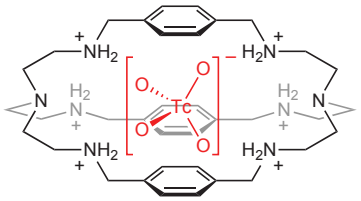
ANION BINDING

Trapping technetium

Angew. Chem. Int. Ed. http://doi.org/fz59tg (2012)



Technetium-99 is a long-lived radioactive isotope with a half-life of more than 200,000 years and, as the pertechnetate ion (TcO_4^-), is a notable component of spent nuclear fuel. The high solubility of this oxoanion in water means that it can spread quite widely in the environment. The development of molecules that can selectively trap this hazardous species could lead to materials that extract it from nuclear-waste streams. Owing to its radioactivity, much academic research on the design of receptors for TcO_4^- has used the structurally similar perrhenate ion (ReO_4^-) as an analogue. Those studies that have focused on TcO_4^- itself have not typically been done in water.

Now, a team of researchers based in Italy and Switzerland, led by Valeria Amendola at the University of Pavia, have shown that a poly-protonated azacryptand (pictured) has a high binding affinity for $^{99}TcO_4^-$ in aqueous solution. This cage-like compound had previously been shown to bind ReO_4^- in water and so was an ideal candidate as a receptor for the analogous pertechnetate anion. Isothermal titration calorimetry experiments revealed that the receptor binds $^{99}TcO_4^-$ with a slightly greater affinity than ReO_4^- and exhibits the strongest binding of $^{99}TcO_4^-$ in aqueous solution for any receptor reported so far. The researchers suggest that the lower hydration energy of the pertechnetate anion — which makes it easier to desolvate than its rhenium analogue — explains its increased affinity for binding with the azacryptand.

The interaction between the $^{99}TcO_4^-$ ion and the azacryptand host was also studied using NMR spectroscopy, looking at both ^1H and ^{99}Tc spectra. In the ^{99}Tc experiments, the linewidth of the ^{99}Tc signal was observed to broaden as more of the receptor was added, up to a limiting value where all of the $^{99}TcO_4^-$ ion is bound to the azacryptand. Finally, further proof that the $^{99}TcO_4^-$ ion binds inside the cavity of the azacryptand receptor was provided by single-crystal X-ray diffraction data, which showed the anion sitting just off-centre forming hydrogen bonds to the protonated amine groups — directly, as well as through water bridges. *SC*

ELECTROCHEMISTRY

Better together

Angew. Chem. Int. Ed. http://doi.org/fz6cwv (2012)

The search for alternatives to fossil fuels has led to a huge research effort aimed at developing efficient fuel cells. Of the possible fuels being studied, hydrogen is the most popular, but problems with its storage and transfer make it unsuitable for portable applications. An alternative fuel for mobile use is formic acid. Unlike hydrogen, it is liquid at room temperature and it can be oxidized on a platinum electrode, which forms the central reaction of a direct formic acid fuel cell. The mechanism of formic

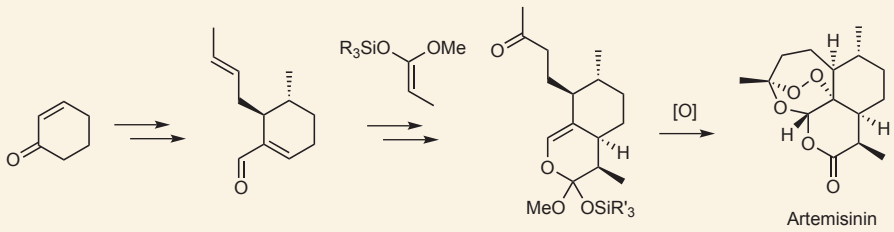
MALARIA TREATMENT

Totally synthetic solution

J. Am. Chem. Soc. **134,** 13577–13579 (2012)

Hundreds of thousands of people die each year from malaria. The natural product artemisinin has been used as a treatment alone or as part of a combination therapy, but the expense of this drug — arising from the need to extract it from a natural source (the sweet wormwood plant) — has encouraged underdosing and ultimately contributed to the development of resistant strains of the disease. Now, Chunyin Zhu and Silas Cook from Indiana University have reported a short total synthesis of (+)-artemisinin starting from inexpensive achiral starting materials.

Although several total syntheses of (+)-artemisinin have been reported, they have not been competitive on price with extraction from the natural source. The most promising current approach is semisynthetic and relies on the conversion of microbially produced (+)-artemisinic acid to the final product. A fully biosynthetic approach to (+)-artemisinin remains elusive. Zhu and Cook's aim was to design a synthesis (pictured) that relied on readily available and cheap starting materials such that their route might truly begin to compete with the semisynthetic or extraction routes.



Starting with cyclohexenone, an enantioselective copper-catalysed conjugate addition–alkylation sequence was used to set the configurations of two of the six stereocentres in the natural product while creating a compound with 11 of the 15 carbon atoms in artemisinin. The remaining carbons are introduced in a sequence involving a Shapiro reaction and an unusual Lewis-acid catalysed [4+2]-cycloaddition. The requirement for cheap starting materials in the first step meant that a Wacker oxidation was needed at this stage, but Zhu and Cook ultimately hit upon some straightforward conditions using palladium chloride and excess hydrogen peroxide.

Discovery of conditions for the final oxidative rearrangement also required some experimentation, but Zhu and Cook found success in a molybdenum-catalysed decomposition of hydrogen peroxide (which produces singlet oxygen *in situ*) followed by treatment with acid. The complete synthetic sequence is achieved in only five pots and, although further optimization would still be required for large-scale production, has been used to produce just over a gram of artemisinin so far. *SD*