Just add water: modulating the structure-derived acidity of catalytic

hexameric resorcinarene capsules

David A. Poole III, Simon Mathew, Joost N. H. Reek*

Homogeneous, Supramolecular, and Bioinspired Catalysis group, van't Hoff Institute for Molecular Science (HIMS), University of Amsterdam (UvA), Science Park 904, 1098 XH Amsterdam, The Netherlands

Contents:

1. Forcefield parameterization of resorcin[4]arene structures	4
Figure S1	4
2. General procedures for CMD simulations	5
Table S1	5
3. CMD studies of interfacial hydrogen bonding	6
Figure S2	6
4. GIST thermodynamic analysis of water association	6
5. Materials	7
6. Analysis methods	7
7. Synthesis of undecyl-resorcin[4]arene (^{C11} R ₁)	7
8. Assembly of hexameric undecyl-resorcin[4]arene capsules (^{C11} R ₆)	7
9. Preparation of ^{C11} R ₆ samples with varied water content	7
Figure S3	8
Figure S4	9
Figure S5	10
10. ^{C11} R ₆ catalyzed Diels–Alder cycloaddition	11
Figure S6	11
11. Uncatalyzed Diels-Alder cycloaddition:	12
Figure S7	12
12. ³¹ P NMR studies of ^{C11} R ₆ internal acidity	13
Figure S8	13
Figure S9	14
Figure S10	15
Figure S11	16
Figure S12	17
13. Model of water-mediated ^{C11} R ₆ formation	18
Figure S13	18
Equation S1	18
14. Models of chemical exchange	19
Figure S14	19
15. Rearrangement of bridging waters in ^{C11} R ₆ -B.	20
Figure S15	20
16. Hydrogen-Bond Network in ^{C11} R ₆ -B	21
Figure S16	21
17. Computational Modelling of Sorbyl Alcohol Isomerization	22
Figure S17	22

18. Model Data for ^{C11} R ₁ monomer	23
Table S2	23
Table S3	24
Supplementary Material.	24
References	25

1. Forcefield parameterization of resorcin[4]arene structures

Model structures for hexameric methyl-resorcin[4]arene ($^{C1}\mathbf{R}_6$) and undecyl-resorcin[4]arene ($^{C11}\mathbf{R}_6$) capsules were constructed, inclusive of 8 structural water molecules and minimized by DFT at a B3LYP/def2SVP level of theory with Gaussian 16 Rev C.¹ Atom types, following GAFF2, and charge assignments, by RESP method, were made for the output structures using antechamber.² The optimized $^{C1}\mathbf{R}_6$ model served as a starting point for a short molecular dynamics simulation using xtb at a GFN2-xTB³ level of theory and implicit chloroform solvation.⁴ A total of 200 frames were extracted from the trajectory by random selection and single point energies were computed for these structures using DFT at a B3LYP/def2SVP level of theory using Gaussian 16 Rev C.¹ A sample of 100 structures and single point energies were used to fit bond, angle, and torsion parameters from randomly generated values using paramfit.⁵ The remaining 100 structures and single point energies were used to validate the accuracy of the resulting forcefield in reproducing B3LYP/def2SVP energies in comparison to other common techniques as shown in Figure S1.



Figure S1. Comparison of optimized hexameric resorcin[4] arene capsule forcefield to common classical mechanics and semi-empirical techniques.

The genetically optimized parameter set demonstrated significant improvements over generalized forcefield methods, GAFF2⁶ and UFF⁷, and performed comparably to GFN2-xTB³ in reproducing DFT energies.

Modelling the complete C11 **R**₆ capsule required additional parameters for the pendant undecyl groups, the optimization of which would be computationally expensive. Instead, these parameters were obtained from the GAFF2 forcefield which is well developed for simple sp³ hydrocarbons.⁶

2. General procedures for CMD simulations

Simulation environments were prepared using packmol,⁸ and contained a single ^{C11}**R**₆ capsule with 8–24 SPC-flexible water molecules,⁹ and 1000 chloroform molecules in a 35 angstrom cube. In all simulations 8 water molecules were specifically placed at the vertex positions of the ^{C11}**R**₆ capsule. Classical mechanics dynamics simulations were carried using pmemd.CUDA^{10,11} following standard equilibration and productive phases indicated by the input files shown below in Table S1.

Table S1. Control input files for molecular dynamics simulations used in computational investigations used in a standard sequence of minimization, heating, density equilibration, thermal equilibration and productive molecular dynamics. Thermal equilibration and productive molecular dynamics used the same input file with appropriate simulation lengths (listed here as '###').

Phase 1. Minimization	Phase 2. NVT / Initial Heating
&cntrl imin = 1, irest = 0, ntx = 1, ntb = 1, maxcyc= 1250, ncyc = 250, ntpr = 1, ntwx = 0, ig = -1, cut = 10, ntpr = 500, ntwx = 500, ioutfm=1, ntxo = 2	&cntrl imin = 0, irest = 1, ntx = 7, ntb = 1, ntp = 0, taup = 5.0, cut = 8, ntr = 0, ntc = 1, ntf = 1, tempi = 0.0, temp0 = 300.0, ntt = 3, gamma_ln = 5.0, dt = 0.001, nstlim = 100000, nscm = 5000, ntpr = 5000, ntwr = 5000, ntwr = 5000, ioutfm= 1, ntxo = 2
Phase 3. NPT / Density equilibration	Phase 4 & 5. NVT / Productive MD
&cntrl imin = 0, irest = 1, ntx = 7, ntb = 2, ntp = 1, taup = 5.0, cut = 8, ntr = 0, ntc = 1, ntf = 1, tempi = 300.0, temp0 = 300.0, ntt = 3, gamma_ln = 0.5, dt = 0.001, nstlim = 1500000, nscm = 1000, ntpr = 1000, ntwr = 1000, ioutfm= 1, ntxo = 2	&cntrl imin = 0, irest = 1, ntx = 7, ntb = 1, ntp = 0, taup = 5.0, cut = 8, ntr = 0, ntc = 1, ntf = 1, tempi = 300.0, temp0 = 300.0, ntt = 3, gamma_ln = 0.5, dt = 0.001, nstlim = ###, nscm = 5000, ntpr = 5000, ntwr = 5000, ntwr = 5000, ioutfm= 1, ntxo = 2

3. CMD studies of interfacial hydrogen bonding

A total of 550 simulations were constructed containing 9–24 water molecules in order to observe the association of water and its effect on hydrogen bonding between the phenolic functional groups of adjacent resorcin[4]arene facial monomers. These simulations were propagated for 20 ns of productive molecular dynamics, and the resulting trajectories analyzed to compute hydrogen bonding between the resorcin[4]arene monomers as shown in Figure S2. A large number of trajectories were used in order to mitigate potential bias.



Figure S2. Hydrogen bond analysis results. The number of hydrogen bonds between resorcin[4]*arene monomers were determined by standard analysis procedures implemented in cpptraj.*¹⁰

We observed a propensity that simulations with ≥ 14 water molecules resulted a disruption of interfacial hydrogen bonds, corresponding to the opening of 1–2 edges of the capsule's cubic structure as depicted in Figure 2. This change fundamentally alters the structure, resulting in an 'open state' distinct from typical portrayals or structural models of the 'closed state' capsule.

4. GIST thermodynamic analysis of water association

A set of 28 molecular dynamics simulations were constructed featuring 8–22 waters. Trajectories from these simulations were propagated for 800 ns each to sample the distribution of water within the capsule environment (Table S1). These trajectories were then analyzed using grid inhomogeneous solvation theory (GIST) to estimate the thermodynamics of water association.¹² The energy per water molecule was determined from the volume sum of the entropic and enthalpic components divided among the water molecules. The relative energy compared to 8 water molecules per capsule then signifies the thermodynamics of water association, as illustrated in Figure 2.

5. Materials

Resorcinol was purchased from Sigma Aldrich; darker crystals were removed manually during weighing as a means of purification before use. Decanal was similarly purchased from Sigma and used immediately after receipt without any purification. Ethanol, concentrated aqueous HCl, methanol, and acetone were purchased from VWR and used directly without purification. All NMR samples were prepared in CDCl₃, purchased from Sigma Aldrich and filtered through a column of dry activated basic alumina before use.

6. Analysis methods

¹H and ³¹P spectra were measured on a Bruker ARX 300 at a constant temperature of 298 K. Spectral data were referenced to residual solvent protons (7.26 ppm for CDCl₃) for ¹H measurements, or the internal deuterium lock signal for ³¹P measurements

Karl-Fisher titrations were carried out using a Metrohm 831 KF Coulometer system.

7. Synthesis of undecyl-resorcin[4]arene (^{C11}R₁)

The synthesis of the title compound was carried out with slight modification from reported procedures.¹³ A round bottom flask was charged with resorcinol (20.0 g, 90.8 mmol) dissolved in a mixture of ethanol (30 mL) and concentrated aqueous hydrochloric acid (15 mL). The flask was then cooled in an ice bath and solution of dodecanal (15.3 g, 18.0 mL, 89.6 mmol) in ethanol (15 mL) was added dropwise by an addition funnel over approximately 1 hour. The ice bath was removed and the mixture was heated (50° C) while stirring overnight (20 h). Over time a yellow to red color developed in the solution, and the next morning an off-white precipitate was observed. This precipitate was collected by vacuum filtration and washed with a solution of saturated aqueous sodium bicarbonate (50 mL) to neutralize remaining acid, and then demineralized water (3×50 mL) to remove any remaining bicarbonate. The filtrate was dissolved in hot acetone (ca. 200 mL) and upon cooling the near-white precipitated solid was collected and washed with cold acetone until the washings were colorless. The filtrate was then dissolved and precipitated upon cooling from hot methanol to obtain the final product as a white solid (9.0 g, 38% yield).

8. Assembly of hexameric undecyl-resorcin[4]arene capsules (^{C11}R₆)

A suspension of ^{C11}**R**₁ (37.5 mg, 34.1 μ Mol) in CDCl₃ (1 mL) was produced in a screw cap vial (5 mL). The vial was held above a beaker of hot water (60–70° C) and mixed with magnetic stirring. We found that the steam provided from the hot water bath afforded sufficient moisture for capsule formation and prevented the addition of excessive water to the solution which may later phase-separate.

9. Preparation of ^{C11}R₆ samples with varied water content

Samples of ^{C11}**R**₆ were prepared and an addition of water (2 uL, 110 μ Mol) was added by micropipette. A small quantity (ca. 5-6 pieces) of molecular sieves (3.0 Å) were added to the sample vial with a small Teflon stir bar. The sample was stirred for up to 3 hours to remove water before being filtered into an NMR tube for analysis. Quantitation by ¹H NMR spectroscopy, shown in Figure S5, indicates minimal changes aside water content and phenolic peak distribution, indicating that ^{C11}**R**₆ is chemically stable under these conditions.

A separate sample was prepared for DOSY NMR following identical protocols. Using the auto-diffusion of residual CHCl₃ to correct for changes in solvent viscosity, we estimate the Stokes radii of C11 **R**₆ to be 22 Å for both assemblies, which is reasonable for the hexameric species.

Transmission FTIR was then used to obtain vibrational spectra of C11 **R**₆ before and after the drying process to specifically identify potential chemical changes, or the formation of dimeric (C11 **R**₂) species which have been previously analyzed by this method.¹⁴



Figure S3. ¹H NMR (500 MHz, CDCl₃) spectra obtained from $C^{11}R_6$ as prepared (a) and after drying (b).



Figure S4. ¹H DOSY diffusograms (500 MHz, 19-point decay) of ^{C11} \mathbf{R}_6 (5.38 mM) in CDCl₃ before (a) and after (b) drying by molecular sieves. Diffusion was determined by exponential fit using Topspin 4.0.9 "DOSY 2d" automation program with a 2-component fitting of the ¹H spectra obtained at 19 gradient strengths using a standard LED-type pulse program (ledbpgb2s).



Figure S5. FTIR Spectra (KBr cell, 100 μ m) obtained from solution state samples of ^{C11}**R**₆ in CDCl₃ as prepared (103.12 mM H₂O), and after drying by molecule sieves (44.03 mM H₂O).

These spectral features match previously reported spectra of the hexameric hexyl resorcin[4]arene capsules and not their dimeric analogs which feature a sharp band at 3500 cm⁻¹.¹⁴ Therefore we conclude that despite changes in size, C11 **R**₆ remains a hexamer in CDCl₃ containing between 44–103 mM water.

10. C11R6 catalyzed Diels-Alder cycloaddition

Solutions of sorbic alcohol (24 mM) and maleimide (24 mM) were prepared in CDCl₃/0.1% TMS and dried using molecular sieves (3 Å). Additionally, a series of ^{C11}**R**₆ solutions were prepared and dried following the above procedures in CDCl₃/0.1% TMS to afford samples of the capsule in the presence of 48 to 130 mM of water as determined by automated Karl Fischer titration. A catalytic experiment was conducted by the addition of the sorbic alcohol solution (24 mM, 125 µL), CDCl₃/0.1% TMS (125 µL), maleimide solution (24 mM, 125 µL) and a ^{C11}**R**₆ solution to a dry NMR tube by micropipette. This sample was vortexed briefly (ca. 3 seconds) and inserted immediately into the NMR for analysis where ten ¹H NMR spectra (300 MHz, T_r = 25 seconds) were obtained over 40 minutes. The NMR sample chamber as well as the laboratory environment were temperature controlled to 25° C. The depletion of maleimide ($\delta = 6.72$ ppm) was computed with reference to the internal TMS standard. A linear fit was used to determine the initial reaction velocity as shown in Figure S7. Slight variation was apparent in the initial concentration of maleimide, likely due to differences in timing from sample mixing to the completion of the first measurement.



Figure S6. Maleimide depletion observed by ¹H NMR for a ^{C11} R_6 catalyzed Diels–Alder cycloaddition reaction at water contents (c_{wat}) spanning 8.76–25.95 mM, shown with linear fits used to determine the reaction rate.

11. Uncatalyzed Diels-Alder cycloaddition:

Solutions of sorbic alcohol (24 mM) and maleimide (24 mM) were prepared in CDCl₃/0.1% TMS and dried using molecular sieves (3 Å). A reaction was prepared by the sequential addition of the sorbic alcohol solution (125 μ L) and maleimide solution (125 μ L) to either dry or water-saturated CDCl₃/0.1% TMS, followed by brief vortexing (ca. 3 seconds). The samples were periodically analyzed by ¹H NMR (300 MHz, T_r = 25 s) overnight, and the depletion of maleimide ($\delta = 6.72$ ppm) was determined with reference to the internal TMS standard. A linear fit was used to estimate the reaction velocity from data obtained over the first 5 hours as shown in Figure S8. The reaction rate of the water-saturated or 'wet' reaction was found to be 0.21±0.01 mM hr⁻¹, ca. 31% faster than the rate observed for the reaction in the absence of water, 0.16±0.01 mM hr⁻¹. The observed rates are significantly slower than the ^{C11}**R**₆ catalyzed reactions (0.6–1.1 mM hr⁻¹), and the effect of water upon the rates is significantly less in these uncatalyzed reactions (ca. 31% vs. ca. 182% increase).



Figure S7. Maleimide depletion observed by ¹H NMR for the uncatalyzed Diels–Alder cycloaddition reaction in ordinary CDCl₃ ('dry', red), and 50% volume water-saturated CDCl₃ ('wet', black). Linear fits on the initial 5 hours of the reaction time were computed to determine the initial reaction velocity.

12. ³¹P NMR studies of ^{C11}R₆ internal acidity

Two samples of ^{C11}**R**₆ (2 mL, 5.38 mM) were prepared as described above in CDCl₃. To each of these samples a quantity of solid Bu₃PO was added (either 1.52 mg or 8.73 mg) to produce samples with 0.65 or 3.72 equivalents of guest. These solutions were divided into two separate aliquots, one which was dried by molecular sieves (3.0 Å), and the other, 'wet' solution, remained with its initial water content. These solutions were then analyzed directly by ¹H NMR ($T_r = 1 \text{ s}$, 300 MHz), and ³¹P NMR (¹H decoupled, 121.44 MHz, $T_r = 0.2 \text{ s}$, ns = 256) as shown in Figures S10, S11, & S12. The dried solutions were then titrated with the 'wet' solutions to observe ³¹P chemical shifts of the encapsulated and free species over a range of water contents. From the resulting ¹H spectra, the integrated area of the water peak relative to ^{C11}R₆ ($\delta = 6.22$ ppm, 24H) was used to determine water content assuming a stable ^{C11}R₆ concentration (5.38 mM). After titration was complete, the sample featuring 24.00 mM of Bu₃PO guest was analyzed by ¹H-³¹P HMBC to assist peak assignment (Figure S13), DOSY NMR to validate capsule integrity and identify peaks of the encapsulated Bu₃PO by ¹H NMR (Figure S14).

In the dried sample (44.34 mM Water) containing the lower concentration of Bu₃PO (3.50 mM), we observed the near total (95.90 %) encapsulation of Bu₃PO by ¹H NMR, resulting in a remarkably sharp NMR spectrum (Figure S10). Upfield peaks (δ -2.0 – 0.5) correspond to the ³¹P coupled protons of the encapsulated species.



Figure S8. ¹H (left and middle), and ³¹P (right) NMR spectra obtained for a sample of ^{C11} \mathbf{R}_6 (5.38 mM) at low water content (44.18 mM) showing the encapsulation of Bu₃PO (middle, $\delta = -2.0-0.5$ ppm) and a single species appears in ¹H decoupled ₃₁P NMR.

In these ¹H decoupled ³¹P spectra, a major and minor peak are observed, we putatively assign this major peak ($\delta_{31P} = 64.28 \text{ ppm}$) to the ^{C11}**R**₆ encapsulated Bu₃PO. The minor downfield peak ($\delta_{31P} = 65.06 \text{ ppm}$) could not be attributed to a particular species experimentally due to its low intensity and fast relaxation. This peak is observable in ³¹P spectra at both high and low concentrations of Bu₃PO (Figures S11 & S12, respectively), decreasing in intensity with increasing water content.

During the titration of samples with a low (3.50 mM) and high (24.00 mM) concentrations of Bu₃PO we observed a third peak which we assigned to the free Bu₃PO. Interestingly, in ¹H NMR we observe the decrease of encapsulated Bu₃PO concomitant with increasing water content. We attribute this decrease of encapsulation to the favorable formation of hydrogen bonds between Bu₃PO and free water in the non-polar medium. Given the relatively high concentration of water compared to Bu₃PO, we surmise that while free water may compete with ^{C11}R₆ for Bu₃PO association, free Bu₃PO is unlikely to compete with ^{C11}R₆ for the association of the large excesses of free water. However, the effect of competition by free water for hydrogen bonded guests is interesting, and may impact catalytic applications—perhaps resulting in performance limitations as observed in this study (Figure 6).



Figure S9. NMR spectra obtained for a solution of ^{C11} R_6 (5.38 mM) and Bu₃PO (3.50 mM) in CDCl₃ at water concentrations ranging from 46.52–110.19 mM as labeled. ¹H NMR spectra shows the capsule (left), with upfield shifted encapsulated Bu₃PO (middle). Both free (**n**) and encapsulated (**v**) Bu₃PO were observed by both ¹H NMR (left, middle) and ³¹P NMR (right). Peaks corresponding to ^{C11} R_6 (*), water (w) and CDCl₃ (c) are annotated for reference with overlapping peaks featuring double annotation (e.g., c*).



Figure S10. NMR spectra obtained for a solution of ^{C11} R_6 (5.38 mM) and Bu₃PO (24.00 mM) in CDCl₃ at water concentrations ranging from 43.05–86.53 mM as labeled. ¹H NMR spectra shows the capsule (left), with upfield shifted encapsulated Bu₃PO (middle). Both free (**■**) and encapsulated (**▼**) Bu₃PO were observed by both ¹H NMR (left, middle) and ³¹P NMR (right). Peaks corresponding to ^{C11} R_6 (*), water (w) and CDCl₃ (c) are annotated for reference with overlapping peaks featuring double annotation (e.g., c*).



Figure S11. ${}^{1}H^{-31}P$ HMBC (${}^{1}H = 300$ MHz, ns = 5120, td = 64) spectra obtained for a sample of Bu₃PO (24.00 mM) and ${}^{C11}\mathbf{R}_{6}$ (5.38 mM) in CDCl₃ with a water content of 75.49 mM based on ${}^{1}H$ NMR integration. Internal ${}^{1}H$ trace (green) is obtained as the vertical sum of the 2d spectrum. External ${}^{1}H$ and ${}^{31}P$ traces are plotted from data obtained by separate measurement of the individual nuclear spectra, shown above in Figure S12.



Figure S12. ¹H DOSY diffusogram (300 MHz, 19-point decay) of ^{C11} R_6 (5.38 mM) and Bu₃PO (20 mM) in CDCl₃ with a water content of 75.49 mM determined by ¹H NMR. Diffusion was determined by contin fit using Topspin 4.0.9 "DOSY 2d" automation program with a 2-component fitting of the ¹H spectra obtained at 19 gradient strengths using a standard LED-type pulse program (ledbpgb2s). Peaks are attributed as annotated, with similar diffusing species highlighted highlighted, ^{C11} R_6 -A and encapsulated Bu₃PO (red), free Bu₃PO (green), water (light blue), residual CHCl₃(grey).

13. Model of water-mediated ^{C11}R₆ formation

The water dependent equilibrium between ^{C11}**R**₆-**A** and ^{C11}**R**₆-**B** may be modelled by a bimolecular association model for the association of non-structural water. A non-linear fit of the ¹H NMR data provides reasonable estimates of the maximum conversion ($\theta_{Max} = 0.43 \pm 0.03$) and equilibrium constant ($K_{eq} = 13.17 \pm 1.75$ mM). For practical purposes the analysis of our data used an empirical function (Equation S1) which includes terms to offset the 8 water molecules for the formation of the capsule.



Figure S13. Plot showing the water dependent conversion of $C^{11}R_6-A$ to $C^{11}R_6-B$ with non-linear fit of an empirical model detailed below in Equation S1.

$$\theta_{\rm B} = \frac{444.174 * c_{\rm wat}}{c_{\rm wat} + 0.05} - 443.578$$

Equation S1. Empirical function used for modeling of conversion between ${}^{C11}R_6$ -A and ${}^{C11}R_6$ -B based on the water content (c_{wat} , mM) determined by non-linear fitting.

14. Models of chemical exchange

Chemical exchange is often considered either 'fast' when a single peak is observed, or 'slow' when two peaks are apparent, in this section we provide detailed guidance on the NMR observation of chemically exchanging species, in particular the criterion for 'fast' exchange phenomenon, and how they appear in the experimental results of this study.



Figure S14. Examples of chemical exchange that appear 'fast' on the NMR time scale. (a) peaks are too similar in frequency to be distinguished, resulting in an observable peak (C). (b) exchange is very rapid, resulting in a single observable peak (C). (c) The combination of the previous two phenomenon as observed in this study.

If chemical exchange between two (or more) states faster than NMR can distinguish between the peaks corresponding to the individual states, then a single peak will be observed in the NMR spectrum that is the superposition of the two or more states—this is referred to as "fast exchange". The limit which NMR may distinguish between peaks is determined by their separation of those peaks (in Hz) as provided below in Equation S2.

$$k_{lim} = \frac{\Delta v}{\pi \sqrt{2}}$$

Equation S2. The limit to distinguish peaks for nuclei in chemical exchange by NMR (k_{lim}) is a consequence of the difference in peak frequency (Δv), given in Hertz (Hz, or s⁻¹).

This necessitates that if exchanging peaks are too similar in resonance frequency (in Hz), then they cannot distinguish even at seemingly slow rates of exchange (Figure S14a), this leads to the appearance of a single peak for aromatic peaks of ^{C11}R₆-A and ^{C11}R₆-B. Similarly, even if they are well separated, a sufficiently fast exchange will result in a single peak (Figure 14b), as was observed with the association of water. In the case of encapsulated Bu₃PO, the combination of a rapid exchange between hydrogen-bond adducts (Bu₃PO: ^{C11}R₆) and encapsulated (Bu₃PO@ ^{C11}R₆) states and the too similar frequencies of the environment within ^{C11}R₆-A or ^{C11}R₆-B, results in a single observable peak (Figure S14c) that is the population-weighted superposition of the four states.

15. Rearrangement of bridging waters in ^{C11}R₆-B

In our CMD simulations we observed rare rearrangement of the incorporated water molecules which form C11 **R**₆-**B**, an example of which is shown below in Figure S17. These events were rare with some simulations showing no rearrangements while others featuring several. Because of the rarity of this event, we are unfortunately unable to provide a quantitative analysis of the water bridge rearrangement using CMD.



Figure S15. An example of bridging water re-arrangement observed in the ^{C11} R_6 -B form of the capsule by a CMD simulation featuring a total of 18 water molecules. Renderings of individual states before, during, and after the transition of the water bridge (top), alongside a rolling average of the interfacial hydrogen bonds showing three transition events (red lines) over the course of the first 400 ns of an 800 ns total CMD trajectory (bottom). The six resorcin[4]arene faces, rendered in a CPK representation, are individually colored to distinguish movement of the incorporated water from the red-yellow edge to the cyan-yellow edge via an intermediate which features encapsulated water molecules (rendered in van der Waal volume spheres colored by atom). These renderings omit alkyl pendant groups and non-hydroxy hydrogen atoms for clarity, though they are included in the CMD models.

16. Hydrogen-Bond Network in ^{C11}R₆-B



Figure S16. Rendering depicting a typical hydrogen bond network of the associated water molecules found in $^{C11}R_6$ -B. Aryl and alkyl hydrogen atoms and alkyl pendant groups, and distant resorcin[4] arene monomer, omitted for clarity.





Figure S17. Depiction of the isomerization between Diels-Adler inactive s-trans sorbyl alcohol and its Diels-Adler active s-cis isomer (a), the free energies computed by DFT at a B3LYP/def2tzv theory level obtained from a relaxed energy scan of the central dihedral. Energies for the s-trans (red), intermediate (green) and s-cis isomers are highlighted for reference. The intermediate isomer was optimized separately as a transition state resulting in a minimum barrier of 7.96 kcal mol⁻¹, these calculations revealed a single imaginary vibrational frequency ($v_{ts} = -167.50 \text{ cm}^{-1}$), corresponding to the dihedral rotation.

18. Model Data for ^{C11}R₁ monomer

Table S2. Mol2 data file with atom information (left) and connectivity (right) for monomer subunit used in MD.

0 <tripos-molecule< td=""><td>0-TRIPOS-BOND</td></tripos-molecule<>	0-TRIPOS-BOND
R4A	1 1 33 1
180 184 1 0 1	1 1 32 1
SMALL USER_CHARGES	$ \begin{array}{c} 3 \\ 4 \\ 2 351 \end{array} $
U <tripos-atom I C1 -5.419000 1.746000 -0.136000 ca 1 R4A 0.2023 **** D c2 - 5 755000 1.550000 1.435000 ca 1 R4A 0.2723 ****</tripos-atom 	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
\$ C5 -4:638000 6:3633000 -2:357000 Ca 1 K4A -0:5053 **** 4 C4 -3:653000 0:435900 -3:85000 -3 K4A -0:718 ****	
5 C5 -3.332000 0.648000 -0.510000 Ca 1 R4A -0.2437 ****	10 5 36 1
6 C6 -4.203000 1.276000 0.389000 ca 1 R4A -0.0718 ****	11 5 6 1
/ C/ -2.625000 -0.222000 -2.820000 C3 1 R4A -0.2534 ***** 8 C8 -2.042000 -1.530000 -2.241000 C3 1 R4A -0.1341 **** 9 C9 -2.666000 -4.245000 -1.566000 ca 1 R4A -0.233 ****	
10 C10 2.666000 5.199000 -0.580000 ca 1 R4A -0.2772 ****	15 7 22 1
11 C11 2.170000 4.897000 0.694000 ca 1 R4A 0.2023 ****	16 8 38 1
12 C12 1.589000 3.641000 0.959000 ca 1 R4A -0.0718 **** 13 C13 1.563000 2.712000 -0.99000 ca 1 R4A -0.2437 ****	17 8 39 1 18 8 97 1 19 0 0 10 1
15 C15 0.934000 3.350000 2.315000 c3 1 R4A 0.2534 ****	20 9 10 1
16 C16 1.333000 1.980000 2.903000 c3 1 R4A -0.1341 ****	21 9 14 1
17 C17 -1.879000 1.669000 -4.381000 ca 1 R4A 0.2023 ****	22 10 42 1
18 C18 -0.399000 2.601000 -4.822000 ca 1 R4A 0.20772 ****	23 10 11 1
10 C10 0.312500 2.601000 -4.32000 ca 1 R4A 0.20772 ****	34 10 11 1
20 C20 0.661000 1.831000 -3.147000 ca 1 R4A -0.0718 **** 21 C21 -0.314000 0.933000 -2.731000 ca 1 R4A -0.2437 ****	
22 C22 -1.581000 0.788000 -3.316000 ca 1 R4A -0.0718 **** 23 C23 2.041000 1.921000 -2.489000 c3 1 R4A 0.2534 ****	27 12 15 1 28 13 43 1 29 13 14 1
24 C24 2.05000 0.05000 -2.03200 C3 1 R4A -0.1341 -0.233 **** 25 C25 -1.122000 4.880000 2.314000 ca 1 R4A -0.223 **** 26 C26 -2.499000 5.087000 2.232000 ca 1 R4A -0.2772 ****	30 14 23 1 31 15 16 1
27 C27 -3.375000 4.010000 2.072000 ca 1 R4A 0.2023 **** 28 C28 -2.883000 2.688000 2.010000 ca 1 R4A 0.0718 **** 20 C20 1.0220 0.0220 0.0220 0.0020 0.0020 0.0000 0.0000 0.0000 0.00000 0.000000 0.000000	32 15 44 1 33 15 30 1
29 C29 -1.95000 2.52000 2.05000 Ca 1 R4A -0.0718 **** 30 C30 -0.582000 3.575000 2.245000 ca 1 R4A -0.0718 **** 31 C31 -3.842000 1.502000 1.662000 c3 1 R4A 0.2334 ****	35 16 46 1 36 16 133 1
32 C32 -3.351000 0.229000 2.596000 C3 1 R4A -0.1341 ****	37 17 47 1
33 01 -6.275000 2.402000 0.724000 ch 1 R4A -0.4696 ****	38 17 22 1
34 U23.199000 1.990000 -3.65000 ha 1 R4A -0.4056 **** 35 H1 -6.711000 1.920000 -1.866000 ha 1 R4A 0.1315 **** 36 H2 -2.364000 0.312000 -0.135000 ha 1 R4A 0.1487 ****	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
37 H3 -3.206000 -0.541000 -3.699000 hc 1 R4A 0.0134 ****	42 19 48 1
38 H4 -1.371000 -1.321000 -1.390000 hc 1 R4A 0.0257 ****	43 19 20 1
40 03 3.064000 4.533000 -2.865000 ch 1 R4A -0.4696 ****	45 20 23 1
41 04 2.240000 5.821000 1.702000 ch 1 R4A -0.4696 ****	46 21 50 1
42 H6 3.095000 6.187000 -0.768000 ha 1 R4A 0.1515 ****	47 21 22 1
43 H7 1.102000 1.740000 0.094000 ha 1 R4A 0.1487 ****	48 23 24 1
44 H8 1.338000 4.091000 3.023000 hc 1 R4A 0.0134 *****	49 23 51 1
45 H9 1.061000 1.164000 2.211000 hc 1 R4A 0.0267 ****	50 24 52 1
46 H10 0.7340000 1.8100000 3.814000 hc 1 R4A 0.0267 ****	51 24 53 1
47 05 -3.082000 1.665000 -5.030000 oh 1 R4A -0.4696 ****	52 24 125 1
48 05 1.159000 3.630000 -4.720000 oh 1 R4A -0.4696 ****	53 25 54 1
-2.112 - 1.120000 - 3.230003.032000 ina 1.184A 0.1213 **** 50 H12 - 0.062000 0.2380001.0122000 ha 1.R4A 0.1487 **** 51 H13 2.732000 2.2800003.267000 hc 1.R4A 0.0134 ****	55 25 26 1 56 26 36 1
52 H14 1.962000 0.080000 -1.296000 hc 1 R4A 0.0267 **** 53 H15 3.562000 0.773000 -1.487000 hc 1 R4A 0.0267 ****	57 26 27 1 58 27 55 1 27 30 1
>= u/ -u.s=>>uu >.y=9uuu 2.4=\$uuu on 1 R4A -U.4=\$U\$ **** 55 o8 -4.703000 4.321000 2.009000 oh 1 R4A -0.4696 **** 56 H16 -2.910000 6.096000 2.287000 ha 1 R4A -0.1515 ****	60 28 29 1 61 28 31 1
57 HI7 -1.058000 1.506000 2.049000 Ha 1.84A 0.11487 ****	62 29 37 1
58 H18 -4.772000 1.790000 2.376000 hc 1.84A 0.0134 ****	63 29 30 1
J9 RL2 = 2.580000 U.500000 3.210000 RC I N4A U.020 ⁷ **** 60 H20 = 2.580000 - 0.291000 2.001000 RC I R4A 0.0267 **** 61 H21 0.6688000 5.771000 2.466000 h0 I R4A 0.3451 ****	65 31 58 1 66 32 59 1
62 H22 -7.062000 2.699000 0.248000 ho 1 R4A 0.3451 ****	67 32 60 1
63 H23 -5.638000 1.502000 -4.030000 ho 1 R4A 0.3451 ****	68 32 69 1
64 H34 2.355000 -5.640000 ho 1 R4A 0.3451 ****	69 32 61 1
65 H25 2:050000 6:730000 1:351000 H6 1 R4A 0:3451 ****	70 34 63 1
66 H26 -3.715000 1:049000 -4.606000 h0 1 R4A 0:3451 ****	71 40 64 1
67 H27 1.878000 3.879000 -4.096000 ho 1.84A 0.3451 ****	72 41 65 1
68 H28 -5.255000 3.994000 1.662000 ho 1.84A 0.3451 ****	73 47 66 1
69 H38 -4.440000 -0.7272000 3.094000 r3 1.84A 0.0198 ****	74 48 67 1
70 H37 -3.970000 -1.501000 3.692000 hc 1 R4A -0.0091 ****	75 54 61 1
71 H38 -5.204000 -0.251000 3.606000 hc 1 R4A -0.0091 ****	76 55 68 1
72 C34 -5.138000 -1.543000 1.873000 c3 1 R4A 0.0116 ****	77 69 70 1
73 H39 -5.672000 -0.831000 1.223000 hc 1 R4A -0.0129 ****	78 69 71 1
74 H40 -4.372700 -2.020000 1.227000 hc 1 R4A -0.0129 ****	70 69 72 1
73 c35 -6.137000 -2.850000 2.350000 c3 1 R4A 0.0010 ****	80 72 73 1
76 H41 -6.853000 -2.147000 3.057000 hc 1 R4A -0.0050 ****	81 72 74 1
// H42 = -6./39000 = -2.952000 1.484000 hC 1 R4A = -0.0050 *****	82 72 75 1
78 C36 = -5.505000 = -3.523000 3.010000 C3 1 R4A = -0.0390 *****	83 75 76 1
79 H43 = -4.873000 = -3.523000 3.857000 hC 1 R4A = 0.0053 ****	84 75 77 1
80 H44 -4.818000 -4.325000 2.288000 hc 1 R4A 0.0053 ****	85 75 78 1
81 c37 -6.508000 -4.885000 3.527000 c3 1 R4A -0.0213 ****	86 78 79 1
82 H45 -5.95000 -5.654000 4.097000 hc 1 R4A 0.0068 *****	87 78 80 1
83 H46 -7.180000 -4.397000 4.254000 hc 1 R4A 0.0068 *****	88 78 81 1
84 C38 -7.330000 -5.580000 2.433000 c3 1 R4A -0.0179 ****	89 81 82 1
85 H47 -8.001000 -4.850000 1.946000 hc 1 R4A 0.0257 ****	90 81 83 1
86 H48 -6.632000 -5.9340000 1.642000 hc 1 R4A 0.0257 ****	91 81 84 1
87 C39 -6.153000 -6.198000 2.68300 C3 1 R4A -0.0539 *****	92 64 65 1
88 H49 -6.535000 -7.278000 1.942000 hc 1 R4A 0.0068 *****	93 84 86 1
89 H50 -7.556000 -7.547000 3.342000 hc 1 R4A 0.0068 ****	94 84 87 1
90 C40 -9.378000 -6.534000 3.778000 c3 1 R4A 0.0800 ****	95 87 88 1
91 H51 -10.099000 -7.338000 3.635000 hc 1 R4A -0.0171 ****	96 87 89 1
92 H52 -9,90000 -3,024000 3,32000 HC 1 R4A -0.0171	97 87 90 1 98 90 91 1 99 90 92 1
95 H54 -8.441000 -5.565000 5.521000 hc 1 R4A 0.0261 ****	100 90 93 1
96 H55 -10.017000 -6.308000 5.854000 hc 1 R4A 0.0261 ****	101 93 94 1
07 H25 -11 202000 -1.202000 5.217100 hc 1 R4A 0.01261 *****	102 102 103 104 1
98 H56 - 1.994000 -2.632000 +6.1000 hc 1 R4A -0.0091 ****	102 93 96 1
99 H57 -0.490000 -1.798000 -3.722000 hc 1 R4A -0.0091 ****	104 97 98 1
100 C43 -0.713000 -3.696000 -2.712000 c3 1 R4A 0.0116 **** 101 H58 -0.021000 -3.450000 -1.857000 hc 1 R4A -0.0129 ****	105 97 99 1 106 97 100 1 107 100 1
105 C44 -0.756000 -4.717000 -2.237000 c3 1 R4A 0.0010 ****	106 100 102 1
104 H60 -2.311000 -4.309000 -1.372000 hc 1 R4A -0.0050 ****	109 100 103 1
105 H61 -2.506000 -4.841000 -3.039000 hc 1 R4A -0.0050 ****	110 103 104 1
106 C45 -1.230000 -6.112000 -1.860000 C3 1 R4A -0.0053 ****	111 103 105 1
107 H62 -2.111000 -6.752000 -1.681000 hc 1 R4A -0.0053 ****	112 103 106 1
108 H63 -0.714000 -6.559000 -2.730000 hc 1 R4A 0.0104 ****	113 106 107 1
109 c46 -0.310000 -6.196000 -0.624000 c3 1 R4A -0.0162 ****	114 106 108 1
110 Hb4 -0.4/7000 -7.169000 -0.132000 hc 1 R4A 0.0119 *****	115 106 109 1
111 H65 -0.622000 -5.435000 0.117000 hc 1 R4A 0.0119 *****	116 109 110 1
112 cd7 1.191000 -6.048000 -0.909000 c3 1 R4A -0.0128 ****	117 109 111 1
113 H66 1.504000 -6.852000 -1.601000 hc 1 R4A 0.0308 ****	118 109 112 1
114 H67 1.375000 -5.105000 -1.449000 hc 1 R4A 0.0308 ****	119 112 113 1
116 H67 1.375000 -5.032000 -0.322000 hc 1 R4A 0.0308 ****	119 112 113 1
115 C46 2.092000 -6.078000 0.335000 C5 1 R4A -0.0308 ****	120 112 114 1
116 H68 3.124000 -5.826000 0.027000 hc 1 R4A 0.0119 ****	121 112 115 1
117 H69 1.784000 -5.272000 1.028000 hc 1 R4A 0.0119 ****	122 115 116 1
118 C49 2.123000 -7.409000 1.094000 c3 1 R4A 0.0851 **** 119 H70 1.111000 -7.660000 1.457000 hc 1 R4A -0.0120 ****	123 115 117 1 124 115 118 1 124 115 118 1
120 H/1 2,40000 -8,42000 2,278000 c3 1 R4A -0.1235 ****	125 118 120 1
121 C50 3.092000 -7,405000 2,278000 c3 1 R4A -0.1235 ****	127 118 121 1
123 H/3 4.125000 -7.201000 1.951000 hc 1 R4A 0.0312 ****	128 121 122 1
124 H/4 2.822000 -6.631000 3.015000 hc 1 R4A 0.0312 ****	129 121 123 1
125 c51 2.912700 -0.402700 -3.12840 0.0248 ****	130 121 123 1
126 H75 3.597000 0.083000 -3.900000 hc 1 R4A -0.0040 ****	130 125 126 1
127 H76 1.988000 -0.614000 -3.738000 hc 1 R4A -0.0040 ****	132 125 127 1
129 C.22. 2. 340000 -1.728000 -2.717000 c5 1 R4A 0.0157 **** 129 H77 4.457000 -1.512000 -2.140000 hc 1 R4A -0.0078 **** 130 H78 2.852000 -2.729000 -2.010000 hc 1 R4A -0.0078 ****	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
131 C53 3.860000 -2.687000 -3.865000 C3 I R4A 0.0001 **** 132 H79 4.567000 -2.197000 -4.564000 hc 1 R4A 0.0002 ****	136 128 131 Ī 137 131 132 1 138 131 132 1
134 C54 4.427000 -4.050000 -3.446000 c3 1 R4A -0.0339 ****	139 131 134 1
135 H81 3.721000 -4.356000 -2.747000 hc 1 R4A -0.0104 ****	140 134 135 1
136 H82 4.467000 -4.706000 -4.334000 hc 1 R4A 0.0104 ****	141 134 136 1
137 C55 5.821000 -4.007000 -2.869000 c3 1 R4A -0.0162 ****	142 134 137 1
138 H83 5.801000 -3.382000 -1.807000 hc 1 R4A -0.012	143 137 138 1
139 H84 6.520000 -3.502000 -3.502000 -1.844 0.0119 ****	144 137 139 1
140 C56 6.374000 -5.390000 -2.452000 c3 1 R4A -0.0128 ****	145 137 140 1
141 H03 3.0700UU -3.432UUU -1./352UUU NC 1 R4A 0.0308 ****	140 141 141 1
142 H85 6.390000 -6.015000 -3.362000 hc 1 R4A 0.0308 ****	147 140 142 1
143 C57 7.771000 -3.349000 -1.820000 c3 1 R4A -0.050R ****	148 140 143 1
144 H87 8.475000 -4.868000 -2.526000 hc 1 R4A 0.0119 ****	149 143 144 1
145 H88 7.738000 -4.689000 -0.934000 hc 1 R4A 0.0119 ****	150 143 145 1
146 C58 8.335000 -6.713000 -1.398000 c3 1.84A 0.0851 ****	151 143 146 1
147 H89 7.635000 -7.190000 -0.687000 hc 1.84A -0.0120 ****	152 146 147 1
148 W0 9.768000 -6.547000 -0.831000 hc 1.84A -0.0120 ****	153 146 148 1
149 C59 8.623000 -7.678000 -2.552000 C3 1 R4A -0.1235 *****	154 146 149 1
150 H91 7.708000 -7.948000 -3.104000 hc 1 R4A 0.0312 *****	155 149 150 1
152 H92 9.377000 -7.234000 -3.270000 RC 1 R4A 0.0312 ****	150 149 151 1
152 H93 9.072000 -8.615000 -2.185000 RC 1 R4A 0.0312 ****	157 149 152 1
153 C60 2.822000 1.8560000 3.246000 C3 1 R4A 0.0249 ****	158 153 154 1
154 H94 3.089000 2.662000 3.967000 hc 1 R4A -0.0040 ****	159 153 155 1
155 H95 3.420000 2.066000 2.341000 hc 1 R4A -0.0040 ****	160 153 156 1
130 H92 2.553000 0.302000 4.7799000 H2 1 R4A -0.0078 ****	162 156 158 1
158 H97 2.969000 -0.290000 3.102000 hc 1 R4A -0.0078 ****	163 156 159 1
159 Cb2 4.667000 0.372000 4.276000 C3 1 R4A 0.0061 *****	164 159 160 1
160 H98 4.790000 -0.586000 4.813000 hc 1 R4A 0.0001 *****	165 159 161 1
161 H99 4.8900000 1.162000 5.015000 hc 1 R4A 0.0001 *****	166 159 167 1
162 C63 5.689000 0.422000 3.132000 c3 1 R4A -0.0339 ****	167 162 163 1
163 H100 5.639000 1.403000 2.625000 hc 1 R4A 0.0104 ****	168 162 164 1
109 H1U1 5.359000 -0.520000 6.353000 c3 1 R4A -0.0162 **** 165 C64 7.141000 0.154000 3.553000 c3 1 R4A -0.0162 **** 166 H102 7.199000 -0.830000 4.055000 hc 1 R4A 0.0119 ****	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
167 H103 7.761000 0.061000 2.642000 hc 1 R4A 0.0119 ****	172 165 168 1
168 C65 7.765000 1.222000 4.460000 c3 1 R4A -0.0128 ****	173 168 169 1
169 U104 7 668000 1.220000 hc 1 R4A -0.0128 ****	174 168 170 1
170 H105 7, 193000 1, 297000 5, 402000 hc 1 R4a 0, 0308 ****	175 168 171 1
171 c66 9, 236000 0, 947000 4, 79500 c3 1 R4A -0, 0508 ****	176 171 172 1
172 H106 9.821000 0.903000 3.857000 hc 1 R4A 0.0119 ****	177 171 173 1
173 H107 9.313000 -0.062000 5.241000 hc 1 R4A 0.0119 ****	178 171 174 1
174 c67 9.887000 1.958000 5.750000 c3 1 R4A 0.0851 ****	179 174 175 1
175 HIDS 5.3070000 1.3590000 6.691000 hc 1 RMA -0.0120 ****	180 174 176 1
175 HIDS 10.857000 1.557000 6.028000 hc 1 RMA -0.0120 ****	181 174 177 1
178 H110 10.608000 3.377000 4.251000 hc 1 R4A -0.0312 **** 178 H110 10.608000 3.837000 4.251000 hc 1 R4A 0.0312 ****	102 1/7 1/9 1 183 177 179 1 184 177 180 1
180 H112 10.547000 4.036000 5.901000 hc 1 R4A 0.0312 ****	0 <tripos>SUBSTRUCTURE</tripos>
@ <tripos>BOND</tripos>	1 R4A 1 **** 0 ****

Table S3. Amber forcefield file used during simulations.

Supplementary Material.

monomer.mol2 — Contains charges, coordinates and connectivity of monomer (Table S2)

sim.frcmod — Contains forcefield parameters in Amber format (Table S3)

References

1. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian 16 Revision C.01, Gaussian Inc., Wallingford CT, 2016.

2. Wang, J.; Wang, W.; Kollman P. A.; Case, D. A. Automatic atom type and bond type perception in molecular mechanical calculations. J. Mol. Graph. Model. 2006, 25, 247260.

3. Bannwarth, C.; Ehlert, S.; Grimme, S. GFN2-xTB—An Accurate and Broadly Parametrized Self-Consistent Tight-Binding Quantum Chemical Method with Multipole Electrostatics and Density-Dependent Dispersion Contributions. J. Chem. Theory Comput. 2019, 15 (3), 1652–1671, DOI: 10.1021/acs.jctc.8b01176.

4. Fox, T., & Kollman, P. A. Application of the RESP Methodology in the Parametrization of Organic Solvents. J. Phys. Chem. B 1998, 102(41), 8070–8079, DOI:10.1021/jp9717655.

5. Betz, R. M., & Walker, R. C. Paramfit: Automated optimization of force field parameters for molecular dynamics simulations. J. Comput. Chem. 2014, 36(2), 79–87, DOI:10.1002/jcc.23775.

6. Wang, J., Wolf, R. M.; Caldwell, J. W.;Kollman, P. A.; Case, D. A. Development and testing of a general AMBER force field. J. Comput. Chem. 2004, 25, 1157–1174.

7. Rappe, A. K.; Casewit, C. J.; Colwell, K. S.; Goddard, W. A. III; Skiff, W. M. UFF, a full periodic table force field for molecular mechanics and molecular dynamics simulations. J. Am. Chem. Soc. 1992, 114, 10024–10039.

8. Martínez, L.; Birgin, R.; Birgin, E. G.; Martínez, J. M. Packmol: A package for building initial configurations for molecular dynamics simulations. J. Comput. Chem. 2009, 30(13), 2157–2164.

9. Wu, Y.; Tepper, H. L.; Voth, G. A. Flexible simple point-charge water model with improved liquid-state properties. J. Chem. Phys. 2006, 124(2), 024503, DOI:10.1063/1.2136877

10. Case, D. A.; Cerutti, D. S.; Cheatham, T. E., III; Darden, T. A.; Duke, R. E.; Giese, T. J.; Gohlke, H.; Goetz, A. W.; Izadi, S.; Janowski, P.; Kaus, J.; Kovalenko, A.; Lee, T. S.; LeGrand, S.; Li, C.; Lin, T. L., Luo, R.; Madej, B.; Mermelstein, D.; Merz, K. M.; Monard, G.; Nguyen, H.; Nguyen, I.; Omelyan, A. O., Roe, D. R.; Roitberg, A.; Sagui, C.; Simmerling, C. L.; Botello-Smith, W. M.; Swails, J.; Walker, J. W., Wolf, R. M.; Wu, X.; Xiao, L.; Kollman, P. A. AMBER 2016, University of California, San Francisco, 2016.

11. Salomon-Ferrer, R.; Goetz, A.W.; Poole, D.; Le Grand, S.; Walker, R.C. Routine microsecond molecular dynamics simulations with AMBER on GPUs. 2. Explicit solvent Particle Mesh Ewald. J. Chem. Theory Comput. 2013 9, 3878–3888.

12. Ramsey, S.; Nguyen, C.; Salomon-Ferrer, R.; Walker, R. C.; Gilson, M. K.; Kurtzman, T. Solvation thermodynamic map-ping of molecular surfaces in AmberTools: GIST. J. Comput. Chem. 2016, 37 (21), 2029–2037, DOI: 10.1002/jcc.24417.

13. Elidrisi,I.; Negin, S.; Bhatt, P. V.; Govender, T.; Kruger, H. G.; Gokel, G. W.; Maguire, G. E. M. Pore formation in phospholipid bilayers by amphiphilic cavitands. Org. Biomol. Chem. 2011, 9, 4498–4506, DOI: 10.1039/C0OB01236J.

14. Stirling, C. J. M.; Fundin, L. J.; Williams, N. H. Trimorphism in solid resorcinarenes. Chem. Commun. 2007, (17), 1748–1750, DOI: 10.1039/b700469a.

15. Payne, R. M.; Oliver, C. L. A propanol-seamed C-methylcalix[4]resorcinarene hexamer accessible via solution crystallization, liquid-assisted grinding and vapour sorption. CrystEngComm 2018, 20 (14), 1919–1922, DOI:10.1039/c8ce00294k.