COMMUNICATION

ChemComm
www.rsc.org/chemcomm

# An outer-sphere ligand for uranyl carbonate†

**Anthony R. Prudden, Nathan R. Lien‡ and Jason R. Telford‡***
*Department of Chemistry, University of Iowa, Iowa City, IA, USA 52242-1294.*
*E-mail: jason-telford@uiowa.edu; Fax: 01 319-335-1270; Tel: 01 319-353-1971*

*Received (in Columbia, MO, USA) 12th August 2003, Accepted 19th November 2003*
*First published as an Advance Article on the web 8th December 2003*

**A novel supramolecular host for the uranyl carbonate complex has been designed and synthesized. The modified cyclodextrin host binds uranyl carbonate in water with a stability of 253 $M^{-1}$.**

The reactivity of a metal ion is controlled by inner- and outer-sphere influences. In metalloproteins, Nature provides inner-sphere coordination by the amino acids and cofactors capable of binding a metal, and outer-sphere influences are a result of (usually) protein secondary and tertiary structure. In all instances characterized to date, proteins recognize specific small inorganic substrates, such as phosphate or iron complexes, by providing a binding site with a spatial arrangement of weak interactions, hydrogen bonds or hydrophobic patches complementary to their substrate.[1] These weak interactions contribute to an overall stability constant large enough to remove the substrate from solution. In many cases, there is no exchange of ligands (replacement of a water by a protein-based ligand, for example), but rather the inorganic complex is recognized *in toto*.

The same features that Nature uses to mediate recognition can also be incorporated into smaller host architectures.[2] Defined synthetic molecular recognition agents have potential non-biological applications in remediation technology, biological or environmental monitoring, and the development of novel catalysts based on the operational principles of enzymes.[3] Most examples of synthetic molecular recognition target organic or oxyanion substrates, since their coordination environment and molecular interactions can easily be predicted or modelled.[4] Metal complexes, on the other hand, comprise a widely variable set of substrates since they have much more diverse coordination preferences. The design of a receptor for a given metal complex must include a topological consideration of the substrate, including symmetry, hydrogen bond donor/acceptor preferences and van der Waals interactions.[5]

In addition to its relevance as an environmental hazard, the uranyl carbonate ion $[UO_2(CO_3)_3]^{4-}$ is well-suited structurally as a target guest molecule for our designs.[6] The complex is charged, with a symmetric ($D_{3h}$) coordination environment and potential hydrogen bond acceptors decorating the ion in the equatorial plane.[7]

We have designed a host for uranyl carbonate based on these features. The architectural scaffold of the receptor is provided by a cyclodextrin (CyD, Fig. 1). The torus is an appropriate size (~12 Å) to encapsulate the guest uranyl complex (~8 Å diameter in the equatorial plane). The CyD was functionalized† by substituting ethylenediamine groups for the primary hydroxyls to give per-(6-deoxy-6-ethylenediamine)-α-cyclodextrin (per-en-α-Cyd, Fig. 1).[8] The amino groups form an array of hydrogen bond donors on one face of the torus, thus providing a moderately preorganized binding site for the uranyl complex.

The interaction of per-en-α-Cyd with the substrate, uranyl carbonate, was determined by $^1$H NMR titration. These titrations were carried out in $D_2O$ under conditions of constant pH (8.5) and ionic strength (0.1 M $Na_2CO_3$–$NaHCO_3$ buffer). In several trials, aliquots of a standard solution of uranyl carbonate (0.1015 M, 0.1 M carbonate buffer) were added to a buffered 1–10 mM solution of per-en-α-Cyd.

Fig. 2 shows a typical titration curve based on the $^1$H NMR shifts of the ethylenediamine protons with increasing uranyl carbonate concentration. While these protons are broad in the absence of uranyl-guest, the signals sharpen and shift upfield at higher complex concentrations. Small, though significant shifts are also seen with the cyclodextrin $C_1$, $C_4$, $C_5$, $C_6$ and $C_6'$ protons. These data were fit to yield a 1 : 1 binding constant of 253 (22) $M^{-1}$. We see no evidence for higher stoichiometries by MS or NMR.

In an aqueous system under the conditions of these titrations, the first coordination sphere of the uranyl ion is certainly carbonate.† The solution equilibria with water and hydroxide are complex, and involve polynuclear species, but modelling of the system indicates that water/hydroxide cannot compete effectively with carbonate as a ligand under these conditions, as the formation constant of uranyl ion with carbonate is $\log \beta_{130} = 21.0$.[9] Nitrogen donors are even weaker ligands for the metal ion and amine groups are unable to compete with even water as a ligand.[10] However, the amino group is an excellent hydrogen bond donor.

The complexation induced chemical shifts (CIS) of protons adjacent to the nitrogens (ethylenediamine backbone) and inside the cavity of the cyclodextrin derivative are sensitive to uranyl binding. An upfield shift is observed for protons $H_1$ and $H_4$, which are oriented to the interior of the cyclodextrin cavity, and for the ethylene protons, but no change is seen for $H_2$ or $H_5$, which are oriented toward the outside of the torus. The shifts of the $C_4$ proton, as well as the ethylene protons support the proposed model of an encapsulated metal complex rather than a simple electrostatic interaction.[11]

It is important to note that the per-en-α-Cyd forms an inclusion complex with the substrate in aqueous solution. This is in contrast to most synthetic hydrogen-bond mediated host–guest complexes which must be characterized in non-polar media, since water is an

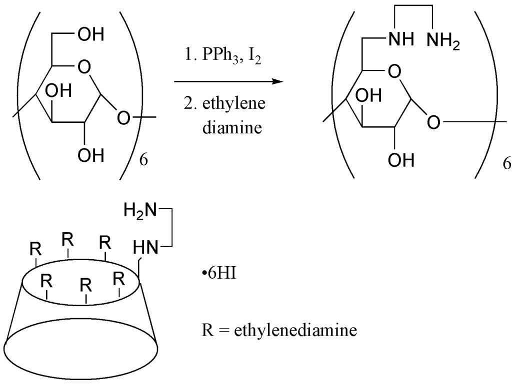

**Fig. 1** Synthetic scheme used in constructing the molecular host.

---

† Electronic supplementary information (ESI) available: spectroscopic characterization of per-(6-deoxy-6-ethylenediamine)-α-cyclodextrin, 2D NMR data, fit of the $H_1$ proton to the binding isotherm, calculated species distribution of uranyl ion *vs.* pH in seawater and in the presence of per-(6-deoxy-6-ethylenediamine)-α-cyclodextrin. See http://www.rsc.org/suppdata/cc/b3/b309733a/

‡ A.R.P. and N.R.L. are both undergraduate researchers. J.R.T. would like to acknowledge a U. Iowa, Carver Foundation Research Grant. N.R.L. would like to thank the NSF for the opportunity to participate in a summer research experience for undergraduates through the University of Iowa, Center for Global and Regional Environmental Research, http://www.cgrer.uiowa.edu

DOI: 10.1039/b309733a

effective competitor for hydrogen bonding interactions. Natural systems, such as proteins, may have much higher affinities for substrates like phosphate, but these proteins are generally highly preorganized for a substrate. In an equilibrium speciation model of seawater (pH 8–8.3) and freshwater (pH 7–8), the interaction of per-en-α-Cyd with uranyl carbonate is strong enough to complex 70–75% of aqueous uranyl carbonate ion based on this thermodynamic model.† Although there are several examples of hydrogen bonding interactions with uranyl species, to our knowledge, this is the first example of entirely outer-sphere coordination of a uranyl carbonate complex.[12]

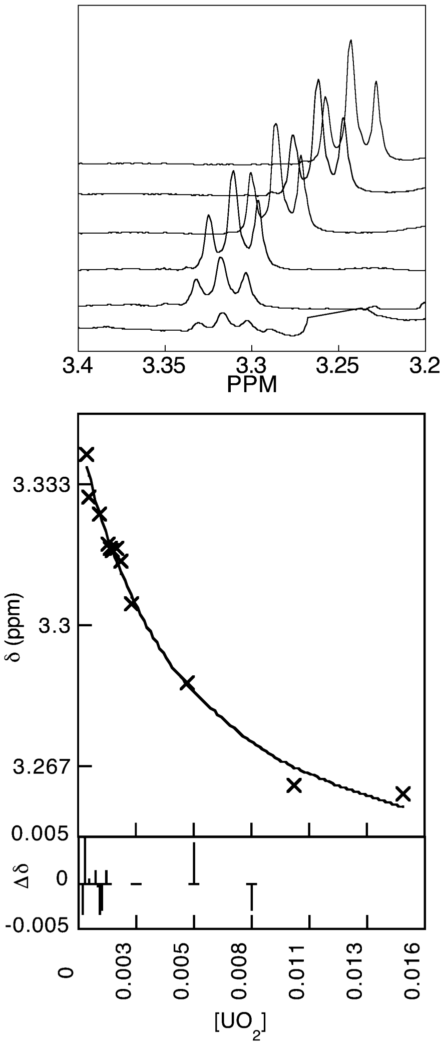

**Fig. 2** (Top) $^1$H NMR spectra of the ethylenediamine proton region and trend in chemical shifts during titration. (Bottom) Data (×) and fit to a 1 : 1 isotherm (—) with $K_{assoc}$ = 253 (22) $M^{-1}$.

## Notes and references

1 P. S. Ledvina, A. I. Tsai, Z. Wang, E. Koehl and F. A. Quiocho, *Protein Sci.*, 1998, **7**, 2550; B. L. Jacobson and F. A. Quiocho, *J. Mol. Biol.*, 1988, **204**, 783; A. D. Ferguson, E. Hofmann, J. W. Coulton, K. Diederichs and W. Welte, *Science*, 1998, **282**, 2215.

2 P. D. Beer and D. K. Smith, *Prog. Inorg. Chem.*, 1997, **46**, 1; K. Connors, *Chem. Rev.*, 1997, **5**, 1325; R. Ludwig, *Fresenius' J. Anal. Chem.*, 2000, **367**, 103.

3 T. S. Snowden and E. V. Anslyn, *Curr. Opin. Chem. Biol.*, 1999, **3**, 740; Y. Tsuji, M. Tokunaga and Y. Obora, *Yuki Gosei Kagaku Kyokaishi*, 2002, **60**, 942; J. Yu, Y. Zhao, M. J. Holterman and D. L. Venton, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 2705.

4 P. A. Gale, *Coord. Chem. Rev.*, 2000, **199**, 181; P. A. Gale, *Coord. Chem. Rev.*, 2001, **213**, 79; P. A. Gale, *Coord. Chem. Rev.*, 2003, **240**, 191.

5 D. R. Alston, P. R. Ashton, T. H. Lilley, J. F. Stoddart, R. Zarzycki, A. M. Z. Slawin and D. J. Williams, *Carbohydr. Res.*, 1989, **192**, 259; B. Siegel and R. Breslow, *J. Am. Chem. Soc.*, 1975, **97**, 6869.

6 D. L. Clark, D. E. Hobart and M. P. Neu, *Chem. Rev.*, 1995, **95**, 25.

7 G. Bernhard, G. Geipel, T. Reich, V. Brendler, S. Amayri and H. Nitsche, *Radiochim. Acta*, 2001, **89**, 511; A. Coda, A. D. Giusta and V. Tazzoli, *Acta Crystallogr., Sect. B*, 1981, **37**, 1496.

8 A mixture of per-6-iodo-6-deoxy-α-cyclodextrin in 1,2-diaminoethane was heated at 60 °C for 14–16 h. The excess amine was evaporated and 50 mL of absolute EtOH were added. The precipitate which formed was collected and washed with absolute EtOH to give the HI salt, which was purified by chromatography on LH20 with water as the mobile phase. MS is consistent in mass and isotope distribution with the proposed formulation; P. Ashton, R. Koniger and J. Stoddart, *J. Org. Chem.*, 1996, **61**, 903; B. I. Gorin, R. J. Riopelle and G. R. J. Thatcher, *Tetrahedron Lett*, 1996, **37**, 4647.

9 L. Alderighi, P. Gans, A. Ienco, D. Peters, A. Sabatini and A. Vacca, *Coord. Chem. Rev.*, 1999, **184**, 311; T. W. Newton and J. C. Sullivan, in *Actinide Carbonate Complexes in Aqueous Solution*, ed. A. J. Freeman and C. Keller, North-Holland, Amsterdam, 1985; I. Grenthe and B. Lagerman, *Acta Chem. Scand.*, 1991, **45**, 122.

10 A. Cassol, P. Di Bernardo, R. Portanova, M. Tolazzi, G. Tomat and P. Zanonato, *Inorg. Chem.*, 1990, **29**, 1079; A. Cassol, P. Di Bernardo, R. Portanova, M. Tolazzi and P. L. Zanonato, *J. Chem. Soc., Dalton Trans.*, 1995, 733.

11 V. Rudiger and H. Schneider, *Chem.-Eur. J.*, 2000, **6**, 3771; H. Schneider, F. Hacket and R. Volker, *Chem. Rev.*, 1998, **98**, 1755.

12 D. A. Beauchamp and S. J. Loeb, *Chem.-Eur. J.*, 2002, **8**, 5084; K. Zamaraev, *New J. Chem.*, 1994, **18**, 3; L. A. Goinez, J. Lin, M. Munoz, A. W. Coleman and A. Kaifer, *J. Chem. Soc., Faraday Trans.*, 1996, **92**, 645; B. Masci, M. Gabrielli, S. L. Mortera, M. Nierlich and P. Thuery, *Polyhedron*, 2002, **21**, 1125; P. H. Walton and K. N. Raymond, *Inorg. Chim. Acta*, 1995, **240**, 593; A. P. Zazhogin, A. A. Zazhogin and A. I. Serafimovich, *Khim. Fiz.*, 1997, **16**, 11; A. R. Van Doorn, R. Schaafstra, M. Bos, S. Harkema, J. Van Eerden, W. Verboom and D. N. Reinhoudt, *J. Org. Chem.*, 1991, **56**, 6083.