Highlight Review

Elastic Cycles as Flexible Hosts: How Tubes Built by Cyclic Chalcogenaalkynes Individually Host Their Guests

Rolf Gleiter* and Daniel B. Werz

(Received August 18, 2004; CL-048012)

Abstract

Tubular structures arise in the solid state through close chalcogen–chalcogen contacts. Several examples containing sulfur and selenium centers are presented. In the case of cyclic systems of ring size 22–33 the resulting tubes are capable of including π-systems as guest molecules. For hexaselenacyclotriacontahexayne **8**(5) it is shown that the cycle is flexible and adopts a smaller space in the case of furan or *n*-hexane as compared with that of mesitylene. This behavior is attributed to the relatively low torsional barrier at the chalcogen-substituted butadiyne unit.

♦ Introduction

During biological evolution the hydrogen bond has proven to be the most effective directional force.[1] Well-known supramolecular structures[2] which are based on hydrogen bonds[3] are ice, the pairing of bases in DNA or RNA, the folding of peptides, the alignment of cellulose molecules or the helical structure of amylose. Alternative directional forces which can lead to supramolecular structures are interactions between Lewis-acidic metal centers and Lewis bases,[4] ion dipole interactions,[5] and π–π stacking[6] to name the most important competitors to hydrogen bonding.

The most prominent supramolecular structures resulting from these forces are helices and tubes which have attracted attention of chemists due to their occurrence in nature and, in the latter case, also due to their potential in material science. The tubular structures can be subdivided into those whose skeleton is determined by covalent bonding or by noncovalent interactions. Examples of the first kind are inorganic tubular constructs such as zeolites[7] or carbon nanotubes[8] to name the most important ones.

To illustrate tubular species based on noncovalent forces we mention carbohydrate-based species such as stacks of cyclodextrins,[9] polymer lipid-based tubes,[10] or nanotubes from cyclic peptides.[11]

Concepts for constructing molecular tubes based on noncovalent interactions can be borrowed from biology and its technique. The inclusion of iodine into amylose is long known to chemists. The 1,4-glycosydic linkage of α-D-glucose units results in a helical structure with a hollow core in which iodine molecules can be included. A second building concept is found in trans membrane channels. Here bundles of helical proteins form a hollow tube. As examples, we mention the potassium channel[12] and maltoporin channel.[13] The tobacco mosaic virus exemplifies a third idea. This system consists of sector-shaped peptide units which are attached on a helical RNA "wire" to form a helical structure with a tubular core.[14] This motif is also found for a number of dipeptides such as L-Val-L-Ala.[15] In these structures head-to-tail hydrogen bonding between the dipeptides is observed leading to a tubular arrangement of six dipeptide units per turn. The resulting channels of 10-Å diameter are hydrophobic at the outside and hydrophilic in the center.[15] A rather flexible technique for building tubular constructs is the stacking of cyclic units. This concept can be varied in different ways: the tori can either be connected with each other by strong forces along the stacking direction only (Figure 1a) or along the stacking direction and sidewise. The first approach leads to a dense packing of rods as found in cyclodextrines[9] or cyclic peptides.[11] A strong in-plane connectivity, but weak inter-stack connections are found for shape-persistent macrocycles with phenol units as building blocks (Figure 1b).[16] Due to the π–π repulsion of the aromatic subunits the planes are shifted sidewise. If the connectivity occurs in a zigzag fashion (Figure 1c), the tubuli are stacked on top of each other. Usually the distances between the rings within one stack are larger than in the situations shown in Figures 1a and 1b. There are many examples of tubular structures assembled according to the situation shown in Figures 1a and 1b, but only recently the zigzag connection emerged as an alternative concept.[17] Therefore we will focus this Highlight Review on this case.

♦ Chalcogen–Chalcogen Interactions

A further directional force which leads to self-assembly of molecules are short interactions between halogen centers[18] and between chalcogen centers.[19] These forces are ascribed as van der Waals forces which usually do not show much directionality. As a result, two- and three-dimensional networks were reported, but no helical or tubular structures.

Our in-depth studies on cyclic tetrachalcogenadiynes such as **1**(*n*) and **2**(*n*)[17a,20] revealed a series of molecules in which

Prof. Dr. R. Gleiter, Dr. D. B. Werz#
Organisch-Chemisches Institut der Universität Heidelberg, Im Neuenheimer Feld 270, D-69120 Heidelberg, Germany
E-mail: rolf.gleiter@urz.uni-heidelberg.de
 # Present Address: Laboratorium für Organische Chemie, ETH-Hönggerberg, CH-8093 Zürich, Switzerland
E-mail: werz@org.chem.ethz.ch

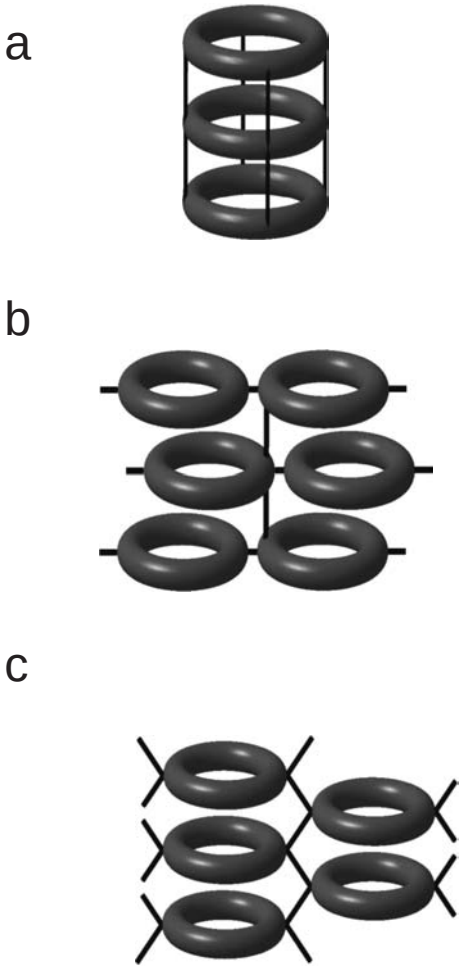


Figure 1. Three possible strategies to interconnect rings to form tubes in the solid state.

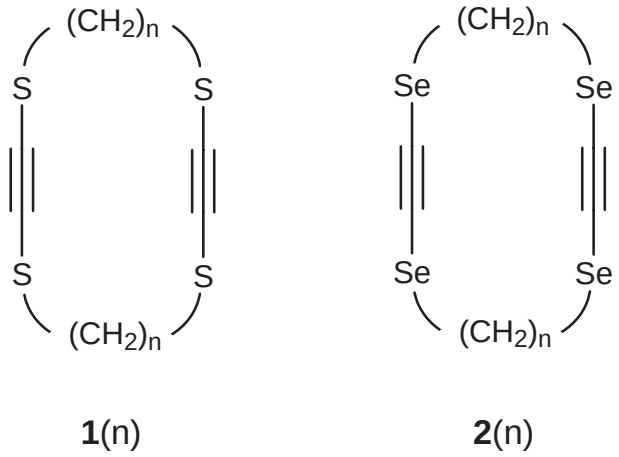


Chart 1.

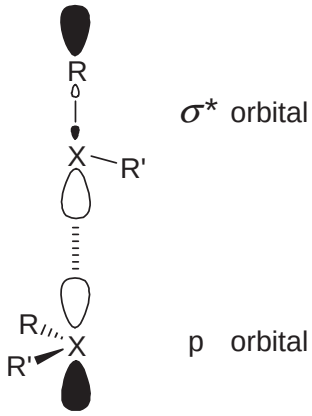


Figure 2. Directional bonding of two chalcogen centers in R–X–R′ units by interaction of an occupied p orbital with an empty X–C(sp) σ^* orbital.

the rings form tubular structures. A detailed investigation revealed that in the solid state the rings associate in such a way that the chalcogen center of one ring keeps close contact with two chalcogen centers of two rings in a neighboring stack. This interaction leads to tubes as shown schematically in Figure 1c. A zigzag arrangement of the chalcogen centers results. Our investigations reveal two main contributions to the chalcogen–chalcogen interactions: the isotropic dispersion forces and the interaction between an occupied p orbital at the chalcogen center with the unoccupied X–C(sp) σ^* orbital (see Figure 2).

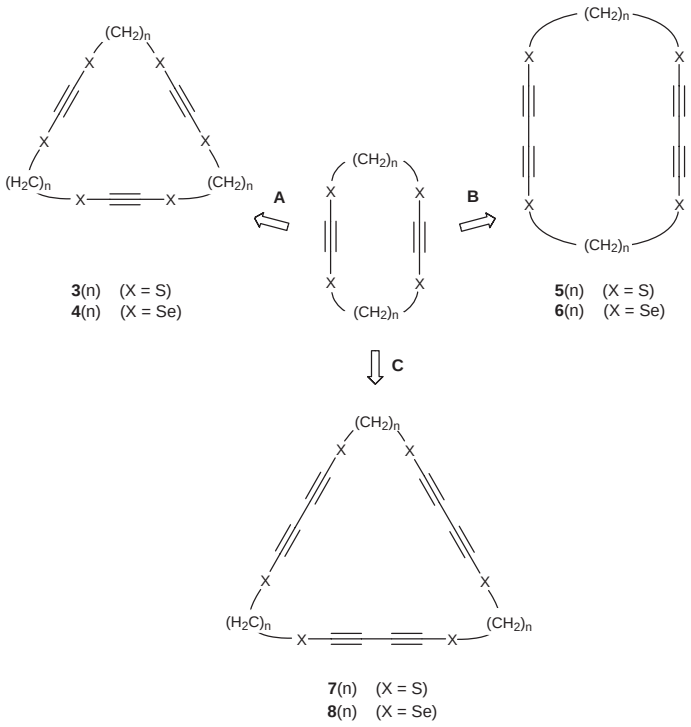
This p–σ^* interaction determines the directionality of the bonding.[17,20] However, also dispersion forces contribute significantly. In Figure 3 we show the calculated (MP2 level) potential energies for the interaction of a dimethylchalcogen $(CH_3)_2X$ with a methylethynylchalcogen CH_3–X–C_2H for X = S, Se, Te.[21] These results reveal that the intermolecular interaction depends upon the chalcogen centers (Te > Se > S). This variation is anticipated from the afore mentioned contributions. The stabilization energies vary between 2 and 4 kcal/mol.[21] Thus, these attractive forces are in the same range as weak to medium hydrogen bonds.

In the cases of **1**(*n*) and **2**(*n*) the hollow core resulting from stacking the molecules on top of each other is not large enough to include any guest molecules. To achieve this goal one has to enlarge the ring size. In Scheme 1 we have outlined how this problem was solved:

- In **A** simply a further repetition of the rigid 1,4-dichalcogenaalkyne unit was applied.
- In **B** the triple bond was replaced by the longer 1,3-butadiyne unit.
- In **C** we combined **A** and **B** to get rings with three 1,6-dichalcogena-2,4-hexadiyne units.

The latter seems to be the most promising approach. Concept **A** needed no further synthetic efforts because ring systems with three 1,4-dichalcogenaalkyne units were side products of the synthesis of **1**(*n*) and **2**(*n*), respectively. When we recrystallized **3**(4) from *n*-hexane we obtained single crystals which showed a tubular stacking of the rings by including *n*-hexane in a disordered fashion. Increasing the ring size by simple elongation of the alkane chains between the rigid units led to **3**(6). Now the potential cavity created by the ring system collapsed (Figure 4) to yield columns of T-shaped molecules which are stacked in AAA fashion, favored by short intercolumnar S···S interactions. This structural examination demonstrates that the rig-

Published on the web (Advance View) December 25, 2004; DOI 10.1246/cl.2005.126



Scheme 1.

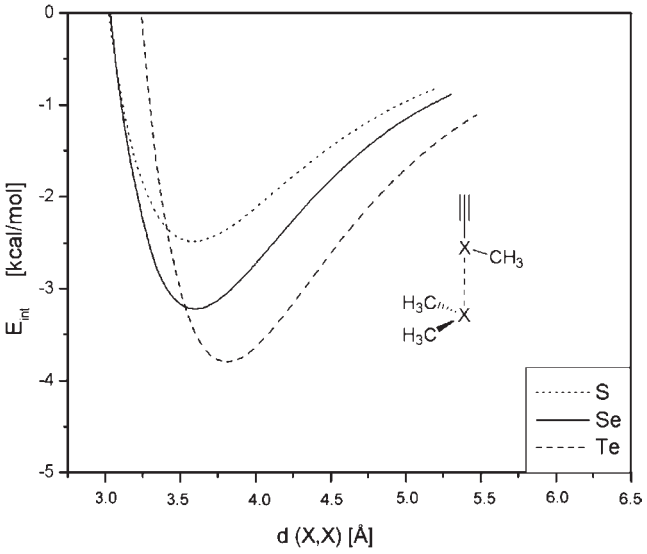


Figure 3. Interaction energies E_{int} calculated at the MP2 level [kcal/mol] between Me_2X and $MeXC_2H$ (X = S, Se, Te) units *vs* the interchalcogen distance d (X, X) [Å] in the most favorable arrangement.

id units are essential to guarantee a hollow core.

The molecular structures of the tetraynes **5**(*n*) and **6**(*n*) (*n* = 2–5) according to concept **B** adopt in the solid state mostly conformations with a center of inversion. In all cases the triple bonds are oriented approximately parallel to each other.

For **5**(5) and **6**(5) we noticed channel-like structures in the solid state which included solvents.

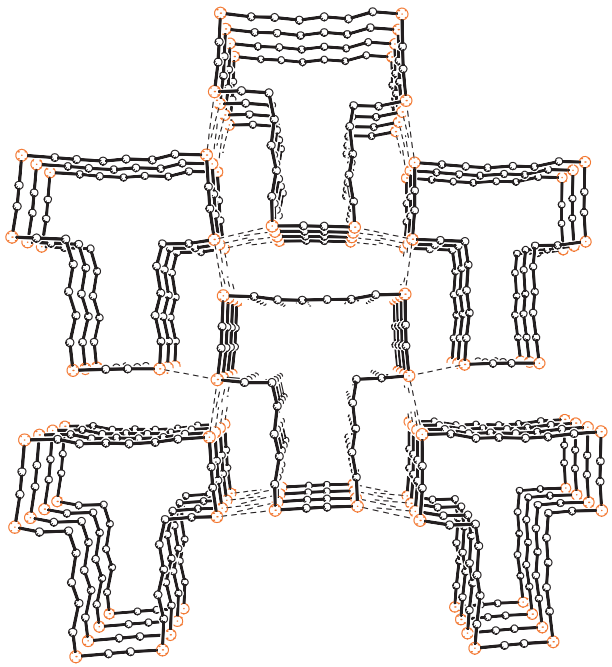


Figure 4. Top view of the columnar structure of **3**(6). The short S···S distances are indicated, the hydrogen atoms are omitted for the sake of clarity.

By recrystallization of **5**(5) from toluene we observed the inclusion of one aromatic species per two ring units in a regular manner as shown in Figure 5 (left).

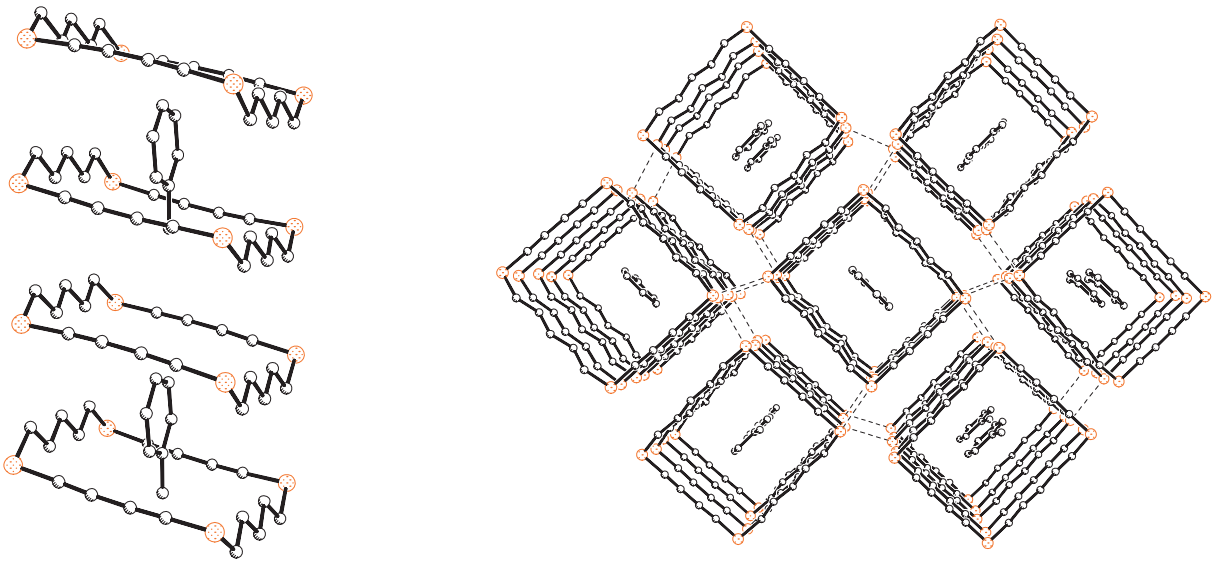


Figure 5. Side and top view of **5**(5) with included toluene guest molecules. The hydrogen atoms are omitted for the sake of clarity.

The rings adopt a chair conformation in the crystal and are stacked in a AAA fashion with short contacts between the sulfur atoms of neighboring stacks. The channel diameter varies within the stack; the cavity itself inside a cycle is still too small to house the aromatic ring, only the methyl group of the guest is included. The arene unit itself is situated between two molecules of the stack.

In the case of **8**(5),[22] a compound following the concept **C**, the larger ring incorporates one aromatic molecule per hexaselenacyclohexayne ring (Figure 6). The rings are stacked in a ABAB fashion as well as are their guests. In line with the case of **5**(5) the stacks are held together by short chalcogen–chalcogen contacts which lead to a hexagonal arrangement of the tubes similar to those observed for α-cyclodextrine.[9]

The 33-membered ring of **8**(5) with its three rigid 1,6-diselena-2,4-hexadiyne units proved to be a neat example to demonstrate the elastic properties of the ring scaffold. A systematic study with 12 different guest molecules (see Table 1), aliphatic as well as aromatic, electron-rich as well as electron-poor ones, revealed tubular structures with inclusion of solvents. It turned out that all structures show very similar primitive unit cells. In Table 1 each structure is denoted by a greek letter (from α to μ). In those cases where the trigonal space group $R\bar{3}$ was observed (α to ζ) the guest molecules could not be localized at well-defined positions. In all the other cases (η to μ) a triclinic space group resulted ($P\bar{1}$) in which the guests were found on well-defined positions. We ascribe the observation that the solvent molecules were incorporated in **8**(5) in an ordered fashion to weak C–H$\cdots\pi$ interactions[3] between the alkane chains of the host and the π-system of the aromatic guest. Two examples of triclinic structures of **8**(5) are depicted in Figure 7.

In Table 1 we have listed the solvent-accessible volume (per unit cell) in the solid state calculated by the PLATON program.[23] This volume is increasing from the inclusion of furan (19%) to that of mesitylene (26%). Obviously, the diameter of the tube within the **8**(5) scaffold depends on the size of the incorporated guest. The larger the guest, the more space is provided.

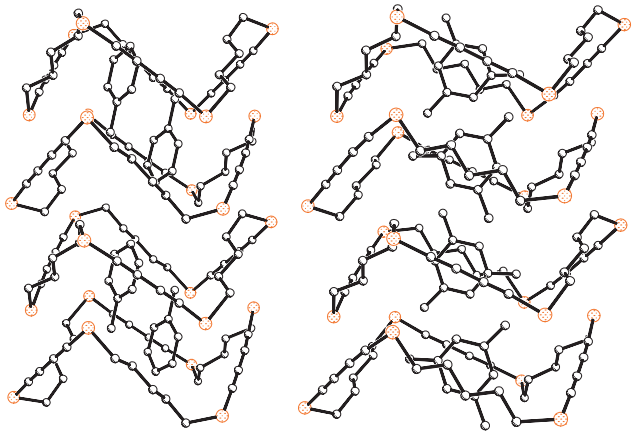


Figure 6. Side view of two modifications of **8**(5): (left) with inclusion of toluene and (right) with inclusion of mesitylene showing a flattening of the ring in comparison to toluene. The hydrogen atoms are omitted for the sake of clarity.

To understand the origin of this flexibility we have also listed in Table 1 the angle ϕ which is defined as the angle between the medium plane of the macrocycle and the vectors of the SeC_4Se units. A straight forward, almost linear correlation between the solvent-accessible volume and the angle ϕ is found: The smaller ϕ, the larger the cavity. The angle ϕ is most efficiently influenced by the torsional angle γ between the Se–CH_2 bonds of the rigid units. The smaller γ is, the flatter is the cyclic system and the smaller is ϕ. As DFT calculations have shown the rotational energy for a diselena-substituted butadiyne moiety amounts to 2 kcal/mol,[24] representing a rather flat potential which facilitates the reduction of γ and thus allows a flattening of the ring. In turn a larger solvent-accessible volume is provided inside the tube. We favor this rationalization as compared with the less favorable bending of the 1,3-butadiynyl units or

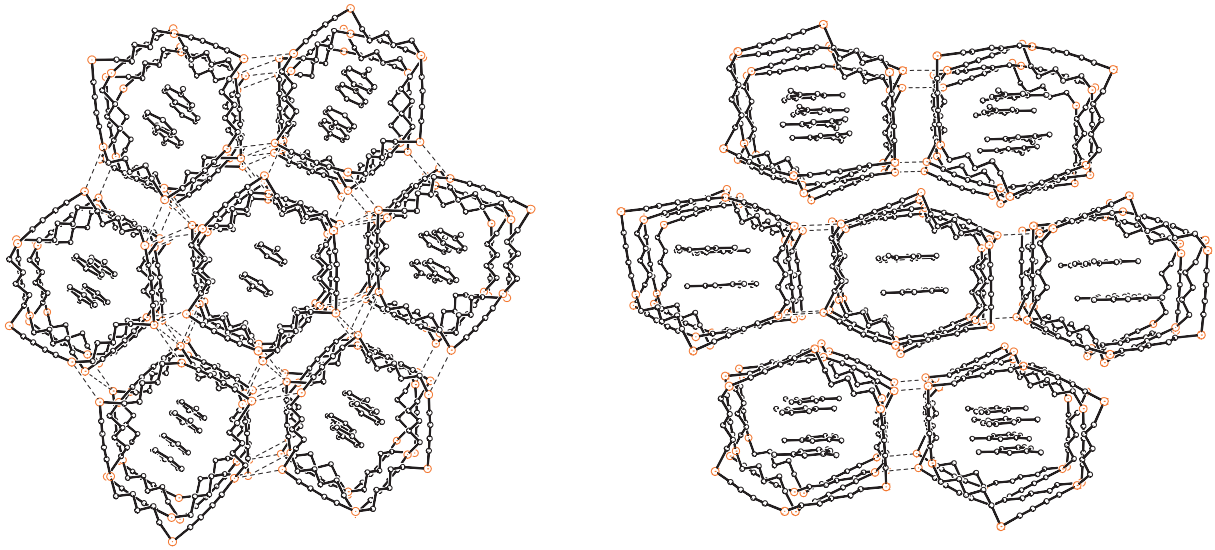


Figure 7. Top view of two modifications of **8**(5): (left) with inclusion of toluene and (right) with inclusion of mesitylene showing a structure with larger cavities. The hydrogen atoms are omitted for the sake of clarity.

Table 1. Solid-state data of **8**(5) with different guests

Structure	Guest molecule	Crystal system	Volume /%[a]	Angle ϕ /deg[b]
8(5) α	furan	trigonal	18.9	37.8
8(5) β	*n*-hexane	trigonal	19.2	37.6
8(5) γ	thiophene	trigonal	20.0	36.6
8(5) δ	benzene	trigonal	20.3	36.1
8(5) ε	aniline	trigonal	20.4	36.0
8(5) ζ	chlorobenzene	trigonal	20.7	35.9
8(5) η	nitrobenzene	triclinic	20.8	35.5
8(5) θ	toluene	triclinic	20.8	35.3
8(5) ι	anisole	triclinic	21.0	35.1
8(5) κ	*p*-xylene	triclinic	23.3	34.1
8(5) λ	4-bromoanisole	triclinic	23.5	33.6
8(5) μ	mesitylene	triclinic	25.6	30.6

[a]Solvent-accessible volume of the unit cell, calculated with PLATON.[23]
[b]Angle ϕ between the medium plane of the macrocycle and the Se–C_4–Se unit(s).

a stretching of the alkyl chains by enlarging the tetrahedral C–C–C angle.

♦ Conclusion

The synthesis of large ring systems, of ring size between 22 and 33 heavy atoms, provided cycles with a cavity, large enough for the inclusion of molecules between the size of *n*-hexane and mesitylene. One prerequisite for the inclusion of guests was a sufficient number of rigid fragments in order to avoid a collapse of the cavity. Essential for the formation of tubular structures was the presence of chalcogen centers with effective p–σ* interactions. The most interesting finding during the studies of these large cycles is their flexibility due to a lower force constant of changing the torsional angle in the R–X–C≡C–C≡C–X–R units. This hinge-like mechanism allows a specific hosting of guests: more space for bigger guests.

♦ Acknowledgments

We are grateful to Dr. F. Rominger for numerous X-ray investigations. For technical support we thank C. Bleiholder, P. Bischof, and P. Krämer. Financial support was provided by the Deutsche Forschungsgemeinschaft (DFG), the Federal State of Baden-Württemberg, and the Fonds der Chemischen Industrie. D. B. Werz is grateful to the Studienstiftung des deutschen Volkes for a graduate fellowship.

References

1 a) J. W. Steed and J. L. Atwood, "Supramolecular Chemistry," John Wiley & Sons, Chichester (2000). b) H. J. Schneider and A. Yatsimirsky, "Principles and Methods in Supramolecular Chemistry," John Wiley & Sons, Chichester (2000).
2 a) J.-M. Lehn, "Supramolecular Chemistry: Concepts and Perspectives," VCH, Weinheim (1995). b) F. Vögtle, "Supramolekulare Chemie," Teubner, Stuttgart (1992). c) D. Philip and J. F. Stoddart, *Angew. Chem.*, **108**, 1243 (1996); *Angew. Chem., Int. Ed. Engl.*, **35**, 1155 (1996).
3 T. Steiner, *Angew. Chem.*, **114**, 50 (2002); *Angew. Chem., Int. Ed.*, **41**, 48 (2002); G. R. Desiraju and T. Steiner, "The Weak Hydrogen Bond: Applications to Structural Chemistry and Biology," Oxford University Press (1999).
4 a) M. Fujita, *Chem. Soc. Rev.*, **6**, 417 (1998). b) S. Leiniger, B. Olenyuk, and P. J. Stang, *Chem. Rev.*, **100**, 853 (2000).
5 J. C. Ma and D. Dougherty, *Chem. Rev.*, **97**, 1303 (1997).
6 C. A. Hunter and J. K. M. Saunders, *J. Am. Chem. Soc.*, **112**, 5525 (1990).
7 a) G. Gottardi, *Pure Appl. Chem.*, **58**, 1343 (1986). b) G.

Calzaferri, M. Pauchard, H. Maas, S. Huber, A. Khatyr, and T. Schaafsma, *J. Mater. Chem.*, **12**, 1 (2002).
8 a) P. M. Ajayan, *Chem. Rev.*, **99**, 1787 (1999). b) M. Terrones, W. K. Hsu, H. W. Kroto, and D. R. M. Walton, *Top. Curr. Chem.*, **199**, 189 (1999).
9 W. Saenger in "Inclusion Compounds Vol. 2," ed. by J. L. Atwood, J. E. Davies, and D. D. McNicol, Academic Press, London (1984), pp 231–259.
10 Y.-S. Lee, J.-Z. Yang, T. M. Sisson, D. A. Frankel, J. T. Gleeson, E. Aksay, S. L. Keller, S. M. Gruner, and D. F. O'Brien, *J. Am. Chem. Soc.*, **117**, 5573 (1995).
11 a) J. D. Hartgerink, T. D. Clark, and M. R. Ghadiri, *Chem.—Eur. J.*, **4**, 1367 (1998). b) D. T. Bong, T. D. Clark, J. R. Granja, and M. R. Ghadiri, *Angew. Chem.*, **113**, 1016 (2001); *Angew. Chem., Int. Ed.*, **40**, 988 (2001).
12 D. A. Doyle, J. M. Cabral, R. A. Pfuetzner, A. Kuo, J. M. Gulbis, S. L. Cohen, B. T. Chait, and R. McKinnon, *Science*, **280**, 69 (1998).
13 T. Schirmer, T. A. Keller, Y.-F. Wang, and J. P. Rosenbusch, *Science*, **267**, 512 (1995).
14 A. Klug, *Angew. Chem.*, **95**, 579 (1983); *Angew Chem., Int. Ed. Engl.*, **22**, 565 (1983).
15 C. H. Görbitz, *Chem.—Eur. J.*, **7**, 5153 (2001).
16 a) D. Ventakaraman, S. Lee, J. Zhang, and J. S. Moore, *Nature*, **371**, 591 (1994). b) Y. Tobe, N. Utsumi, K. Kawabata, A. Nagano, K. Adachi, S. Araki, M. Sonoda, K. Hirose, and K. Naemura, *J. Am. Chem. Soc.*, **124**, 5350 (2002). c) O. Henze, D. Lentz, and A.-D. Schlüter, *Chem.—Eur. J.*, **6**, 2362 (2000). d) S. Höger, D. L. Morrison, and V. Enkelmann, *J. Am. Chem. Soc.*, **124**, 6734 (2002).
17 a) D. B. Werz, T. H. Staeb, C. Benisch, B. J. Rausch, F. Rominger, and R. Gleiter, *Org. Lett.*, **4**, 339 (2002). b) R. Gleiter, D. B. Werz, and B. J. Rausch, *Chem.—Eur. J.*, **9**, 2676 (2003).
18 V. R. Pedireddi, D. S. Reddy, B. S. Goud, D. C. Craig, A. D. Rae, and G. R. Desiraju, *J. Chem. Soc., Perkin Trans. 2*, **1994**, 2353.
19 J. M. Williams, J. R. Ferraro, R. J. Thom, K. D. Carlson, U. Geiser, H. H. Wang, A. M. Kini, and M.-H. Whangbo, "Organic Superconductors," Prentice Hall, Englewood Cliffs, N. J. (1992).
20 D. B. Werz, R. Gleiter, and F. Rominger, *J. Org. Chem.*, **67**, 2490 (2002).
21 C. Bleiholder, D. B. Werz, H. Köppel, and R. Gleiter, unpublished results.
22 D. B. Werz, R. Gleiter, and F. Rominger, *J. Org. Chem.*, **69**, 2945 (2004).
23 A. L. Spek, "A. M. C. T. PLATON," Utrecht University, Utrecht, The Netherlands (1998).
24 D. B. Werz and R. Gleiter, *J. Org. Chem.*, **68**, 9400 (2003).