Self-Assembly

DOI: 10.1002/anie.200601594

Supramolecular Assemblies of Chiral Propargylic Alcohols**

Marilise Hyacinth, Maksymilian Chruszcz, Ki Sung Lee, Michal Sabat, Ge Gao, and Lin Pu**

Chiral propargylic alcohols are very useful synthetic precursors to many organic compounds.[1] A few propargylic alcohols were also found to form interesting supramolecular structures through intermolecular interactions of the hydroxy groups and the π electrons of the C≡C bonds.[2–4] Another supramolecular interaction based on the quadrupole π–π attraction between an aryl and a perfluoroaryl moiety was used to create new materials for applications in solid-state photopolymerization, liquid crystals, hydrogels, and so forth.[5] We have initiated a program to combine the four functional groups, including the aryl, perfluoroaryl, C≡C, and OH groups, to make the diaryl-substituted chiral propargylic alcohols and to explore their potential in supramolecular chemistry. Herein, we present some of findings that indicate that the presence of the functional groups not only makes the self-assembly of propargylic alcohols possible but it also allows for a finely tuned cooperation of interactions on a scale rarely seen in other supramolecular systems. We show herein that diaryl-substituted chiral propargylic alcohols can form cyclic hexameric supramolecular assemblies as a result of the cooperation between three major intermolecular forces: O–H···O hydrogen bonding, C–H···F–C hydrogen bonding involving organic fluorine atoms, and π–π stacking interactions between the pentafluorophenyl and phenyl rings. We believe that this synergy of intermolecular forces could be utilized in a variety of applications, including molecular recognition and discrimination.

We synthesized the racemic propargylic alcohol *rac*-**1** from the reaction of phenylacetylene with pentafluorobenzaldehyde in the presence of Et_2Zn and HMPA at room

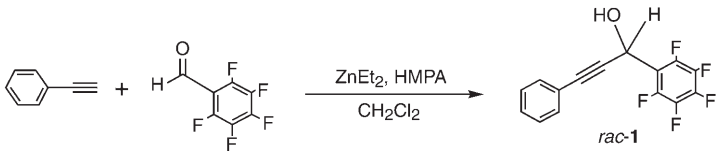
[*] M. Hyacinth, K. S. Lee, Dr. M. Sabat, Dr. G. Gao, Prof. L. Pu
Department of Chemistry
University of Virginia
Charlottesville, VA 22904-4319 (USA)
Fax: (+1) 434-924-3170
E-mail: ms5c@virginia.edu
lp6n@virginia.edu

M. Chruszcz
Department of Molecular Physiology and Biological Physics
University of Virginia
Charlottesville, VA 22908 (USA)

[**] We thank Professor Wladek Minor (University of Virginia Medical School) for helpful discussions and the Rigaku/MSC for loan of the RAPID system. Partial support of this work from the National Institute of Health (R01GM58454/R01EB002037) and from the HKL Research Inc. (GI11496) is gratefully acknowledged.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

temperature (Scheme 1). X-ray analysis of the crystals of *rac*-**1** gave a hexameric supramolecular structure that contained alternating *RSRSRS* enantiomers (Figure 1). The crystal structure of *rac*-**1** consists of centrosymmetric hexamers



Scheme 1. Synthesis of the propargylic alcohol *rac*-**1**. HMPA = hexamethyl phosphoramide.

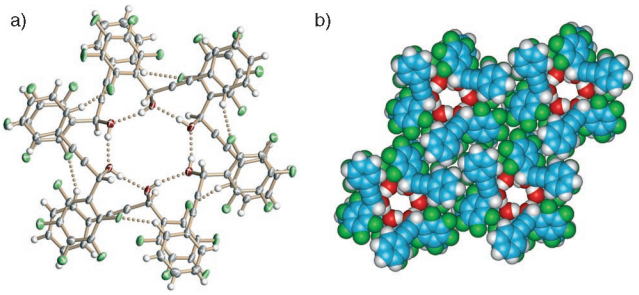
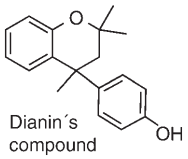


Figure 1. a) The network of O–H···O hydrogen bonds, face-to-face π–π stacking interactions, and C–H···F hydrogen bonds that cooperatively form the hexameric structure of *rac*-**1**. b) Channels formed along the crystallographic *a* axis.

formed by alternating *R* and *S* enantiomers (Figure 1). The hexamers are held together by O–H···O hydrogen bonds with O···O donor–acceptor distances of 2.808, 2.771, and 2.777 Å. The pentafluorophenyl and phenyl rings are almost exactly parallel, with an average separation of 3.52 Å between the ring planes. Additional stabilization comes from a network of C–H···F–C hydrogen bonds between the *ortho* C–H groups of the phenyl ring and the *ortho* C–F groups of the pentafluorophenyl ring, with the C···F separations of 3.25, 3.36, and 3.27 Å comparable with analogous distances found in systems with organic fluorine atoms.[6]

The hexameric structures of *rac*-**1** stack with each other along the unit-cell axis with the alternating parallel phenylethynyl–pentafluorophenyl π–π interaction to form infinite channels. In a hexameric unit of *rac*-**1**, three *R* enantiomers are up and three *S* enantiomers are down (Figure 2a). The two stacking hexamers in a channel generate a cage that can include guest molecules, such as dioxane and dichloromethane. Figure 2b is the cross section of one channel in the crystal structure of *rac*-**1** and shows two cages, with each including a dioxane molecule. Figure 2c gives the dimension of two cages in *rac*-**1**. The diameters A and B are 7.85 and 8.35 Å for each cage, respectively.



The supramolecular assembly of *rac*-**1** is similar to that of Dianin's compound.[7] Dianin's compound was found to be able to host a wide range of organic and inorganic guests, such as glycerol, argon, small carbohydrates, and SF_6. It is useful in the storage and transport of volatile species.

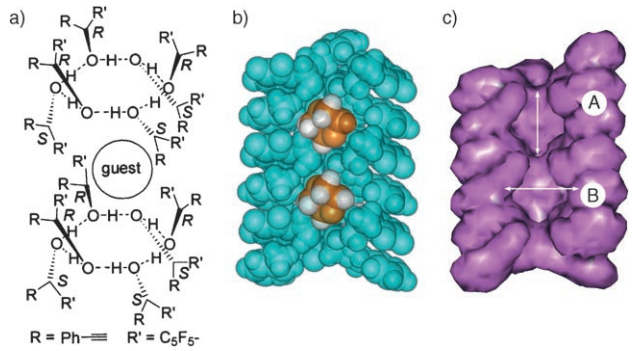
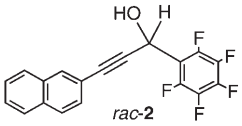


Figure 2. Cages in the crystal structure of *rac*-**1**.

In the same way as the preparation of *rac*-**1**, we also synthesized the racemic compound *rac*-**2** from the addition of



2-ethynylnaphthalene to perfluorobenzaldehyde. The crystal structure of this compound shows the same hexameric channel-like supramolecular structure as *rac*-**1** (Figure 3). The cages inside *rac*-**2** are similar to those of *rac*-**1** (Figure 2c). The diameters A and B are 7.76 and 8.46 Å for each cage in *rac*-**2**, respectively.

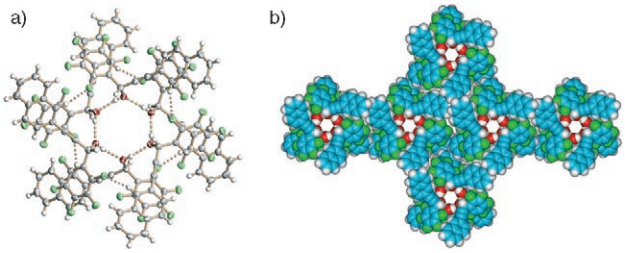
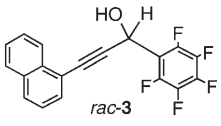


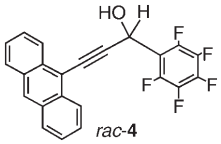
Figure 3. a) The network of O–H···O hydrogen bonds, face-to-face π–π stacking interactions, and C–H···F hydrogen bonds that cooperatively form the hexameric structure of *rac*-**2**. b) Channels formed along the crystallographic *a* axis.

We synthesized the 1-naphthyl-substituted analogue *rac*-**3** to explore the role of the C–H···F–C hydrogen bonds in the supramolecular structures of *rac*-**1** and *rac*-**2**. This compound contains one less C–H group *ortho* to the triple bond than *rac*-**1** and *rac*-**2**, and was thus expected to have less C–H···F–C hydrogen bonds. The X-ray analysis of the single crystal of *rac*-**3** showed no hexameric structure.



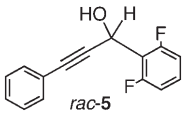
Instead, this compound formed a centrosymmetric *RRSS* tetrameric assembly, stabilized by a network of O–H···O hydrogen bonds in the solid state. No significant C–H···F–C interactions were present in the crystal lattice of *rac*-**3**. Additional stabilization of the tetramer came from the face-to-face π–π stacking interactions involving the naphthylethynyl and pentaflurophenyl units of the adjacent molecules.

We further synthesized the 9-anthrancenyl-substituted compound *rac*-**4**, which contained no C–H group *ortho* to the triple bond. This compound was also unable to form the hexameric structure of *rac*-**1** and *rac*-**2**. Its crystal structure was similar to that of *rac*-**3** with the centrosymmetric *RRSS* tetrameric assembly. Thus, the study of *rac*-**3** and *rac*-**4** demonstrates that the C–F···H–C hydrogen bonds are very important for the hexameric supramolecular structures of *rac*-**1** and *rac*-**2**.



rac-**4**

We synthesized compound *rac*-**5**, which contained a difluorophenyl group in place of the pentafluorophenyl unit in *rac*-**1** and *rac*-**2**, to assess the importance of the π–π attraction of the aryl–perfluorophenyl system. The subsequent structural determination of *rac*-**5** revealed a linear assembly of the opposite enantiomers held together by O–H···O hydrogen bonds rather than the hexameric structure of *rac*-**1** and *rac*-**2**. Some weak C–H···F interactions were also found. However, no apparent stacking forces were observed in this structure.



rac-**5**

Our study of the various diaryl-substituted propargylic alcohols demonstrates that the cooperation of three noncovalent forces, O–H···O hydrogen bonds, aryl–pentafluorobenzene π–π interactions, and C–H···F hydrogen bonds, in *rac*-**1** and *rac*-**2** is crucial for their supramolecular structures. Decreasing any of the forces, as shown in the structures of *rac*-**3**, *rac*-**4**, and *rac*-**5**, leads to a complete disruption of the hexameric channel-like assembly. The supramolecular assembly of *rac*-**1** also exhibits promising host–guest interactions, as evidenced by its complexation with molecules such as dichloromethane and dioxane in the cages between the $(O–H)_6$ planes. Further research is in progress to explore the utility of these structures and functions. We are also preparing the optically active analogues of these compounds by using a catalytic asymmetric synthetic method to construct the optically active supramolecular structures;[8] for example, the combination of (*R*)-**1** with (*S*)-**2** could potentially generate optically active crystals and chiral cages.

Received: April 23, 2006
Published online: July 17, 2006

Keywords: π–π interactions · fluorine · hydrogen bond · propargylic alcohols · supramolecular chemistry

[1] Selected examples: a) *Modern Acetylene Chemistry* (Eds.: P. J. Stang, F. Diederich), VCH, Weinheim, **1995**; b) J. A. Marshall, X. J. Wang, *J. Org. Chem.* **1992**, *57*, 1242–1252; c) M. E. Fox, C. Li, J. P. Marino, Jr., L. E. Overman, *J. Am. Chem. Soc.* **1999**, *121*, 5467–5480; d) A. G. Myers, B. Zheng, *J. Am. Chem. Soc.* **1996**, *118*, 4492–4493; e) B. M. Trost, M. J. Krische, *J. Am. Chem. Soc.* **1999**, *121*, 6131–6141; f) W. R. Roush, R. J. Sciotti, *J. Am. Chem. Soc.* **1994**, *116*, 6457–6458; g) E. J. Corey, K. A. Cimprich, *J. Am. Chem. Soc.* **1994**, *116*, 3151–3152; h) N. K. Anand, E. M. Carreira, *J. Am. Chem. Soc.* **2001**, *123*, 9687–9688; i) L. Pu, *Tetrahedron* **2003**, *59*, 9873–9886.

[2] J. W. Steed, J. L. Atwood, *Supramolecular Chemistry*, Wiley, Chichester, **2000**.

[3] G. R. Desiraju, T. Steiner, *The Weak Hydrogen Bond in Structural Chemistry and Biology*, Oxford University Press, Oxford, **1999**.

[4] a) N. N. L. Madhavi, C. Bilton, J. A. K. Howard, F. H. Allen, A. Nangia, G. R. Desiraju, *New J. Chem.* **2000**, *24*, 1–4; b) C. Bilton, J. A. K. Howard, N. N. L. Manhavi, A. Nangia, G. R. Desiraju, F. H. Allen, C. C. Wilson, *Acta Crystallogr. Sect. B* **2000**, *56*, 1071–1079; c) J. G. Garcia, B. Ramos, A. Rodriguez, *Acta Crystallogr. Sect. C* **1995**, *51*, 2674–2676; d) D. Braga, F. Grepioni, D. Walther, K. Heubach, A. Schmidt, W. Imhof, H. Görls, T. Klettke, *Organometallics* **1997**, *16*, 4910–4919; e) F. H. Allen, J. A. K. Howard, V. J. Hoy, G. R. Desiraju, D. S. Reddy, C. C. Wilson, *J. Am. Chem. Soc.* **1996**, *118*, 4081–4084; f) N. N. L. Madhavi, G. R. Desiraju, C. Bilton, J. A. K. Howard, F. H. Allen, *Acta Crystallogr. Sect. C* **2000**, *56*, 1359–1360; g) R. Banerjee, R. Mondal, J. A. K. Howard, G. R. Desiraju, *Cryst. Growth Des.* **2006**, *6*, 999–1009.

[5] a) C. R. Patrick, G. S. Prosser, *Nature* **1960**, *187*, 1021; b) A. P. West, S. Mecozzi, D. A. Dougherty, *J. Phys. Org. Chem.* **1997**, *10*, 347–350; c) J. H. Williams, J. K. Cockcroft, A. N. Fitch, *Angew. Chem.* **1992**, *104*, 1666–1669; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1655–1657; d) J. H. Williams, *Acc. Chem. Res.* **1993**, *26*, 593–598; e) T. Dahl, *Acta Chem. Scand.* **1994**, *48*, 95–106; f) R. E. Gillard, J. F. Stoddart, A. J. P. White, B. J. Williams, D. J. Williams, *J. Org. Chem.* **1996**, *61*, 4504–4505; g) F. Cozzi, F. Ponizi, R. Annunziata, M. Cinquini, J. S. Siegel, *Angew. Chem.* **1995**, *107*, 1092–1094; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1019–1020; h) G. W. Coates, A. R. Dunn, L. M. Henling, J. W. Ziller, E. B. Lobkovsky, R. H. Grubbs, *J. Am. Chem. Soc.* **1998**, *120*, 3641–3649.

[6] A. Schwarzer, W. Seichter, E. Weber, H. Stoeckli-Evans, M. Losada, J. Hulliger, *CrystEngComm* **2004**, *6*, 567–572.

[7] J. L. Flippen, J. Karle, I. L. Karle, *J. Am. Chem. Soc.* **1970**, *92*, 3749–3655.

[8] G. Gao, R.-G. Xie, L. Pu, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5417–5420.

