Electronic Supplementary Material (ESI) for CrystEngComm.


# Enantiospecific recognition of 2-butanol by an inherently chiral cavitand in the solid state

G. Brancatelli,[a] C. Nicosia,[b] T. Barboza,[b] L. Guy,[c] J.-P. Dutasta,[c] R. De Zorzi,[a] N. Demitri,[a] E. Dalcanale,[b] S. Geremia[a]*and R. Pinalli[b]*

a. CEB Centre of Excellence in Biocrystallography, Department of Chemical and Pharmaceutical Sciences, University of Trieste, Via L. Giorgieri 1, 34127, Trieste, Italy

b. Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma and INSTM UdR Parma, Parco Area delle Scienze 17/A, 43124 Parma (Italy).

c. Laboratoire de Chimie, CNRS and École Normale Supérieure de Lyon, Lyon 07, France

## Electronic Supplementary Information

**Characterization of achiral cavitand 5**

**$^{1}$H NMR (300 MHz, $CDCl_3$)**: δ = 8.17 (m, 2H, P(S)$ArH_{ortho}$); 8.08 (m, 4H, P(O)$ArH_{ortho}$); 7.69-7.50 (m, 9H, P(X)$ArH_{para}$, P(X)$ArH_{meta}$, X=O,S); 7.28 (m, 4H, $ArH_{down}$); 6.83 (s, 2H, $ArH_{up}$); 6.81 (s, 2H, $ArH_{up}$); 5.70 (d, 1H, $CH_{2(out)}$, J=7.4 Hz); 4.92 (d, 1H, $CH_{2(in)}$, J=7.4 Hz); 4.68 (m, 4H, ArCH); 2.37 (m, 8H, $CH_2CH_3$); 1.07 (m, 12H, $CH_2CH_3$);

**$^{31}$P NMR (162 MHz, $CDCl_3$)**: δ = 78.70 (s, 1P, P=S); 8.82 (s, 2P, P=O)

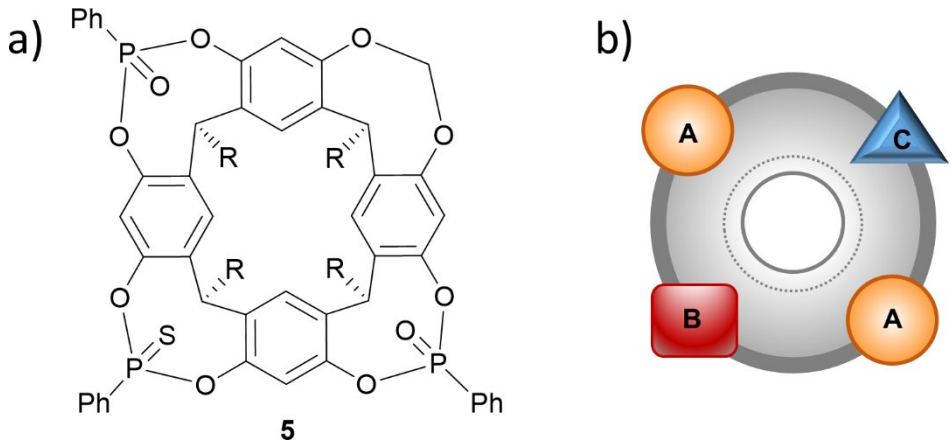


**Figure S1.** Achiral cavitand **5** (a) in a ABAC configuration (b).

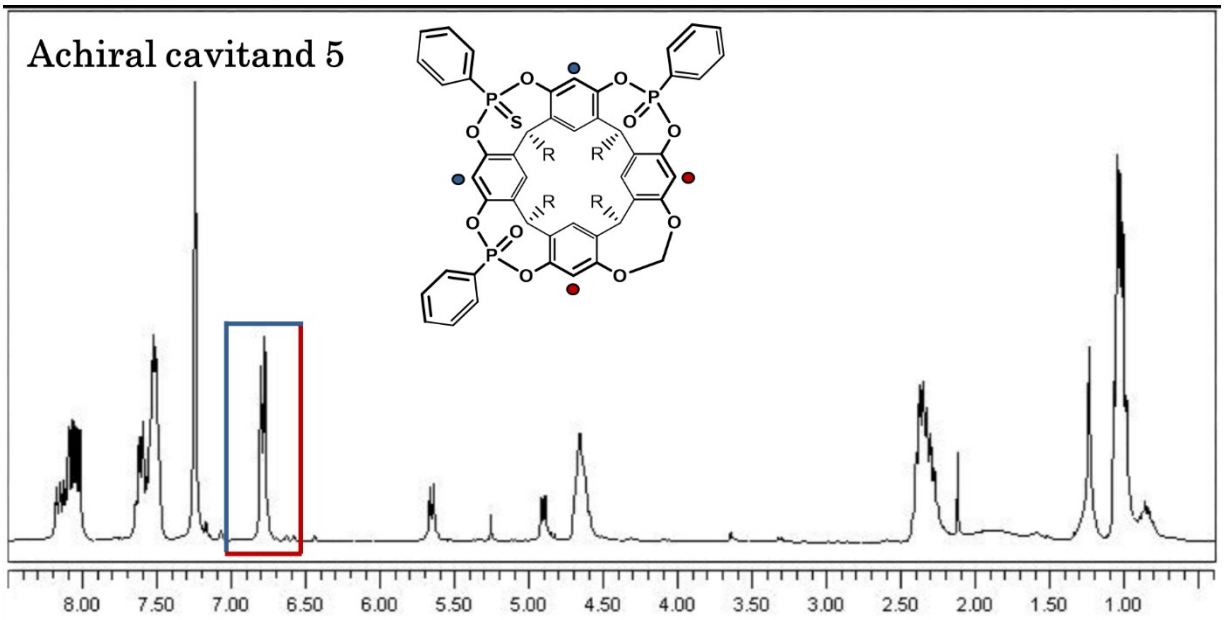


**Figure S2.** $^{1}$H NMR of the achiral cavitand **5.** The two signals corresponding to the apical protons are highlighted.

**Characterization of cR/cS-cav**

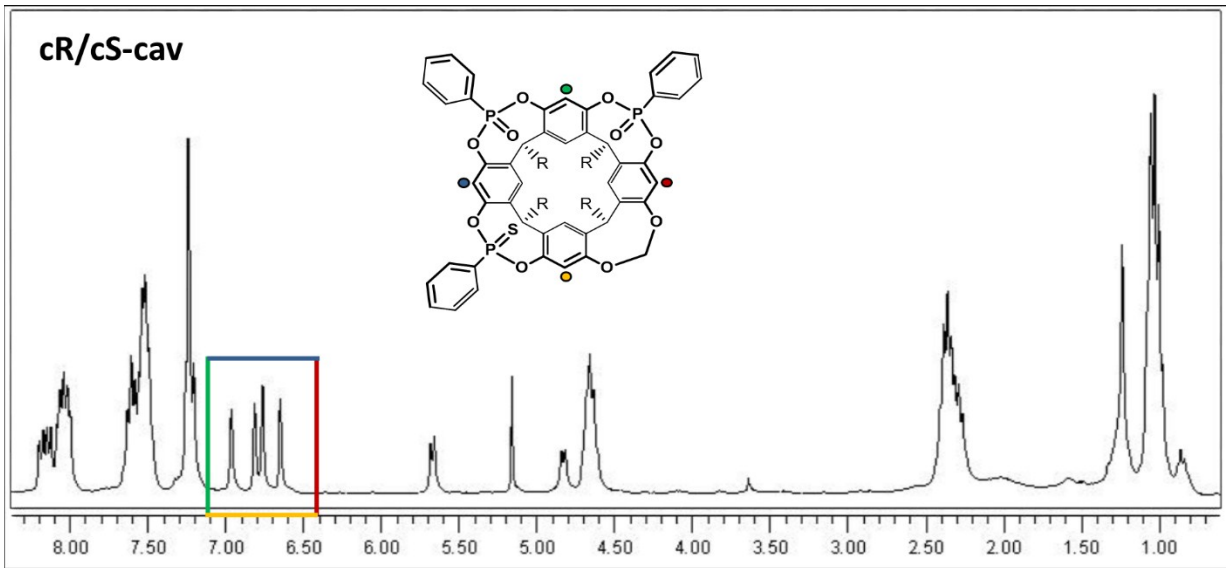


**Figure S3.** $^{1}$H NMR of the chiral isomer cR/cS-cav. The four different apical signals are highlighted.

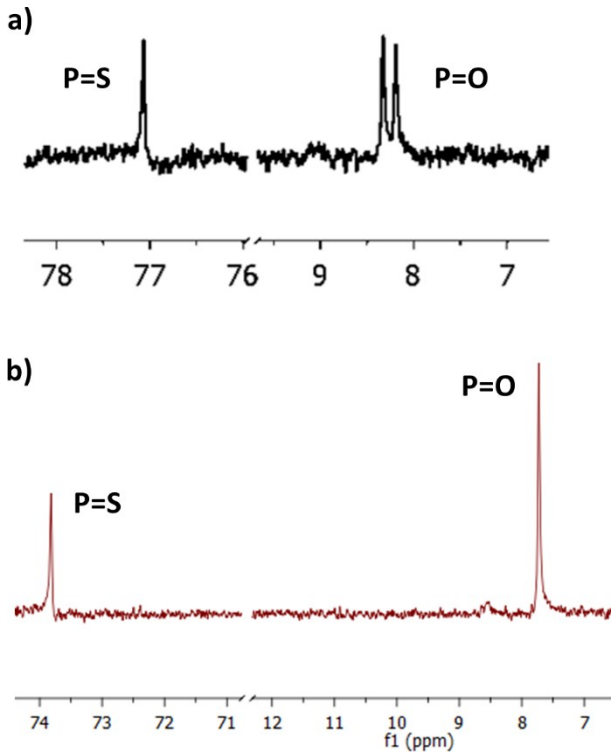


**Figure S4.** Comparison between the $^{31}$P NMR of the chiral isomer cR/cS-cav and cavitand **5**.

**Chiral HPLC chromatogram**

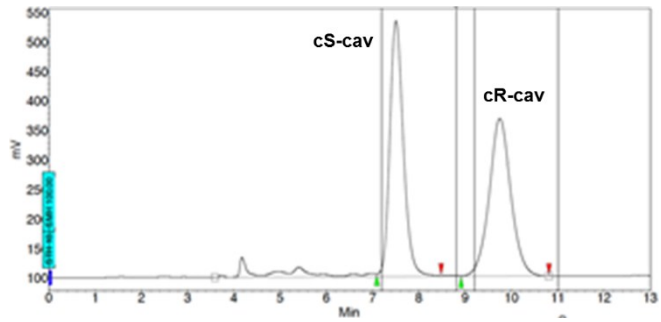


**Figure S5.** Analytical HPLC chromatogram of the cR/Cs cavitands chiral resolution.

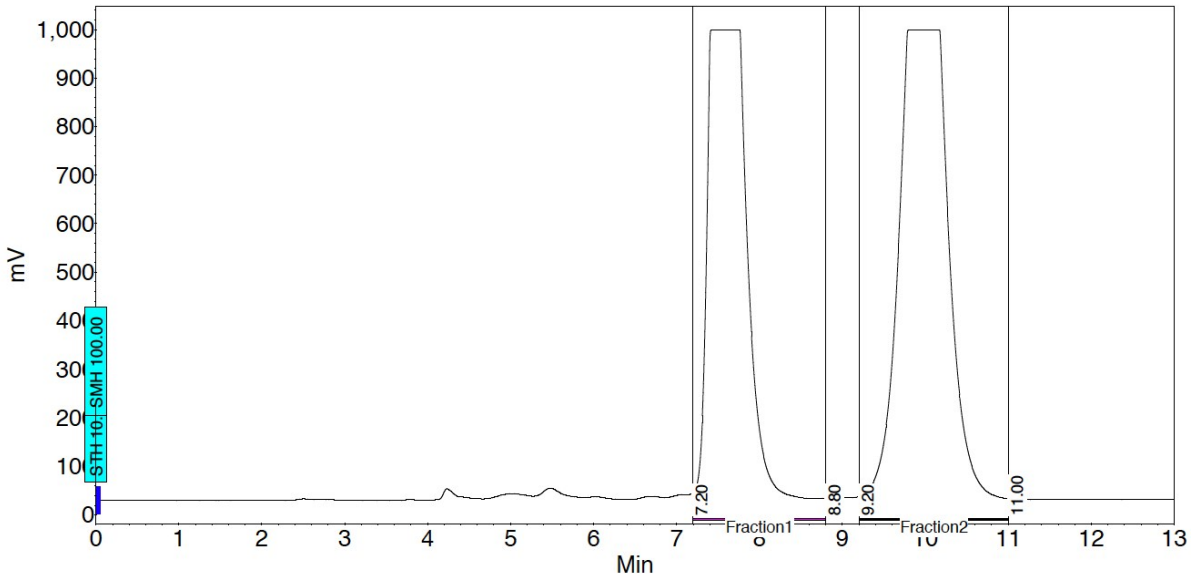


**Figure S6.** Chromatogram performed by semi-preparative HPLC on concentrated samples. Column: chiral pack IC (10x250mm). Eluent: $CH_3CN/H_2O$/Acetone 8/2/2. Flow rate 4.5 mL/min .

**Crystals structure of the complexes**

In the picture below the structure of the racemic complexes of the cavitand with 2-butanol is shown.

In the asymmetric unit of the crystal two cavitand molecules with opposite configuration were identified, together with three 2-butanol molecules and two water molecules (Figure S7). In the cavity of each cavitand a 2-butanol guest alcohol molecule was located. The two enantiomeric cavitands were hosting the two enantiomers of the 2-butanol: the cavity of the S-cavitand was occupied by the 2-butanol molecule with S configuration, and similarly the cavity of the R-cavitand hosted the R-2-butanol, as observed in Figure S8. Conversely from what observed in the structure of the enantiopure R-cavitand with the R-2- butanol, in the structure of the racemic mixture the methyl group of the alcohol guest molecule is pointing towards the cavity.

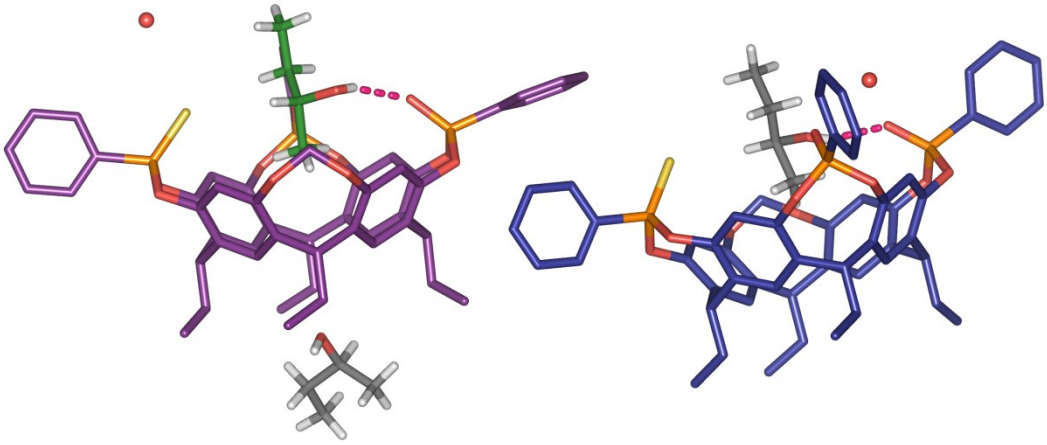

**Figure S7.** Asymmetric unit content of the crystals of the racemic mixture of cavitands with 2-butanol. Unit cell dimensions: $P2_1/n$, a = 24.150(5), b = 15.847(3), c = 31.397(6) Å, α = 90, β = 96.99(3), γ = 90, V = 11927(4), Z = 8, ρ = 1.252, $R_1$ 0.1031, w$R_2$ = 0.2556, total reflections 9333.

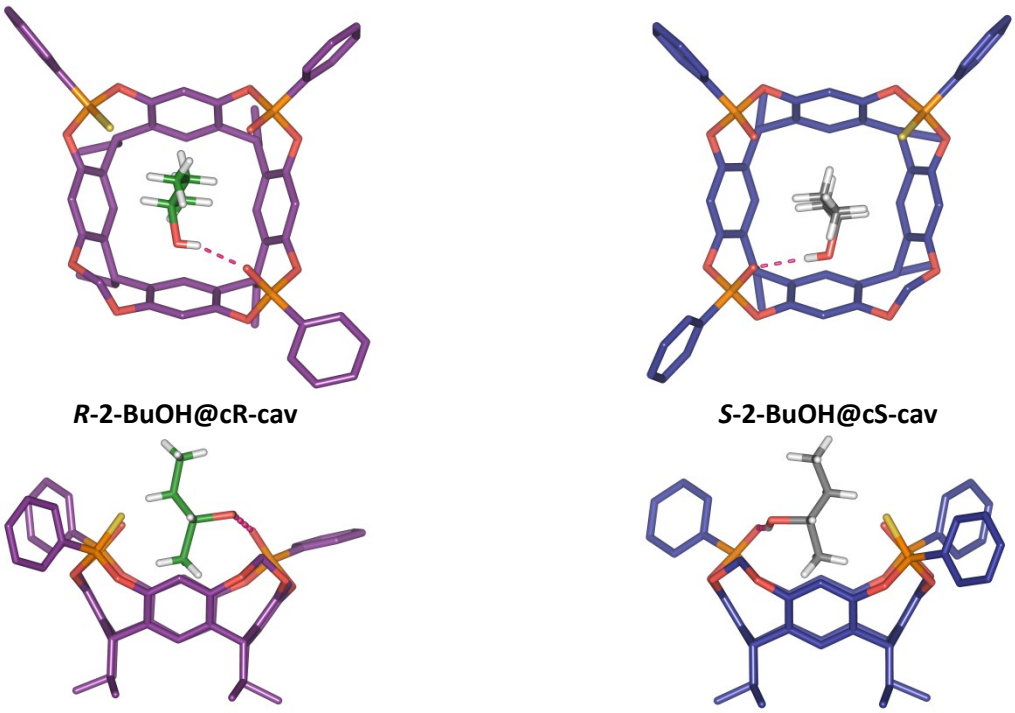


**Figure S8.** Top and side views of the diastereomeric complexes, obtained by co-crystallization of the racemic mixture of the cavitand in the presence of R/S-2-butanol.

**Table S1. Crystallographic data and refinement details for (±)-2-butanol@cS/cR-cav.**

| | **(±)-2-butanol @ cS/cR-cav** |
|---|---|
| Empirical formula | $C_{55}H_{49}O_{10}P_3S$, 2.7 $C_4H_{10}O$, $H_2O$ |
| Formula weight | 1213.07 |
| T (K) | 100(2) K |
| $\lambda$ (Å) | 1.542 |
| Crystal system | Monoclinic |
| Space group | $P\ 2_1/n$ |
| Unit cell dimensions (Å, °) | $a$ = 24.150(5)<br>$b$ = 15.847(3), $\beta$ = 96.99(3)<br>$c$ = 31.397(6) |
| $V$ (Å$^3$) | 11927(4) |
| $Z$ | 8 |
| $\rho_{calc}$ (g/cm$^3$) | 1.351 |
| μ (mm$^{-1}$) | 1.700 |
| F(000) | 5147.2 |
| Crystal size (mm$^3$) | 0.200 x 0.100 x 0.100 |
| θ range (°) | 2.184 to 44.494 |
| Reflections collected | 23805 |
| Independent reflections | 9333 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data/restraints/parameters | 9333 / 9 / 740 |
| GooF | 1.042 |
| $R_1$, $wR_2$ [I>2σ(I)] | 0.1031, 0.2556 |
| $R_1$, $wR_2$ (all data) | 0.1112, 0.2622 |

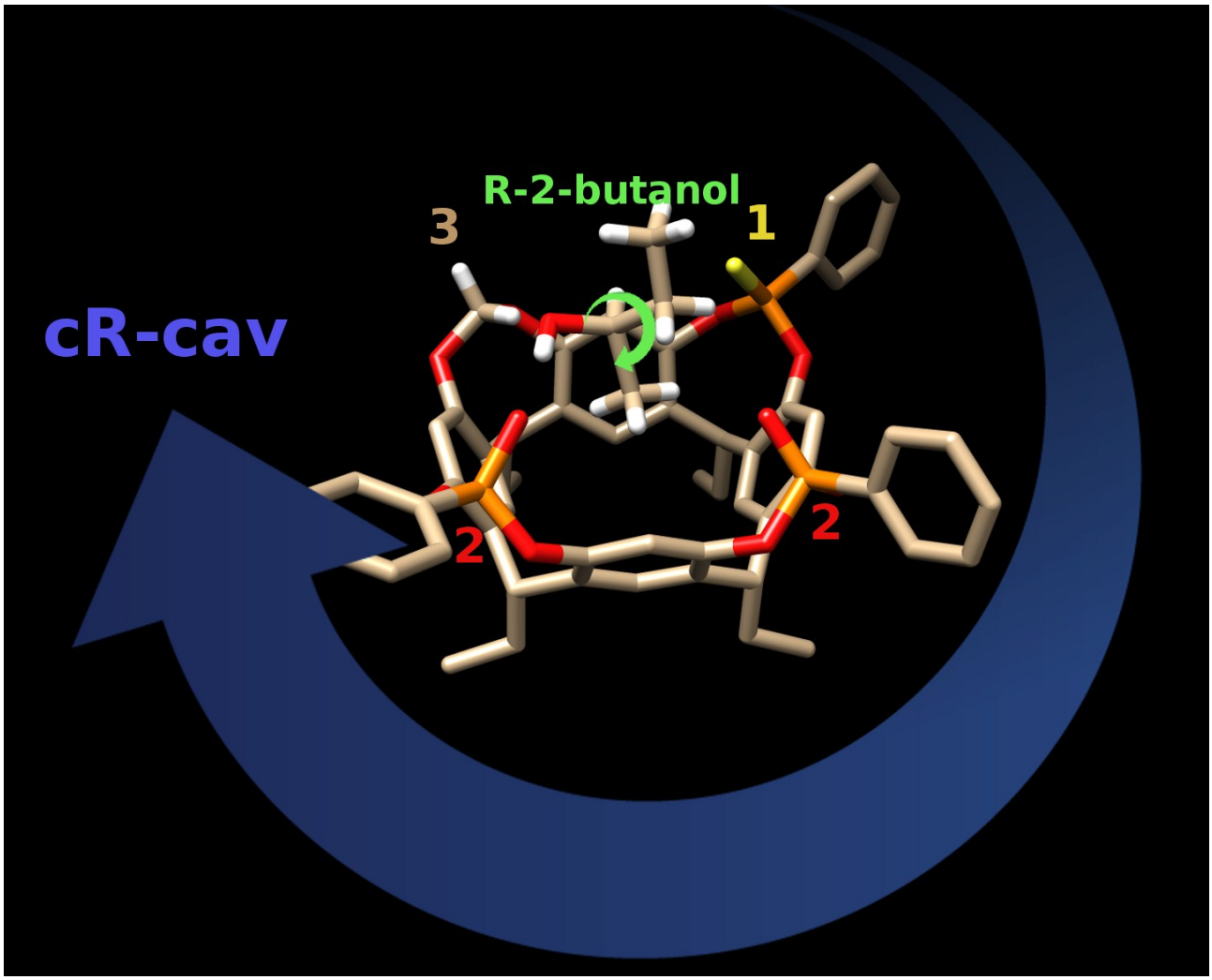


**Figure S9.** Chirality assignment for the R-2-butanol@cR-cav from the (±)-2-butanol@cS/cR-cav crystal structure, according to the rule summarized in Figure 2 in the main article.

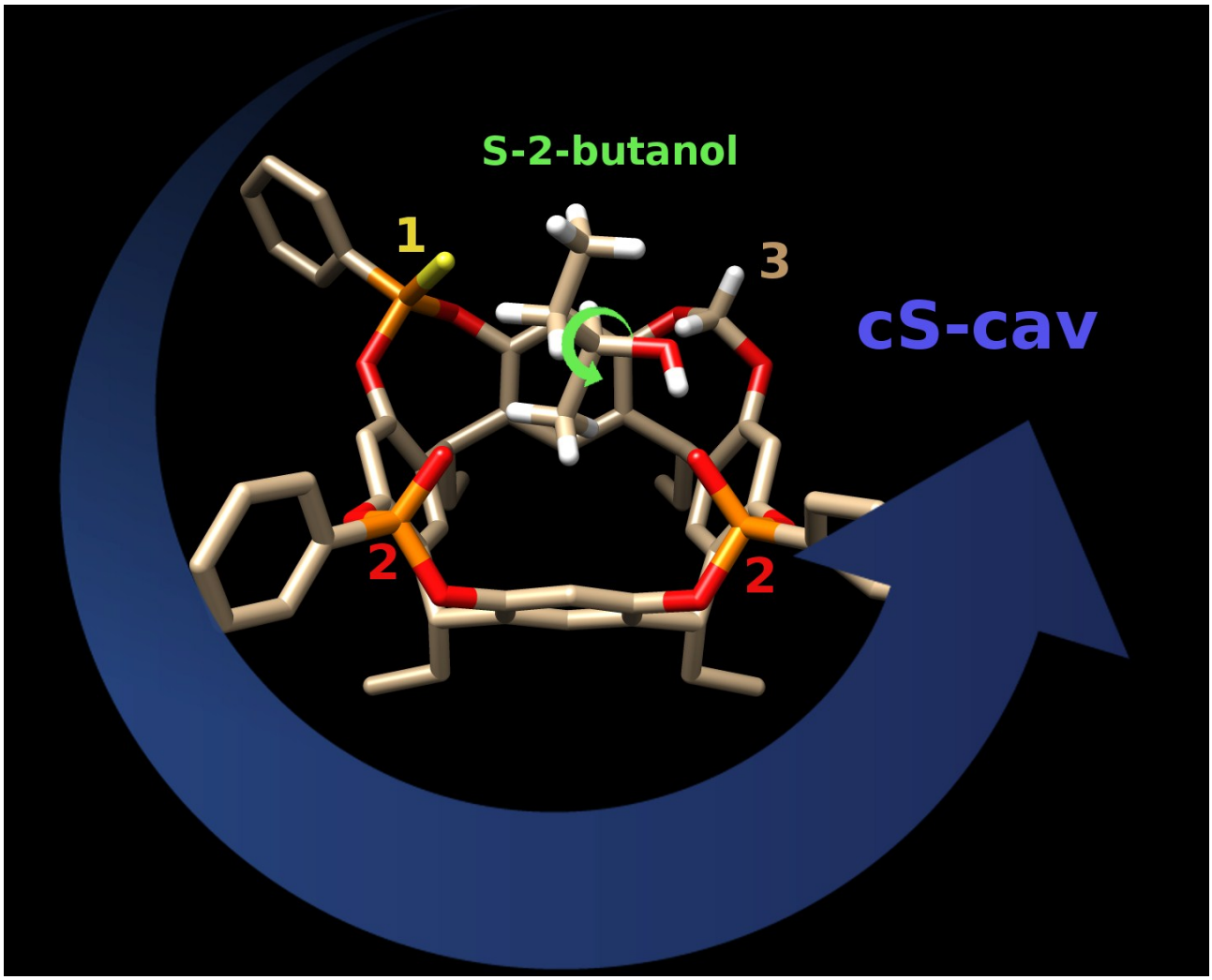


**Figure S10.** Chirality assignment for the S-2-butanol@cS-cav from the (±)-2-butanol@cS/cR-cav crystal structure, according to the rule summarized in Figure 2 in the main article.

**Calculation with CSM (Continuous Symmetry Measures)**

The calculation of the chirality values was performed at the website: http://chirality.ch.huji.ac.il/new/?cmd=chirality.25

The calculation without hydrogens was used to estimate the chirality value for the cavitands cR-cav and Tiiii[H,$CH_3$,$CH_3$] and for the host-guest complex R-BuOH@cR-cav. In Table S2 the chirality values of hosts and guests mentioned in the paper are reported.

**Table S2: chirality values of different species mentioned in the paper.**

| Chemical species | Chirality value |
|---|---|
| **alanine** | 10.7 |
| **2-butanol** | 1.9 |
| **cR-cav** | 11.5 |
| **Tiiii[H,$CH_3$,$CH_3$]** | 0.1 |
| **R-BuOH@cR-cav** | 13.7 |