J|A|C|S
COMMUNICATIONS

Published on Web 07/31/2009

Supramolecular Rhombic Grids Formed from Bimolecular Building Blocks

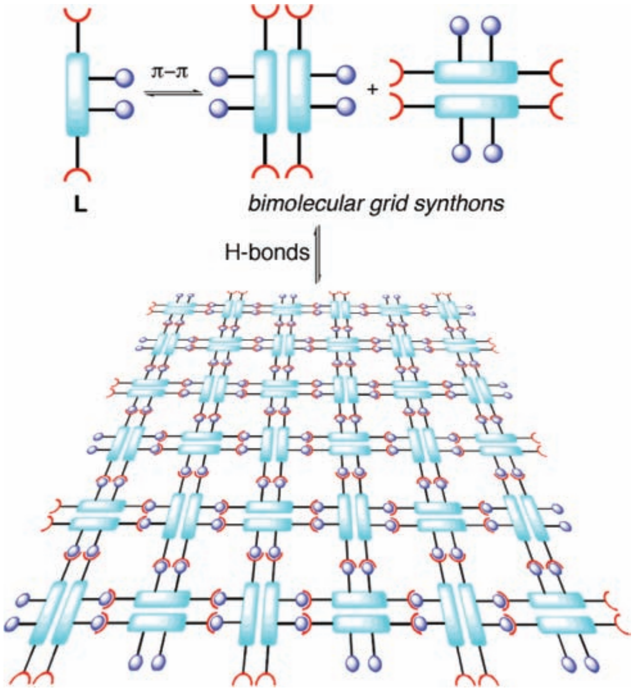
Neng-Fang She,† Meng Gao,† Xiang-Gao Meng,† Guang-Fu Yang,† Johannes A. A. W. Elemans,‡
An-Xin Wu,*,† and Lyle Isaacs*,§

Key Laboratory of Pesticide & Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University, Hubei, Wuhan 430079, P. R. China, Institute for Molecules and Materials, Radboud University Nijmegen, Toernooiveld 1, 6525 ED Nijmegen, The Netherlands, and Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland 20742

Received June 16, 2009; E-mail: chwuax@mail.ccnu.edu.cn; LIsaacs@umd.edu

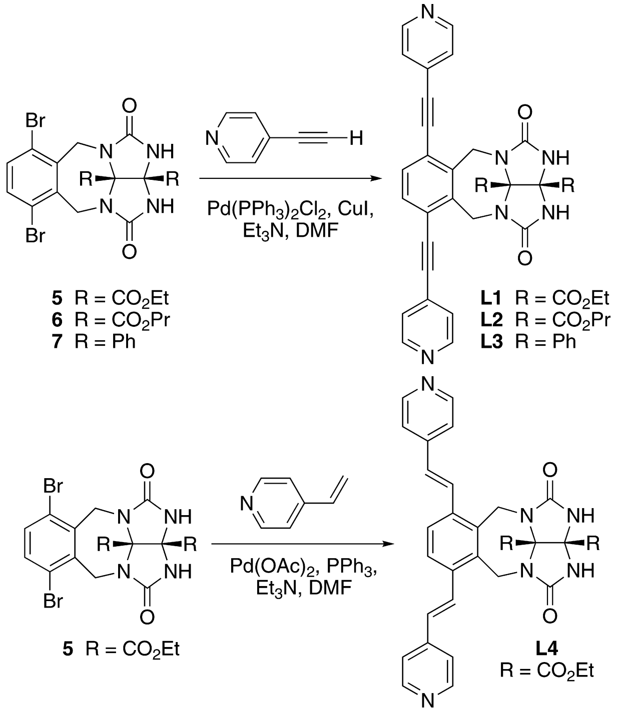
Crystal engineering is blossoming as a powerful strategy for the construction of functional materials for use in application areas as diverse as nonlinear optics, drug delivery, and energy storage.[1] To achieve proper function of the crystalline material, it is necessary to precisely position the component molecules within the crystal lattice by means of appropriate noncovalent interactions between molecules. Among the common noncovalent interactions, hydrogen bonds and coordination interactions have been extensively employed because of their strength and high directionality. In contrast, the use of weaker and less highly directional forces, especially $\pi-\pi$ interactions, have remained challenging to employ in a predictable manner.[2] In this paper, we demonstrate that increasing the π surface area of suitable building blocks results in a concomitant increase in the free energy of the resulting $\pi-\pi$ interactions to a point where such building blocks can be used in programmed assembly processes to build up supramolecular rhombic grids.

Scheme 1. Schematic Representation of the Buildup of a Grid Network Structure from **L**



For our initial demonstration of this concept, we decided to target the formation of noninterpenetrated grid networks, which are of great interest because of the range of applications enabled by selective guest inclusion. To date, grid networks have been constructed using either metal−ligand interactions or hydrogen bonds.[3,4] Although H-bonded grid networks have been prepared in single- or multicomponent processes by the use of templating guests,[5] their preparation from a single component in a nontemplated manner is rare.[6] Conceptually, we decided to target a set of compounds (**L**) which contain π surfaces (aqua), H-bond donors (blue spheres), and H-bond acceptors (red semicircles), as shown in Scheme 1. We planned that **L** would undergo dimerization by $\pi-\pi$ interactions to generate bimolecular grid synthons (**L**$_2$). The bimolecular grid synthons, which feature orthogonal donor−donor (DD) and acceptor−acceptor (AA) H-bond arrays, should then undergo H-bond-mediated assembly to form the desired grid network (Scheme 1).

Scheme 2. Supramolecular Synthons (**L1**−**L4**) and Synthetic Intermediates (**5**−**7**) Used in This Study



To implement the strategy outlined in Scheme 1, we designed compounds **L1**−**L4** (Scheme 2). Compounds **L1**−**L4** are based on the well-known glycoluril scaffold, with its rigid concave geometry and abundance of H-bond-accepting and -donating functionalities, which we and others are developing as a scaffold for crystal

---

† Central China Normal University.
‡ Radboud University Nijmegen.
§ University of Maryland.

10.1021/ja904920r CCC: $40.75

engineering.[7] Compounds **L1**−**L3** (**L4**) contain two 4-ethynylpyridine (4-ethenylpyridine) rings, which define a large electron-poor π surface that holds two excellent H-bond-accepting N atoms oriented collinearly. The two unsubstituted ureidyl N−H groups are directed roughly parallel to one another and define a DD H-bonding array. The synthesis of compounds **L1**−**L3** was achieved by Pd-catalyzed Sonogashira coupling reactions[8] between glycoluril derivatives **5**−**7** and 4-ethynylpyridine in 67−78% yield (Scheme 2).[7c,9] For the preparation of **L4**, we conducted the Pd-catalyzed Heck coupling reaction[10] between **5** and 4-vinylpyridine in 90% yield (Scheme 2). Details of the synthesis and complete characterization of **L1**−**L4** are given in the Supporting Information.

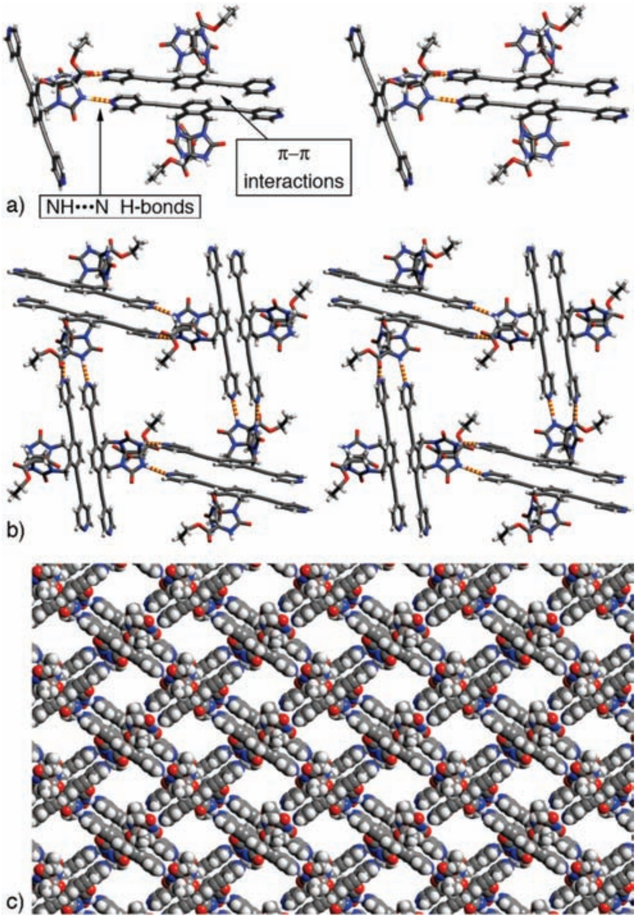


Figure 1. (a) Cross-eyed stereoview of a portion of the X-ray structure of **L1**, illustrating the $\pi-\pi$ stacking and H-bonding interactions. (b) Cross-eyed stereoview of the rhombic-grid subunit built from $(\mathbf{L1}_2)_4$. (c) CPK representation of the two-dimensional rhombic grid formed from **L1**. Color code: C, gray; H, white; N, blue; O, red; H bonds, red-yellow striped.

We were fortunate to obtain X-ray-quality crystals of **L1**−**L4** as plates from 1:1 (v/v) CH_2Cl_2/MeOH solution. The crystal structures of **L1**−**L4** were all solved in the monoclinic system. Figure 1 shows the X-ray structure of **L1**. Figure 1a illustrates the dimerization of **L1** by $\pi-\pi$ interactions between the extended π systems. To maximize the $\pi-\pi$ interactions, the two π systems assume an offset stacked geometry with a separation of ~3.46 Å between the mean planes of the π systems.[11] This $\pi-\pi$ stacking interaction occurs between the convex faces rather than within the concave pseudocavity of molecular-clip building block **L1**. Figure 1a also illustrates how this bimolecular grid synthon ($\mathbf{L1}_2$) engages a third molecule of **L1** through NH•••N hydrogen-bonding interactions.[12] On the basis of Etter's rules[13] we were not surprised that the best H-bond acceptor (e.g., pyridyl N) and the best H-bond donor (e.g., ureidyl N−H) preferentially formed hydrogen bonds. Consequently, the ureidyl C═O H-bond-accepting group, which is so important in the recognition behavior of glycoluril molecular clips,[14] remains unsatisfied in the crystal of **L1**. Figure 1b shows a stereoview of the rhombic subunit of the crystal lattice of **L1** built up from four $\mathbf{L1}_2$ bimolecular grid synthons. The lengths of the sides of these rhomboids are 16.4 Å, and they have diagonals of 21.5 and 24.8 Å. Figure 1c illustrates how these rhombic subunits pack to form a two-dimensional grid network. It is interesting to note that no interpenetration of the network was observed for these crystal forms, despite their large grid size.[15] The rhombic grids pack on top of each other with a slipped geometry stabilized by weak C−H•••O interactions.[16]

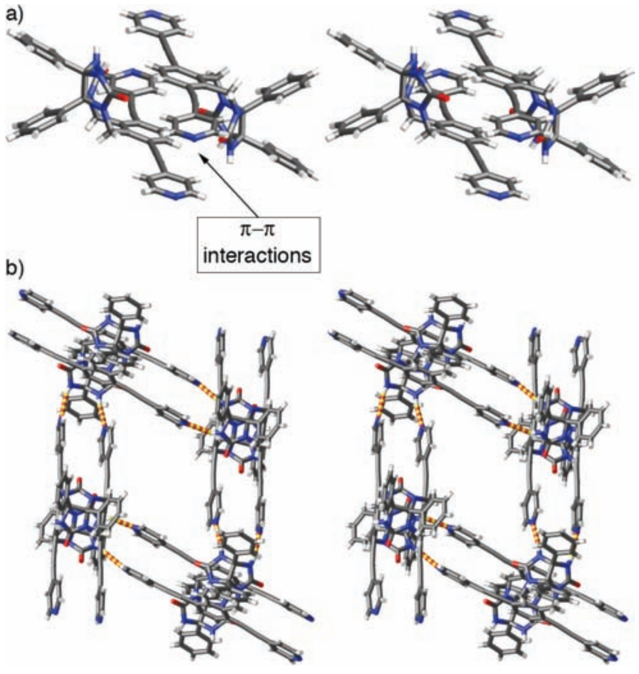


Figure 2. (a) Cross-eyed stereoview of $\mathbf{L3}_2$ from the X-ray structure of **L3**, illustrating the concave-face $\pi-\pi$ stacking interaction. (b) Cross-eyed stereoview of the rhombic grid subunit built from $(\mathbf{L3}_2)_4$. Color code: C, gray; H, white; N, blue; O, red; H bonds, red-yellow striped.

In order to establish the robustness of the rhombic grid motif, we investigated the X-ray crystal structures of **L2**−**L4**. Compound **L2** differs from **L1** in the length of the alkyl ester functional group. Not surprisingly, **L2** also crystallizes in the form of a rhombic grid. The side lengths of the rhomboids are 16.6 Å, and the lengths of the diagonals are 22.2 and 24.7 Å. We next examined the X-ray crystal structure of **L3**, which contains Ph rings on the convex face of the molecule. Even in the presence of these Ph groups, which might be expected to compete for $\pi-\pi$ interactions with the bis(ethynylpyridyl)-substituted *o*-xylylene sidewall, **L3** reliably forms a rhombic grid network. The dimensions of this rhombic grid (side length = 13.5 Å; diagonals = 15.4 and 22.1 Å) are somewhat smaller than those observed for **L1** and **L2**. Figure 2 shows a stereoview of the rhombic subunit of the crystalline form of **L3**. In contrast to the assemblies formed from **L1** and **L2**, **L3** undergoes initial dimerization by $\pi-\pi$ interactions between the π surfaces on the concave face of **L3**, yielding bimolecular grid synthon $\mathbf{L3}_2$ (Figure 2a). As for **L1** and **L2**, grid synthon $\mathbf{L3}_2$ then undergoes H-bond-mediated assembly between its DD- and AA-substituted faces to yield a rhombic grid network. The consequence of the $\pi-\pi$ dimerization of **L3** via its concave face is a reduction in the side length of the rhomboid and a concomitant decrease in the size of the holes in the grid network. Similar to **L3**, compound **L4**, with its 4-ethenylpyridine arms, also reliably forms a rhombic grid network via $\pi-\pi$ interactions involving its concave π surface followed by H-bond-mediated oligomerization. The rhombic subunit formed from **L4** has side lengths of 12.4 Å and diagonal dimensions of 16.0 and 18.9 Å.

In conclusion, we have reported the synthesis of glycoluril building blocks **L1**−**L4** and their supramolecular organization into two-dimensional rhombic grids. Such rhombic grids, when grafted to surfaces or organized into porous solids, have promise for the development of materials for controlled sorption and desorption processes such as hydrogen storage, drug delivery, and remediation applications. Beyond the wide range of potential applications for rhombic grid materials, we believe that the construction strategy described herein is significant. Through the use of aromatic walls with large π surfaces and interaction energies, it was possible to predictably promote dimerization of building blocks **L1**−**L4** by $\pi-\pi$ interactions even in the presence of competing aromatic rings. When these robust $\pi-\pi$ interactions are used in combination with NH···N hydrogen-bonding interactions, building blocks **L1**−**L4** reliably deliver the rhombic grid networks. The strength, directionality, and orthogonality of the $\pi-\pi$ and H-bond-mediated assembly steps on a common length scale suggests its description as a programmed self-sorting process.[17] This system presents a clear-cut example of a $\pi-\pi$ interaction system that satisfies Etter's criteria[18] regarding the use of sufficiently strong and directional noncovalent interactions in crystal engineering. Ongoing work aims to use **L1**−**L4** and related compounds in self-assembly processes in homogeneous solution and for solid-state storage and release applications.

Acknowledgment. We thank the National Laboratory of Applied Organic Chemistry, Lanzhou University, and the National Natural Science Foundation of China (Grants 20672042 and 20872042), the Dutch Organization for Scientific Research (Vidi Grant to J.A.A.W.E), and the U.S. National Science Foundation (CHE-0615049 and CHE-0914745) for financial support.

Supporting Information Available: Details of the synthesis, characterization, and X-ray crystal structures (CIF) obtained for **L1**−**L4**. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Desiraju, G. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2311–2327. (b) Hosseini, M. W. *Acc. Chem. Res.* **2005**, *38*, 313–323. (c) Wong, M. C.; Bosshard, C.; Gunter, P. *Adv. Mater.* **1997**, *9*, 837–842. (d) Hollingsworth, M. D. *Science* **2002**, *295*, 2410–2413. (e) Aoyama, Y. *Top. Curr. Chem.* **1998**, *198*, 131–161. (f) Hamilton, T. D.; MacGillivray, L. R. *Adv. Phys. Org. Chem.* **2005**, *40*, 109–152. (g) Garcia-Garibay, M. A. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 10771–10776. (h) Tranchemontagne, D. J.; Ni, Z.; O'Keeffe, M.; Yaghi, O. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 5136–5147. (i) Braga, D.; Brammer, L.; Champness, N. R. *CrystEngComm* **2005**, *7*, 1–19. (j) Holman, K. T.; Pivovar, A. M.; Ward, M. D. *Science* **2001**, *294*, 1907–1911. (k) Dalgarno, S. J.; Thallapally, P. K.; Barbour, L. J.; Atwood, J. L. *Chem. Soc. Rev.* **2007**, *36*, 236–245. (l) Barbour, L. J. *Chem. Commun.* **2006**, 1163–1168. (m) Shan, N.; Zaworotko, M. J. *Drug Discovery Today* **2008**, *13*, 440–446. (n) Desiraju, G. R. *Angew. Chem., Int. Ed.* **2007**, *46*, 8342–8356. (o) Evans, O. R.; Lin, W. *Chem. Mater.* **2001**, *13*, 2705–2712. (p) Wang, Z.; Cohen, S. M. *J. Am. Chem. Soc.* **2007**, *129*, 12368–12369.

(2) (a) Meyer, E. A.; Castellano, R. K.; Diederich, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1210–1250. (b) Waters, M. L. *Curr. Opin. Chem. Biol.* **2002**, *6*, 736–741. (c) Hunter, C. A.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5525–5534. (d) Klarner, F. G.; Kahlert, B. *Acc. Chem. Res.* **2003**, *36*, 919–932.

(3) (a) Fujita, M.; Kwon, Y. J.; Washizu, S.; Ogura, K. *J. Am. Chem. Soc.* **1994**, *116*, 1151–1152. (b) Biradha, K.; Fujita, M. *J. Chem. Soc., Dalton Trans.* **2000**, 3805–3810. (c) Biradha, K.; Hongo, Y.; Fujita, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 3843–3845. (d) Biradha, K.; Fujita, M. *Chem. Commun.* **2001**, 15–16. (e) Maji, T. K.; Ohba, M.; Kitagawa, S. *Inorg. Chem.* **2005**, *44*, 9225–9231. (f) Plater, M. J.; Gelbrich, T.; Hursthouse, M. B.; De Silva, B. M. *CrystEngComm* **2006**, *8*, 895–903.

(4) (a) Dahal, S.; Goldberg, I. *J. Phys. Org. Chem.* **2000**, *13*, 382–387. (b) Holy, P.; Závada, J.; Císarová, I.; Podlaha, J. *Angew. Chem., Int. Ed.* **1999**, *38*, 381–383.

(5) (a) Biradha, K.; Dennis, D.; MacKinnon, V. A.; Sharma, C. V. K.; Zaworotko, M. J. *J. Am. Chem. Soc.* **1998**, *120*, 11894–11903. (b) Zaman, Md. B.; Tomura, M.; Yamashita, Y. *Org. Lett.* **2000**, *2*, 273–275.

(6) Lazar, A.; Danyluk, O.; Suwinska, K.; Perret, F.; Coleman, A. W. *Chem. Commun.* **2006**, 903–905.

(7) (a) Johnson, D. W.; Palmer, L. C.; Hof, F.; Iovine, P. M.; Rebek, J., Jr. *Chem. Commun.* **2002**, 2228–2229. (b) Wu, A.; Fettinger, J. C.; Isaacs, L. *Tetrahedron* **2002**, *58*, 9769–9777. (c) Reek, J. N. H.; Elemans, J. A. A. W.; de Gelder, R.; Beurskens, P. T.; Rowan, A. E.; Nolte, R. J. M. *Tetrahedron* **2003**, *59*, 175–185. (d) She, N.; Meng, X.; Gao, M.; Wu, A.; Isaacs, L. *Chem. Commun.* **2008**, 3133–3135. (e) Kölbel, M.; Menger, F. M. *Chem. Commun.* **2001**, 275–276. (f) Kurth, D. G.; Fromm, K. M.; Lehn, J.-M. *Eur. J. Inorg. Chem.* **2001**, 1523–1526. (g) Moon, K.; Chen, W.-Z.; Ren, T.; Kaifer, A. E. *CrystEngComm* **2003**, *5*, 451–453.

(8) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467–4470. (b) Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627–630.

(9) (a) Wu, A.; Chakraborty, A.; Witt, D.; Lagona, J.; Damkaci, F.; Ofori, M. A.; Chiles, J. K.; Fettinger, J. C.; Isaacs, L. *J. Org. Chem.* **2002**, *67*, 5817–5830. (b) Wang, Y.-Z.; Gao, M.; Cao, L.-P. *Acta Crystallogr.* **2007**, *E63*, o3419.

(10) (a) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146–151. (b) Chang, C. C.; Chen, K. J.; Yu, J. J. *J. Org. Chem.* **1999**, *64*, 5603–5610.

(11) In **L1**, the central aryl ring and the pyridyl arms are approximately coplanar. Each pyridyl ring and *o*-xylylene sidewall lie in an offset face-to-face π-stacked geometry (pyridyl ring centroid−centroid distance, 3.82 Å; aryl ring centroid−centroid distance, 3.94 Å).

(12) H-bonding parameters: N5−N2, 2.889(2) Å; H5−N2, 1.961(10) Å; N5−H5−N2, 176(3)°; N6−N1, 2.890(2) Å; H6−N1, 1.979(12) Å; N6−H6−N1, 168(3)°.

(13) Etter, M. V. *Acc. Chem. Res.* **1990**, *23*, 120–126.

(14) Rowan, A. E.; Elemans, J. A. A. W.; Nolte, R. J. M. *Acc. Chem. Res.* **1999**, *32*, 995–1006.

(15) (a) Hirsch, K. A.; Wilson, S. R.; Moore, J. S. *Chem.*−*Eur. J.* **1997**, *3*, 765–771. (b) Kumar, D. K.; Jose, D. A.; Das, A.; Dastidar, P. *Inorg. Chem.* **2005**, *44*, 6933–6935.

(16) The ester and phenyl substituents from a given layer protrude into the cavities on the adjacent layers, thereby producing a close-packed structure with no volume available for guest binding.

(17) (a) Wu, A.; Isaacs, L. *J. Am. Chem. Soc.* **2003**, *125*, 4831–4835. (b) Wang, F.; Han, C.; He, C.; Zhou, Q.; Zhang, J.; Wang, C.; Li, N.; Huang, F. *J. Am. Chem. Soc.* **2008**, *130*, 11254–11255. (c) Lin, J.-B.; Xu, X.-N.; Jiang, X.-K.; Li, Z.-T. *J. Org. Chem.* **2008**, *73*, 9403–9410. (d) Jiang, W.; Winkler, H. D. F.; Schalley, C. A. *J. Am. Chem. Soc.* **2008**, *130*, 13852–13853.

(18) In ref 13, Etter made the following suggestion: "Other intermolecular interactions that occur in organic systems may also be candidates for 'intermolecular syntheses' when they are sufficiently strong and sufficiently directional to give rise to recognizable and reproducible molecular assemblies."

JA904920R