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ARTICLE TYPE

Dimeric Packing of Molecular Clips Induced by Interactions Between π-Systems

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In order to investigate the self-association of asymmetric glycoluril clips, compounds **1**-**7** with a common *p*-dimethoxy-*o*-xylylene ring sidewall were synthesized and their structures were analyzed by X-ray crystallography. As expected, the clip molecules formed dimers promoted by π-π interactions between their aromatic sidewalls. Interestingly, the nature of the substitutents on the differentially substituted sidewall caused appreciable differences in the observed dimerization motifs in the crystalline state. For example, **1** and **2** adopted the *out-out* dimeric motif with its diaromatic-vinyl-*o*-xylylene rings bound in the cleft of the neighboring molecular clip by π–π stacking interactions. In contrast, compounds **3** – **7** adopted the *in-in* dimeric motif in the solid state, in which the *p*-dimethoxy-*o*-xylylene rings were sandwiched by the adjacent clip driven by π–π and OCH_3•••O=C H-bonding interactions. X-ray crystallographic analysis of compounds **1** – **7** indicates that the conformational preferences induced by the linking group between the *o*-xylylene sidewalls and the terminal aromatic rings plays a critical role in determining which mode of dimerization (*in-in* versus *out-out*) and three dimensional packing predominates. The ability to control the selective dimerization of asymmetric glycoluril derived molecular clips *via* π–π interactions promises to expand the use of these building blocks to design complex and functional solid state architectures.

INTRODUCTION

A fundamental pursuit of chemists is the delineation of the connection between structure and function. To physical organic chemists these structure property relationships focus on differences in the arrangement of covalent bonds and the resulting changes in molecular properties.[1] For medicinal and biological chemists, the focus is on differences in the arrangements of non-covalent interactions between two or more species in homogenous solution.[2] In recent years, chemists with interests in materials have sought to control the three dimensional arrangement in the solid state to create materials with enhanced solubility,[3] nonlinear optical properties,[4] gas sorption capacity,[5] and energy conversion.[6] All of these applications rely on our ability to understand and predictably control non-covalent interactions between molecules. Accordingly, supramolecular chemists and crystal engineers[7] have focused on learning how to control the three dimensional ordering in crystals by using non-covalent interactions like H-bonding,[8] coordination interactions,[9] π–π interactions,[10] toward the creation of complicated supramolecular architectures from small molecule building blocks.[11] Our interests in this area have focused on the development of glycoluril derived supramolecular synthons.

Glycoluril and its derivatives are widely used as building blocks to construct a variety of more sophisticated structures and supramolecular objects.[12] Among these versatile structures, glycoluril-derived molecular clips containing a single glycoluril unit and two aromatic sidewalls has attracted substantial scientific attention due to their diverse function including acting as excellent receptors,[13,14] as components of supramolecular vesicles and organogel,[15] and as enzyme mimics.[16] In addition, due to the curved but rigid skeleton and their ability to engage in a diverse array of non-covalent interactions within their concavity, on their convex surfaces, and at their ureidyl C=O groups, these structures have also emerged as a versatile building block for studies of crystal engineering.[17,18,19] Most relevant to their use as building blocks for crystal engineering is the fact that the distance between the two aromatic sidewalls of glycoluril molecular clips generally fall in the range of 6.1 – 7.1 Å, which allows them to engage in π–π interactions with aromatic guest molecules. Because glycoluril-derived molecular clips contain two aromatic sidewalls they readily undergo dimerization both in solution and the solid state driven by the reciprocal inclusion of an aromatic sidewall in the cavity of the opposing clips.[13,14,17,18,19,20] Whereas molecular clips that contain two identical sidewalls can form only a single dimer driven by π–π interactions, asymmetric clips that contain two different aromatic sidewalls may adopt three different diastereomeric homodimers (*in-in*, *in-out*, and *out-out*) as shown in Figure 1. In this paper, the *in* or *out* nomenclature refers to the location of the dimethoxy substituted *o*-xylylene sidewall of one clip with respect to the cavity of its dimeric partner.

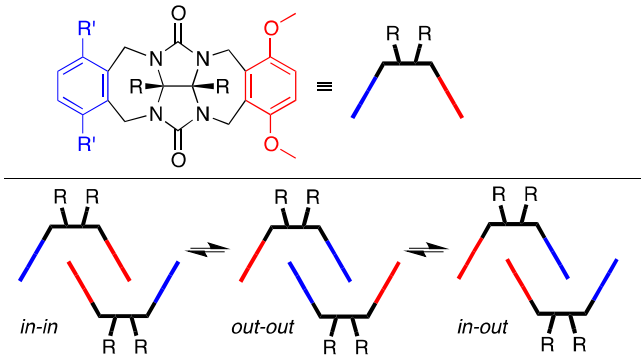


Figure 1. Illustration of the three diastereomeric dimers (*in-in*, *out-out*, *in-out*) that can be formed by dimerization of an asymmetric glycoluril derived molecular clip.

In previously published work, we have found that glycoluril based molecular clips containing a *p*-dimethoxy-*o*-xylylene sidewall preferred to form in-in dimeric motif driven by π–π interactions between the *p*-dimethoxy-*o*-xylylene sidewalls and OCH_3•••O=C H-bonding interactions.[18] A CSD search of the *p*-dimethoxy-*o*-xylylene sidewall containing molecular clip framework retrieved 36 x-ray structures; 13 exist as monomer whereas 22 exist as dimeric entities in the crystal. All of the 22 dimers display the *in-in* motif, and there is no out-out motif observed previously (See Suporting Information for details). In continuation of our work toward the use of glycoluril derived molecular clips as robust synthons for crystal engineering we have used these building blocks to construct one-dimensional chains, molecular bowls, and an artificial bilayer.[19,21] In this paper, we continue along this line of inquiry and report the X-ray crystal structures of seven asymmetric glycoluril based molecular clips which contain a common 3,6-dimethoxy-*o*-xylylene sidewall and a differentially substituted *o*-xylylene sidewall containing expanded aromatic π-surfaces. We analyze the structural features of their extended aromatic sidewalls of **1**–**7** that influence the balance between the *in-in* and the *out-out* dimers in the crystalline state.

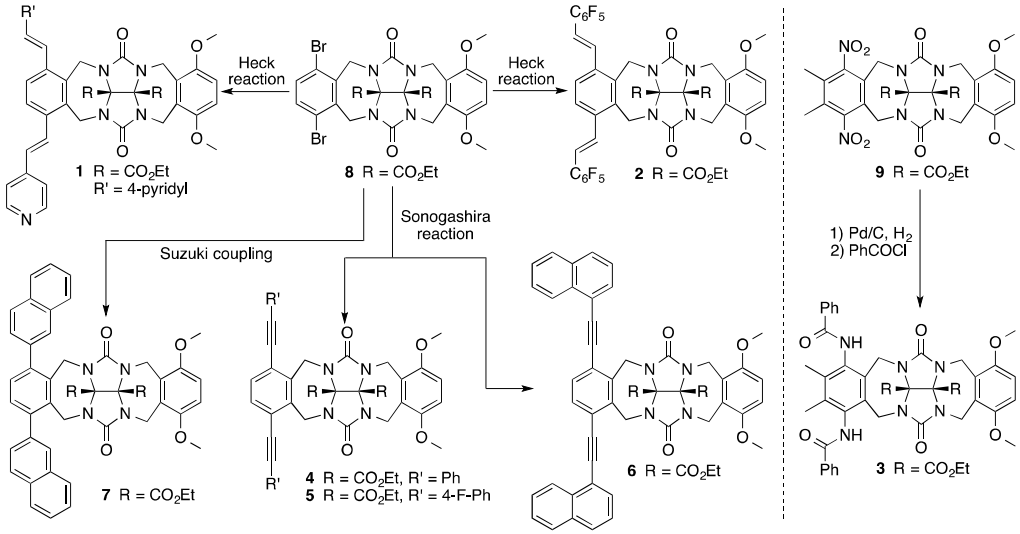
EXPERIMENTAL SECTION

Materials and Instrumental

The reagents and solvents employed were commercially available and used as received without further purification. DMSO was distilled from CaH_2 immediately before use. NEt_3 was distilled from KOH immediately before use. IR spectra were recorded on a Perkin-Elmer PE-983 infrared spectrometer as KBr pellets over the 4000-400 cm^{-1} range. NMR spectra were recorded on 400 or 600 MHz spectrometers and chemical shifts are reported (δ) in parts per million relative to internal tetramethylsilane (TMS). HRMS were obtained on a Bruker Apex-Ultra 7.0T FTMS equipped with an electrospray source (ESI). Melting points were determined using XT-4 apparatus and were not corrected.

Crystal Growth and X-ray Diffraction Analysis

Crystals of compounds **1** – **7** that were suitable for structure determination by X-ray crystallography were prepared by slow evaporation: **1** from $CHCl_3$ and MeOH, **2** from $CHCl_3$ and MeOH, **3** from $CHCl_3$ and MeOH, **4** from $CHCl_3$, **5** from CH_2Cl_2 and MeOH, **6** from $CHCl_3$ and MeOH, and **7** from $CHCl_3$. Diffraction data for **1**-**7** were collected on a Bruker Apex CCD area detector diffractometer (MoKα radiation, λ = 0.71073 Å) at 100 or 220 K. SMART and SAINT software packages were used for data collection and data integration. Collected data were corrected for absorbance by using SADABS. Structure solution and refinement were carried out with the SHELXTL-PLUS software package and the structure solved by the direct method. Full-matrix least-squares refinement was carried out by minimizing $(Fo^2-Fc^2)^2$.[22] All non-hydrogen atoms were refined anisotropically; hydrogen atoms were located and refined isotropically or assigned isotropic displacement coefficients U(H)=1.2U(N-H) or 1.5U(O-H), and their coordinates were allowed to ride on their respective atoms. The crystal parameters, data collection, and refinement results for all compounds are summarized in Table S1. Crystallographic .cif files (CCDC 992389-992394 and 996879) are available at www.ccdc.cam.ac.uk/data_request/cif or as part of the Supporting Information.



Scheme 1. Synthetic route for the preparation of **1-3**

RESULTS AND DISCUSSION

This results and discussion section is organized as follows. First, we discuss the synthesis of asymmetric molecular clips **1** – **7**. Next, we describe the molecular structure of clips **1** – **7** in the crystal. Subsequently, we present the supramolecular dimeric structures formed by **1** – **7**, their arrangement in the crystalline state, and analyze the factors that lead to the preference for either the *in-in* or the *out-out* dimers.

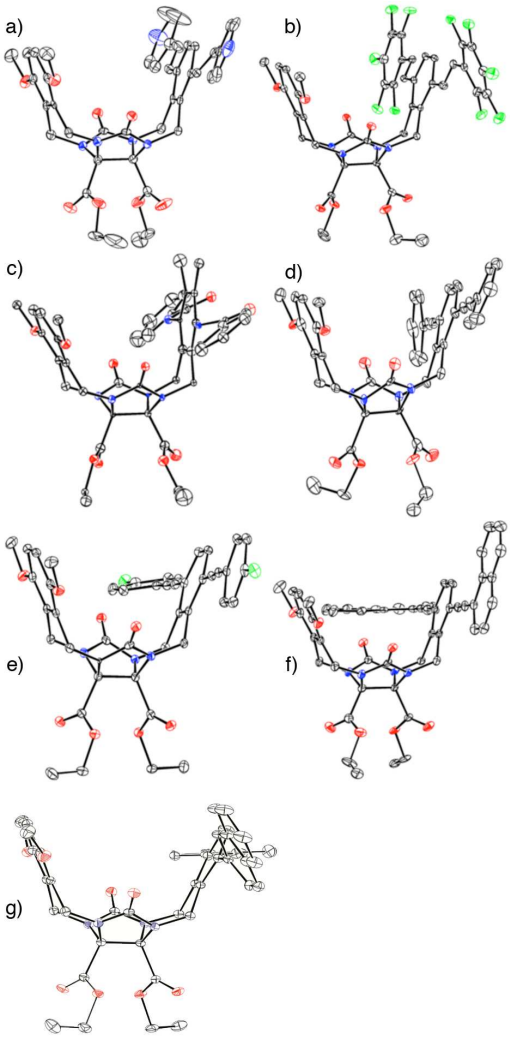


Figure 2. ORTEP plots of the X-ray crystal structures of: a) **1**, b) **2**, c) **3**, d) **4**, e) **5**, f) **6**, g) **7** drawn at the 30% probability levels. Color coding: C, gray; F, green; N, blue; O, red. Hydrogen atoms have been omitted for clarity.

Design and Synthesis of Asymmetric Molecular Clips 1 – 7. As a starting material for asymmetric molecular clips **1**, **2**, and **4** – **7** we selected compound **8**[23] bearing one dimethoxy-*o*-xylylene and one dibromo-*o*-xylylene sidewall and CO_2Et solubilizing groups (Scheme 1). We selected the CO_2Et derived clips for these studies because of their generally good solubility in nonpolar organic solvents as well as to avoid the competing π-π stacking motifs possible with clips derived from diphenyl glycoluril. The Heck reaction between **8** and 4-vinylpyridine or pentafluoro styrene smoothly delivered molecular clips **1** (75%) and **2** (61%) in good yield. We employed the Sonogashira reaction between **8** and phenylacetylene, 4-fluorophenylacetylene, or 1-ethynylnaphthalene to deliver molecular clips **4** (56%), **5** (65%), and **6** (66%) in good yields. Molecular clip **7** was obtained in 90% yield by the Suzuki coupling between **8** and naphthalene-2-boronic acid. To prepare molecular clip **3** we reduced the known molecular clip **9**[24] followed by acylation with benzoyl chloride to yield **3** in 85% yield. The ^1H, ^{13}C, and mass spectra recorded for these new compounds are fully consistent with the depicted structures (Supporting Information).

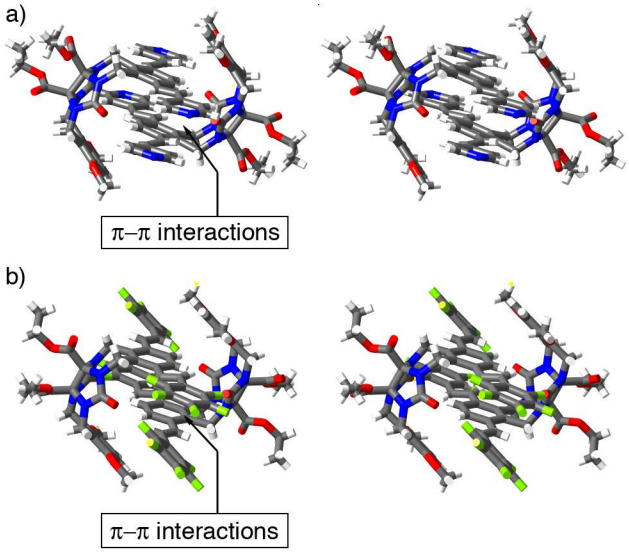


Figure 3. Stereoscopic representations of the dimeric packing unit in the X-ray crystal structures of a) **1** and b) **2**. Color coding: C, gray; F, green; N, blue; O, red.

Molecular Structure of 1 – 7 in the Crystal. We were fortunate to obtain single crystals of **1** – **7** that were suitable for X-ray crystallographic structure determination by recrystallization from $CHCl_3$, CH_2Cl_2, and MeOH, or mixtures thereof. Figure 2 shows the ORTEP plots for the molecular components **1** – **7** from the X-ray structures. The bond lengths, bond angles, and other geometrical features of **1** – **7** proved similar to those reported previously.[13,14,15,16,17,18,19,21,23,25,26] For example, the crystal structure were all present in their *aa* conformation[14,25] and the *cis*-fused five-membered rings bearing CO_2Et groups were seen to enforce their cup-shaped geometry. The angle between the mean planes defined by the *o*-xylylene sidewalls were 62.50–65.84° and the distances between the centroids of the substituted *o*-xylylene rings ranged from 6.2 to 6.6 Å, which is appropriate for the formation of dimers promoted by π–π interactions between the inner walls of each clip of the dimer.

The *out-out* dimerization of compounds 1 and 2. The molecular structure of compound **1** features two vinylpyridyl units connected to the *o*-xylylene ring of the sidewall of the glycoluril derived molecular clip. We were able to obtain single crystals of **1** that proved suitable for X-ray crystal structure determination by slow evaporation of its $CHCl_3$ solution. As seen in Figure 3a, two molecules of **1** form a dimer due to the

formation of offset π–π interactions between all three of the aromatic rings of the extended aromatic sidewall. The distance between the mean planes of the pairs of aromatic rings involved in π···π interactions were 3.362 Å (R(C8-C13)•••R(C8-13)), 3.350 Å (R(N2-C16-C20)•••R(N1-C1-C5)) and 3.382 Å (R(N1-C1-C5)•••R(N2-C16-C20)), respectively. The corresponding dihedral angles between the related aromatic rings were 0.00˚, 7.25˚ and 7.25˚, which indicated that the π-π connected aromatic rings are nearly coplanar. The dimerization also appears to benefit from C-H•••O=C interactions (distance: 3.212 and 3.293 Å; C-H••O angle: 136 and 119˚) between pyridyl C-H and alkenyl C-H groups of the sidewall and the ureidyl C=O group of its dimeric partner. As commonly observed with these glycoluril derived molecular clips, the outer and inner Ar sidewalls are not coplanar. In the crystal, these dimers **1•1** arrange themselves into tapes (Figure 4a) that extend along the b-axis driven by interactions between the external dimethoxy-*o*-xylylene walls (interplanar separation: 3.563 Å). In particular, C-H groups on the convex face of the clip appear to engage in C-H•••π interactions (H to mean plane distance: 2.659 and 2.773 Å) with the adjacent units of dimers **1•1**. These tapes align their long axes in a parallel fashion along the a-axis aided by C-H•••π interaction between one C-H group on the convex face of the extended *o*-xylylene sidewall and a pyridyl ring in an adjacent tape (H to mean plane distance: 2.433 Å) to give slabs; these slabs pack parallel to one another along the c-axis separated by molecules of solvating $CHCl_3$.

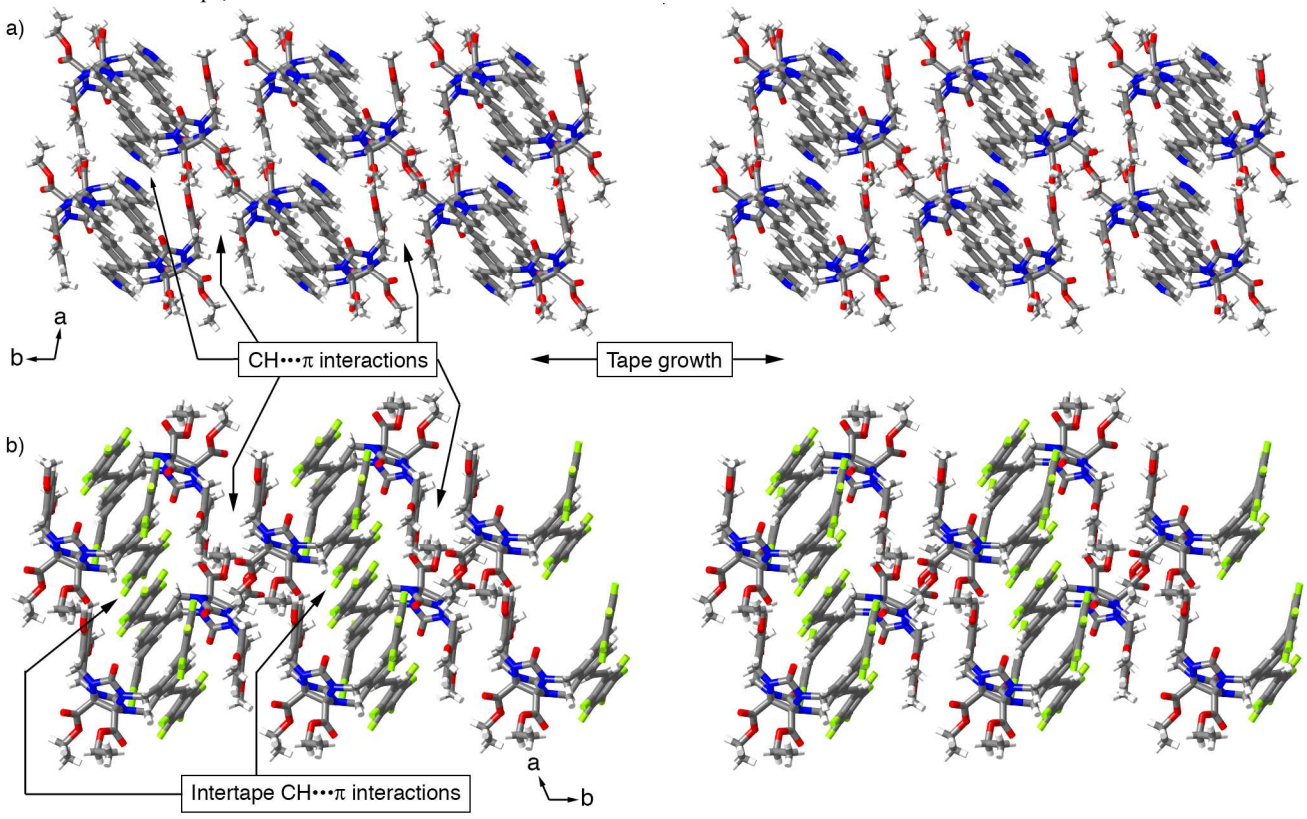


Figure 4. Cross eyed stereoviews of the packing of tapes in the crystal structures of a) **1** and b) **2**. Color coding: C, gray; F, green; N, blue; O, red.

Single crystals of **2** – which features a pentafluorophenylvinyl-o-xylylene sidewall – was obtained by recrystallization from $CHCl_3$. Similar to **1•1**, the X-ray crystal structure of **2** is based on the formation of the *out-out* dimer **2•2** via π–π interactions between the expanded aromatic sidewalls (Figure 3b). The distance between the two mean planes of the *o*-xylylene rings sidewalls were 3.372 Å which represents an ideal π–π stacking distance. The corresponding dihedral angles of the related aromatic rings were 0.00°, 28.47° and 28.47°. The fact that the four terminal C_6F_5 rings in dimer **2•2** are not coplanar will be shown to arise from the three dimensional packing of **2•2** in the crystal as discussed below. The dimerization also benefits from C-H•••O=C interactions between the protons on the *o*-xylylene ring and alkenyl linker with the ureidyl C=O group of its dimeric partner (distances: 3.367 and 3.570 Å; C-H•••O angle: 158 and 130˚). The geometrical characteristics of these π···π interactions are shown in Table 1. Dimers **2•2** pack into tapes along the b-axis driven by CH•••□ (H to mean plane distance: 2.615 and 2.726 Å) and π–π interactions (mean interplanar separation: 3.568 Å) between the dimethoxy-o-xylylene substituted sidewalls (Figure 4b). Interestingly, the packing of these tapes along the a-axis appears to be driven by CH•••π interactions between one of the C_6F_5 rings in one tape and the convex face of the o-xylylene ring of the fluorinated sidewall of a clip in the adjacent tape (H to mean plane distances: 2.561 and 2.773 Å). We believe this is one of the reasons the C_6F_5 rings within dimer **2•2** (Figure 3b) are not coplanar. The resulting slabs of **2•2** dimers oriented in the ab-plane then stack along the c-axis to generate the three dimensional structure of the crystal which results in an offset stacked arrangement between the two out-of-plane C_6F_5 rings.

The *in-in* dimerization of compounds 3-7. To probe the structural features that promoted the *in-in* dimerization observed for **1** and **2** we prepared and solved the X-ray crystal structures for **3** - **7** which differ in the nature of the linking group between the aromatic rings of the extended aromatic wall (e.g. alkene versus amide versus alkyne versus no linker) and the terminal aromatic rings (e.g. phenyl versus fluorophenyl versus naphthyl).

Single crystals of **3** were obtained from $CHCl_3$. As illustrated in Figure 5a, compound **3** adopted an *in-in* dimeric form with its *p*-dimethoxy-*o*-xylylene ring sidewall sandwiched in the neighboring clip. The mean planes of the two internal aromatic rings are separated by 3.359 Å indicating that these aromatic rings benefit from direct π-π interactions in the dimerization (Table 1). The 1,4-dimethoxy-*o*-xylylene wall promotes the *in-in* dimerization because of OCH_3•••O=C H-bonding interactions (C•••O distances: 3.603 and 3.570 Å; C-H•••O angles: 123 and 132˚). The amide linking groups are rotated out-of-plane of the *o*-xylylene sidewall in order to engage in intramolecular NH•••O H-bonding interactions with the ureidyl C=O groups. Two of the solvating $CHCl_3$ molecules form H-bonds to the amide C=O groups of each dimer **3•3** (C•••O distance: 3.055 Å; C-H•••O angle: 176˚). The terminal Ph rings remain conjugated with the amide group and are thus roughly orthogonal to the aromatic sidewall. These out-of-plane terminal Ph rings sterically prevent the usual formation of tapes driven by CH•••O and π–π interactions *via* a head to tail arrangement of dimeric units. Accordingly, units of **3•3** pack along the a-axis in the head-to-head manner shown in Figure 5a mediated by interactions between the CH_3-groups on the tips of the aromatic rings of **3•3**. The linear assemblies of **3•3** pack with their long axes parallel along the c-axis mediated by interdigitation of the CO_2Et groups to form sheets. Finally, these sheets pack parallel to one another – separated by solvating $CHCl_3$ groups – along the b-axis that appears to be promoted by π–π interactions (mean interplanar separation = 3.31 Å) between pendant Ph rings in adjacent sheets as depicted in Figure 5b. Compound **4** features two phenylethynyl arms on one of its sidewalls. Similar to **3**, compound **4** undergoes dimerization to yield the *in-in* dimer **4•4** (Figure 6). This dimerization benefits from π–π interactions between the inside dimethoxy-*o*-xylylene rings (mean plane separation: 3.404 Å) and OCH_3•••O=C H-bonding interactions (C•••O distances: 3.288 and 3.176 Å; C-H•••O angles: 127 and 126˚). The pendant phenylethynyl substituents are almost coplanar (18.0 and 7.4˚) with respect to the central *o*-xylylene sidewall. Somewhat surprisingly, the dimeric building blocks **4•4** do not grow by π–π interactions between the extended π-surfaces of these building blocks. Instead they arrange themselves into rods oriented along the a-axis as shown in Figure 6 perhaps benefitting from pairs of weak but reciprocal C-H•••π interactions (C-H•••π distances: 2.908 and 3.041 Å) between the convex face of one dimethoxy-o-xylylene sidewall and a C≡CPh sidearm on an adjacent **4•4** dimer. These rods align themselves with their long axes parallel to one another in the ab-plane to form sheets in a process that results in packing and interdigitation of the pendant Ph groups and one of the CO_2Et groups on the convex face of **4**. No direct π–π or CH•••π interactions are noted. Finally, these sheets stack along the c-axis. Alternating layers of the sheets are rotated with respect to one another.

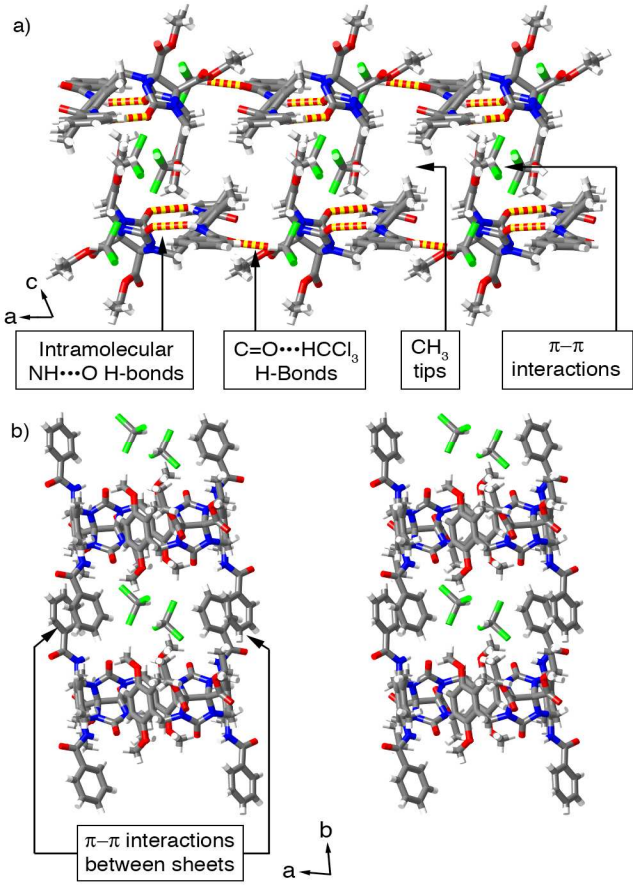


Figure 5. a) Crystal packing of units of **3•3** along the a-axis. b) Stereoview of the intersheet π–π interactions in the crystal structure of **3**. Color coding: C, gray; F, green; N, blue; O, red.

Single crystals of **5** were obtained from mixtures of CH_2Cl_2 and MeOH. The most relevant structural feature of monomeric **5** is that one of its 4-fluorophenyl ethynyl arms (C1-C8-F2) is roughly coplanar with the *o*-xylylene sidewall (7.6˚) whereas the second 4-fluorophenyl ethynyl arm (C15-C22-F1) is rotated significantly out-of-plane (59.7˚). Compound **5** – just like compounds **3** and **4** – forms the *in-in* dimer driven by π–π interactions between the internal dimethoxy-*o*-xylylene sidewalls (mean plane separation: 3.492 Å) and OCH_3•••O=C H-bonding interactions (C•••O distances: 3.227 and 3.379 Å; C-H•••O angles: 123 and 132˚) as shown in Figure 7a. In contrast to compounds **1**, **2**, and **3**, compound **5** does not undergo tape formation driven by CH•••π and π–π interactions between the two *o*-xylylene rings, but instead does so by shifting out-of-register such that the in-plane fluorophenyl ring of **5** engages in CH•••π (C-H•••π distances: 2.722 and 2.758 Å) and π–π interactions (mean plane separation: 3.30 Å) with its neighbor and vice versa. In concert, the out-of-plane fluorophenyl ring of **5** engages in two different edge-to-face interactions: a) the C-H groups of the C_6H_4F ring interact with the face of a neighboring dimethoxy-*o*-xylylene sidewall (H to mean plane distance: 2.720 and 2.895 Å, C-H•••Ar angle =135˚), and b) the face of the C_6H_4F interacts with the C-H groups on the *o*-xylylene ring of an adjacent 4-fluorophenyl ethynylated sidewall (H to mean plane distance: 2.642 and 2.846 Å, C-H•••Ar angle = 147^o). The sheets created by these two types of π–π interactions stack along the c-axis

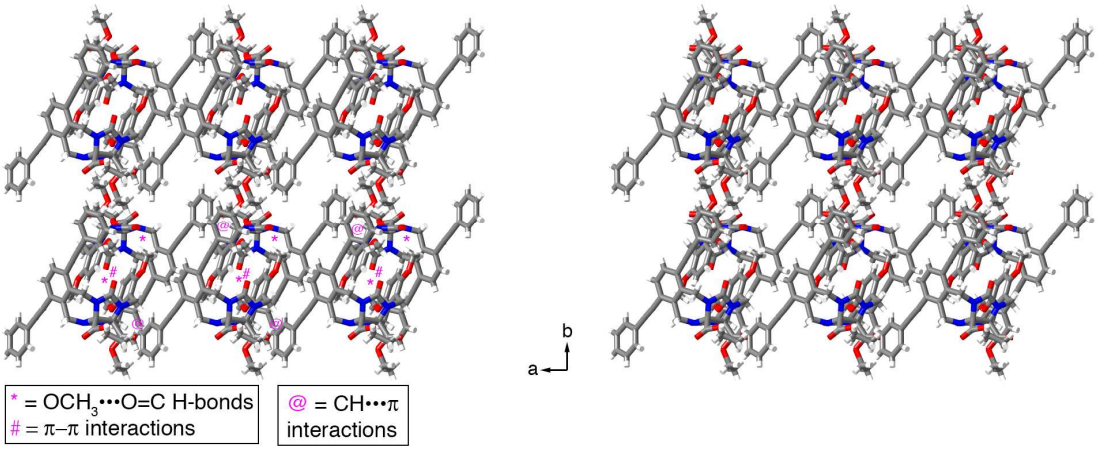


Figure 6. Cross eyed stereoview of the packing of **4•4** in the ab-plane. Color coding: C, gray; H, white; N, blue; O, red.

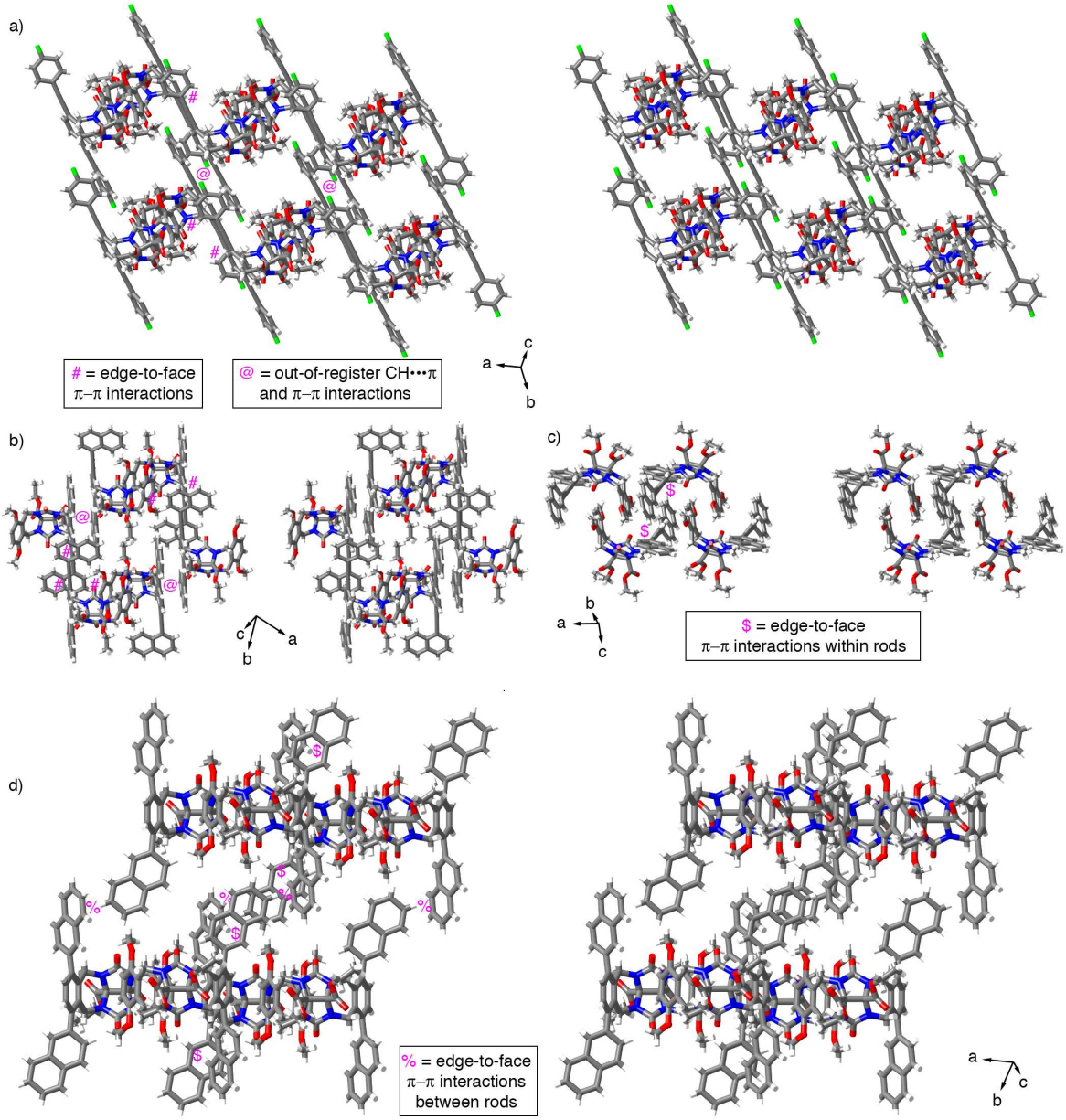


Figure 7. Cross eyed stereoviews of the packing of: a) **5•5**, b) **6•7**, c) tapes of **7•7**, and d) sheets of **7•7** in the ab-plane. Color coding: C, gray; H, white; F, green; N, blue; O, red.

Table 1. Selected Parameters from the X-ray Crystal Structures **1-7.**

	Dimeric motif	Ar•••Ar centroid distance (Å)	Ar•••Ar mean plane angles (˚) in monomer				Ar•••Ar mean plane angles (˚) and separation distances (Å) within the dimer	
			R1-R2	R2-R3	R2-R4	R3-R4	R(i) – R(j) (˚)*	R(i) – R(j) (Å)*
1	*out-out*	6.396	36.16	8.74	6.81	7.25	0.00 (i = j = 2)[a] 7.25 (i = 3, j =4)[a]	3.362, 3, 350, 3.382[a]
2	*out-out*	6.424	37.83	6.41	34.85	28.47	0.00 (i = j = 2)[b] 28.47 (i = 3, j =4)[b]	3.372[b]
3	*in-in*	6.221	30.26	43.65	53.07	9.42	0.00[c]	3.359[c]
4	*in-in*	6.484	38.74	18.00	7.38	24.80	0.02[d]	3.407[d]
5	*in-in*	6.634	42.77	59.68	7.64	67.21	0.00[e]	3.492[e]
6	*in-in*	6.598	41.47	73.16	6.81	78.92	0.00[f]	3.512[f]
7	*in-in*	6.925	49.82	59.40	60.52	60.16	0.00[g]	3.551[g]

R1 = dimethoxy-o-xylylene ring; R2 = o-xylylene ring substituted with extended aromatic arms; R3 and R4 = aromatic rings of extended arms. * i = j = 1 unless otherwise noted. [a]Symmetry codes: (i) 2-X, 2-Y, 1-Z. [b]Symmetry codes: (i) 1-X, 1-Y, 1-Z. [c]Symmetry codes: (i) 2-X, 1-Y, 1-Z. [d]Symmetry codes: (i) 1-X, 1-Y, 2-Z. [e]Symmetry codes: (i) -X, 1-Y, 1-Z. [f]Symmetry codes: (i) 1-X, -Y, 1-Z. [g] Symmetry codes: (i) -X, -Y, 1-Z.

facilitated by the interdigitation of the CO_2Et groups on the convex faces of the **5•5** dimers that compose the sheets.

The X-ray crystal structure of **6** was solved for crystals grown from $CHCl_3$ and MeOH. Similar to compound **5**, one of the 1-napthyl ethynyl arms of monomeric **6** is roughly coplanar with the *o*-xylylene sidewall whereas the second naphthyl ethynyl arm is rotated significantly out-of-plane (Figure 2e). Because the 1-naphthyl ethynyl arms are unsymmetric, the naphthyl groups can be oriented in two possible directions. The in-plane naphthyl arm is oriented away from the cavity of the clip whereas the out-of-plane arm is oriented toward the cavity. Compound **6** forms *in-in* dimeric building blocks (**6•6**) driven by π–π interactions between the dimethoxy-*o*-xylylene sidewalls (mean plane separation: 3.511 Å) and CH•••O interactions (C•••O distances: 3.364 and 3.458 Å; CH•••O angles: 131 and 136˚) between the OCH_3 groups and the ureidyl C=O groups of the opposing clip (Figure 7b). Similar to compound **5**, the dimeric building blocks **6•6** form sheets in the ab-plane driven by CH•••π and π–π interactions. For example, dimeric building blocks **6•6** assemble by π–π (mean plane separation: 3.40 Å) and CH•••π (CH•••π distances: 2.753 and 2.792 Å) interactions in an out of register fashion between the in-plane naphthyl ring of one equivalent of **6•6** and the *o*-xylylene unit of the naphthylethynyl subsitituted sidewall of the adjacent **6•6** and vice versa. Simultaneously, the out-of-plane naphthyl arms of pairs of adjacent **6•6** dimers interact by edge to face π–π interactions (H to mean plane distances: 2.752 and 2.807 Å) between the C-H groups of the *o*-xylylene ring of the naphthylethynyl substituted sidewall and the π-system of the naphthyl ring (Figure 7b). The sheets stack along the c-axis aided by the interdigitation of the CO_2Et groups on the convex face of the **6•6** building blocks.

In compound **7**, the terminal naphthalene rings have been completely removed. We expected that terminal naphthalene substituents would be oriented out-of-plane with respect the *o*-xylylene sidewall because of the biaryl nature of the linkage. We obtained single crystals of **7** by crystallization from $CHCl_3$. Figure 7c shows that **7** adopts the *in-in* dimeric motif as its basic building block in the crystal driven by π–π interactions between the dimethoxy-*o*-xylylene rings (mean plane separation: 3.551 Å) and perhaps benefitting from OCH_3•••O=C interactions (C•••O distances: 3.515 and 3.582 Å; CH•••O angles: 119 and 152˚). As observed previously for **3**, the presence of the out-of-plane arms precludes the packing of units of **7•7** into tapes in a head-to-tail fashion that was observed in the crystal structures of **1** and **2**. Instead the dimeric building blocks **7•7** grow along the a-axis to give rod-like assemblies driven by reciprocal pairs of edge-to-face π–π interactions (CH•••π distances: 2.997 and 2.894 Å) between the two different naphthalene arms of adjacent units of **7•7** (Figure 7c). These rod-like assemblies orient their long axes parallel to one another and form sheets in the ab-plane. These sheets benefit from the formation of additional edge-to-face π–π interactions (CH•••π distances: 2.701 Å) between the naphthalene substituents of different rods. Finally, the sheets stack along the c-axis driven by interdigitation of the CO_2Et groups on the convex face of **7** between the sheets.

Factors Governing the Packing of 1 – 7 in the Crystal. Previously, we have shown that *p*-dimethoxysubstituted *o*-xylylene sidewalls reliably control the *in-in* dimerization of glycoluril derived molecular clips.[18] In this paper we explored the role of extended aromatic arms and their linking groups on the organization in the crystal. For compounds **1** and **2** which feature electron deficient extended aromatic arms connected to the *o*-xylylene sidewall via ethylene spacers, we observe the *out-out* dimers **1•1** and **2•2** as the basic building blocks in the crystal. For **1** and **2**, the enhanced π–π interactions and the presence of ArH•••O=C interactions between the electron deficient Ar-H groups of the extended aromatic walls and the ureidyl carbonyl of the opposing molecular clip overcome the previously observed preference for the *in-in* dimerization driven by OCH_3•••O=C interactions. The geometrical preferences of the ethylene linking group supports the overall planarity of the extended sidewalls of **1** and **2** which appears critical to obtain the *out-out* dimeric geometry. In contrast, the amide linker of **3** and the absence of a linker in compound **7** dictate that the extended aromatic arms are not coplanar with the *o*-xylylene ring to which they are attached. For **3**, the amide groups rotate out-of-plane to form NH•••O H-bonds to the ureidyl carbonyl groups whereas **7** does so because of the well known conformational preferences of the biaryl linkage. Accordingly, compounds **3** and **7** form the *in-in* dimers as the basic building block in the crystal driven by π–π interactions between the internal dimethoxy-*o*-xylylene rings and

also by OCH_3•••O=C H-bonding interactions. The presence of the out-of-plane aromatic arms of **3** and **7** also prevents the formation of tape-like motifs by head-to-tail π–π and CH•••π interactions between the external aromatic walls of the dimers. The situation is more complex for compounds **4** – **6** which feature ethynyl linkers which result in freely rotatable diaryl ethynyl units. Despite the fact that the phenylethynyl arms of **4** are nearly coplanar with their *o*-xylylene sidewall, **4** forms the *in-in* **4**-**4** dimer probably because these arms lack suitably polarized C-H groups to compete with the OCH_3•••O=C interactions formed by the internal dimethoxy-*o*-xylylene rings. In the crystal, compounds **5** and **6** feature one arylethynyl arm that is roughly coplanar to and one arm that is out-of-plane with respect to the attached *o*-xylylene ring. This geometry allows for out-of-register π–π and CH•••π interactions between the external coplanar extended aromatic walls of adjacent *in-in* dimers to form tapes. The out-of-plane C≡CAr arms are critical to the formation of the observed crystalline geometries of **5** and **6** because they form key edge-to-face π–π interactions that support the three dimensional packing. Accordingly, the two most important features controlling the packing geometry in the **1** – **7** appear to be the conformational properties of the linking groups and the electronic nature of the extended aromatic sidewall (e.g. electron deficient).

Conclusion. We have presented the X-ray crystal structures of seven asymmetric glycoluril-based molecular clips (**1** – **7**) featuring a common *p*-dimethoxy-*o*-xylylene ring sidewall and a series of different extended aromatic sidewalls. We observed that compound **1** and **2** display the uncommon *out-out* dimers as the fundamental building blocks of their crystal structures. In contrast, compounds **3** – **7** display the *in-in* dimers as their basic building blocks which benefit from π–π interactions between the internal dimethoxy-*o*-xylylene rings and also OCH_3•••O=C H-bonding interactions. We find that the conformational preferences of the linking groups (e.g. alkenyl, alkynyl, amide, no linker) play a critical role in determining the mode of dimerization and the subsequent mode of packing. Linkers that prevent the planarity of the extended arms with the *o*-xylylene ring (e.g. amide and no linker) preclude the formation of the out-out dimers and also prevent the commonly observed head-to-tail packing of the dimers via π–π stacking between the external extended sidewalls. The freely rotatable ethynyl linker of **5** and **6** resulted in one coplanar and one out-of-plane aryl ethynyl arm which simultaneously allows tape formation by offset π–π stacking and CH•••π interactions and also edge-to-face π–π interactions between tapes. The electronic nature of the extended sidewall (e.g. electron deficient) also play an important role by modulating the strength of the constituent interactions (e.g. ArH•••O=C and π–π). The work provides further guidelines for the design of asymmetric molecular clips that undergo predictable organization in the solid state. Enhanced levels of control over crystalline geometry promises to expand the use of these building blocks to create complex and functional solid state architectures.

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† Electronic Supplementary Information (ESI) available: [Preparation of compounds in this work, ^{1}H NMR and ^{13}C NMR Spectra of the target compounds, CSD search result, X-ray crystallographic information files (CIF) for compounds **1**-**7**]. See DOI: 10.1039/b000000x/.

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Dimeric Packing of Molecular Clips Induced by Interactions Between π-Systems

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We report the first observation synthesis and x-ray structures of seven glycoluril clips that feature extended aromatic sidewalls; compounds **1** and **2** are the first examples of the out-out dimeric motif.