Self-Sorting

International Edition: DOI: 10.1002/anie.201502983
German Edition: DOI: 10.1002/ange.201502983

Shape-Controlled Synthesis and Self-Sorting of Covalent Organic Cage Compounds[**]

Stefanie Klotzbach and Florian Beuerle*

Abstract: *The directional bonding approach is a powerful tool to rationally control both shape and stoichiometry of three-dimensional objects built from rigid building blocks under dynamic covalent conditions. Co-condensation of catechol-functionalized tribenzotriquinacene derivatives which have 90° angles between the reactive sites and diboronic acids with bite angles of 60°, 120°, and 180°, led to the efficient formation of, respectively, bipyramidal, tetrahedral, or cubic covalent organic cage compounds in a predictable manner. Investigations on the self-sorting of ternary mixtures containing two competitive boronic acids revealed either narcissistic or social self-sorting depending on the stability of the segregated cages relative to feasible three-component assemblies.*

Since the humble beginnings of sophisticated synthesis, molecular cage structures have aroused fascination among chemists not only because of their aesthetic beauty but also because of the tempting possibilities of controlling both size and interior of the intrinsic cavities for functional purposes. Owing to their complex structures, traditional synthetic approaches, such as the landmark synthesis of cubane,[1] suffered from tedious multistep routes and very low yields, particularly for the final cyclization steps. However, the rise of dynamic approaches based on metallasupramolecular[2] or dynamic covalent[3] bond formations proceeding under thermodynamic control provided easy access to a wide variety of self-assembled cage structures.[4] The geometry and shape of the molecular objects obtained this way are usually governed by the structures of the respective molecular precursors and a rational prediction of the geometrical outcome of such assemblies is highly desirable. As a powerful strategy, the directional bonding approach[2a] was established in the 1990s by Fujita et al.[5] and Stang and Cao[6] in their seminal studies on the formation of metal-coordinated squares. According to this concept, the geometrical shape of a self-assembled cage is solely dependent on the rigid bite angles of the complementary precursors and their mixing in the appropriate stoichiometric ratio and can therefore be precisely predicted based on basic geometrical considerations. Following this strategy, a variety of metallasupramolecular assemblies[4a–d] have been designed and synthesized in recent years with in large part excellent control over stoichiometry and geometry of the obtained cages. One of the most impressive examples is by the Fujita group and involves the synthesis of either $M_{12}L_{24}$ or $M_{24}L_{48}$ polyhedra with a clear-cut transition between the two species achieved simply by changing the ratio of two ligands which have different bite angles.[4e] For purely organic systems, a notably smaller number of cages having octahedral,[7] cubic,[8] or cuboctahedral[9] shape have been presented in recent years. Cooper et al. were able to govern the formation of either [2+3]- or [4+6]-imine cages[10] from trialdehydes and diaminoalkanes depending on the number of carbon atoms between the two amino groups. An odd/even effect was observed. With even numbers of carbon atoms between the two amino functions [4+6]-assemblies were formed and for odd numbers of carbon atoms [2+3]-cages formed. Mastalerz and co-workers presented the formation of either [4+6]-[11] or [2+3]-cages[12] for the co-condensation of a tritopic triptycene triamine and aromatic dialdehydes with either *meta-* or *ortho*-relationship between the two functional sites. By changing the solvent, Liu and Warmuth could selectively synthesize either octahedral, tetrahedral, or square-antiprismatic cages derived from the very same precursors through imine condensation.[13]

For multi-component systems comprising competitive building blocks, increased levels of complexity could eventually result in molecular recognition or self-sorting effects. Despite being intensively studied in supramolecular chemistry in recent years,[14] examples regarding covalent organic cages are still very rare in the current literature.[15] One of the very first examples for self-sorting of covalent organic cages is the "molecular marriage" of two isostructural dialdehydes and two diamines presented by the Mukherjee group.[15b] For this mixture, the exclusive formation of two out of four possible imine cages is observed depending on the rigidity of the precursors. Note that a rational prediction of cage geometry and stoichiometry solely based on the structure of the precursor units and efficient control of self-sorting properties for more complex mixtures containing competitive reactive components is still in its infancy. The appealing prospect of saving time and resources in targeted syntheses of organic cage compounds of any imaginable molecular shape and topology makes such strategies still worthwhile goals in synthetic chemistry.

Herein we report on the design and synthesis of a series of covalent organic cage compounds with predictable geomet-

---

[*] S. Klotzbach, Dr. F. Beuerle
Universität Würzburg, Institut für Organische Chemie & Center for Nanosystems Chemistry (CNC)
Am Hubland, 97074 Würzburg (Germany)
E-mail: florian.beuerle@uni-wuerzburg.de

[**] We would like to thank Prof. Dr. Frank Würthner for his generous support and assistance as well as Elfriede Ruckdeschel and Dr. Matthias Grüne for DOSY-NMR measurements. Financial support from the Collaborative Research Network "Solar Technologies Go Hybrid" of the Bavarian Ministry of Science, Research and the Arts and the Fonds der Chemischen Industrie (doctoral fellowship for S.K. and Liebig fellowship for F.B.) is gratefully acknowledged.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201502983.

rical shape synthesized by co-condensation of a catechol-functionalized tribenzotriquinacene[16] (TBTQ) derivative and three different diboronic acids with varying angles between the two reactive sites. In addition, initial studies on the self-sorting behavior for ternary mixtures containing two different diboronic acids revealed either so-called "narcissistic" or "social" self-sorting depending on the deployed boronic acids.

Recently, we reported on the efficient formation of molecular cubes[8b] through co-condensation of catechol-functionalized TBTQ and *para*-phenylene diboronic acid under water removing conditions. In terms of the directional bonding approach, such [8 + 12]-assemblies can be classified as a combination of tritopic 90° subunits **A** and ditopic 180° linkers **D** with 8:12 ratio (see Figure 1). However, different geometrical shapes with [4+6]- or [2+3]-stoichiometry should be more favorable with ditopic building blocks with smaller angles. Based on general geometrical considerations, we therefore calculated the optimum angles for trigonal-bipyramidal [2+3]- and tetrahedral [4+6]-assembly to be 70.5° and 141.1°, respectively (see Figure 1 and Supporting Information for more details on the geometrical calculations). Molecularly, such spatial orientations are realized in bisfunctional phenylene derivatives with *ortho*- or *meta*-substitution patterns in contrast to *para*-derivatives which result in cubic [8 + 12]-assembly (see Figure 1).

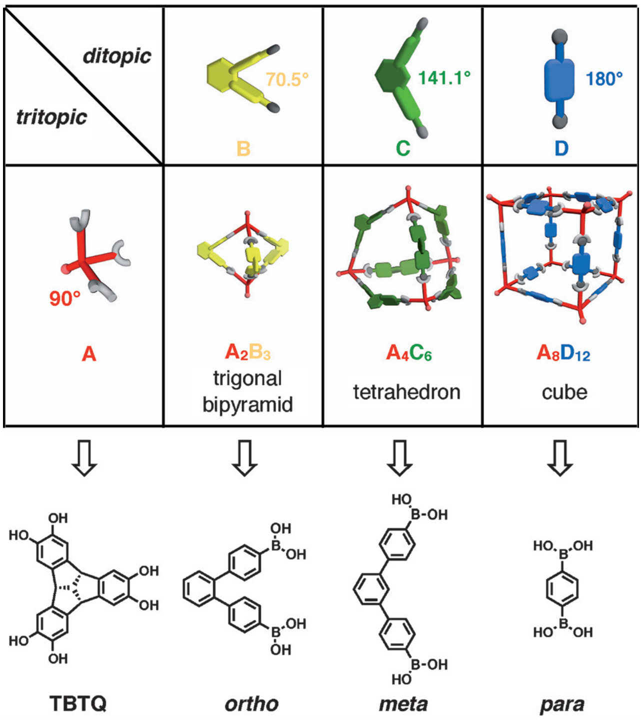
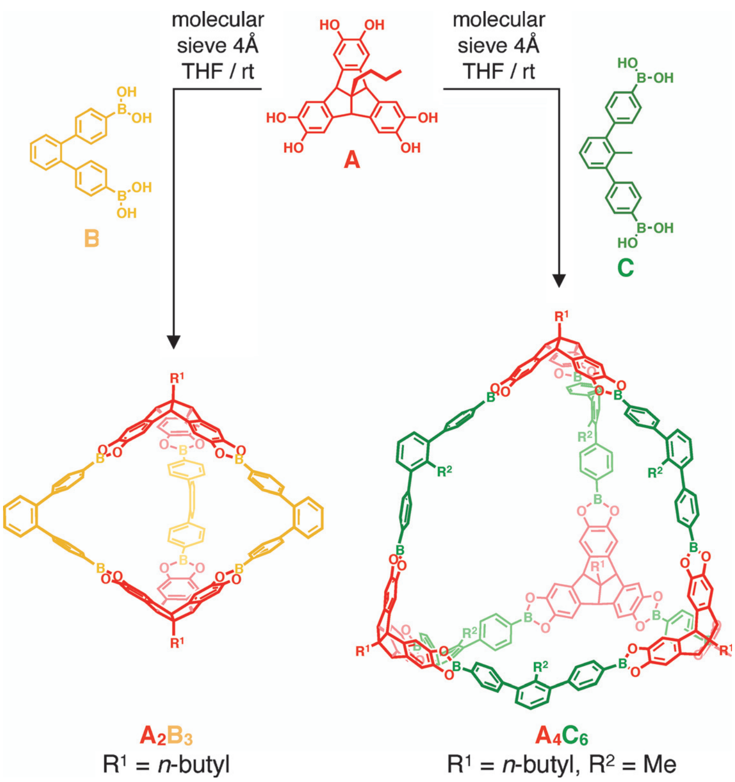


Figure 1. Shape-selective synthesis of molecular cage compounds from orthogonal tritopic units and ditopic linkers with varying angular disposition based on the directional bonding approach. TBTQ derivatives and phenylene diboronic acids provide suitable scaffolds for appropriate molecular building blocks.

To test this hypothesis, we synthesized diboronic acids **B** and **C** (see Supporting Information for experimental procedures and characterization details) possessing the desired 1,2- and 1,3-substitution pattern at the central phenylene ring and investigated their reactivity in the presence of appropriate catechols under conditions we recently established for the efficient formation of boronate ester cages.[8b] Reactions of tritopic TBTQ **A** with either **B** or **C** in 2:3 molar ratio (see Scheme 1) were performed in [D$_8$]THF at room temperature and monitored by ^{1}H NMR spectroscopy. Several hours after initial mixing, complex equilibria of various oligomeric intermediates were reached (see Supporting Information Figure S15) which did not change further even over the course of several days. However, the addition of 4 Å molecular sieves initiated complete conversion into highly symmetrical and monodisperse organic cages as the only detectable products after several days. ^{1}H NMR spectra of the respective molecular precursors and the reaction mixtures after completion of cage formation are shown in Figure 2. Final products could be isolated after filtration to remove the molecular sieves and eventual precipitates, washing with *n*-hexane, and drying under high vacuum. Both cages were fully characterized by ^{1}H- and DOSY-NMR spectroscopy as well as elemental analysis.

Formation of $\mathbf{A_2B_3}$ bipyramids was also confirmed by MALDI-TOF mass spectrometry showing only one peak at *m*/*z* 1601.41 (calculated 1602.27 for $\mathbf{A_2B_3}$, see Figure S7 in the Supporting Information), whereas in the case of the tetrahedral $\mathbf{A_4C_6}$ assembly, no cage compounds could be detected in the mass



Scheme 1. Synthesis of trigonal-bipyramidal $\mathbf{A_2B_3}$ and tetrahedral $\mathbf{A_4C_6}$ cages under water-removing conditions from TBTQ **A** and diboronic acids **B** or **C**.

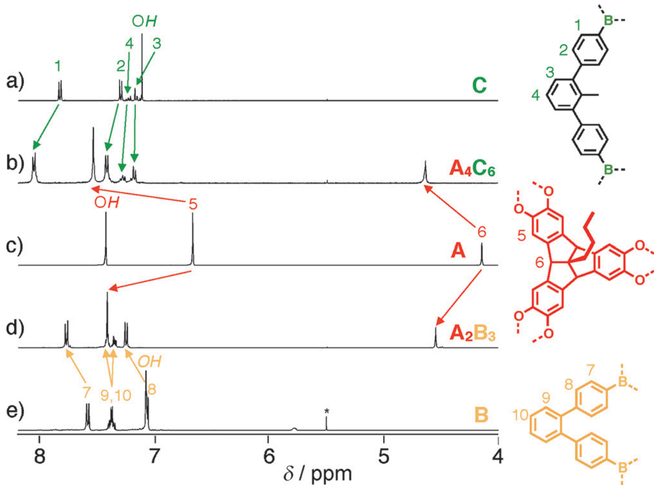


Figure 2. Aromatic and TBTQ-C*H* regions of ^{1}H NMR spectra (400 MHz, [D$_8$]THF, RT) of a) *meta*-diboronic acid **C**, b) tetrahedral **A$_4$C$_6$** cage, c) tripodal TBTQ **A**, d) trigonal-bipyramidal **A$_2$B$_3$** cage, e) *ortho*-diboronic acid **B**; spectra of cage compounds were measured directly from the reaction mixtures indicating quantitative formation of the organic cage compounds; full data and spectra of the isolated cages are provided in the Supporting Information; * CH$_2$Cl$_2$.

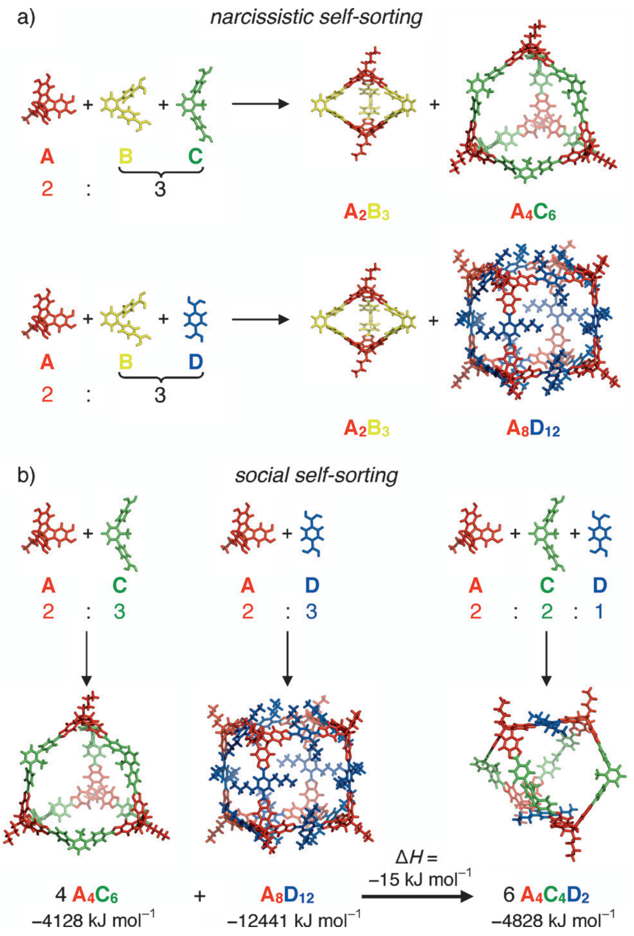


Figure 3. a) Narcissistic self-sorting into separate two-component assemblies for ternary mixtures containing TBTQ **A** and competitive diboronic acids **B**/**C** or **B**/**D** in a 2:3 molecular ratio; b) social self-sorting into three-component cage **A$_4$C$_4$D$_2$** for ternary mixture of TBTQ **A** and diboronic acids **C**/**D** in a 2:2:1 molecular ratio; all molecular structures are PM6-minimized[17] models, graphics were produced with the PyMOL software.[19]

spectra. The actual angle between the two boronic acids is 120°, which is considerably different to the optimum angle for tetrahedral assembly of 141.1°. We therefore speculated that this significantly higher inherent strain energy for **A$_4$C$_6$** might lead to decomposition of the cages under ionizing conditions as was also reported for other boronate cages.[9b] Semi-empirical calculations[17] on the PM6 level provided further indications for the inherent strain energy by revealing significant bending of the linear boronate ester moieties (see Figure S34a).

As one possibility to increase the stability for the tetrahedral assemblies, we envisioned changing some of the 120° linkers **C** for linear diboronic acids **D**. After formal replacement of one or two opposite **C** units, we identified **A$_4$C$_5$D** and **A$_4$C$_4$D$_2$** assemblies as the least-strained mixed cages. For **A$_4$C$_4$D$_2$** which has the shape of the Johnson solid J_{26} gyrobifastigium,[18] an optimum angle for the bent ditopic building blocks of 120° was calculated (see Figure S33 in the Supporting Information) making such cage structures promising targets for covalent organic cage formation based on mixtures of *meta*- and *para*-substituted diboronic acids.

Consequentially, we started to get interested in more complex reaction mixtures containing different types of both tritopic and ditopic linkers which have been rarely studied in the field of organic cage compounds to date. As the next level of complexity, we investigated ternary 2:3 mixtures containing **A** as a tripodal building block and two different ditopic linkers from **B**, **C**, or **D**. The question arises whether narcissistic self-sorting into segregated binary cages or social self-sorting into unprecedented mixed assemblies, such as the predicted **A$_4$C$_4$D$_2$** cage, occurs. In unfortunate cases, these complex mixtures might lead to enhanced formation of polymeric side products. According to the directional-bonding approach, no stable mixed assemblies can be envisioned for combinations of **A** with **B**/**C** or **B**/**D**, predicting narcissistic self-sorting into the individual high-symmetry cages (see Figure 3a) will occur. In fact, ternary mixtures of both **A**/**B**/**C** and **A**/**B**/**D** resulted in the exclusive formation of the individual binary cages **A$_2$B$_3$** and **A$_4$C$_6$** or **A$_2$B$_3$** and **A$_8$D$_{12}$**, respectively, as evidenced by NMR spectroscopy. The ^{1}H NMR spectra after completion of cage formation show overlaying signals for the respective individual cages (see Figure S20 and S23). For the **A**/**B**/**D** case, both cages were also identified by MALDI-TOF mass spectrometry with signals at m/z 1625 for $[\mathbf{A_2B_3}+\mathrm{Na}]^+$ and m/z 5953 for $[\mathbf{A_8D_{12}}]^+$ (see Figure S27). Furthermore, DOSY-NMR spectroscopy revealed the co-existence of two distinct species with different diffusion coefficients in both cases (see Figure 4c and Figures S21 and S24). According to the Stokes–Einstein equation, we calculated molecular diameters of 2.0 and 2.9 nm for the **A**/**B**/**C** mixture and 2.2 nm and 3.9 nm for the **A**/**B**/**D** mixture. These values are in good agreement with diameters of 1.9, 3.0, and 3.5 nm for the individual cages **A$_2$B$_3$**, **A$_4$C$_6$**, and **A$_8$D$_{12}$**, respectively, which are depicted as semi-

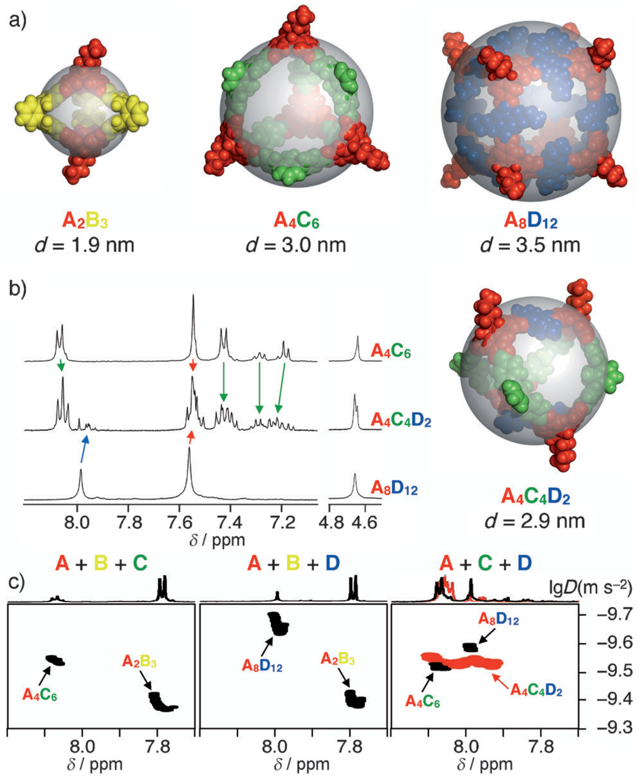


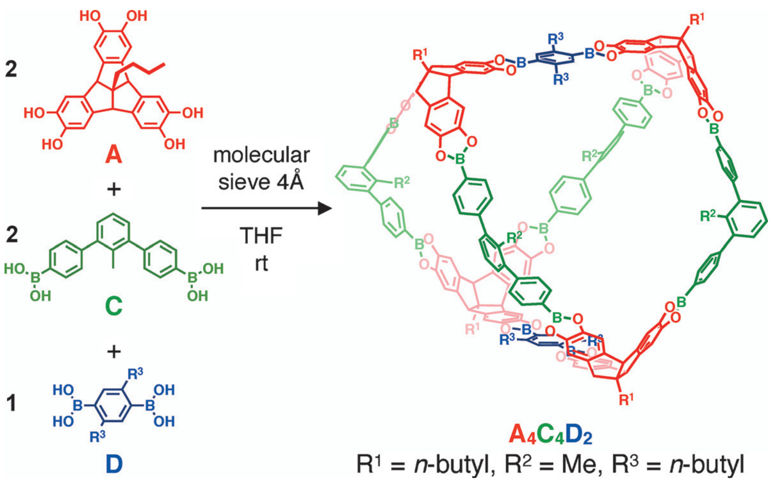
Figure 4. a) PM6-minimized[17] space-filling models of $\mathbf{A_2B_3}$, $\mathbf{A_4C_6}$ and $\mathbf{A_8D_{12}}$ cages. Hydrodynamic diameters as obtained from the Stokes–Einstein equation from DOSY-NMR spectroscopy are shown as transparent gray spheres; b) Aromatic and TBTQ-C*H* regions of ^{1}H NMR spectra ([D$_8$]THF, 400 MHz, RT) of $\mathbf{A_4C_6}$ (top), $\mathbf{A_8D_{12}}$ (bottom), and three-component cage $\mathbf{A_4C_4D_2}$ (middle); c) DOSY-NMR spectra ([D$_8$]THF, 600 MHz, RT) for ternary mixtures **A**/**B**/**C** (left), **A**/**B**/**D** (middle), and **A**/**C**/**D** (right, red signals); DOSY-NMR for a mixture of separately prepared cages $\mathbf{A_4C_6}$ and $\mathbf{A_8D_{12}}$ is shown in black in the right spectrum.

transparent gray spheres in the PM6-minimized[17] space-filling models in Figure 4a. Altogether, these findings clearly indicate narcissistic self-sorting for both systems.

For an **A/C/D** mixture however, besides narcissistic self-sorting into individual cages also emergent formation of three-component cages, for example, $\mathbf{A_4C_5D}$ or $\mathbf{A_4C_4D_2}$, is feasible depending on the relative thermodynamic stability of the mixed assemblies in comparison to the segregated cages. To estimate the position of the equilibria between both mixed and segregated cages, we calculated heats of formation (PM6 semi-empirical molecular modeling)[17] of −4128, −4479, −4828, and −12441 kJ mol^{-1} for $\mathbf{A_4C_6}$, $\mathbf{A_4C_5D}$, $\mathbf{A_4C_4D_2}$, and $\mathbf{A_8D_{12}}$, respectively. Based on these results, we identified $\mathbf{A_4C_4D_2}$ as the most stable species and calculated a reaction enthalpy of −15 kJ mol^{-1} for the formal transformation of four $\mathbf{A_4C_6}$ tetrahedra and one $\mathbf{A_8D_{12}}$ cube into six $\mathbf{A_4C_4D_2}$ cages (see Figure 3b and Figure S27b). Although we have to admit that these calculations are only rough estimations based on gas phase data without taking any solvent effects or entropic contributions into account, we still believe that such calculations might provide good estimations for inherent strain effects. According to these data, we can anticipate that there might be a significant penalty for the segregated cages because of the inherent strain energy of $\mathbf{A_4C_6}$ which might shift the equilibrium towards the mixed assemblies and especially $\mathbf{A_4C_4D_2}$ as the only or at least major product.

Indeed, reaction of **A/C/D** (see Scheme 2) in a 2:2:1 ratio in [D$_8$]THF in the presence of 4 Å molecular sieves resulted in a NMR spectrum significantly differing from a simple overlay of the spectra for a cube and tetrahedron. Owing to the lower symmetry of the $\mathbf{A_4C_4D_2}$ cages, more complex signal splitting is observed, for example, two sets of duplets for the aromatic protons of the boronate containing phenyl ring (see Figure 4b). MALDI-TOF-MS of the reaction mixture showed one weak signal for the molecular ion at *m*/*z* 3185 (see Figure S21). Most convincingly, DOSY-NMR spectroscopy indicated the formation of one monodisperse molecular species with a diameter of 2.9 nm (see red signals in Figure 4c and Figure S19).

In contrast to the reaction of **A/C/D** in a 2:2:1 ratio, a 4:1 mixture of individually prepared cages $\mathbf{A_4C_6}$ and $\mathbf{A_8D_{12}}$ with an effective ratio of 2:2:1 for building blocks **A/C/D** in [D$_8$]THF (see Equation in Figure 3b) appeared to be stable over several weeks in the presence of molecular sieves and the coexistence of both cages was confirmed by DOSY-NMR spectroscopy (see black signals in the right part of Figure 4c and Figure S19). Thus, the final cage compounds appear to be kinetically inert and do not undergo transformations into thermodynamically more stable products. Therefore, the often-proposed reversibility of dynamic covalent reactions might only be true for the initial reaction steps, whereas late propagation steps as for example the final ring-closure reactions might end up in kinetically trapped states. Currently, we are working on the synthesis of cages with higher solubility to investigate the direct transformation of preformed binary cages into more stable three-component assemblies.



Scheme 2. Synthesis of three-component cage $\mathbf{A_4C_4D_2}$ under water-removing conditions from TBTQ **A** and diboronic acids **C** and **D** in a 2:2:1 molecular ratio.

In summary, we have demonstrated the shape-selective formation of covalent organic cages with trigonal-bipyramidal, tetrahedral, or cubic geometry from hydroxy-functionalized TBTQ and diboronic acids depending on the bite angle of the diboronic acids. This directed approach offers rational control over the final cage geometries and is therefore a significant step towards a tailor-made synthesis of covalent organic cage compounds. For ternary mixtures containing two competitive diboronic acids, we obtained either narcissistic self-sorting into segregated cages $\mathbf{A_2B_3}$/$\mathbf{A_4C_6}$ and $\mathbf{A_2B_3}$/$\mathbf{A_8D_{12}}$ or social self-sorting in the case of three-component cages $\mathbf{A_4C_4D_2}$. To our knowledge, the formation of these mixed assemblies is the first example of social self-sorting to give mixed cages from ternary mixtures of two different diboronic acids and one catechol. It offers unique insights into the thermodynamic and kinetic stabilities of spherical boronate ester assemblies. Investigations into the porosity of these cages and synthetic efforts to functionalize their interior and periphery are underway and will be reported in due course.

Keywords: boronate esters · cages compounds · dynamic covalent chemistry · self-sorting · tribenzotriquinacenes

How to cite: *Angew. Chem. Int. Ed.* **2015**, *54*, 10356–10360
Angew. Chem. **2015**, *127*, 10497–10502

---

[1] P. E. Eaton, T. W. Cole, *J. Am. Chem. Soc.* **1964**, *86*, 3157–3158.

[2] a) P. J. Stang, B. Olenyuk, *Acc. Chem. Res.* **1997**, *30*, 502–518; b) D. L. Caulder, K. N. Raymond, *Acc. Chem. Res.* **1999**, *32*, 975–982; c) M. Fujita, M. Tominaga, A. Hori, B. Therrien, *Acc. Chem. Res.* **2005**, *38*, 369–378.

[3] a) S. J. Rowan, S. J. Cantrill, G. R. L. Cousins, J. K. M. Sanders, J. F. Stoddart, *Angew. Chem. Int. Ed.* **2002**, *41*, 898–952; *Angew. Chem.* **2002**, *114*, 938–993; b) K. Severin, *Dalton Trans.* **2009**, 5254–5264; c) M. E. Belowich, J. F. Stoddart, *Chem. Soc. Rev.* **2012**, *41*, 2003–2024; d) Y. Jin, C. Yu, R. J. Denman, W. Zhang, *Chem. Soc. Rev.* **2013**, *42*, 6634–6654; e) Y. Kubo, R. Nishiyabu, T. D. James, *Chem. Commun.* **2015**, *51*, 2005–2020.

[4] a) R. Chakrabarty, P. S. Mukherjee, P. J. Stang, *Chem. Rev.* **2011**, *111*, 6810–6918; b) M. M. J. Smulders, I. A. Riddell, C. Browne, J. R. Nitschke, *Chem. Soc. Rev.* **2013**, *42*, 1728–1754; c) K. Harris, D. Fujita, M. Fujita, *Chem. Commun.* **2013**, *49*, 6703–6712; d) M. Han, D. M. Engelhard, G. H. Clever, *Chem. Soc. Rev.* **2014**, *43*, 1848–1860; e) Q. F. Sun, J. Iwasa, D. Ogawa, Y. Ishido, S. Sato, T. Ozeki, Y. Sei, K. Yamaguchi, M. Fujita, *Science* **2010**, *328*, 1144–1147; f) M. Mastalerz, *Angew. Chem. Int. Ed.* **2010**, *49*, 5042–5053; *Angew. Chem.* **2010**, *122*, 5164–5175; g) G. Zhang, M. Mastalerz, *Chem. Soc. Rev.* **2014**, *43*, 1934–1947.

[5] M. Fujita, J. Yazaki, K. Ogura, *J. Am. Chem. Soc.* **1990**, *112*, 5645–5647.

[6] P. J. Stang, D. H. Cao, *J. Am. Chem. Soc.* **1994**, *116*, 4981–4982.

[7] a) X. Liu, Y. Liu, G. Li, R. Warmuth, *Angew. Chem. Int. Ed.* **2006**, *45*, 901–904; *Angew. Chem.* **2006**, *118*, 915–918; b) J. Sun, R. Warmuth, *Chem. Commun.* **2011**, *47*, 9351–9353; c) K. E. Jelfs, X. Wu, M. Schmidtmann, J. T. A. Jones, J. E. Warren, D. J. Adams, A. I. Cooper, *Angew. Chem. Int. Ed.* **2011**, *50*, 10653–10656; *Angew. Chem.* **2011**, *123*, 10841–10844.

[8] a) D. Xu, R. Warmuth, *J. Am. Chem. Soc.* **2008**, *130*, 7520–7521; b) S. Klotzbach, T. Scherpf, F. Beuerle, *Chem. Commun.* **2014**, *50*, 12454–12457; c) S. M. Elbert, F. Rominger, M. Mastalerz, *Chem. Eur. J.* **2014**, *20*, 16707–16720.

[9] a) P. Skowronek, B. Warżajtis, U. Rychlewska, J. Gawroński, *Chem. Commun.* **2013**, *49*, 2524–2526; b) G. Zhang, O. Presly, F. White, I. M. Oppel, M. Mastalerz, *Angew. Chem. Int. Ed.* **2014**, *53*, 1516–1520; *Angew. Chem.* **2014**, *126*, 1542–1546.

[10] K. E. Jelfs, E. G. B. Eden, J. L. Culshaw, S. Shakespeare, E. O. Pyzer-Knapp, H. P. G. Thompson, J. Bacsa, G. M. Day, D. J. Adams, A. I. Cooper, *J. Am. Chem. Soc.* **2013**, *135*, 9307–9310.

[11] a) M. Mastalerz, *Chem. Commun.* **2008**, 4756–4758; b) M. Mastalerz, M. W. Schneider, I. M. Oppel, O. Presly, *Angew. Chem. Int. Ed.* **2011**, *50*, 1046–1051; *Angew. Chem.* **2011**, *123*, 1078–1083; c) M. W. Schneider, H.-J. S. Hauswald, R. Stoll, M. Mastalerz, *Chem. Commun.* **2012**, *48*, 9861–9863.

[12] M. W. Schneider, I. M. Oppel, M. Mastalerz, *Chem. Eur. J.* **2012**, *18*, 4156–4160.

[13] X. Liu, R. Warmuth, *J. Am. Chem. Soc.* **2006**, *128*, 14120–14127.

[14] a) K. Osowska, O. Š. Miljanić, *Angew. Chem. Int. Ed.* **2011**, *50*, 8345–8349; *Angew. Chem.* **2011**, *123*, 8495–8499; b) K. Osowska, O. Š. Miljanić, *Synlett* **2011**, 1643–1648; c) M. M. Safont-Sempere, G. Fernández, F. Würthner, *Chem. Rev.* **2011**, *111*, 5784–5814; d) M. L. Saha, M. Schmittel, *Org. Biomol. Chem.* **2012**, *10*, 4651–4684; e) Z. He, W. Jiang, C. A. Schalley, *Chem. Soc. Rev.* **2015**, *44*, 779–789.

[15] a) K. Ziach, M. Ceborska, J. Jurczak, *Tetrahedron Lett.* **2011**, *52*, 4452–4455; b) K. Acharyya, S. Mukherjee, P. S. Mukherjee, *J. Am. Chem. Soc.* **2013**, *135*, 554–557; c) K. Acharyya, P. S. Mukherjee, *Chem. Eur. J.* **2014**, *20*, 1646–1657; d) K. Acharyya, P. S. Mukherjee, *Chem. Commun.* **2015**, *51*, 4241–4244.

[16] a) D. Kuck, *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 508–509; *Angew. Chem.* **1984**, *96*, 515–516; b) M. Harig, B. Neumann, H.-G. Stammler, D. Kuck, *Eur. J. Org. Chem.* **2004**, 2381–2397; c) E. U. Mughal, D. Kuck, *Eur. J. Org. Chem.* **2012**, 3416–3423; d) T. Wang, Y.-F. Zhang, Q.-Q. Hou, W.-R. Xu, X.-P. Cao, H.-F. Chow, D. Kuck, *J. Org. Chem.* **2013**, *78*, 1062–1069; e) W.-R. Xu, H.-F. Chow, X.-P. Cao, D. Kuck, *J. Org. Chem.* **2014**, *79*, 9335–9346.

[17] *Spartan'14*, Wavefunction, Inc., Irvine, CA, USA.

[18] N. W. Johnson, *Canad. J. Math.* **1966**, *18*, 169–200.

[19] The PyMOL Molecular Graphics System, Version 1.7.4 Schrödinger, LLC.

Received: March 31, 2015