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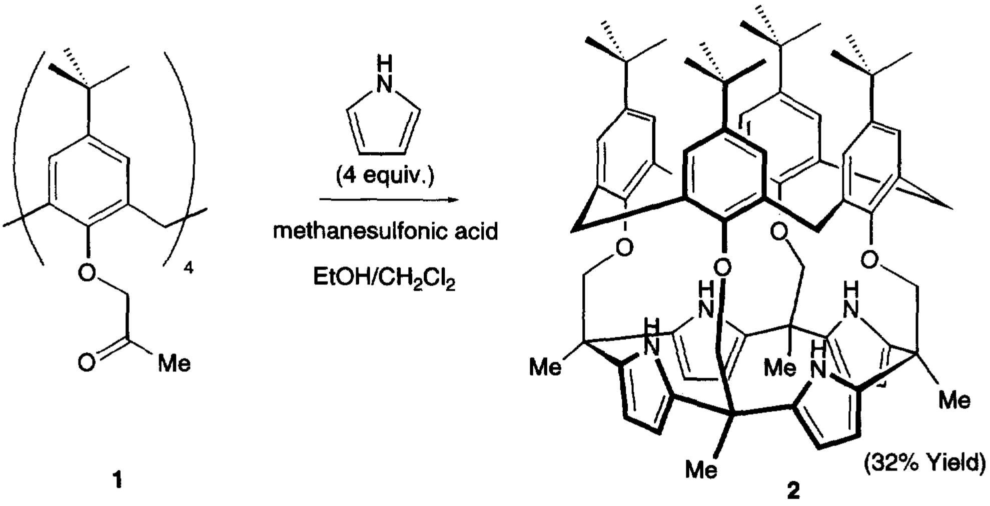
Synthesis of a New Cylindrical Calix[4]arene-Calix[4]pyrrole Pseudo Dimer

Philip A. Gale, Jonathan L. Sessler,* Vincent Lynch and Petra I. Sansom

Department of Chemistry and Biochemistry, University of Texas at Austin, Austin, Texas 78712-1167, USA.

Abstract: The synthesis of a new calixarene-capped calixpyrrole **2** has been achieved using *p-tert*-butylcalix[4]arene tetramethyl ketone **1** as a template. Using this approach, the stereochemistry at the calixpyrrole *meso*-carbons is automatically defined. The X-ray crystal structure of **2** has been elucidated and reveals hydrogen bonding between the pyrrole NH groups and the oxygens at the lower rim of the calixarene. NMR studies confirm the importance of these interactions in solution.

The construction of new polypyrrolic macrocycles capable of anion chelation constitutes a synthetic challenge that has inspired us increasingly over the last few years.[1] Our recent discovery that calix[4]pyrroles (*meso*-octaalkylporphyrinogens)[2] are both selective and easy-to-make anion binding agents[3] led us to consider strategies for synthesizing expanded calix[*n*]pyrroles (*n*>4). Calix[*n*]arenes are macrocyclic molecules composed of phenol rings linked by methylene groups.[4] It occurred to us that the calix[*n*]arene skeleton could be used as a template, around which a calix[*n*]pyrrole could form.[5] As a first step towards testing this strategy, we have synthesized a calix[4]arene-calix[4]pyrrole pseudo dimer (compound **2**) and elucidated its solid state structure *via* X-ray diffraction analysis. Although calixarene-linked[6(a)-(b)] and calixarene-capped porphyrins [5, 6(c)-(d)] as well as calixarenes linked to pyrrole groups[7] are known, to the best of our knowledge, compound **2** represents the first example of a calixarene capped-calixpyrrole.



Scheme 1. Synthesis of compound **2**

SYNTHESIS

p-tert-Butylcalix[4]arene tetramethyl ketone **1** was synthesized according to literature procedures.[8] Reaction of compound **1** (0.5 g, 0.57 mmol) with pyrrole (0.153 g, 2.29 mmol) in a dichloromethane/ethanol mixture, in the presence of methanesulfonic acid, followed by column chromatography on silica gel (CH_2Cl_2, eluant) afforded the calixpyrrole-calixarene dimer **2** in 32% yield (Scheme 1). Compound **2** gave spectroscopic and analytical data in accord with the assigned structure.[9] As a consequence of this template synthesis, the stereochemistry at the calixpyrrole *meso*-carbons is automatically defined.

CRYSTALLOGRAPHY

Crystals were obtained by slow evaporation of a dichloromethane solution of compound **2**. The crystals were then subject to X-ray diffraction structural analysis.[10] The resulting structure shows the calixarene adopting a cone conformation. The pyrrole NH groups are within hydrogen bonding distance of the lower rim calixarene oxygen atoms.

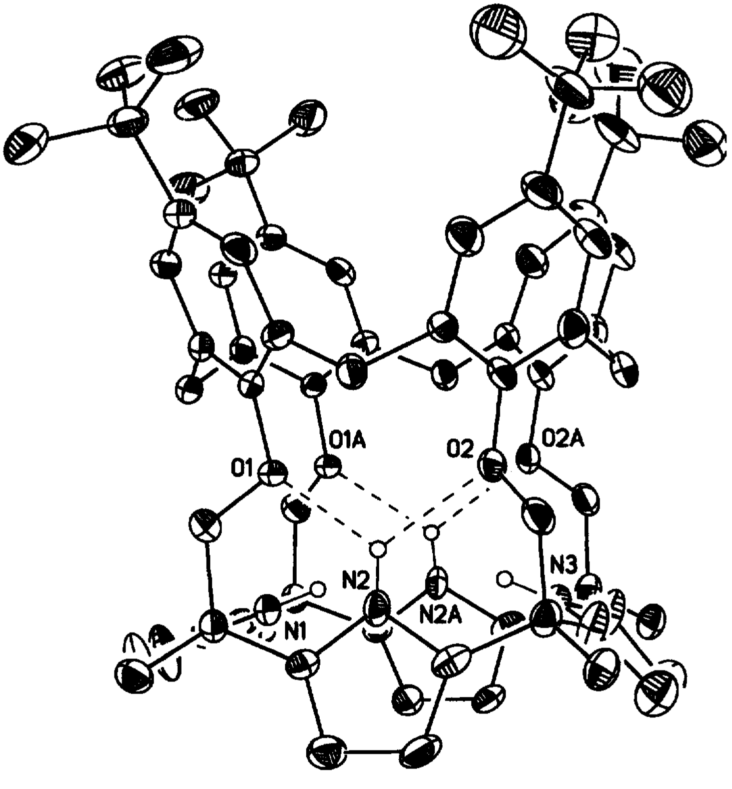


Fig. 1. The X-ray crystal structure of compound **2** showing the intramolecular H-bonding. Dashed lines are indicative of the H-bonding interaction with relevant geometry: N2···O1 2.701(6) Å, N2···O2 2.739(6) Å. A crystallographic mirror plane of symmetry bisects the pyrrole rings containing N1 and N3. Thermal ellipsoids are scaled to the 30% probability level.

NMR STUDIES

The ^{1}H NMR spectrum of **2** in dichloromethane-d_2 (Figure 2) shows that the pyrrole NH protons, which are normally observed at around 7 ppm in other calix[4]pyrroles,[3] resonate at 11.22 ppm. This can be attributed to hydrogen bonding between the pyrrole NH groups and the calixarene oxygen atoms. CD_3OD was added to the NMR solution in an attempt to disrupt this hydrogen bonding interaction, however this had a negligible effect on the ^{1}H NMR spectrum. Similarly, addition of 10.0 equiv. tetrabutylammonium fluoride (which has been shown to bind strongly to other calix[4]pyrroles)[3(a)] caused no changes in the NMR spectrum. Based on these findings, we conclude that the dimer is adopting a cylindrical conformation in solution due to these clearly favorable NH - O hydrogen bonds.

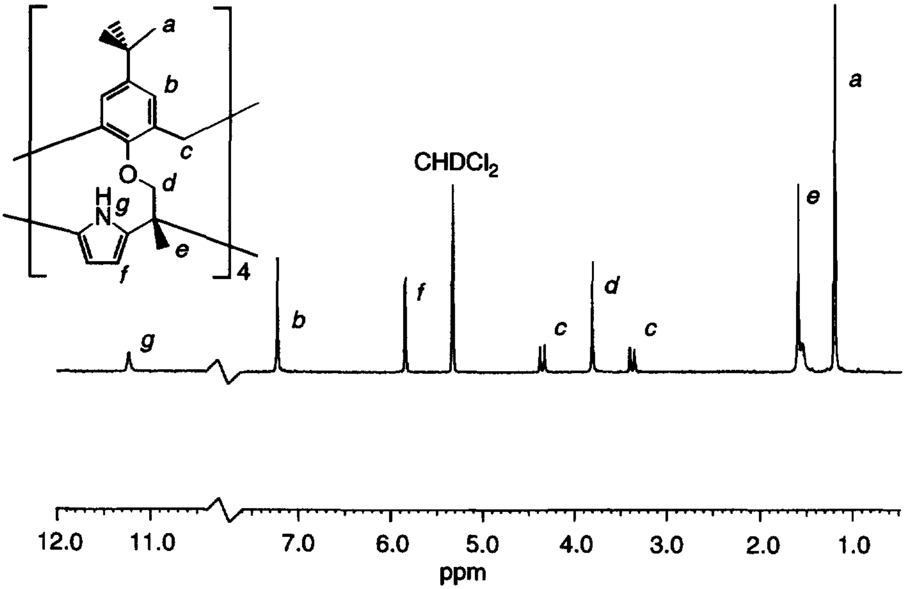


Fig. 2. ^{1}H NMR spectrum of compound **2** in dichloromethane-d_2

CONCLUSIONS

The synthesis of a calix[4]pyrrole-calix[4]arene cylindrical dimer by a template type synthesis has been achieved successfully. We are currently working towards using larger calix[*n*]arenes (n > 4) and other molecules, such as cyclodextrins, as templates to produce both expanded calixpyrroles and expanded porphyrins. We are also investigating other template type syntheses involving cleavable linking groups between the calixarene and ketone moiety and also ketone moieties which are attached to the template *via* non-covalent interactions.[11] Such an approach may eventually lead to new syntheses of expanded porphyrins and calixpyrroles.

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REFERENCES AND NOTES

1. (a) Shionoya, M.; Furuta, H.; Lynch, V.; Harriman, A.; Sessler, J. L. *J. Am. Chem. Soc.* **1992**, *114*, 5714-5722. (b) Sessler, J. L.; Cyr, M.; Furuta, H.; Král, V.; Mody, T.; Morishima, T.; Shionoya, M.; Weghorn, S. J. *Pure and Applied Chem.* **1993**, *65*, 393-398. (c) Král, V.; Sessler, J. L. *Tetrahedron* **1995**, *51*, 539-554. (d) Král, V.; Andrievsky, A.; Sessler, J. L. *J. Am. Chem. Soc.* **1995**, *117*, 2953-2954.
2. (a) Baeyer, A. *Ber. Dtsch. Chem. Ges.* **1886**, *19*, 2184-2185. (b) Dennstedt, M.; Zimmermann, J. *Chem. Ber.* **1887**, *20*, 850-857. (c) Dennstedt, M. *Ber. Dtsch. Chem. Ges.* **1890**, *23*, 1370-1374. (d) Jacoby, D.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *J. Chem. Soc. Chem. Commun.* **1991**, 220-222. (e) Jacoby, D.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *J. Chem. Soc. Chem. Commun.* **1991**, 790-792.
3. (a) Gale, P. A.; Sessler, J. L.; Král, V.; Lynch, V. *J. Am. Chem. Soc.* **1996**, *118*, 5140-5141. (b) Sessler, J. L; Andrievsky, A.; Gale, P. A.; Lynch, V. *Angew. Chem.* **1996**, In press.
4. Böhmer, V. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713-745.
5. For related approaches to the synthesis of calixarene capped porphyrins, see Kobayashi, N.; Mizuno, K.; Osa, T. *Inorg.Chem. Acta* **1994**, *224*, 1-3.
6. (a) Asfari, Z.; Vicens, J.; Weiss, J. *Tetrahedron Lett.* **1993**, *34*, 627-628. (b) Rudkevich, D. M.; Verboom, W.; Reinhoudt, D. N. *Tetrahedron Lett.* **1994**, *35*, 7131-7134. (c) Nagasaki, T.; Fujishima, H.; Shinkai, S. *Chem. Lett.* **1994**, 989-992. (d) Nagasaki, T.; Fujishima, H.; Takeuchi, M.; Shinkai, S. *J. Chem. Soc. Perkin Trans. 1* **1995**, 1883-1888.
7. Chen, Z.; Gale, P. A.; Beer, P. D. *J. Electroanal. Chem.* **1995**, *393*, 113-117.
8. Arnaud-Neu, F.; Collins, E. M.; Deasy, M.; Ferguson, G.; Harris, S. J.; Kaitner, B.; Lough, A. J.; McKervey, M. A.; Marques, E.; Ruhl, B. L.; Schwing-Weill, M. J.; Seward, E. M. *J. Am. Chem. Soc.* **1989**, *111*, 8681-8691.
9. Analytical and spectroscopic data for compound **2**. Analysis for $C_{72}H_{84}N_4O_4$: Calculated C 80.86%; H 7.92%; N 5.24%. Found C 80.57%; H 7.95%; N 5.11%. High resolution positive ion FABMS: Calculated ($C_{72}H_{84}N_4O_4$) 1068.649; Found 1068.648 (Δ 1.4 ppm). ^{1}H NMR (CD_2Cl_2) δ: 11.22 (s, 4H, NH), 7.22 (s, 8H, ArH), 5.83 (d, J = 2.5 Hz, 8H, CH), 4.35 (d, J = 12.5 Hz, 4H, ArCH_2Ar), 3.80 (s, 8H, OCH_2), 3.37 (d, J = 12.5 Hz, ArCH_2Ar), 1.58 (PyCCH_3), 1.18.(s, 36H, ^{t}Bu). ^{13}C NMR ($CDCl_3$) δ: 151.3, 146.8, 137.2, 134.4, 126.1, 101.7, 90.2, 37.9, 34.1, 31.4, 29.6, 21.1.
10. Crystallographic summary for **2**.xCH_2Cl_2. Large regions of disordered solvent of unknown stoichiometry in this structure presented difficulties with this analysis, however the structure of the calixarene-calixpyrrole pseudo dimer is a reliable description of this unique and interesting molecule. Faintly yellow crystals, monoclinic, *C2/m*, *Z* = 4 in a cell of dimensions *a* = 25.836(5)Å, *b* = 20.139(3)Å, *c* = 15.46(2)Å, *β* = 106.0(1)°, *V* = 7719(2)Å^3. ρ_{calc}: x = 4; 1.21 gcm^{-3}; x = 6, 1.36 gcm^{-3}. 9112 unique reflections of which 4121 were observed (I > 2σ(I)). Data collected at -90°C on a Siemens P3 diffractometer. The final R = 0.148.
11. Hoss, R.; Vögtle, F. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 375-384.

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