**Inherently chiral phosphonate cavitands as enantioselective receptors for mono-methylated L-amino acids.**

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

**Table S1.** Crystallographic data and refinement details for crystals of the diastereomeric complexes of the racemic mixture cS/cR-cav **1** with *N*-methyl-D/L-leucine.

|  |  |
| --- | --- |
| Empirical formula | C55H49O10P3S1, C7H15N1O2, 2.75 (C2H3F3O1)a |
| Formula weight | 1415.23a |
| *T* (K) | 100(2) |
| *λ* (Å) | 0.700 |
| Crystal system | Monoclinic |
| Space group | *P* 21/n |
| Unit cell dimensions (Å, °) | *a* = 16.272(1), *α* = 90 |
|  | *b* = 18.162(1), *β* = 91.033(3) |
|  | *c* = 23.712(2), *γ* = 90 |
| *V* (Å3) | 7006.5(8) |
| *Z* | 4 |
| *ρ*calc (g/mm3) | 1.342a |
| F(000) | 2950a |
| Reflections collected | 38307 |
| Independent reflections | 12525 [R(int) = 0.1057] |
| Resolution limit (Å) | 23.71 − 0.70 |
| Completeness to theta = 24.835° | 96.9 % |
| Data / restraints / parameters | 12525 / 54 / 951 |
| GooF | 1.025 |
| *R*1, *wR*2 [I > 2 σ (I)] | 0.0790, 0.2068 |
| *R*1, *wR*2 (all data) | 0.0899, 0.2143 |
| CCDC number | 1432693 |

a Empirical formula, FW, density and F(000) values were corrected by taking into account also the contribute of the disordered TFE solvent molecule, removed from the crystallographic model by the SQUEEZE function.

**Treatment of the disorder in the crystallographic model of the host-guest complex.**

Difference Fourier maps and structure refinements evidenced the presence of a statistically disordered model of the host-guest complex. In particular,the electron density of two complexes: c*S*-cav@*N*-methyl-L-leucine and c*R*-cav@*N*-methyl-D-leucine overlapped in the same site of the asymmetric unit for most of the atoms of the complex. Few not overlapped atoms of these two models were refined with occupancy factor 70% and 30%, respectively (Figure 6). Despite the presence of several disordered moieties, the refinement led to a good determination of the crystallographic model, as witnessed by the *R* value, GooF and data/parameters ratio (Table 1).

The disorder present in the crystallographic model can be detailed as:

1) The cavitand showed a limited disorder at the level of the two distal P=O and P=S units: the two sites of the atom bound to the phosphorous atom by a double bond, were mutually shared by an oxygen atom and a sulfur atom. In the first unit the partial occupancy was refined respectively at 70% for the oxygen atom and 30% for the sulfur atom. In the second unit the partial occupancy of the sulfur atom was refined at 70% and the one of the oxygen atom at 30%. As a consequence, in the asymmetric unit it was found that the receptor with 70% of partial occupancy was the cS-cav **1** hosting the *N*-methyl-L-leucine, refined also at 70% of partial occupancy. On the other hand, the receptor cR-cav **1** refined at 30% of partial occupancy was hosting the *N*-methyl-D-leucine, refined with the same partial occupancy. Since the complexes crystallized in a centrosymmetric space group, the overall crystal resulted in a racemic mixture of the two diastereomeric complexes.

2) The phenyl groups linked to the phosphorous atoms were disordered over two orientations, refined at 70% and 30% of partial occupancy, in all cases.

3) The complex showed a more important disorder at the level of the guest molecule: the presence of both L (*S*) and D (*R*) enantiomers of *N*-methyl-leucine was distinguished inside the cavity. The cavity site was occupied by the L (*S*) enantiomer for the 70% and by the D (*R*) by the 30%. Restrains on geometrical parameters (bond distances and angles) were introduced for the two enantiomers of *N*-methyl-leucine.

4) In the asymmetric unit also three disordered trifluoroethanol (TFE) molecules were found. Two orientations were distinguished for two of them, and refined at 50/50% and 60/40% of partial occupancy. For the third TFE molecule the appropriate modeling of the disorder resulted highly difficult, even by introducing restraints on geometrical and thermal parameters for the atoms involved in the fragment. Therefore, the SQUEEZE/PLATON1 procedure was used to remove the contribution of this disordered TFE molecule to the overall scattering. In the void volume (corresponding to 6.7% of the cell volume) 161 electrons were computed, ascribable to about 3 TFE molecules.



**Figure S2**. Picture showing the overlapping orientations of the disordered moieties in the crystallographic model of the crystal.

(1) (a) Spek, A. L. *Acta Crystallogr.* **2015**, *C71*, 9; (b) van der Sluis, P.; Spek, A. L. *Acta Crystallogr*. **1990**, *A46*, 191.