

Encapsulation of oligoethylene glycols and perfluoro-*n*-alkanes in a cylindrical host molecule†

Byron W. Purse and Julius Rebek, Jr.*

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Oligoethylene glycols and perfluoro-*n*-alkanes are suitable guests for the synthetic cylindrical host molecule **1**₂; an investigation of these host-guest systems is reported.

Guest molecules encapsulated in larger molecular hosts are known to adapt their conformation and in some cases isomeric distribution to maximize attractive interactions and minimize repulsive interactions with the host.^{1,2} The coiling of long alkyl chains into helices within cavitands and capsules is such an adaptation.^{1b,c} Compensation for the *gauche* interactions is provided by favorable CH- π and other interactions with the cavity interior. Here we describe the behavior of oligoethylene glycols (OEGs) and perfluoro-*n*-alkanes as occupants of the cavity of cylindrical capsule **1**₂ (Fig. 1).

This host molecule self-assembles to form a dimeric capsule stabilized in part by a seam of bifurcated hydrogen bonds. The cavity has an elongated shape, with a length of approximately 16 Å and a volume of 425 Å³. A broad range of guests are accommodated in mesitylene-*d*₁₂ solution; this solvent does not compete to occupy the cavity. Modelling studies suggested how this cylindrical capsule could accommodate OEGs and perfluoro-*n*-alkanes (Fig. 2). Given the length of the cavity at 16 Å, no more

† Electronic supplementary information (ESI) available: detailed experimental procedures and NMR spectra of host-guest complexes. See <http://www.rsc.org/suppdata/cc/b4/b408878f/>
*jrebek@scripps.edu

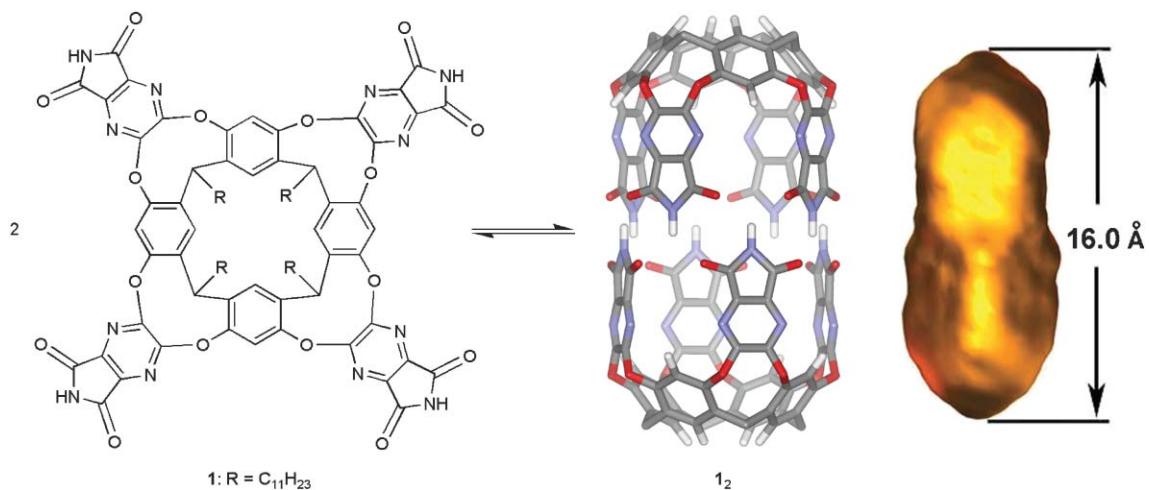


Fig. 1 Structure of cylindrical capsule half **1**, MM+ minimized model of capsule **1**₂, and a model of the cavity interior space. R groups in the model structure have been removed for clarity.

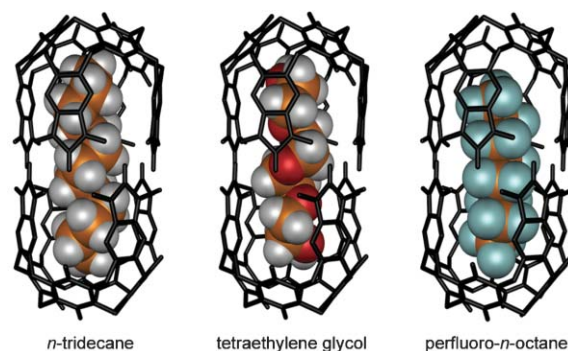


Fig. 2 Model structures of *n*-tridecane, tetraethylene glycol, and perfluoro-*n*-octane in cylindrical capsule **1**₂.

than 10 contiguous carbon atoms can be accommodated in a fully staggered conformation (MM+ minimized model).

In organic solvents, OEGs adopt an extended helical conformation with *gauche* dihedrals about their C-C bonds and *trans* dihedrals about their C-O bonds. It has been proposed that the *gauche* configuration about the C-C bonds is the result of stereoelectronic effects or attractive *gauche* interactions, when polar bonds are present.³ Alternatively, matrix-isolation infrared spectroscopy indicates that the fully *trans* extended conformation is the most stable; the introduction of *gauche* interactions during coiling allows for more favorable intermolecular interactions

between OEGs.⁴ In any event, the native coiled conformation of OEGs has too great a helical diameter to fit within the capsule, but introduction of *gauche* dihedrals about the C–O bonds can contract the helix and allow it to be accommodated.

In contrast, the native conformations of perfluoro-*n*-alkanes are well suited to the host: they adopt twisted staggered conformations with dihedral angles typically around 167°, and the diameter of the perfluoroalkyl chain is sufficient to make van der Waals contacts (if appropriate) with the cavity walls without additional coiling. This conformational preference is governed predominately by the steric demands of the fluorine atoms which disfavor a truly staggered configuration.⁵

Minimization (MM+ force field) of triethylene glycol monomethyl ether (seven CH₂ + four O) in the capsule gives a fully staggered conformation, but minimization of triethylene glycol dimethyl ether results in a deviation from this conformation as coiling begins. An extra main-chain atom is accommodated in the oligoethylene glycol because a C–O bond is 0.1 Å shorter than a C–C bond.

Binding studies in mesitylene-*d*₁₂ gave the relative association constants (Table 1; ESI†). A difference in the distribution of chain lengths bound is immediately apparent between the three classes of guests (Fig. 3). The alkanes show a marked preference for a guest which is longer (in its staggered conformation) than the host cavity and therefore must coil to be bound. This is undoubtedly due to the greater breadth of the coiled structure which allows it to make more favourable contacts with the host walls (see Fig. 1). A similar trend is observed for the OEGs, though notably the maximum chain length bound was two atoms longer than the longest alkane.‡ This is due, in part, to the shorter C–O bond length compared to C–C bonds, though pentaethylene glycol is still longer than tetradecane by 0.8 Å. A second contributing factor is that approximately one third of the *gauche* interactions inherent in a tightly coiled conformation are already present in the

Table 1 Relative association constants and packing coefficients of *n*-alkanes, OEGs, and perfluoro-*n*-alkanes and cylindrical capsule **1**₂ in mesitylene-*d*₁₂

Length ^a	Guest	<i>K</i> _{rel}	PC ^b
8	<i>n</i> -octane	0 ^c	0.32 ^c
9	<i>n</i> -nonane	0.3 ^c	0.36 ^c
10	<i>n</i> -decane	17 ^c	0.39 ^c
11	<i>n</i> -undecane	100 ^c	0.44 ^c
12	<i>n</i> -dodecane	24 ^c	0.47 ^c
13	<i>n</i> -tridecane	1 ^c	0.52 ^c
14	<i>n</i> -tetradecane	13 ^c	0.56 ^c
15	<i>n</i> -pentadecane	0 ^c	0.61 ^c
7	Perfluoro- <i>n</i> -heptane	<0.05	0.43
8	Perfluoro- <i>n</i> -octane	0.91	0.48
9	Perfluoro- <i>n</i> -nonane	1.3	0.54
10	Perfluoro- <i>n</i> -decylidide	<0.05	0.66
11	Triethylene glycol monomethyl ether	0	0.36
12	Triethylene glycol dimethyl ether	2.1	0.41
13	Tetraethylene glycol	0.42	0.42
14	Tetraethylene glycol monomethyl ether	1.2	0.45
15	Tetraethylene glycol dimethyl ether	0.17	0.50
16	Pentaethylene glycol	<0.04	0.51

^a Number of carbon plus oxygen atoms. ^b Packing coefficient = the volume of the guest divided by the volume of the host cavity. ^c Data from ref. 6.

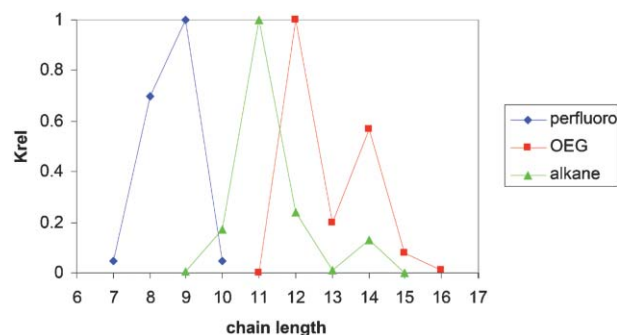


Fig. 3 Relative association constants *K*_{rel} as a function of guest chain length (number of C + O). Relative association constants are normalized for each series and cannot be compared directly in this chart.

oligoethylene glycol's native conformation and do not have to be induced on encapsulation. The tapered ends of the cavity are suited to a primary OH function.

The perfluoro-*n*-alkanes exhibit different behaviour. The eight and nine carbon chains are selected with longer and shorter lengths showing little or no binding. Because these molecules are unable to coil inside the host, those structures that best fill the cavity in their native conformation are favored.

Packing coefficients are reported in Table 1. Typically, packing coefficients of around 0.55 are preferred for hosts with neutral guests. For the cases at hand, we observe a competition between the filling of the cavity's length and space; OEGs and *n*-alkanes of sufficient volume to fill the space optimally must coil to reduce their length. In contrast, the perfluoro-*n*-alkanes efficiently occupy the cavity in their native conformations.

In studies of the *n*-alkanes bound in this capsule, no evidence was observed for the diastereotopic differentiation of geminal hydrogens, as would be expected of a fixed helical conformation. We attribute this to rapid racemization of the helix through a partial uncoiling mechanism. The same phenomenon was observed in the ¹H NMR spectra of encapsulated OEGs. The coiled conformations shown in Fig. 2 maximize the favorable intermolecular contacts of the oligoethylene glycol (or *n*-alkane) to make with the host interior and minimize the unfavourable intramolecular contacts (steric repulsion) in the guest. Because the conformation of the guest is dynamic, the average conformation seen on the NMR time scale maintains the *D*_{4d} symmetry of the capsule.

The perfluoro-*n*-alkanes are likely bound in their twisted staggered conformation (Fig. 2). Like the encapsulated *n*-alkanes and OEGs, this is a chiral conformation that racemizes quickly on the NMR timescale. Computational studies estimate the barrier to rotation from a –167° to a +167° dihedral to be less than 1 kcal mol^{–1}.⁷

The driving force for encapsulation of OEGs and perfluoro-*n*-alkanes is two-fold. First, attractive interactions between host and guest, including CH–π interactions and van der Waals contacts, help drive assembly in the case of the OEGs. The perfluoro-*n*-alkanes can interact with the host interior, though it is not known how favorable these interactions are. Second, host–guest complex formation is driven enthalpically by the formation of the hydrogen-bonded seam of the host. Assembly of the capsule does not occur in the

absence of a suitable guest; a highly unfavorable 425 Å³ vacuum would be the result. *n*-Alkanes, OEGs, and perfluoro-*n*-alkanes all make sufficiently favorable contacts with the interior of the host to allow them to fill this space and facilitate assembly.

In conclusion, we have shown that cylindrical host molecule **1**₂ can accommodate OEG and perfluoro-*n*-alkane guests. The OEG guests coil to fill the cavity whereas the perfluoro-*n*-alkanes are already organized for encapsulation.

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Byron W. Purse and Julius Rebek, Jr.*

*The Skaggs Institute for Chemical Biology and the Scripps Research Institute, 10550 N. Torrey Pines Rd., La Jolla, CA 92037, USA.
E-mail: jrebek@scripps.edu; Fax: +1 (858)-784-2876;
Tel: +1 (858)-784-2855*

Notes and references

‡ In both the *n*-alkane series and the OEG series the guest with chain length 13 is less favorably bound than either the length 12 or length 14 guest. The reason is unknown.

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