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Anion-Free Bambus[6]uril and Its Supramolecular Properties

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Abstract: Methods for the preparation of anion-free bambus[6]uril (BU6) are presented. They are based on the oxidation of iodide anion, which is bound inside the macrocycle, utilizing dark oxidation by hydrogen peroxide or photooxidation in the presence of titanium dioxide. Anion-free BU6 was found to be insoluble in any of the investigated solvents; however, it dissolves in methanol/chloroform (1:1) or acetonitrile/water (1:1) mixtures in the presence of the tetrabutylammonium salt of a suitable anion. The association constants with halide ions, BF_4^-, NO_3^-, and CN^-, were measured by ^1H NMR spectroscopy. The highest association constant ($8.9\times10^5\,M^{-1}$) was found for the 1:1 complex of BU6 with I^- in acetonitrile/water mixture. A number of crystal structures of BU6 complexes with various anions were obtained. The influence of the anion size on the macrocycle diameter is discussed together with an unusual arrangement of the macrocycles into separate layers.

Keywords: anion receptors · halides · host–guest systems · macrocycles · supramolecular chemistry

Introduction

Development of anion receptors is of growing interest among scientists.[1,2] Macrocyclic molecules have been investigated particularly for their ability to bind anions within their preorganized cavity interior. In the late 1960s, macrocyclic katapinands were recognized as the first artificial compounds exhibiting complexation properties towards halide ions.[3] Since then, a number of macrocycles with structurally different binding motifs, including ammonium,[4,5] guanidinium,[6,7] urea,[8,9] amide,[10,11] and pyrrole[12–14] derivatives, have been developed. As early studies were dedicated especially to the preparation of these structurally different receptors, the current interest aims at the modification of already known structures to obtain receptors with chemically tuned composition showing both high affinity and selectivity towards the corresponding anion.

Recently, some of us designed and synthesized a new macrocyclic compound and named it bambus[6]uril (BU6; Figure 1).[15] This compound consists of six 2,4-dimethylglycoluril units, accommodating an alternate conformation, which are connected through one row of methylene bridges. Two methine hydrogen atoms on the convex face of each glycoluril unit are pointed into the cavity center. We have shown that the cavity interior is suited for the encapsulation of one halide ion, which is stabilized inside a positively charged cavity (Figure 1). We were able to show that BU6 binds halide ions with a high affinity and selectivity preferentially in the order $I^- > Br^- > Cl^-$ in $CD_3OD/CDCl_3$ mixture (2:1) by using ^1H NMR spectroscopy. Prepared BU6 was isolated from the reaction mixture as a complex with

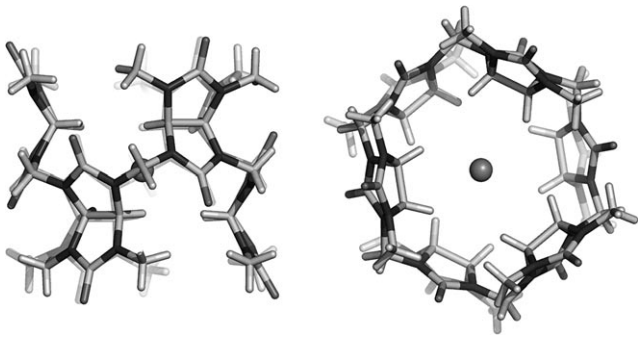

Figure 1. X-ray crystal structure of BU6·Cl^- complex (side and top views) and the chemical formula of BU6.

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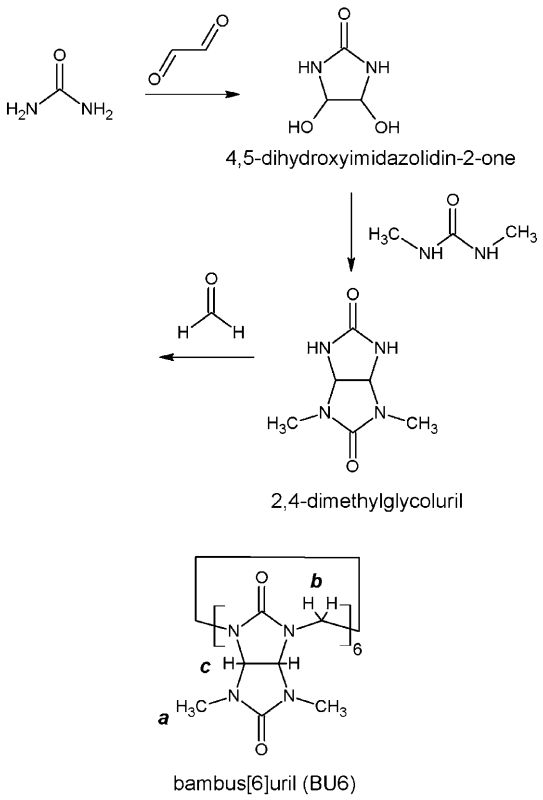
HCl. This complex did not dissociate at millimolar concentrations. The addition of one equivalent of the tetrabutylammonium (TBA^+) salt of Br^- or I^- to BU6·HCl solution resulted in complete replacement of Cl^- by the competing anion in the cavity. Therefore, we were not able to calculate the equilibrium association constants (K_a) of BU6 complexes with halide ions.

Herein, we provide some important insights into the world of BU6. We were able to prepare anion-free BU6, which allowed us to determine K_a values of BU6 complexes with various anions by using ^{1}H NMR spectroscopy. We show that BU6 is able to bind halide ions not only in organic solvents but also in aqueous media, while still preserving its high affinity and selectivity. We show that BU6 acts as a ditopic receptor binding simultaneously both the anion and the corresponding counter cation, based on X-ray diffractometry and ESI mass spectrometry analyses. Moreover, the crystal structures of BU6 with various anions are presented and the influence of the anion size on the macrocycle structural parameters is discussed. Finally, the electrochemical behavior of the complex between BU6 and bromide ion is also presented.

Results and Discussion

Synthesis of BU6: Inexpensive starting materials and straightforward and relatively easy synthesis are significant advantages of BU6 applications (Scheme 1). The preparation of the BU6 macrocycle by the acid-catalyzed polycondensation of formaldehyde and 2,4-dimethylglycoluril was reported recently.[15] The macrocycle was isolated from the reaction mixture by simple filtration; the resulting solid did not require any purification except washing with solvent. The starting monomer, 2,4-dimethylglycoluril,[16, 17] and its precursor, 4,5-dihydroxyimidazolidin-2-one,[18, 19] were also prepared before. During our attempts to prepare these two heterocyclic compounds according to the published procedures, we found that there are some important aspects to which one should pay attention in order to avoid possible difficulties. In this work, we initially synthesized 2,4-dimethylglycoluril in a one-pot arrangement. The condensation of glyoxal and urea under basic conditions gave a solution of 4,5-dihydroxyimidazolidin-2-one. Then the solution was acidified, 1,3-dimethylurea was added, and the resulting 2,4-dimethylglycoluril precipitated out after evaporation of the solvent. Unfortunately, removal of byproducts, such as nonsubstituted glycoluril and hidantoins, was indispensable in a subsequent purification step. Therefore, we decided to isolate pure 4,5-dihydroxyimidazolidin-2-one that was allowed to react with dimethylurea in the next step. This approach could eliminate the formation of side products and increase the yield of glycoluril. Initial attempts to isolate pure 4,5-dihydroxyimidazolidin-2-one were not successful because we obtained a mushlike material, which was very difficult to handle. However, the product was successfully isolated when urea and glyoxal (40% aqueous solution)



Scheme 1. Preparation of BU6.

were used in a 2:1 molar ratio without addition of any other solvent; the pH of the reaction mixture was kept between 8 and 9 during the preparation and isolation steps. The first portion of the product precipitated from the solution after 1 h. The second portion of the product formed as colorless crystals after the filtrate was left in the refrigerator for two days. The remaining urea was removed by washing the solid with ethanol to give pure 4,5-dihydroxyimidazolidin-2-one in 69% yield. Reaction of 4,5-dihydroxyimidazolidin-2-one with dimethylurea gave 2,4-dimethylglycoluril as sole product in 78% yield. Therefore, we recommend that 2,4-dimethylglycoluril be prepared from isolated 4,5-dihydroxyimidazolidin-2-one rather than by one-pot synthesis.

Anion removal—oxidation by H_2O_2 in the dark: BU6 was prepared by acid-catalyzed polycondensation between 2,4-dimethylglycoluril and paraformaldehyde in aqueous HCl according to a previously published procedure.[15] Use of HCl appeared to be very important for the formation of this macrocyclic product because the chloride ion acted as a template. After reaction, the macrocycle was isolated as a complex, in which one chloride ion was encapsulated inside the BU6 cavity. The complex was very stable and our attempts to remove the anion from the BU6 cavity failed. These attempts included successive washing of the complex with various solvents or treatment of a complex solution with silver nitrate.

In the subsequent step, we replaced chloride by iodide inside the cavity, thereby forming a BU6·HI complex. BU6·HI can be prepared easily by addition of a small excess of HI to the solution of BU6·HCl in methanol/chloroform (1:1), followed by the evaporation of the solvent and washing of the solid with water and acetone. We found that when the solution of BU6·HI in methanol/dichloromethane[20] (1:1) was treated with hydrogen peroxide, the anion-free BU6 precipitated out of the solution in 92% yield. BU6 did not dissolve in any of the investigated solvents, including chloroform, methanol, acetonitrile, water, DMSO, DMF, or their mixtures. However, the addition of TBA halide salt (Cl^-, Br^-, I^-) to the suspension of BU6 in methanol/dichloromethane (1:1) resulted in immediate dissolution of the powder. ^{1}H NMR spectra confirmed the formation of a complex between BU6 and the corresponding halide, which was soluble under the experimental conditions. Later we found that complexes of BU6 with halide ions also dissolved in aqueous solutions. BU6·HI was dissolved in water/acetonitrile (1:1) and, after treatment with hydrogen peroxide, the empty macrocycle was obtained in 90% yield.

Anion removal—photocatalysis: It has been shown that aqueous iodide can be photocatalytically oxidized in the presence of titanium dioxide.[21–24] This reaction occurs in the presence of oxygen, and results in the production of I_2. Flash photolysis studies suggested that the mechanism includes a direct hole–adsorbate electron-transfer process.[24] Formation of a one-electron intermediate (I_2^-) was confirmed to take place on the TiO_2 surface.[25–27] According to these studies, adsorbed I^- can be oxidized by a trapped hole (h^+) to an iodine atom, which subsequently reacts with iodide to give I_2^-. This species disproportionates to I^- and I_3^-. Similarly to photocatalytic oxidation on a semiconductor, hydrogen peroxide[28,29] or singlet oxygen generated in situ by photosensitization[30–35] can oxidize iodide in aqueous solution. We adopted these strategies to oxidize the iodide ion complexed with BU6 and propose a mechanism for the formation of an anion-free (empty) macrocycle molecule.

An oxygenated solution of BU6·HI in water/acetonitrile (1:1) with a catalytic amount of suspended TiO_2 was irradiated at $\lambda = 254$ nm. Formation of the characteristic absorption bands ($\lambda_{max} \approx 290$ and 365 nm), which correspond to those of authentic iodine–iodide (I_3^-) solutions in this solvent mixture, was monitored by UV/Vis spectroscopy (Figure 2). The concentration of the photoproduct was the highest after 21 min of irradiation and then gradually decreased; similar behavior was observed when the sample was irradiated at $\lambda = 365$ nm, although the maximum concentration of the product formed was lower by a factor of 2. The rate of its formation was considerably dependent on the amount of TiO_2 in the mixture; however, the experimental conditions were not optimized. It was, nevertheless, confirmed that I_2 physically adsorbs on the surface of TiO_2 particles in water/acetonitrile suspension in the dark, which resulted in complete disappearance of its absorption bands.

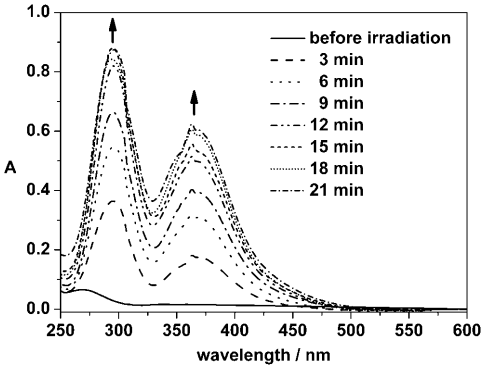


Figure 2. UV/Vis absorption spectra measured following irradiation of an oxygenated BU6·HI solution in the presence of TiO_2 ($\lambda_{irr} = 254$ nm).

Therefore, the above-mentioned experiments were carried out only to identify the released iodine.

The absorption spectra of the iodine–iodide (I_3^-) solutions were also compared to those for samples prepared by dissolving equimolar solutions of I_2 and BU6·HI. The identical absorption maxima and band intensities of equally concentrated samples suggest that the BU6·HI_3 complex may form.

The photooxidation of BU6·HI in a D_2O/acetonitrile mixture to liberate empty BU6 was successfully followed by ^{1}H NMR measurements. Real-time monitoring was not feasible because changes neither in the chemical shifts nor the signal intensities were observed during the first several hours of irradiation, despite the fact that I_3^- was evidently formed in the first few minutes (UV/Vis spectroscopy; see above). However, 6 h of irradiation and a subsequent two days of standing led to precipitation of empty BU6 in 84% yield (Figure 3A,B). This number was calculated by measuring the decreasing intensity of the BU6 methyl NMR signal (peak *a*, Figure 3). Subsequently, addition of KI (3 molar equivalents) recovered the original signal intensity after 2 h of standing. No changes in the NMR shifts were detected, which implies that the bambusuril skeleton did not degrade upon irradiation (Figure 3C). In comparison, non-photochemical (dark) oxidation of BU6·HI in water/acetonitrile (1:1) for 4 h by benzoyl peroxide resulted in 87% production of empty BU6 as a precipitate (NMR spectroscopy).

Based on the known facts[24–27] and our observations, we propose the mechanism of empty BU6 formation through photocatalytic oxidation given in Equations (1)–(3).

$$BU6 \cdot I^- + h^+ \rightarrow BU6 + I \quad (1)$$

$$BU6 \cdot I^- + I \rightarrow BU6 \cdot I_2^- \quad (2)$$

$$BU6 \cdot I_2^- \rightarrow BU6 \cdot I^- + BU6 \cdot I_3^- \quad (3)$$

The first electron-transfer step most likely liberates the bambusuril molecule together with the iodine atom, which couples with another BU6·I^- molecule to form an intermediate BU6·I_2^-. It then disproportionates into BU6·I^- and BU6·I_3^-. At higher reaction conversions, BU6·I^- is not pres-

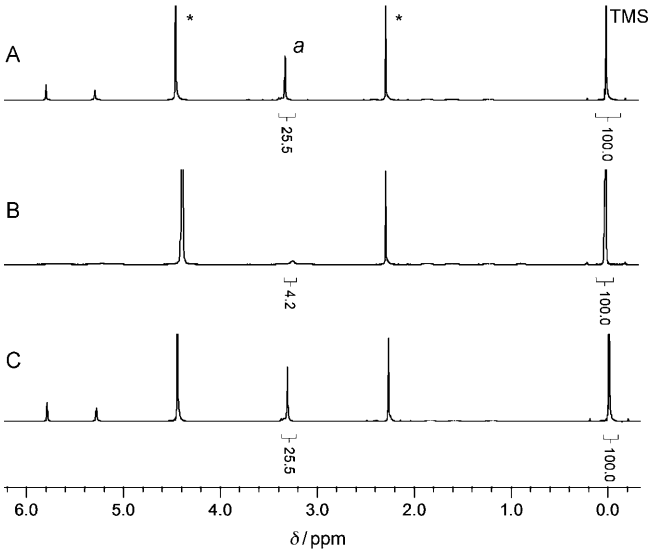


Figure 3. ^{1}H NMR spectra measured following irradiation of BU6·HI in the presence of TiO_2; the monitored peak ($\approx$3.3 ppm, *a*) corresponds to the CH_3 group of the dissolved BU6 derivative: A) before irradiation; B) after 6 h of irradiation at $\lambda = 254$ nm and subsequent 2 days standing; and C) after KI addition. * = HOD and acetonitrile, TMS = tetramethylsilan.

ent in sufficient amounts. As a result, I_2 remains as a dominant side product in the reaction mixture or is possibly oxidized further by species, such as H_2O_2,[16,17,36,37] produced in the irradiated solutions.

Determination of the association constants: We showed in our initial studies that BU6 forms stable complexes with various anions in a methanol/chloroform mixture (2:1).[15] The complexation between BU6 and a halide ion, such as Cl^-, Br^-, or I^-, was slow on the ^{1}H NMR timescale. Unfortunately, we were not able to determine the corresponding association constants, because the complexes of BU6 with a halide were very stable under the experimental conditions. Now, having isolated anion-free BU6, we attempted to determine the association constants (K_a) for the complexes. We took advantage of the insolubility of anion-free BU6 and the good solubility of BU6·halide complexes in a methanol/chloroform (2:1) mixture. This would allow us to determine K_a from solubility measurements.[38] Unfortunately, after addition of an anion to the suspension of BU6, all anions present in the solution were consumed to form the complex, which precluded the calculation of the K_a values. Because of the biological relevance of halide ions,[1] we decided to investigate BU6 complexation in aqueous media. As BU6 complexes are insoluble in water, we used a D_2O/CD_3CN (1:1) mixture. ^{1}H NMR spectroscopy was used to determine the concentration of the complex, which was formed during gradual additions of the TBA salt of the corresponding anion to the suspension of empty BU6. By using these solubility measurements, we calculated the K_a values for BU6 with Cl^-, Br^-, BF_4^-, NO_3^-, and CN^- to be 780, 4.8×10^4, 2.1×10^4, 1.6×10^4, and $5.9\times10^3\,M^{-1}$, respectively (see the Supporting Information). Please note that type of counter-anion does not influence affinity of BU6-cation complex as the $K_{a(Cl)}$ values for BU6·Cl^- complex in the presence of different counter-cations (Cs^+, Na^+, and TBA^+) were found to be similar within an experimental error.

The binding between BU6 and the iodide ion was too strong to be determined by this method. Therefore, we decided to determine K_a of this complex by using ^{1}H NMR competition experiments.[39] A gradual addition of TBA iodide (TBAI) to the solution of a BU6·HCl complex in D_2O/CD_3CN (1:1), containing an excess of NaCl, resulted in a continuous downfield shift of the signal c of the macrocycle, which indicated the replacement of chloride by iodide inside the BU6 cavity (Figure 4). The anion exchange was fast on the NMR timescale (Figure 4). Our experimental data can be fitted to a 1:1 binding isotherm (Figure 5) and

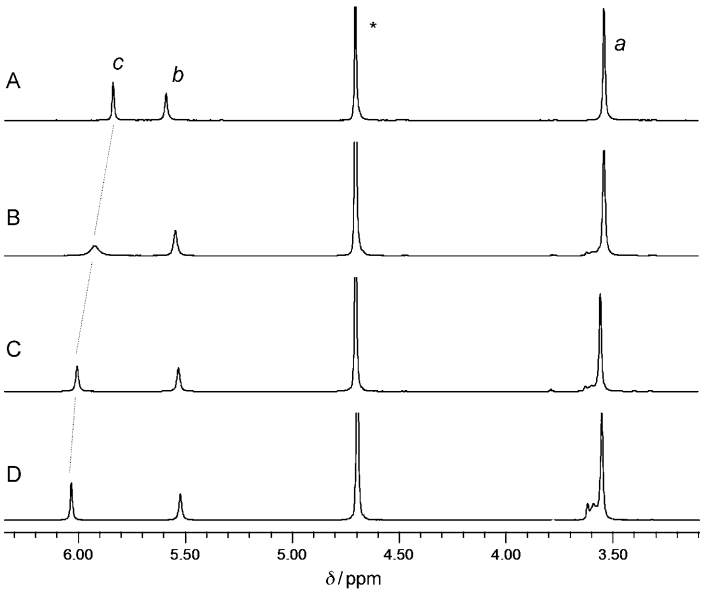


Figure 4. ^{1}H NMR spectra (300 MHz, 0.1 M NaCl, D_2O/CD_3CN (1:1)) of BU6·HCl in the absence (A) and presence of 0.4 (B), 1.0 (C), and 2.0 equiv (D) of TBAI. * = HOD.

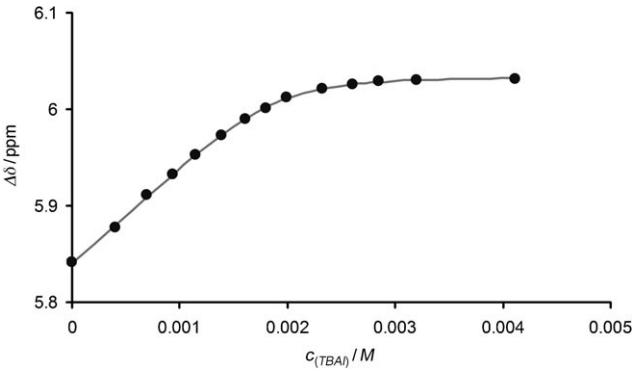


Figure 5. ^{1}H NMR (300 MHz, 0.1 M NaCl, D_2O/CD_3CN (1:1)) titration of BU6·HCl complex with TBAI. The line shows the best fit of the experimental data, which corresponds to a 1:1 binding model.

the value of K_{rel} ($K_{rel}=K_{a(Cl)}/K_{a(I)}$) obtained was used together with the previously determined $K_{a(Cl)}$ value of the BU6·Cl^- complex to calculate the $K_{a(I)}$ between BU6 and the iodide ion to be $8.9\times10^5\,M^{-1}$. A similar $K_{a(I)}$ value was obtained when the BU6·HBr complex and NaBr were used instead of BU6·HCl and NaCl. The competition measurements were also used as the control experiments to determine the K_a values of BU6 complexes with Br^- and BF_4^- indirectly, and the results were in good agreement with those obtained from the solubility measurements. The values clearly showed that BU6 also maintains its high affinity and selectivity in aqueous media. $K_a\approx10^6\,M^{-1}$ for BU6·HI in D_2O/CD_3CN (1:1) makes BU6 one of the most potent, synthetically available neutral receptors for iodide in aqueous media. In this context, the possibility of easy dissociation of the complex described above is very important.

Solid-state complexes: Monocrystals of the BU6 complexes with anions, such as Cl^-, Br^-, I^-, or BF_4^-, were obtained by slow evaporation of a BU6 solution in methanol/chloroform (1:1) containing an excess of TBA salt of the corresponding anion. In all cases, the anion was incorporated in the center of BU6, which is the crystallographic inversion center at the same time. The building glycoluril units of the macrocycle have two different z coordinates, depicted in Figure 6 by colors (blue for an upper position, yellow for a lower position). However, they are symmetry related and have thus the same distance to the central anion. It is expected that glycoluril building units connected by one row of the methylene bridges have limited freedom of motion and, therefore, the macrocycle can adapt its shape to the anion size. The binding modes of all crystallized BU6 complexes and their arrangements within the crystal structure were comparable. This allowed monitoring of the influence of an anion on various parameters within the crystals. The measured parameters are shown in Figures 6 and 7, in which the crystal structure of BU6·I^- is used as an illustrative example; the values are then summarized in Table 1. The parameters $d1$, $d2$, and $d3$ describe the diameter of the circle going through the three oxygen atoms O2, the diameter of the circle going through the carbon atoms C2 and C3, and the diameter of the circle going through the six carbon atoms C5, respectively (see Figure 6). Parameters $h1$ ($h2$) correspond to the average distance between the plane defined by the circle of diameter $d1$ ($d2$) and the plane defined by the circle of diameter $d2$ ($d3$). The height of the macrocycle $h3$ was calculated as the distance between these two planes. Each of the planes is defined by the three oxygen atoms O2, which are located on the opposite portals of the macrocycle. Table 1 shows that the measured diameters increase with increasing anion size. The diameter $d1$ is the most influenced by the anion size, going from 8.76 Å for BU6·Cl^- to 9.88 Å for a tetrafluoroborate anion complex. On the other hand, the heights of the macrocycles do not differ and the widest part of the macrocycle, described by the parameters $d3$, was not influenced much by the anion type.

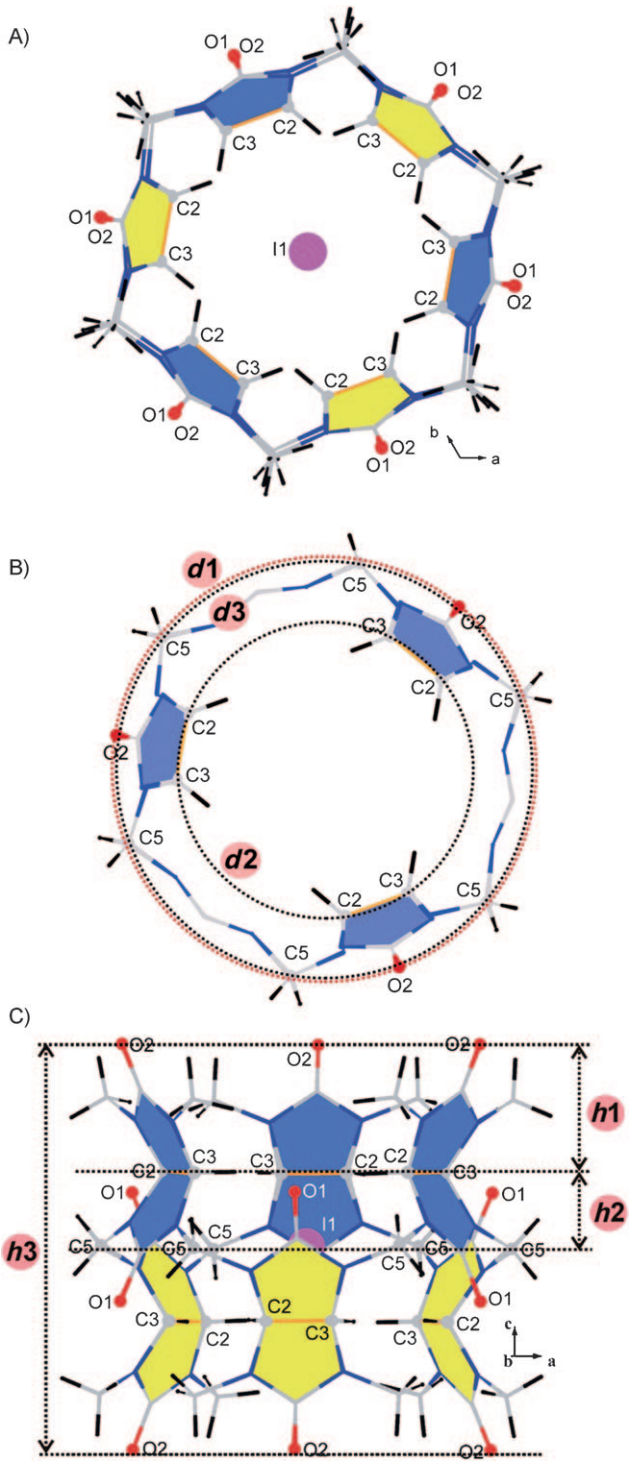


Figure 6. X-ray crystal structure of the BU6·I^- complex: A) top view, B) top view with indication of the measured diameters d, and C) side view with indication of the measured heights h.

It was rather surprising that the structures of all crystals, obtained by crystallization of BU6 from solutions containing various TBA salts, have very similar packing characteristics. The molecules of the macrocycle are arranged into separated layers, which are parallel with the *ab* plane (Figure 7). The macrocycles are connected within van der Waals con-

Table 1. Dimensions of BU6 in various BU6·anion complexes.

	*d*1 [Å]	*d*2 [Å]	*d*3 [Å]	*h*1 [Å]	*h*2 [Å]	*h*3 [Å]	*s*1 [Å]	*s*2 [Å]
BU6·Cl^-	8.76	6.57	9.68	3.17	1.68	9.64	6.18	12.17
BU6·Br^-	9.62	6.83	9.73	3.05	1.76	9.63	6.14	12.10
BU6·I^-	9.79	6.91	9.73	3.04	1.76	9.61	6.22	12.14
BU6·BF_4^-	9.88	6.99	9.75	3.04	1.78	9.64	6.45	12.17

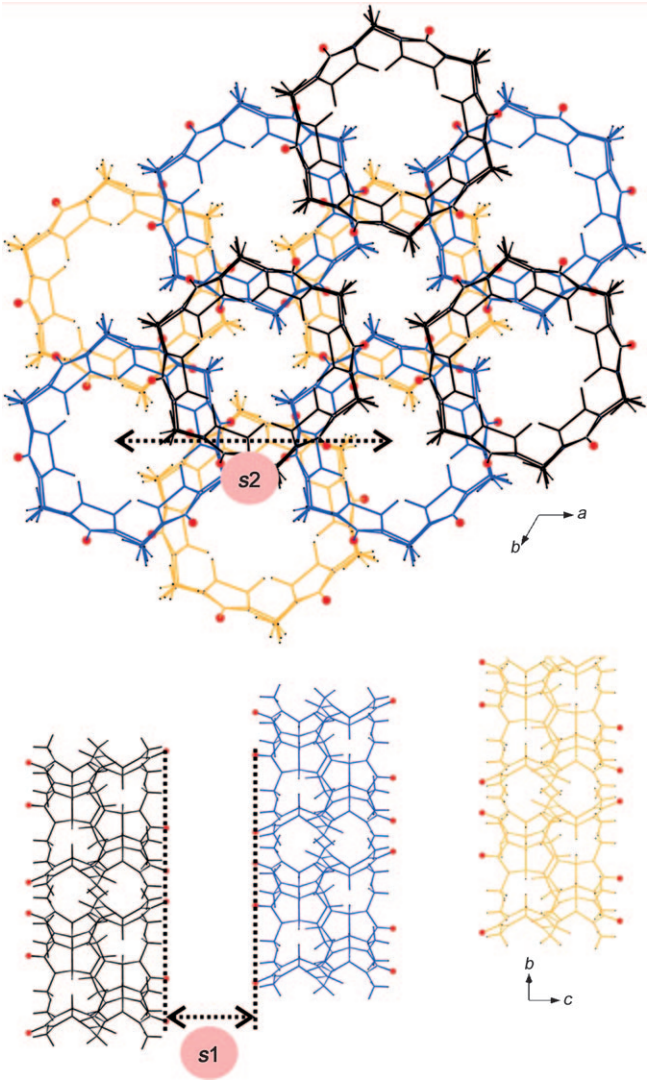


Figure 7. Side and top views of the BU6·I^- packing with indication of the measured distances *s*.

tact distances in one layer. There is a large space between the layers, which is occupied by solvent molecules and/or the TBA ions. The accurate determination of their position was impossible due to strong disorder of the molecules. The exception is the previously determined crystal structure of BU6·Cl^-, in which the molecules of TBA and chloroform occupying the space between the layers of the macrocycles were fully resolved.[15] We calculated the distance *s*1 between the best planes through positions of the oxygen atoms O2 framing free space between the neighboring layers. These distances in the crystal structures differ by no more than 0.27 Å. There is no direct correlation between the *s*1 values and the anion size. The parameter *s*1 is probably influenced by the nature of the molecules and their arrangement in the gap between the layers. The stacking of the layers is illustrated in Figure 7. There are insignificant differences in the distances *s*2 between the centers of the two neighboring macrocycles for different crystal structures.

Electrochemistry: Both iodide and bromide can be electrochemically oxidized at accessible potentials. Iodide oxidation may be complicated by the formation of species such as I_3^-, whereas bromide oxidation is devoid of these complications. Therefore, we decided to investigate the effect of Br^- encapsulation inside the host BU6 on the electrochemical oxidation of this anion. We carried out cyclic voltammetric experiments in CH_3CN/H_2O (1:1) also containing 0.1 M NaF as the supporting electrolyte. Our selection of the supporting electrolyte relied on the knowledge that fluoride does not interact with BU6 at all,[15] thus releasing the macrocycle for binding interactions with anions present at much lower concentrations. Under these conditions, anodic cyclic voltammetry of a 1.0 mM solution of NaBr showed the anticipated oxidation of bromide at a peak potential of 1.16 V versus Ag/AgCl (Figure 8). This peak has all the characteristics of diffusion control, that is, the peak potential is basically invariant with scan rate and the peak current increases linearly with the square root of the scan rate. However, no reverse peak was detected, because the oxidized form (Br•) is highly reactive and expected to be consumed in the timescale of the experiment. We could only observe two minor cathodic peaks at potentials under 0.8 V, which may correspond to

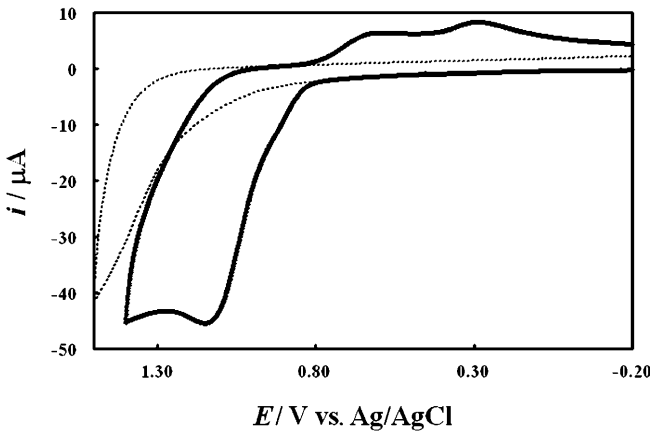


Figure 8. Cyclic voltammetry of 1 mM NaBr in the absence (black) and presence of 1 equiv of BU6 (gray). Medium: 0.1 M NaF, CH_3CN/H_2O (1:1) solution. Scan rate: 0.1 $V s^{-1}$.

the reduction of Br_2. In sharp contrast to this, the BU6·Br^- complex does not exhibit an anodic peak within the accessible potential window. In fact, oxidation of the solvent takes place before we can clearly observe the oxidation of the macrocycle-bound bromide. Therefore, we conclude that the complexation of bromide inside BU6 provides a strong differential stabilization to bromide (versus its oxidized form, Br•), which displaces the corresponding oxidation potential in the positive direction and moves it out of the accessible potential window. We should also point out the possibility that, in addition to the thermodynamic stabilization of bromide upon binding inside BU6, bromide encapsulation may kinetically slow down the heterogeneous rate of electron transfer between the bound anion and the electrode surface. One of us has already reported other examples, in which encapsulation has a strong kinetic effect on the electrochemistry of the bound substrate.[41]

Conclusion

BU6 is a new macrocyclic compound, which is able to bind anions with high affinity and selectivity.[35] Until now BU6 was reported to exist only as a complex with an anion. In this study, we demonstrated that the BU6·HI complex can dissociate through either dark oxidation by H_2O_2 or photocatalytic oxidation of encapsulated iodide anion. We proposed that, under these conditions, the encapsulated I^- is converted to I_2, which does not interact with the macrocycle, thus allowing the isolation of empty BU6 in high yields. In addition to easy and inexpensive synthesis of BU6, its recovery as an anion-free receptor from a stable complex is another important advantage for potential applications. We were able to determine the K_a values for the complexes of BU6 with anions, such as BF_4^-, NO_3^-, or CN^-, in acetonitrile/water (1:1). The highest $K_{a(I)}$ value ($8.9\times10^5\,M^{-1}$) was found for BU6·HI. X-ray diffraction was also used to demonstrate that BU6 has a flexible structure when the glycoluril building blocks adapt their position to the anion size. Furthermore, the crystals obtained from the solution of BU6 and TBA salts showed an unusual arrangement of macrocycles into the layers, which are separated by more than 6 Å by the intervening space filled with solvent molecules and cations. Cyclic voltammetry of BU6·Br^- showed that the anodic peak corresponding to bromide oxidation is shifted substantially in the positive direction.

The presented results indicate that BU6 has great potential in many fields, such as removal and sensing of anions, or crystal engineering. Further studies, which may reveal more exciting properties of BU6, are currently under way in our laboratory.

Experimental Section

General: Starting materials were purchased from commercial suppliers and were used without further purification. NMR spectra were recorded with a Bruker Avance 300 spectrometer operating at frequencies of 300.13 (^{1}H) and 75.77 MHz (^{13}C) and were referenced to the residual peak of the solvent or TMS. UV/Vis spectra were obtained in 1.0 cm quartz cuvettes. Irradiation was carried out with a 45 W Hg lamp equipped with bandpass glass filters ($\lambda=254$ or 366 nm). Diffraction data were collected on an Oxford Diffraction Gemini CCD single-crystal diffractometer equipped with a CCD detector Atlas, with mirror-collimated $Cu_{K\alpha}$ radiation. The temperature during data collection was 120 K. The electrochemical data were recorded with a BAS 100B/W workstation (Bioanalytical Systems), by using a single-compartment cell fitted with a glassy carbon working electrode (0.071 cm^2), a tungsten counter electrode, and a Ag/AgCl reference electrode. The working electrode was polished with 0.05 μm alumina powder (Buehler) on a felt surface lubricated with pure water. All solutions were deoxygenated by passage of high-purity nitrogen gas before the measurements. HRMS data were obtained on a UPLC/MS-TOF apparatus equipped with an ESI interface.

4,5-Dihydroxyimidazolidin-2-one: Urea (42.2 g; 0.70 mol) and glyoxal (40% aqueous solution, 40.1 mL, 0.35 mol) was stirred at 80°C until the starting materials had dissolved completely. The solution was then allowed to cool down and was stirred at room temperature for 1 h. The pH of the solution was kept between 8 and 9 by additions of a concentrated aqueous solution of NaOH during the procedure. The resulting precipitate was collected by filtration; the filtrate was placed in a refrigerator (4°C) and a second portion of solid was collected after 2 days. The solid fractions were combined and washed with ethanol to remove remaining urea. The product was obtained as a white powder in 69% yield. ^{1}H NMR (300 MHz, [D$_6$]DMSO, 30°C, TMS): $\delta=7.09$ (s, 2H; NH); 5.86 (d, 2H; OH); 4.61 ppm (d, 2H; CH); ^{13}C NMR (75 MHz, [D$_6$]DMSO, 30°C, TMS): $\delta=160.7$, 83.9 ppm.

2,4-Dimethylglycoluril: A mixture of 4,5-dihydroxyimidazolidin-2-one (30.0 g, 0.254 mol), 1,3-dimethylurea (22.4 g, 0.254 mol), deionized water (125 mL), and HCl (35%, 4 mL) was stirred at 105°C for 1 h. Most of the liquid was then evaporated to obtain a mushlike solid, which was collected by filtration. After drying under reduced pressure, a white powder was obtained in 78% yield (33.7 g). ^{1}H NMR (300 MHz, [D$_6$]DMSO, 30°C, TMS): $\delta=7.48$ (s, 2H; NH); 5.12 (s, 2H; CH); 2.64 ppm (s, 6H; CH_3); ^{13}C NMR (75 MHz, [D$_6$]DMSO, 30°C, TMS): $\delta=160.9$, 157.6, 67.1, 27.6 ppm.

BU6·HI: BU6·HCl (2 g, 1.77 mmol) was dissolved in chloroform (50 mL) and methanol (50 mL), and an aqueous solution of HI (56%, 0.237 mL) was added. The liquid was then evaporated. The precipitate was washed with water and acetone, and dried under reduced pressure. The yield was 95%. ^{1}H NMR (300 MHz, $CD_3OD/CDCl_3$ (2:1), 30°C, TMS): $\delta=5.62$ (s, 12H; CH), 5.12 (s, 12H; CH_2), 3.17 ppm (s, 36H; CH_3).

Empty BU6: Method A: BU6·HI (1 g, 0.819 mmol) was dissolved in methylene chloride (150 mL) and methanol (150 mL). An aqueous solution of hydrogen peroxide (30%, 0.25 mL) was added dropwise and the resulting mixture was stirred for 1 h at 20°C, heated at reflux for 5 min, and cooled to 20°C. The solvent was evaporated and the resulting precipitate was washed with a mixture of methanol/dichloromethane (1:1) and acetone. Empty BU6 was obtained as a white powder in 92% yield.

Method B: BU6·HI (0.515 g, 0.422 mmol) was dissolved in water/acetonitrile (1:1, 75 mL). An aqueous solution of hydrogen peroxide (30%, 0.25 mL) was added dropwise. The mixture was stirred for 24 h at 20°C. The solvent was evaporated and the resulting precipitate was washed four times with water/acetonitrile (1:1, 75 mL) and acetone (50 mL). Empty BU6 was obtained as a white powder in 90% yield. The product was insoluble in any of the tested solvents. It was therefore characterized as a BU6·TBACl complex, which was formed after addition of TBACl to the suspension of anion-free BU6 in methanol/chloroform (2:1). ^{1}H NMR ($CD_3OD/CDCl_3$ (2:1), 300 MHz); $\delta=5.41$ (s, 12H), 4.20 (s, 12H), 3.17 (t, 8H), 3.03 (s, 36H), 1.62 (m, 8H), 1.39 (m, 8H), 0.99 ppm (t, 12H).

Photocatalysis: Titanium dioxide powder (Aeroxide P25, typically 0.1 mg) was suspended in a solution of BU6·HI (5.0 mM) in acetonitrile/water (1:1, 0.5 mL) in a standard quartz UV cuvette. The mixture was purged with oxygen for 5 min and irradiated at either $\lambda=254$ or 366 nm. UV/Vis and NMR spectra were recorded periodically at the given time

intervals or after 1–2 days of standing at 20 °C. The suspension was always stirred thoroughly and purged with oxygen for 5 min before the photolysis started.

Oxidation of BU6·HI by benzoyl peroxide in the dark: A solution of BU6·HI (6.7 mg, 5.5 μmol) and benzoyl peroxide (1.8 mg, 7.5 μmol) in D_2O/acetonitrile (1:1, 0.5 mL) in an NMR cuvette was stirred and the NMR spectra were recorded periodically at the given time intervals and after 4 h of standing.

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