Pergamon

Tetrahedron Letters, Vol. 37, No. 14, pp. 2327-2330, 1996
Copyright © 1996 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4039/96 $15.00 + 0.00

S0040-4039(96)00287-0

LINKED BIS-ISOPHTHALIC ACID DERIVATIVES AS BUILDING BLOCKS IN THE DESIGN OF SELF-ASSEMBLING STRUCTURES

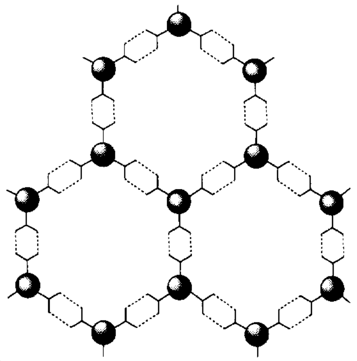
Abdullah Zafar, Ji Yang, Steven J. Geib and Andrew D. Hamilton*

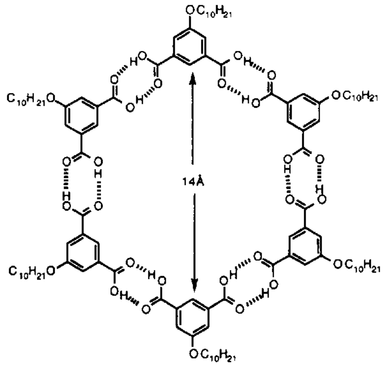
Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

Abstract: In this paper we show that linked bis-isophthalic acid derivatives form ordered molecular structures in the solid state. The key organizing interactions are hydrogen bonds between the isophthalate carboxylic acid substituents on adjacent molecules or to methanol solvent. NMR investigations suggest that alternative aggregates form in solution.
Copyright © 1996 Elsevier Science Ltd

There is presently intense interest in the design of small organic subunits that can self-assemble into ordered molecular aggregates both in solution and in the solid state.[1] Particular attention has been focused on the use of complementary hydrogen bonding interactions as a means of directing and stabilizing the relative orientation of components within the aggregate.[2] In crystal engineering an important goal is the development of solids which contain ordered cavities or channels within the lattice.[3] Such self-assembled, porous structures have the potential for reversible inclusion of organic guests without loss of cavity structure in a manner reminiscent of zeolites.[4] An interesting approach to this problem is suggested by the well-known crystal structure of benzene-1,3,5-tricarboxylic acid (trimesic acid) which forms a hexagonal lattice arrangement in which hydrogen bonds between carboxylic acid groups lead to the formation of cavities defined by six trimesate molecules, as in **1**.[5] The structure is highly catenated with three hexagonal aggregates interpenetrating through each cavity.

We recently introduced[6] 5-substituted isophthalic acid derivatives as key building blocks in the formation of similar cyclic hexameric aggregates (e.g. **2**).[7] A central cavity 14Å in diameter is formed in the aggregate but, instead of showing concatenation, the hexamers stack in three repeating layers and form

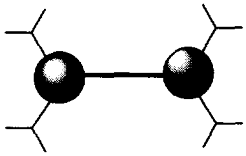

1



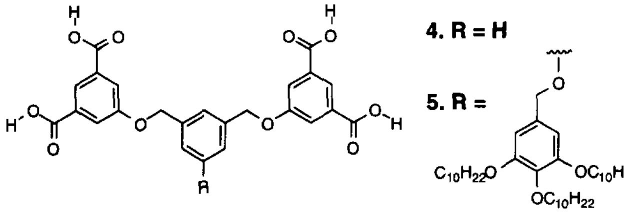
2

channels that encapsulate disordered solvent molecules. An important next step in the generation of more complex aggregates should involve linking two isophthalic acid groups (e.g. **3**) through a suitable spacer.[8]

In this paper we describe the synthesis and structural evaluation, in both the solid state and solution, of a family of bis-isophthalic acid derivatives in which the hydrogen bonding head groups are linked through their 5,5-positions, as in **4** and **5**. We anticipated that the resulting tetraacid might associate in three primary aggregate forms. In the first (Figure 1A) the covalent spacer would act as a link between hydrogen bonded isophthalic acid ribbons to form a layered structure similar to that of trimesic acid (**1**). In the second (Figure 1B) six isophthalic acid dimers would self-associate to form a cylindrical structure composed of two stacked cyclic hexamers (as in **2**) and stabilized by 24 hydrogen bonds. A third possibility (Figure 1C) would be a combination of the two previous forms in which an extensive three dimensional network of hydrogen bonded dimers is formed.



3



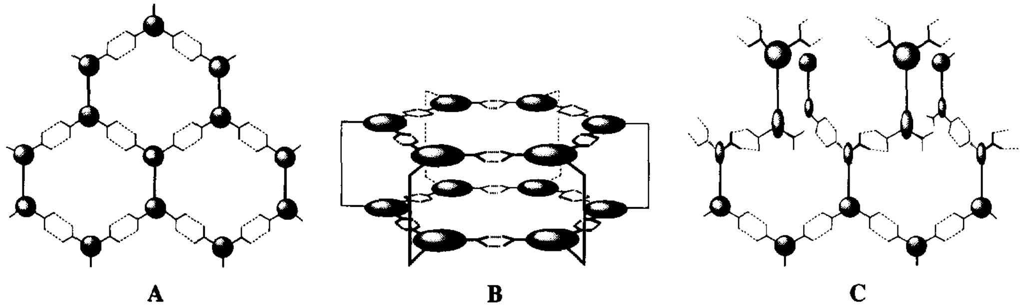


Figure 1. Possible aggregation modes for isophthalic acid dimers.

The key bis-isophthalic acid derivative **4** was prepared from the reaction of dimethyl 5-hydroxyisophthalate with 1,3-bis-(bromomethyl)benzene followed by base-catalyzed deesterification. A more lipophilic derivative **5** was prepared from the reduction of 5-tert-butyldimethylsilyloxyisophthalic acid (with $LiAlH_4$) followed by reaction of the bis-hydroxymethyl derivative with dimethyl 5-hydroxyisophthalate (PPh_3, DEAD) and deprotection (TBAF) to give the tetramethyl 5-hydroxy-derivative of **4**. Further reaction with 1, 2, 3-tridecyloxy-5-bromomethylbenzene (formed from gallic acid by alkylation, $LiAlH_4$ reduction and PBr_3 bromination) using K_2CO_3 as base and deesterification (LiOH, aq. MeOH) gave **5**.

Tetraacid **4** was insoluble in non-polar organic solvents but could be recrystallized from MeOH-DMSO to give large monoclinic crystals. The structure was determined by X-ray crystallography[9] and gave a layer arrangement similar to that shown in Figure 1A. The top view of each layer (Figure 2A) shows a hydrogen bonded network of cavities, each composed of two complete and two partial bis-isophthalic acid

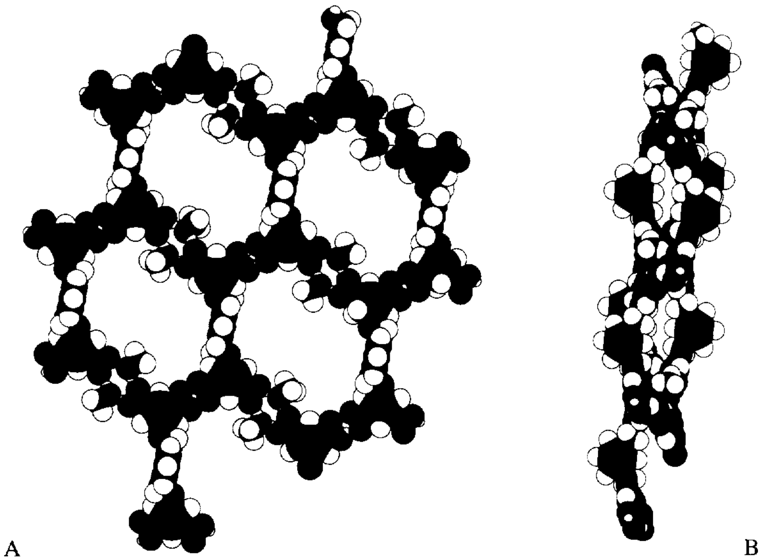


Figure 2. Front (A) and side (B) views of one layer of the crystal packing of **4**.[9]

units. The linking m-xylyl groups project in an alternating up and down arrangement from each layer (Figure 2B). However, a directly hydrogen bonded hexameric aggregate, analogous to those in **1** or **2**, is not formed. In addition to two directly hydrogen bonded carboxylic acid dimers (O....O, 2.61Å), four molecules of methanol are present to form a pair of solvent bridged carboxylic acid dimers (O....O, 2.71 and 2.58Å). The result is a distorted hexagonal cavity with dimensions, measured from isophthalate-2H to opposite isophthalate-2H, of 19.09, 18.30 and 14.30Å. Unlike **2**, no channels are formed with bis-isophthalate **4**. Instead, the larger cavity accommodates stacked xylyl groups from the non-catenated layers directly above and below as well as two isophthalic acid units from two interpenetrating layers (Figure 3).

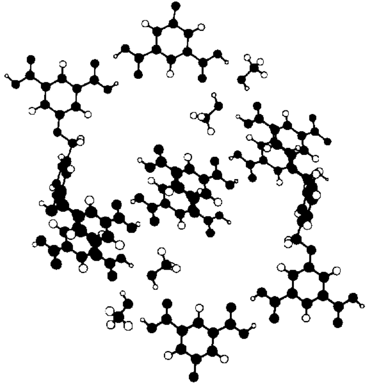


Figure 3. Interpenetrating layers in **4**.

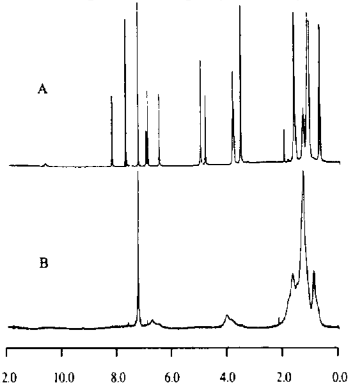


Figure 4. ^{1}H NMR of **5** in A) 20% d_8-THF/CDCl$_3$, B) CDCl$_3$

The solubility of the bis-isophthalic acids could be significantly improved by the attachment of a lipophilic substituent into the 5-position of the bridging m-xylyl group, as in **5**. The ^{1}H NMR spectrum of **5** in 20% d_8-THF/$CDCl_3$ (Figure 4A) showed a well-resolved set of peaks that changed little as a function of concentration, suggesting that no aggregation was occurring in this solvent. This is consistent with earlier observations that neutral hydrogen bonding to carboxylic acids is disrupted in THF.[10] In contrast, the ^1H NMR spectrum of **5** at 5mM in $CDCl_3$ is broad and featureless (Figure 4B). Addition of d_8-THF leads to a regeneration of the spectrum in Figure 4A, indicating that in $CDCl_3$ extensive hydrogen bonded aggregation between the bis-isophthalic acid groups is present. At 10mM **5** forms a gel in $CDCl_3$ presumably involving an extensive three dimensional network of the type shown in Figure 1B. The corresponding gel in tetrachloroethane was stable up to 380°C.[11]

Acknowledgments. We thank the National Science Foundation (CHE 9213937) for support of this work.

References

1. For recent reviews see; Lawrence, D. S.; Jiang, T.; Levett, M. *Chem. Rev.* **1995**, *95*, 2229. Whitesides, G. M.; Mathias, J. P.; Seto, C. T. *Science (Washington, D.C.)* **1992**, *254*, 1312. Lindsey, J. S. *New J. Chem.* **1991**, *15*, 153.
2. Desiraju, G. R. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2311. Fredericks, J.; Yang, J.; Geib, S. J.; Hamilton, A. D. *Proc. Indian. Acad. Sci. (Chem. Sci)* **1994**, *106*, 923.
3. For the designed stabilization of cavity structure by hydrogen bonding see, for example; Kimizuka, N.; Fujikawa, S.; Kuwahara, H.; Kunitake, T.; Marsh, A.; Lehn, J. M. *J. Chem. Soc. Chem. Commun.* **1995**, 2103. Wang, X.; Simarel, M.; Wuest, J. D. *J. Am. Chem. Soc.* **1994**, *116*, 12119. Mahdyarfar, A.; Harris, K. D. *J. Chem. Soc. Chem. Commun.* **1993**, 51-3. By metal chelation see; Venkataraman, D.; Gardner, G. B.; Lee, S.; Moore, J. S. *J. Am. Chem. Soc.* **1995**, *117*, 11600. Fujita, M.; Kwon, Y. J.; Washizu, S.; Ogura, K. *J. Am. Chem. Soc.* **1994**, *116* 1151.
4. Müller, A.; Reuter, H.; Dillinger, S. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2328. MacNicol, D. D. In *Inclusion Compounds;* Atwood, J. L.; Davies, J.E.D.; MacNicol, D.D., Eds.; Academic Press: London, 1984; Vol. 2, pp 1-45.
5. For a recent extensive discussion of the crystal packing behavior of trimesic acid and its derivatives see Herbstein, F. H. in *Comprehensive Supramolecular Chemistry*, Pergamon Press, Oxford. Volume 6. In Press. See also, Duchamp, D. J.; Marsh, R. E. *Acta. Cryst.* **1969**, *B25*, 5.
6. Yang, J.; Marendaz, J. L.; Geib, S. J.; Hamilton, A. D. *Tetrahedron Lett.* **1994**, 3665.
7. For a related approach see; Valiyaveetil, S.; Erkelmann, V.; Müllen, K. *J. Chem. Soc. Chem. Commun.* **1994**, 2097.
8. Yang, J.; Zafar, A.; Marendez, J.-L.; Geib, S. J.; Hamilton, A. D. in *Supramolecular Stereochemistry,* Siegel, J. S. Ed.; Kluwer: Dordrecht, 1995, pp 141-146.
9. Crystal Data for $C_{26}H_{26}O_{12}$: monoclinic, $C\,2/c$, $a = 21.565(10)$, $b = 13.388(7)$, $c = 8.898(4)$ Å, $\beta = 92.04(4)$, $V = 2567(2)$ Å^3, $Z = 4$, $D_c = 1.373$ Mg m^{-3}, 293K. A Siemans P3 diffractometer was used to collect 2390 data points of which 2029 independent data points were used in the solution and refinement. X-ray data were corrected for absorbtion (λ(MoKα) =0.71073 Å). Structure was solved by direct methods which located all non-hydrogen atoms. Hydrogen atom positions were calculated (d(C-H) = 0.96 Å). Structure refined to $R_F = 4.52\%$ and $R_{WF} = 9.57\%$; $GOF = 1.055$, highest final difference peak, 0.22 e/Å^3.
10. Fan, E.; Hamilton, A.D.; van Arman, S. *J. Am. Chem. Soc.* **1993**, *115*, 369.
11. For other studies on hydrogen bonded self-assembly in solution; Sessler, J. L.; Magda, D.; Furuta, H. *J. Org. Chem.* **1992**, *57*, 818. Zimmerman, S. C.; Duerr, B. F. *J. Org. Chem.* **1992**, *57*, 2215. Gallant, M.; Viet, M. T. P.; Wuest, J. D. *J. Org. Chem.* **1991**, *56*, 2284. Wyler, R.; de Mendoza, J.; Rebek, J. Jr., *Angew. Chem. Int. Ed.* **1993**, *32*, 1699. Mathias, J. P.; Simanek, E. E.; Seto, C. T.; Whitesides, G. M. *Angew. Chem. Int. Ed.* **1993**, *32*, 1766. Bonar-Law, R. P.; Sanders, J. K. M. *Tetrahedron Lett.* **1993**, 1677. Seto, C. T.; Whitesides, G. M. *J. Am. Chem. Soc.* **1993**, *115*, 1330. Bonazzi, S.; DeMorais, M. M.; Gottarelli, G.; Mariani, P.; Spada, G. P. *Angew. Chem. Int. Ed.* **1993**, *32*, 248. Drain, C. M.; Fischer, R.; Nolen, E. G.; Lehn, J. M. *J. Chem. Soc. Chem. Commun.* **1993**, 243.

Note added in press. While this paper was under review a report describing related bis-isophthalic acid derivatives appeared; Kolotuchin, S. V.; Fenlon, E. E.; Wilson, S. R.; Loweth, C. J.; Zimmerman, S. C. *Angew. Chem. Int. Ed.* **1995**, *34*, 2654.

(*Received in USA* 10 *January* 1996; *accepted* 30 *January* 1996)