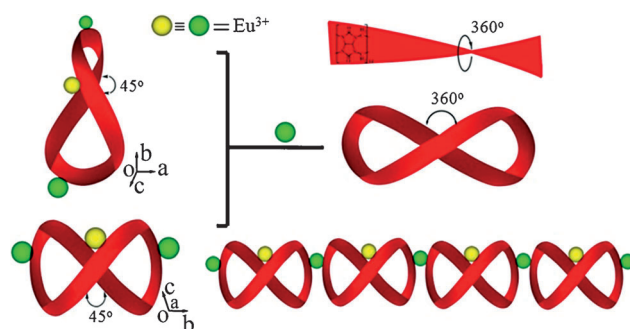


Twisted Cucurbit[14]uril**

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Since the structure of the cucurbituril (Q[6]), a cyclic oligomer of 6 units of glycoluril linked by 12 methylene bridges, was first determined by Mock and co-workers in 1981,^[1] a series of its homologues and derivatives have been reported over the last three decades. The homologues (for example Q[5], Q[7], and Q[8]) were discovered by Day and Kim in 2000,^[2] and cucurbit[10]uril (Q[10]), which includes a Q[5] molecule, was reported by Day in 2002.^[3] The perhydroxylated (HO)2nQ[n] species were synthesized by direct oxidation of Q[n] species with K₂S₂O₈ and realized direct functionalization of the Q[n] species.^[4] In recent years, Isaacs and co-workers reported the preparation of a series of oligomers of glycoluril^[5] and cucurbit[n]uril derivatives with novel structures, such as the inverted cucurbit-[6]uril and inverted cucurbit[7]uril (*i*Q[6] and *i*Q[7]),^[6] the chiral nor-seco-cucurbituril (±)-bis-ns-Q[6],^[7] and the nor-seco-cucurbit[10]uril (ns-Q[10]), which results from formal extrusion of two CH₂ bridges from Q[10].^[8] These new cucurbit[n]urils have inspired further intense interest in the chemistry of the enlarged cucurbit[n]uril family.^[9] Interestingly, Q[n] (*n* > 10) was identified in reaction mixtures,^[10] and these species have only been indicated in calculations by using the density functional theory.^[11] Although Miyahara and co-workers have reported a large hemicucurbit[12]uril,^[12] this does not show typical Q[n] properties.

Herein, we report a new member of the cucurbit[n]uril family, which we name tQ[14]. It is the largest cucurbit[n]uril with 14 normal glycoluril units linked by 28 methylene bridges. However, it consists of 14 units of the -glycoluril-(CH₂)₂- moiety with a 360° twist. As a consequence, it does not have a normal cavity like the most cucurbit[n]urils, and has



Scheme 1. Representations of tQ[14] and the Eu³⁺-tQ[14] complex.

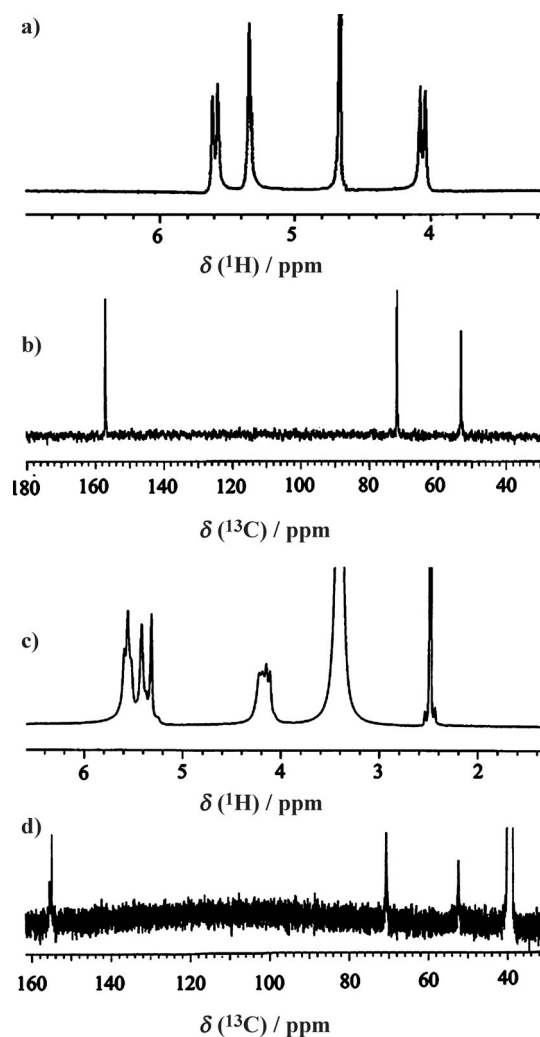


Figure 1. a, b) ¹H and ¹³C NMR spectra of tQ[14] in D₂O; c, d) ¹H and ¹³C NMR spectra of tQ[14] in [D₆]DMSO.

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the appearance of a folded, figure-of-eight conformation (Scheme 1).

Using methods previously reported,^[2a,b] a mixture of Q[n] species can be obtained by precipitating a reaction solution in methanol, and then washing the precipitate with hot water to give a water-soluble fraction that mainly consists of Q[5] and Q[7]. When we separated Q[5] and Q[7] by running a Dowex column, we obtained a white solid that was water-soluble.^[13] The TLC analysis on a silica gel plate showed that this new species was different from any of the known unsubstituted Q[n] species (Supporting Information, Figure S1). The ¹H NMR spectra of this solid in D₂O is that of a typical symmetrical cucurbit[n]uril, having three groups of proton resonances with about 1:1:1 intensity, two doublet groups at $\delta \approx 4.0$ and $\delta \approx 5.6$, and a singlet at $\delta \approx 5.3$. Furthermore, the corresponding ¹³C NMR spectra in D₂O shows three clear

peaks, at $\delta = 53.23$, $\delta = 71.95$, and $\delta = 157.14$, (Figure 1 a,b). Generally, the cucurbit[n]urils with an odd number *n*, such as 5 and 7, are very water-soluble, while the cucurbit[n]urils with an even number *n*, such as 6, 8, and 10, are less water-soluble. Therefore, we speculated that the compound could be the missing Q[9]. By chance, we found that the new cucurbit[*n*]uril can be dissolved in DMSO, and its ¹H and ¹³C NMR spectra in [D₆]DMSO are quite different from those in D₂O (Figure 1 c,d). The ¹H NMR spectrum shows that all proton resonances are split, and the ¹³C NMR spectrum shows two peaks from carbonyl carbon atoms, suggesting that this new Q[n] has an asymmetrical feature or there is a dynamic conformation process occurring around the ring in different solvents. ¹H NMR spectroscopy studies carried out in concentrated DCl (35 %) and NaOD (0.01M) solutions at different temperatures revealed that this new compound is stable

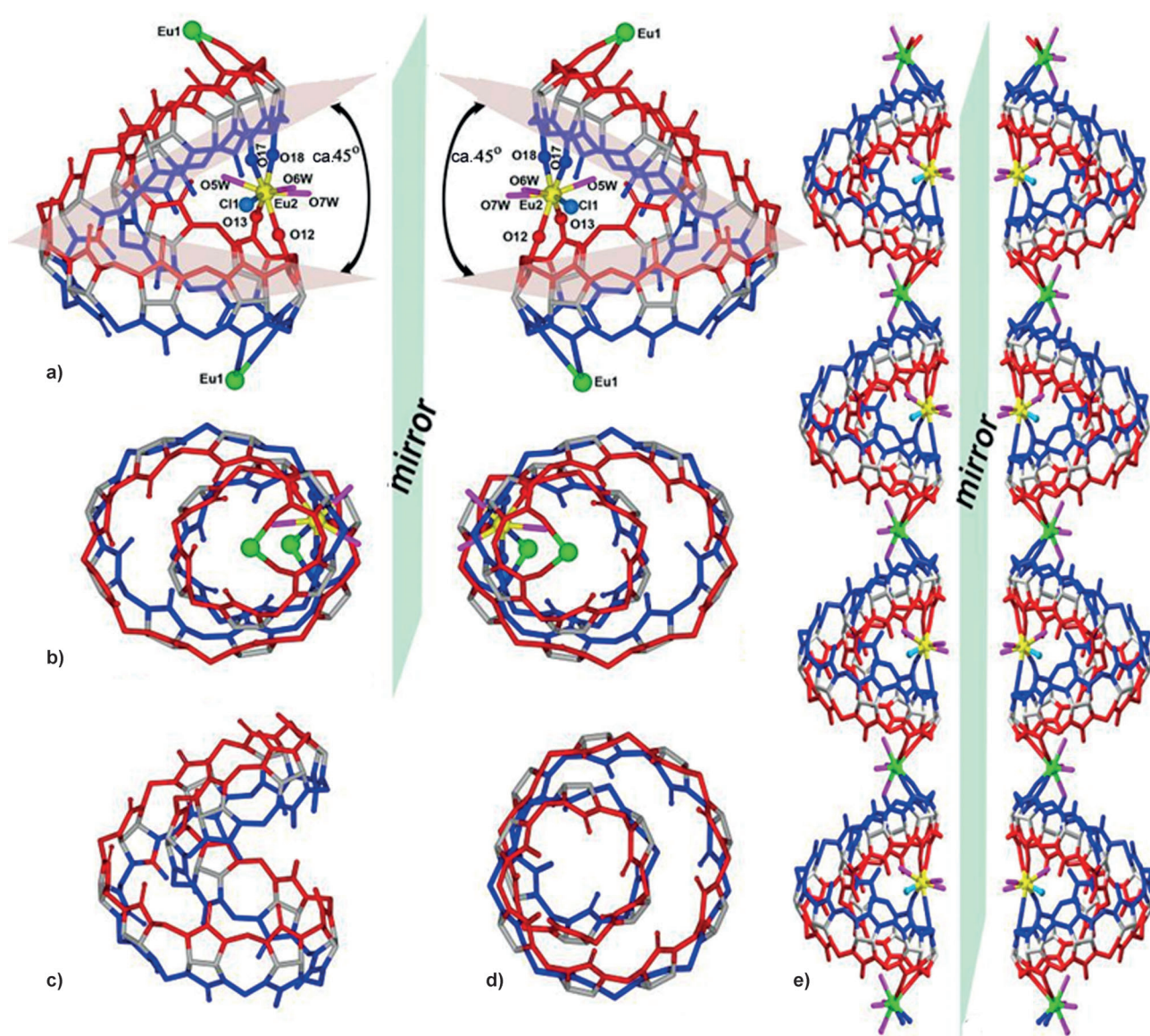


Figure 2. a) Side and b) top view of the two enantiomers of the Eu³⁺-tQ[14] complex in the X-ray crystal structure; c) side and d) top view of tQ[14]; e) a pair of one-dimensional coordination polymers constructed by the Eu³⁺ cations and tQ[14] molecules (hydrogen atoms are omitted for clarity).

under the experimental conditions (Supporting Information, Figures S2–S5).

The host–guest interaction results reveal that the new Q[*n*] cannot include 1-aminopyrene or 1,10-phenanthroline, which can be included by Q[7] and Q[8].^[14] The ¹H NMR spectra reveal that the resonances of these guest compounds show no change (or a slight downfield shift), suggesting at most a portal interaction between the new Q[*n*] and these guests (Supporting Information, Figures S6, S7). Further host–guest results show that the new Q[*n*] can bind guests with an alkyl chain, such as 1,12-diaminododecane, 1,ω-alkylenedi-4,4'-bipyridines, and 1,ω-alkylenedipyridines (Supporting Information, Figures S8–S12). The alkyl chain, pyridine, or 4,4'-bipyridine moieties can be included in the cavities of the new Q[*n*], like Q[6],^[15] suggesting that the portal size of the new Q[*n*] is larger than those of Q[5] and Q[6] but smaller than those of Q[7] and Q[8]. The related stability constant (*K*_a) of host–guest complexes involving with pyridine were determined to be in the range 5.98 × 10³ L mol^{−1} to 1.20 × 10⁶ L mol^{−1} (Supporting Information, Figure S13).

MALDI-TOF mass spectrometry of the new Q[*n*] gave an ion that was equivalent to a Q[14] species (*m/z* = 2347 for the Q[14]-Na ion and *m/z* = 2363 for the Q[14]-K ion; Supporting Information, Figure S14). Using a approach involving inorganic anion-induced coordination of metal ions to cucurbit[7]uril,^[16] we were fortunate to obtain single crystals of the complex formed by Eu³⁺ metal ions with the new Q[14] in 6 M HCl in the presence of Eu³⁺ cation and [CdCl₄]^{2−} anions. The X-ray crystal structure^[17] unambiguously identifies this new Q[14] as having a twist, hence our naming as tQ[14] (Figure 2). A close inspection reveals that this Eu³⁺-tQ[14] complex has chirality depending on the direction of the twist, there are two enantiomers of Eu³⁺-tQ[14] in the crystal structure. The bulk sample of Eu³⁺-tQ[14] should be a racemate of this two enantiomers, hence has no chirality (Figure 2a). Additionally, Figure 2e shows a pair of one-dimensional coordination polymers in which each tQ[14] is coordinated to three Eu³⁺ cations. Two of them (2 Eu1) are further coordinated to the two neighboring tQ[14] molecules, and interestingly, the remaining Eu2 cation coordinates to four carbonyl oxygen atoms of the two portals (O12, O13 and O17, O18) of a tQ[14] molecule (Figure 2a). This is the first observation of a metal ion coordinating to both portals of a cucurbit[*n*]uril molecule owing to the twisted connection in the tQ[14] molecule.

The single crystals of the Eu³⁺-tQ[14] complex show a completely different ¹H NMR spectra from that free of metal ions, so that we thought tQ[14] might have changed into another form or decomposed during the initial stage of preparation of the single crystals in concentrated HCl (Figure 3a). However, adding Eu(NO₃)₃ to a D₂O solution of tQ[14] gave a similar ¹H NMR spectra to that of the single crystals of the Eu³⁺-tQ[14] complex (Figure 3b,c), suggesting that interaction of the tQ[14] molecule with the metal ions is accompanied by a structural transformation, and that tQ[14] might be very flexible. The tQ[14] molecule seems to show a more symmetrical conformation when it interacts with an organic guest (Supporting Information, Figures S8–S12), but shows an asymmetrical conformation when it interacts with

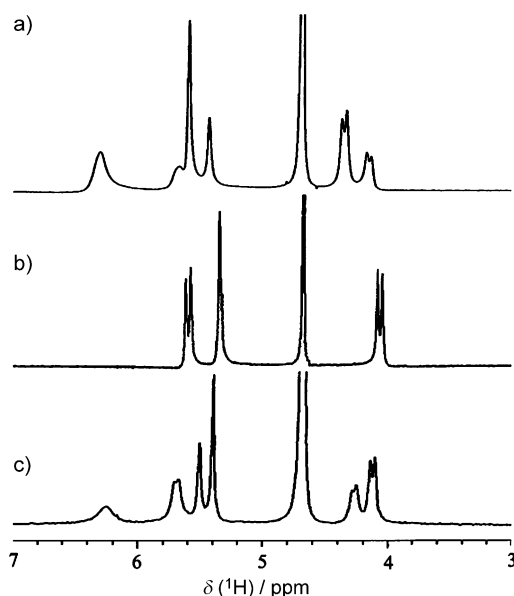


Figure 3. ¹H NMR spectra (400 MHz, D₂O, 25 °C) of a) the Eu³⁺-tQ[14] complex; b) tQ[14]; and c) in the presence of about 2.0 equiv of Eu(NO₃)₃.

metal ions which have multiple positive charges, such as lanthanide metal ions (Supporting Information, Figure S15). When adding 1,12-diaminododecane HCl salt to a D₂O solution of tQ[14], it can be seen that the asymmetrical ¹H NMR spectra of the Eu³⁺-tQ[14] complex changes gradually into a symmetrical ¹H NMR spectra, similar to the normal Q[*n*] (Supporting Information, Figure S16). More interestingly, tQ[14] seems to prefer to include the 4,4'-bipyridine moieties of the 1,6-di(4,4'-bipyridine) guest in [D₆]DMSO, while the 4,4'-bipyridine moieties are at the outside of the portals of tQ[14] in D₂O (Supporting Information, Figures S11, S12), suggesting that tQ[14] shows different binding properties in water and organic solvents. Since the discovery and the development of large-ring cyclodextrin molecules (LR-CDs),^[18] many exciting results have been demonstrated and reported in the last two decades.^[19] From a structural viewpoint, it is therefore believed that some unique supramolecular behavior by tQ[14] can be expected.

In summary, we have isolated and characterized the largest cucurbit[14]uril of the cucurbit[*n*]uril family. Although it does not have the largest portal sizes and cavity volume, which is due to the twisted connection in the twisted cucurbit[14]uril molecule, the discovery of tQ[14] provide the important information that larger oligomers and the corresponding cucurbit[*n*>10]urils could exist in processes of a normal Q[*n*]-synthesis. Moreover, the tQ[14] molecule shows many special properties, such as the structural flexibility, which could be adjusted by binding to organic molecules or metal ions; good solubility in water and organic solvents (DMSO, DMF); and chirality and different selectivity for the moieties of a guest in the different solvents. More detailed host–guest chemistry and coordination chemistry of tQ[14] are currently undergoing.

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- [13] A mixture of glycoluril (50 g, 0.35 mol), paraformaldehyde (26.2 g, 0.86 mol), and conc. HCl (100 mL) was stirred at room temperature for 1 h and then heated at 100°C for 6 h. The resulting solution was cooled to room temperature and precipitated by pouring into MeOH (700 mL) to yield a crude pale yellow solid. The residue was redissolved by boiling water 3 to 4 times (200 mL). The filtrate was collected by filtered and evaporated to give the crude solid, which contains Q[5] and Q[7] as major products, Q[5]@Q[10], tQ[14] and a small amount of unknown solid as minor products. Purification of the mixture was achieved by chromatography on a Dowex 50W×2–400(H) column equilibrated with 1:1 acetic acid/water. The sample (ca. 27 g) was loaded onto the column (5 cm (Ø) × 75 cm), eluting with an eluent (1:1 acetic acid/water (v/v) with an increase of HCl from 0.01 to 2 M during the eluting process) to yield white solid tQ[14] (0.86 g, 1.2%). It should be noted that the eluting period could last at least three months based on 12 h column running time per day. M.p.: > 300°C. IR (KBr): $\tilde{\nu}$ = 1728, 1476, 1423, 1385, 1243, 1237 cm^{−1}. ¹H NMR (400 MHz, D₂O): δ = 5.62 (d, *J* = 9.2, 28H), 5.33 (s, 28H), 4.03 ppm (d, *J* = 9.2, 28H). ¹³C NMR (100 MHz, D₂O): δ = 157.14, 71.95, 53.23 ppm. MS *m/z*: 2347 [M+Na]⁺. The solubility of tQ[14] in a solvent was determined by ¹H NMR spectra. Solubility of tQ[14]: 4.1 × 10^{−2} mol L^{−1} in D₂O, 1.8 × 10^{−2} mol L^{−1} in [D₆]DMSO.
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- [17] Crystal data: colorless parallelepipeds 0.30 × 0.15 × 0.15 mm³, [Eu₂(H₂O)₇Cl·tQ[14]]·5Cl66H₂O, *M_r* = 4157.70, triclinic, space group *P*1̄, *a* = 15.378(2), *b* = 18.510(3), *c* = 29.066(4) Å, *α* = 96.448(5), *β* = 96.450(6), *γ* = 98.667(5)°, *V* = 8055.9(19) Å³, *Z* = 2, ρ_{calcd} = 1.714 g cm^{−3}, *T* = 223 K, Bruker-AXS SMART CCD diffractometer, MoK α (λ = 0.71073 Å), μ = 1.002 cm^{−1}, 95645 reflections measured for $\theta \leq 23^\circ$, *R*₁ (*I* > 2 σ (*I*)) = 0.0792. A number (66) of the water molecules in the unit cell have been taken into account to SQUEEZE option of the PLATON program, but the Eu³⁺·tQ[14] complex is well-defined. CCDC 913620 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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