ChemComm
www.rsc.org/chemcomm

The role of template in the synthesis of *meso*-hexamethyl-*meso*-hexaphenyl-calix[6]pyrrole: trihalogenated compounds as templates for the assembly of a host with a trigonal cavity†

Boaz Turner,[a] Alexander Shterenberg,[a] Moshe Kapon,[a] Kinga Suwinska[b] and Yoav Eichen*[ac]

[a] *Department of Chemistry, Technion-Israel Institute of Technology, Technion City, 32000 Haifa, Israel. E-mail: chryoav@tx.technion.ac.il; Fax: 972-4-8233735; Tel: 972-4-8293708*

[b] *Institute of Physical Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, PL-01 224 Warszawa, Poland. E-mail: kinga@ichf.edu.pl; Fax: 48-22-6325276; Tel: 48-22-6323221*

[c] *Solid-State Institute, Technion-Israel Institute of Technology, Technion City, 32000 Haifa, Israel*

Received (in Cambridge, UK) 11th July 2001, Accepted 13th December 2001

First published as an Advance Article on the web 5th February 2002

Trihalogenated compounds act as effective and selective templates in the template-assisted synthesis of *meso*-hexaphenyl-calix[6]pyrrole.

The host–guest chemistry of calixpyrroles has become the subject of intensive research aimed at gaining understanding and control of recognition of anionic guests.[1,2] Some calix[4]pyrroles exhibit a remarkable selectivity for binding fluoride compared to other halides.[3–5] Recently, expanded cavity calix[n]pyrroles with n = 5,[6,7] 6[8,9] and 8[7] have been prepared. Some of these systems have been shown to host large anions such as iodide, bromide and chloride[10,11] as well as different uncharged *Lewis* bases.[11]

To date, the most simple and efficient route to calix[6]pyrroles is through a two-step acid-catalyzed condensation of dipyrrolemethanes with different aliphatic ketones.[8] Acid catalyzed condensation of pyrrole with some aromatic ketones results in the formation of the respective *di*(aryl)-*di*(2-pyrrole) methanes in moderate to good yields. These *di*(aryl)-*di*(2-pyrrole) methanes react readily with simple aliphatic ketones, such as acetone, in the presence of acid catalysts to form calixpyrroles.

Interestingly, the product distribution of the latter reaction depends on the nature of the acid catalyst. For example, methanesulfonic acid yields exclusively calix[4]pyrrole, while calix[6]pyrrole is the major product when borontrifluoride etherate is used. This remarkable dependence of the nature of the product on the type of acid catalyst used seemed to be in contrast to earlier studies on the role of the acid catalyst in the cyclization of pyrrole with acetone.[12]

We have therefore investigated the role of the acid catalyst in the cyclization reaction between acetone and *di*phenyl-*di*(2-pyrrole) methane. Table 1 depicts the product distribution in the cyclization reaction between *di*phenyl-*di*(2-pyrrole) methane and acetone using different acid catalysts.‡ Table 1 clearly demonstrates that halogenated acids yield calix[6]pyrrole and that the most efficient are the 2,2,2-trihalogenated acids. In contrast, nonhalogenated acids such as acetic acid and methanesulfonic acid yield only calix[4]pyrrole.

The association mode between trihalogenated acetic acids and pyrrolemethane rings is revealed from the crystal structure of the 1 : 1 complex between tetraethyl ammonium trifluoroacetate and calix[4]pyrrole, Fig. 1.§ The complex lies on a crystallographic mirror plane of symmetry. The trifluoroacetate moiety is held by the calix[4]pyrrole cavity through four hydrogen bonds between the four N–H groups of the pyrrole rings and one oxygen atom of the trifluoroacetate ion: $d_{\text{N1-H1}\cdots\text{O1}}$ = 2.15(5) Å; $\alpha_{\text{N1-H1}\cdots\text{O1}}$ = 171(4)°; $d_{\text{N5-H5}\cdots\text{O1}}$ = 2.22(3) Å; $\alpha_{\text{N5-H5}\cdots\text{O1}}$ = 175(3)°; $d_{\text{N11-H11}\cdots\text{O1}}$ = 2.25(4) Å; $\alpha_{\text{N11-H11}\cdots\text{O1}}$ = 156(5)°.

In this arrangement, the three halide-atoms of the trifluoroacetate guest are located above the calix rim. Assuming the same binding mode takes place between the forming oligopyrrolemethane species and trihalogenated acids in the process of formation of hexaphenyl calix[6]pyrrole, simple CPK models show that the three halogen atoms of the acid catalyst may serve as anchoring groups for binding three axial phenyl rings of the forming hexaphenyl calix[6]pyrrole.¶

In such a case, the trihaloacid catalyst plays two different and independent roles, one as the acid catalyst and the other as the template for the cyclization of calix[6]pyrrole. The role of the trihalogenated acid could therefore be performed by a combination of a non halogenated acid catalyst, that by itself yields only calix[4]pyrrole, and a trihalogenated template, such as 2,2,2-trichloroethanol or 2,2,2-trifluoroethanol, that lacks any catalytic properties but can bind both to the forming oligopyrrolemethane

Table 1 Yields of the cyclization reaction between diphenyl-di(2-pyrrole) methane and acetone in dry ethanol[a]‡

Haloacetic derivative	pK_a	Calix[4]pyrrole	Calix[6]pyrrole
Acetic acid	4.76	n.r	n.r
Monofluoroacetic acid	2.72	*	*
Difluoroacetic acid	1.34	**	**
Trifluoroacetic acid	0.47	**	***
Monochloro acetic acid	2.87	*	*
Dichloroacetic acid	1.35	*	**
Trichloroacetic acid	0.26	**	***
Monobromoacetic acid	2.90	*	*
Dibromoacetic acid	1.39	**	**
Tribromoacetic acid	0.66	**	***
BF_3OEt_2		**	***
BI_3		**	***
$MeSO_3H$	~ −2	***	—
TsOH	0.7	***	*
H_2SO_4	~ −3	**	Traces
HCOOH	3.75	n.r	n.r
Phosphoacetic acid		*	**
Phosphopropionic acid		—	*

[a] pK_a values in water. Yields: 1% < * < 10%; 10% < ** < 25%; 25% < *** < 50%.

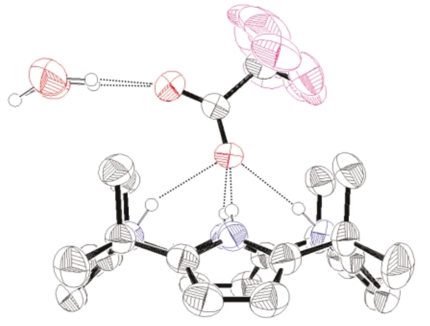
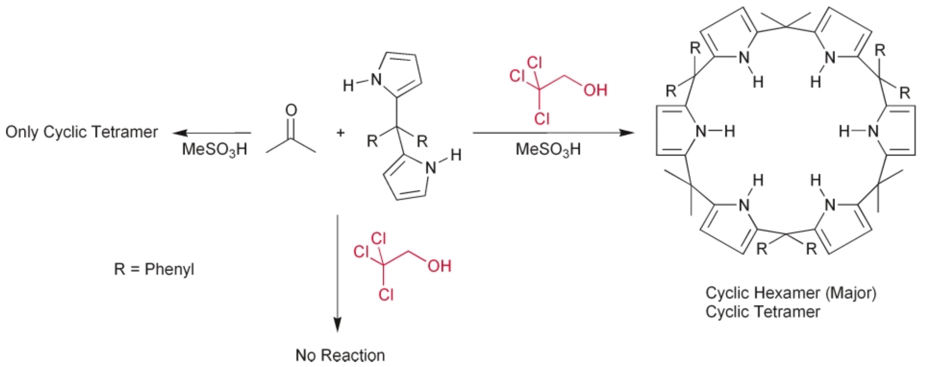


Fig. 1 Side view of the complex between octamethyl calix[4]pyrrole and trifluoroacetate. The counter ion (tetraethylammonium) was removed from the figure for clarity.

---

† Electronic supplementary data (ESI) available: Figs. 1 and 2 showing atom numbering. See http://www.rsc.org/suppdata/cc/b1/b106162n/

DOI: 10.1039/b106162n



Scheme 1

system through hydrogen bonds and to the axial *meso* phenyl ring substituents.

Indeed, the reaction between *di*phenyl-*di*(2-pyrrole) methane and acetone under the same experimental conditions as in Table 1, in the presence of 7.7 mM methane sulfonic acid and 10.5 mM 2,2,2-trichloroethanol yields a mixture of 12% tetraphenyl-calix[4]pyrrole and 45% hexaphenyl-calix[6]pyrrole. Control experiments reveal that calix[6]pyrrole is formed only in the presence of both acid catalyst and template. Methane sulfonic acid by itself produces only calix[4]pyrrole and 2,2,2-trichloroethanol by itself is not acidic enough to induce the reaction, Scheme 1.

The crystal structure‖ of the complex between calix[6]pyrrole and the template 2,2,2-trichloroethanol, depicted in Fig. 2, reveals the role of 2,2,2-trichloroethanol as the template. The 2,2,2-trichloroethanol guest is anchored to the cavity of the calix[6]pyrrole through hydrogen bonds between the disordered oxygen atom of the guest and the acidic hydrogen atoms of three pyrrole rings: $d_{\mathrm{O84b}\cdots\mathrm{H18\text{-}N18}}$ = 2.41(5) Å, $\alpha_{\mathrm{O}\cdots\mathrm{H\text{-}N}}$ = 169.1(7)°; $d_{\mathrm{O84a}\cdots\mathrm{H70\text{-}N70}}$ = 2.41(5) Å, $\alpha_{\mathrm{O}\cdots\mathrm{H\text{-}N}}$ = 175.9(7)°; $d_{\mathrm{O84a}\cdots\mathrm{H44\text{-}N44}}$ = 2.73(5) Å, $\alpha_{\mathrm{O}\cdots\mathrm{H\text{-}N}}$ = 157.0(7)°, two $\pi_{\mathrm{pyrrole}}\cdots$H-O– interactions:** $d_{\pi_{\mathrm{pyrrole(N52,C48–51)}}\cdots\mathrm{O84A}}$ = 2.93(1) Å, $\alpha_{\pi_{\mathrm{pyrrole(N52,C48–51)}}\cdots\mathrm{O84A–C83}}$ = 143.1(7)°; $d_{\pi_{\mathrm{pyrrole(N78,C74–77)}}\cdots\mathrm{O84B}}$ = 3.01(1) Å, $\alpha_{\pi_{\mathrm{pyrrole(N78,C74–77)}}\cdots\mathrm{O84B–C83}}$ = 161.4(7)°, and three $\pi_{\mathrm{phenyl}}\cdots$Cl-C interactions between the Cl atoms of the guest and the π electron clouds of the axial phenyl groups,** $d_{\mathrm{Cl79–\pi(C34–C39)}}$ = 3.62(1) Å; $\alpha_{\mathrm{C82–Cl79–\pi(C34–C39)}}$ = 147.7(7)°; $d_{\mathrm{Cl80–\pi(C60–C65)}}$ = 3.61(1) Å, $\alpha_{\mathrm{C82–Cl80–\pi(C60–C65)}}$ = 148.8(7)°; $d_{\mathrm{Cl81–\pi(C8–C13)}}$ = 3.75(1) Å, $\alpha_{\mathrm{C82–Cl81–\pi(C8–C13)}}$ = 143.8(1)°. The attractive nature of the C-Cl···π interaction is revealed from the close contact between the Cl atom and one of the carbon atoms of each of the phenyl rings: $d_{\mathrm{Cl79–C39}}$ = 3.40(1) Å; $d_{\mathrm{Cl81–C13}}$ = 3.51(1) Å; $d_{\mathrm{Cl80–C62}}$ = 3.18(1) Å. The exact nature and magnitude of this type of interactions are currently under investigation.¶

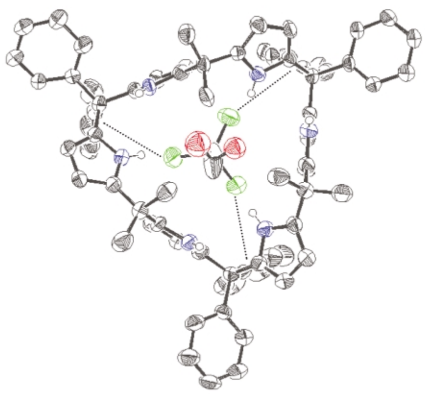


Fig. 2 Top View of the complex between 2,2,2-trichloroethanol and *meso*-hexaphenyl-*meso*-hexamethyl-calix[6]pyrrole. Solvent molecules were removed from the figure for clarity.

Template assisted formation of extended calix[*n*]pyrroles may be a more general case. For example, the crystal structures of β-hexadecafluoro-*meso*-hexadecamethyl-calix[8]pyrrole and β-decafluoro-*meso*-decamethyl-calix[5]pyrrole reveal that the cyclopyrrolemethane ring is folded in a way that hydrogen bonds between the fluoro substituents of the pyrrole rings and the acidic hydrogens of other pyrrole rings are formed.[7] It is possible that these N-H···F bonds form in the course of the formation of the pyrrolemethane oligomer and the specific folding pattern induces ring-size selection.

In conclusion, trihalogenated compounds such as boron trifluoride, 2,2,2-trihaloethanol derivatives and trihaloacetic acids serve as templates in the formation of calix[6]pyrrole from *di*(aryl)-*di*(2-pyrrole) methanes and acetone. The use of different templates for the formation of other extended cavity calixpyrroles is under investigation.

Notes and references

‡ Reaction conditions: a mixture of 60 ml 1 : 1 dry ethanol–acetone, 300 mg (1 mmol) diphenyl-di(2-pyrrole) methane and 10 mmol of the relevant acid catalyst. The mixture was stirred for five days under Argon in the dark.

§ Crystal data for *meso*-octamethyl calix[4]pyrrole·tetraethyl ammonium trifluoroacetate·H₂O: $C_{28}H_{36}N_4{\cdot}C_2F_3O_2{\cdot}C_8H_{20}N_1{\cdot}H_2O$, M = 689.89, a = 12.6000(4), b = 16.7230(7), c = 10.6350(4) Å; β = 120.276(2)°, U = 1935.25(13) Å^3, T = 293(2) K, Space Group: Cm, Monoclinic, Z = 2, GOF = 1.064, R_{int} = 0.0461. CCDC 171004. See http://www.rsc.org/suppdata/cc/b1/b106162n/ for crystallographic data in .cif format. See ESI† for atom numbering.

¶ Bound halide atoms are known to form attractive interactions with different *Lewis* bases, *cf.* P. Metrangolo and G. Resnati, *Chem. Eur. J.*, 2001, **7**, 2511 and references therein. The crystallographic databank also reveals many structures with close C–Cl···π distances.

‖ See ref. 11 for crystal data. See supplementary information for atom numbering.†

** The distance between atoms and rings refer to the distance between the relevant atom and the centroid of the relevant aromatic ring.

1 P. A. Gale, *Coord. Chem. Rev.*, 2001, **213**, 79.
2 P. A. Gale, *Coord. Chem. Rev.*, 2000, **199**, 181.
3 P. A. Gale, J. L. Sessler and V. Král, *Chem. Commun.*, 1998, 1.
4 P. Anzenbacher, Jr., K. Jursíková and J. L. Sessler, *J. Am. Chem. Soc.*, 2000, **122**, 9350.
5 P. Anzenbacher, Jr., A. C. Try, H. Miyaji, K. Jursíková, V. M. Lynch, M. Marquez and J. L. Sessler, *J. Am. Chem. Soc.*, 2000, **122**, 10268.
6 P. A. Gale, J. W. Genge, V. Král, M. A. McKervey, J. L. Sessler and A. Walker, *Tetrahedron Lett.*, 1997, **38**, 8443.
7 J. L. Sessler, P. Anzenbacher Jr., J. A. Shriver, K. Jursíková, V. M. Lynch and M. Marquez, *J. Am. Chem. Soc.*, 2000, **122**, 12061.
8 B. Turner, M. Botoshansky and Y. Eichen, *Angew. Chem., Int. Ed.*, 1998, **37**, 2475.
9 G. Cafeo, F. H. Kohnke, G. L. La Torre, A. J. P. White and D. J. Williams, *Angew. Chem., Int. Ed.*, 2000, **39**, 1496.
10 G. Cafeo, F. H. Kohnke, G. L. La Torre, A. J. P. White and D. J. Williams, *Chem. Commun.*, 2000, 1207.
11 B. Turner, A. Shterenberg, M. Kapon, K. Suwinska and Y. Eichen, *Chem. Commun.*, 2001, 13.
12 J. S. Lindsey and R. W. Wagner, *J. Org. Chem.*, 1989, **54**, 828.