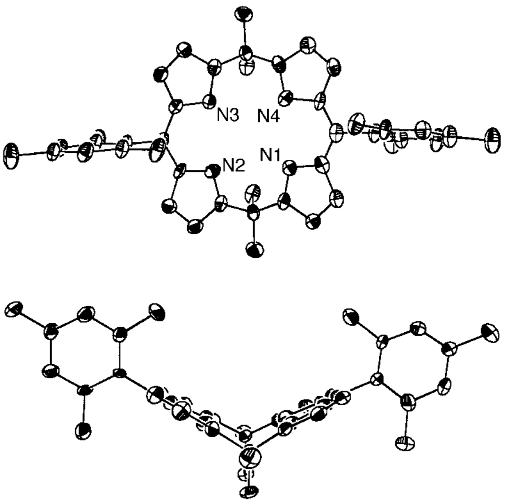

Figure 1. Top and side views of the solid-state structure of **5**. The molecule adopts a winglike conformation, in which the pyrrole-methylene-pyrrole dihedral angles are 55.4°. Thermal ellipsoids are at the 30 % probability level.

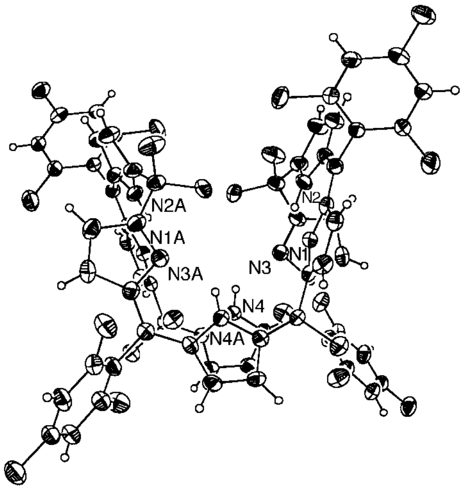

Figure 2. View of the solid-state structure of **7**. The molecule adopts a partially closed bowllike conformation, wherein each of the pyrrole groups are oriented in different directions to its neighbors. Thermal ellipsoids are at the 30 % probability level.

While only a single conformer is observed in the X-ray structures of **5** and **7**, molecular modeling suggested that **5** is likely to be relatively rigid, whereas the higher homologues **6** and **7** might be fluctional in solution. The NMR spectra of **5**–**7** recorded in [D$_1$]chloroform (see Supporting Information) supported this conclusion. Whereas sharp peaks are observed in the ^{1}H NMR spectrum of **5**, broad peaks were seen for the *meso*-CH$_3$ signals of **6** as well as those ascribed to the 2- and 6-CH$_3$-aryl protons of this prototypic calix[6]phyrin, with similar trends also observed in the ^{13}C NMR spectra. As expected for a fully fluctional molecule, no significant broadening of any signals was seen in either the ^{1}H or ^{13}C NMR spectra of calix[8]phyrin **7** at room temperature. However, at low temperature fully resolved sharp signals were observed for both this calixphyrin and its smaller congener **6**.

These hybrid calixpyrrole-porphyrin macrocycles are prototypical of what might be a large class of partially oxidized, mixed condensation products.[13, 14] On account of the rich pyrrolic functionality, they show promise as receptors of exceptional utility. While further study is needed to detail the substrate-binding properties of **5**–**7**, preliminary work confirmed, as expected in light of Floriani's prior studies,[5] that **5** forms complexes with Cu^{II} and Zn^{II}, while its higher homologue **6** coordinates trivalent Co^{III} and Ru^{III} ions. All three calixphyrins bind anions, as judged from changes in the UV/Vis spectra when dichloromethane solutions of **5**–**7** are treated with tetrabutylammonium salts of various anions. Further, peaks corresponding to the proposed calixphyrin–anion complexes are observed by mass spectrometric analysis.

In conclusion, the first rational syntheses of hybrid calixpyrrole–porphyrin macrocycles, porphodimethene (calix[4]phyrin) and its homologues, calix[6]phyrin and calix[8]phyrin, are reported. Taken together with binding studies, these findings suggest that the calixphyrins could provide a useful complement to the calixpyrrole,[3, 4, 7] porphyrin,[1] and expanded porphyrin[8] systems that are known for their rich cation-coordination and anion-binding chemistries.

Experimental Section

A solution of dipyrromethane **8** (0.1 mmol)[9] in dry solvent (acetone, dichloromethane, ethanol, or acetonitrile; 20 mL) and acetone (10–100 molar excess), was degassed by bubbling with argon for 10 min. Catalytic acid (usually TFA (0.03 mL) but also MSA, *p*-TSA, HCl, HBr, PPA) was added. The reaction mixture was stirred under argon for 16–48 h and followed by removing samples for HPLC analysis. Because of the presumed instability of the porphyrinogen-like intermediates, they were not generally isolated. However, for spectroscopic identification, the reaction mixtures were dried in vacuo, redissolved in deoxygenated dichloromethane/hexane (1/4) and filtered through degassed silica gel, all under argon, before being evaporated to dryness again. Compound **11** (the precursor to **5**) was obtained in relatively pure form in this way. For the oxidation procedure, DDQ was added to the initial reaction flask when dichloromethane was used as the solvent. For other solvents, the reaction mixture was evaporated to dryness and redissolved in dichloromethane before addition of DDQ. The product was purified by column chromatography (packing: silica gel; eluent: hexane, with dichloromethane (0–50%) gradient). Single crystals of **5** and **7** were grown from dichloromethane/methanol. Metal complexes were prepared from acetate or acetylacetonate salts of the metal cation in question using either chloroform or a cholorform/methanol mixture as the solvent.[15]

5: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 1.87$ (s, 12 H, *meso*-CH_3), 2.09 (s, 12 H, 2,6-$(CH_3)_2C_6H_2$), 2.32 (s, 6 H, 4-$(CH_3)C_6H_2$), 6.11 (d, ^3J(H,H) = 4 Hz, 4 H, β-pyrrole CH), 6.17 (d, ^3J(H,H) = 4 Hz, 4 H, β-pyrrole CH), 6.86 (s, 4 H, C_6H_2), 13.70 (br s, 2 H, NH); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta =$ 20.11, 21.07, 29.44, 38.15, 76.74, 77.25, 114.06, 126.49, 127.56, 133.53, 136.99, 137.03, 139.04, 140.21, 164.62; UV/Vis (CH_2Cl_2): λ_{max} (ε) = 302 (15726), 418 (72037); HR-MS(CI) for $C_{42}H_{45}N_4$ ($[M+H]^+$): calcd: 605.3644; found: 605.3648; elemental analysis for $C_{42}H_{44}N_4$ (604.36): calcd: C 83.40, H 7.33, N 9.26; found: C 83.31, H 7.35, N 9.23.

Copper(II) complex of **5**: UV/Vis (CH_2Cl_2): λ_{max} 478 nm; HR-MS(CI) for $C_{42}H_{43}N_4Cu$ ($[M+H]^+$): calcd: 666.278372; found: 666.278880; elemental analysis for $C_{42}H_{42}N_4Cu$ (665.28): calcd: C 75.70, H 6.53, N 8.41; found: C 75.41, H 6.27, N 8.22.

Zinc(II) complex of **5**: UV/Vis (CH_2Cl_2): λ_{max} 452 nm; HR-MS(CI) for $C_{42}H_{43}N_4Zn$ ($[M+H]^+$): calcd: 667.277918; found: 667.278392; elemental analysis for $C_{42}H_{42}N_4Zn$ (666.28): calcd: C 75.49, H 6.34, N 8.38; found: C 75.12, H 6.22, N 8.18.

6: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 1.75$ (m, 18 H, *meso*-CH_3), 2.10 (s, 18 H, 2,6-$(CH_3)_2C_6H_2$), 2.30 (s, 9 H, 4-$(CH_3)C_6H_2$), 6.26 (d, 12 H, β-pyrrole CH), 6.85 (s, 6 H, C_6H_2), 13.22 (br s, 3 H, NH); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta =$ 14.11, 20.32, 20.70, 21.09, 22.65, 25.28, 27.81, 29.70, 31.58, 34.52, 34.67, 39.22, 76.75, 77.26, 115.33, 127.12, 127.61, 133.33, 137.05, 138.36, 161.88; UV/Vis (CH_2Cl_2): λ_{max} (ε) = 274 (7470), 438 (11229), 490 (1243); HR-MS(CI) for $C_{63}H_{67}N_6$ ($[M+H]^+$): calcd: 907.542722; found: 907.543616; elemental analysis for $C_{63}H_{66}N_6$ (906.54): calcd: C 83.40, H 7.33, N 9.26; found: C 83.25, H 7.28, N 9.31.

Cobalt(III) complex of **6**: HR-MS(CI) for $C_{63}H_{64}N_6Co$ ($[M+H]^+$): calcd: 963.452444; found: 963.453567; elemental analysis for $C_{63}H_{63}N_6Co$ (962.45): calcd: C 78.56, H 6.59, N 8.73; found: C 78.37, H 6.39, N 8.59.

Ruthenium(III) complex of **6**: HR-MS(CI) for $C_{63}H_{64}N_6Ru$ ($[M+H]^+$): calcd: 1006.423594; found: 1006.420271; elemental analysis for $C_{63}H_{63}N_6Ru$ (1005.42): calcd: C 75.27, H 6.32, N 8.36; found: C 75.06, H 6.21, N 8.18.

7: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 1.52$ (m, 24 H, *meso*-CH_3), 2.12 (m, 24 H, 2,6-$(CH_3)_2C_6H_2$), 2.31 (m, 12 H, 4-$(CH_3)C_6H_2$), 6.12 (d, ^3J(H,H) = 4 Hz, 4 H, β-pyrrole CH), 6.16 (d, ^3J(H,H) = 4, 4 H, β-pyrrole CH), 6.21 (m, 4 H, β-pyrrole CH), 6.22 (m, 4 H, β-pyrrole CH), 6.86 (m, 8 H, C_6H_2), 13.22 (br s, 4 H, NH); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta =$ 1.01, 20.13, 20.47, 21.09, 27.58, 29.44, 29.70, 38.85, 76.74, 77.25, 77.56, 127.61, 133.50, 137.07, 138.05; UV/Vis (CH_2Cl_2): λ_{max} (ε) = 404 (3345), 428 (3080), 448 (2900); HR-MS(CI) for $C_{84}H_{89}N_8$ ($[M+H]^+$): calcd: 1209.721021; found: 1209.720281; elemental analysis for $C_{84}H_{88}N_8$ (1208.72): calcd: C 83.40, H 7.33, N 9.26; found: C 83.14, H 7.18, N 9.14.

9: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 1.81$ (m, 6 H, *meso*-CH_3), 2.09 (m, 12 H, 2,6-$(CH_3)_2C_6H_2$), 2.33 (m, 6 H, 4-$(CH_3)C_6H_2$), 6.09 (m, 2 H, β-pyrrole CH), 6.15 (m, 2 H, β-pyrrole CH), 6.42 (d, ^3J(H,H) = 4.5 Hz, 2 H, β-pyrrole CH), 6.51 (d, ^3J(H,H) = 4.5 Hz, 2 H, β-pyrrole CH), 6.89 (m, 4 H, C_6H_2), 7.12 (m, 2 H, α-pyrrole CH), 12.5 (br s, 2 H, NH); HR-MS(CI) for $C_{39}H_{40}N_4$ ($[M+H]^+$): calcd: 565.3331; found: 565.3337.

10: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 1.71$ (12 H, *meso*-CH_3), 2.12 (m, 18 H, 2,6-$(CH_3)_2C_6H_2$), 2.18 (s, 9 H, 4-$(CH_3)C_6H_2$), 6.04 (m, 3 H, β-pyrrole CH), 6.18 (m, 3 H, β-pyrrole CH), 6.33 (m, 3 H, β-pyrrole CH), 6.46 (m, 3 H, β-pyrrole CH), 6.86 (m, 6 H, C_6H_2), 7.12 (m, 2 H, α-pyrrole CH), 12.30 (br s, 3 H, NH). HR-MS(CI) for $C_{60}H_{62}N_6$ ($[M+H]^+$): calcd: 867.5114; found: 867.5125.

11: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 1.58–1.62$ (m, 12 H, *meso*-CH_3), 1.96–2.01 (m, 12 H, 2,6-$(CH_3)_2C_6H_2$ broadened due to rotation), 2.25 (s, 6 H, 4-$(CH_3)C_6H_2$), 5.67 (s, 2 H, *meso*-CH), 5.97 (m, 8 H, β-pyrrole CH), 6.78 (s, 4 H, C_6H_2), 7.54 (br s, 4 H, NH); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta =$ 20.51, 20.75, 38.30, 76.75, 77.26, 106.48, 108.63, 116.11, 130.31, 131.22, 134.52, 136.55, 137.57; HR-MS(CI) for $C_{42}H_{48}N_4$: calcd: 608.3879; found: 608.3879.

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[10] An alternative approach to preparing porphodimethenes and related systems, involving the mixed condensation of an aldehyde, ketone, and pyrrole, was also tested. As expected, such a reaction generates a statistical mixture of possible products.

[11] Lewis acids were found to be far less efficacious as catalysts to produce only trace quantities of products.

[12] Crystal structure analyses were measured on a Nonius Kappa CCD using graphite-monochromatized $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å) at $-120\,^{\circ}$C. **5**: $C_{42}H_{44}N_4$. Orange plates and lathes grown from CH_2Cl_2, monoclinic, space group *C2/c*, $Z = 12$, $a = 26.618(3)$, $b = 13.546(2)$, $c = 29.934(3)$ Å, $\beta = 104.765(6)^{\circ}$, $V = 10437(2)$ Å^3, $\rho_{calc} = 1.16\ g\,cm^{-3}$, $F(000) = 3888$. A total of 15391 reflections were measured, 9097 unique ($R_{int} = 0.11$). The structure was refined on F^2 to $R_w = 0.218$, $R = 0.145$ (3471 reflections with $F_o > 4\sigma(F_o)$), and GoF = 2.02 for 623 refined parameters. There are two crystallographically independent molecules per asymmetric unit. One molecule lies around a crystallographic two-fold rotation axis. **7**: $C_{84}H_{88}N_8 \cdot CH_2Cl_2$. Orange lathes and needles grown from CH_2Cl_2, orthorhombic, space group *Pccn*, $Z = 4$, $a = 26.183(2)$, $b = 11.1017(8)$, $c = 25.1343(13)$ Å, $V = 7305.9(9)$ Å^3, $\rho_{calc} = 1.18\ g\,cm^{-3}$, $F(000) = 2760$. A total of 10948 reflections were measured, 5795 unique ($R_{int} = 0.10$). The structure was refined on F^2 to $R_w = 0.182$, $R = 0.098$ (2372 reflections with $F_o > 4\sigma(F_o)$), and GoF = 1.34 for 416 refined parameters. The tetrameric calixpyrrole lies around a crystallographic two-fold rotation axis. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-134665 and 134666. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[13] A reaction analogous to that of Scheme 1 but employing a bipyrrole, rather than dipyrromethane derivative, produced, inter alia, a cyclotrimer and a cyclotetramer under a variety of reaction conditions. These compounds will be discussed in a subsequent report.

[14] For an alternative approach to the synthesis of large bipyrrole-derived calixphyrin analogues, see: M. Michels, L. Zander, J. Wytko, *Abstr. 24th Int. Symp. Macrocyc. Chem.* (Barcelona), **1999**.

[15] J.-H. Furhop, K. M. Smith, *Laboratory Methods*, chap. 19, pp. 757–869 in Ref. [1a)].

Synthesis of Geometrically Well Defined, Molecularly Thin Polymer Films[**]

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Here we demonstrate a general method for the fabrication of molecularly thin polymer films with well-defined (in-plane) dimensions. The strategy for the synthesis of these materials starts with a sequence of reactions on a patterned self-assembled monolayer (SAM). This pattern, defined by microcontact printing, determines the size and shape of the polymer films on the micrometer scale. The out-of-plane thickness and composition is defined on a nanometer scale by the sequence of chemical reactions.

These molecularly thin polymer films with in-plane cross-linking are a subset of the class of "two-dimensional polymers".[1] Synthetic routes to two-dimensional polymers include polymerization of reactive monomers in SAMs[2] and lipid bilayers,[3] at oil–water[4] and air–water interfaces,[5] and polymerization of monomers that form self-assembled layered structures.[6] Although certain of these approaches have generated two-dimensional polymeric structures, they have not controlled their lateral (in-plane) dimensions. Our strategy for the fabrication of two-dimensional polymers relies on the work of Grainger et al.,[7] Crooks et al.,[8] and others,[9] who examined covalently bound polymer mono- and multilayers on surfaces. Rubner et al.[10] and Decher[11] also examined structures made up of electrostatically associated layers of polymers. Möhwald et al. described covalently linked hollow shell multilayers[12] and Hammond et al. studied electrostatically deposited multilayers on patterned SAMs.[13] We do not know of any attempts to release these polymeric multilayers into suspension following assembly on a surface.

We began the fabrication of the two-dimensional polymers by using microcontact printing (µCP)[14] to pattern a SAM; this patterned SAM served as a template for the growth of the polymer films (Scheme 1). The synthesis involves four steps: 1) patterning a gold surface by µCP with COOH- and CH_3-terminated SAMs;[15] 2) deposition of an amine-containing polymer (polyethyleneimine, PEI) by ionic adsorption onto the CO_2^--terminated areas;[16] 3) cross-linking the adsorbed PEI covalently by allowing it to react with a polymeric anhydride (poly(octadecene-*alt*-maleic anhydride), POMA, or poly(ethylene-*alt*-maleic anhydride), PEMA);[17] and 4) releasing the film from the surface by dissolving the gold substrate completely in 5 mM sodium dodecylsulfate (SDS)/30% aqua regia/0.5% HF in water.[18] We examined polymeric films patterned into hexagons with 10-µm sides and 10-

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