**Graphical abstract**:

First principles modeling of the dethreading of pseudorotaxanes formed by a dialkylammonium axle and a crown ether ring elucidates the interactions between the components which control the process at the molecular level. Different escape mechanisms are revealed for the *E* and *Z* configurations of the axle: while the former undergoes a one-step process, the dethreading of the latter (see graphic) proceeds through a transition state and an intermediate structure.

**Scheme 1.** Structural formulas of the investigated ring (**R**) and axle (**A**) compounds, and light and heat-induced interconversion between the *EE* and *ZZ* configurational isomers of the axle.

**Figure 1.** Representation of the optimized structures resulting from the structural quantum chemical calculations. Top: two views of the ring (dibenzo[24]crown-8) **R**. Center: stick representation of the axle in the EE (left) and ZZ (right) configuration. Bottom: [**R**⊃EE-**A**] (left) and [**R**⊃ZZ-**A**] (right) complexes. Atom colors code: C, cyan; N, blue; O, red; H, white.

**Figure 2.** Energy profiles for the metadynamics simulation of the dethreading process at 300 K for the [**R**⊃EE-**A**] (left) and [**R**⊃ZZ-**A**] (right) complexes.

**Figure 3.** Graphical representations (stick models) of the minimum energy structure (left), the transition state structure (center), and the intermediate structure (right) predicted by the quantum chemical calculations for the dethreading process of [**R**⊃ZZ-**A**]. Only the protons of the ammonium group are represented. The arrows indicate the exit direction of the axle. Atom colors code: C, cyan; N, blue; O, red; H, white.

**Figure 4.** Graphical representation of the normal mode (green arrows) characterizing the TS structure in the dethreading process of [**R**⊃ZZ-**A**]. Atom colors code: C, gray; N, blue; O, red; H, white.

**Figure 5.** Snapshots from the first principles metadynamics simulation of the dethreading process of [**R**⊃EE-**A**] at 300 K. The arrows indicate the exit direction of the axle. Atom colors code: C, cyan; N, blue; O, red; H, white.

**Figure 6.** Schematic diagram showing the changes in the potential energy (kcal mol−1) along the dethreading profile for the [**R**⊃EE-**A**] (top) and [**R**⊃ZZ-**A**] (bottom) complexes obtained via quantum chemical approaches. Black thick lines refer to calculated energies in vacuum, red thick lines refer to values including solvation energies, blue thick lines refer to values including both solvation and zero-point energies (Table [1](http://onlinelibrary.wiley.com/doi/10.1002/cphc.201501160/full#cphc201501160-tbl-0001)). Thin dashed lines are guides for the eye.