Models for Vanadium–Tunichrome Interactions

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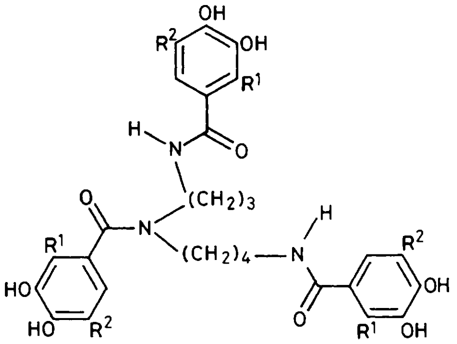
N,N',N''-Tris(2,3,4- and 3,4,5-trihydroxybenzoyl)-1,5,10-triazadecanes have been synthesized as models for the tunichromes thought to be involved in vanadium metabolism of many tunicates.

The spectacular ability of certain species of sessile marine organisms known as tunicates to accumulate vanadium from seawater has engendered much interest by scientists over the past hundred years[1,2]. The vanadium, which may reach an internal concentration of 1.5 M, is stored within blood cells in the reduced +3 or +4 oxidation states.[3] Reduction from the +5 oxidation state of vanadium found in the seawater is thought to involve a class of bright yellow organic pigments called tunichromes. These tunichromes are air-sensitive and readily hydrolysed, features which have thwarted efforts to



(1) $R^1 = OH, R^2 = H$
(2) $R^1 = H, R^2 = OH$

characterize them. Recently however Nakanishi and co-workers have succeeded in identifying extremely small amounts of the pure material as trimers of hydroxydopa.[4] The limited studies that have been conducted suggest that the tunichromes might function both as the reductant for the incoming $\mathrm{V^V}$ and as ligand for the reduced $\mathrm{V^{III}}$. Although, *in vitro* at least, tunichromes will only reduce $\mathrm{V^V}$ to $\mathrm{V^{IV}}$,[5] reduction of vanadyl(acac)$_2$ (acac = acetylacetonato) to a $\mathrm{V^{III}}$ complex has been achieved with pyrogallol itself.[6] In order to understand better the interaction of the tunichromes with vanadium we have begun to synthesize air-stable analogues of these very reactive molecules. The results of our initial efforts are reported here.

The basic structure of the tunichromes suggests a resemblance to the naturally occurring tricatecholate siderophore, enterobactin and the model systems of Raymond *et al.*[7] By the reaction of spermidine with the acid chlorides of either 2,3,4- or 3,4,5-trimethoxybenzoate, followed by deprotection with BBr_3, we have isolated two tunichrome analogues (**1**) and (**2**).[†] Both the 2,3,4 compound (**1**), and 3,4,5 compound (**2**) have been examined because of the report that various tunichromes might differ only in the number and position of the hydroxy groups.[8] The two isomers vary in their ability to form stable tris chelates. Drieding models indicate that (**2**), which most closely resembles the known tunichromes, cannot simultaneously co-ordinate all three rings to a metal ion while (**1**) can easily do so.

As expected, compound (**1**) forms 'tris' complexes[9] in neutral solutions with both $\mathrm{V^{III}}$ and $\mathrm{V^{IV}}$ as determined by optical and e.s.r. spectroscopy.[‡] The bright green $\mathrm{V^{III}}$ complex is air-sensitive and is oxidized to the intensely blue $\mathrm{V^{IV}}$ species over the course of several hours. However in contrast to catechol itself, reaction of the ligand with vanadate yields, not a stable $\mathrm{V^V}$ tris chelate but rather a new dark blue complex of $\mathrm{V^{IV}}$ as determined by e.s.r. This material may well be polymeric as the solution precipitates a dark blue insoluble solid upon standing. The $\mathrm{V^{IV}}$ product that is formed in this reaction is not the same as that produced directly with $\mathrm{V^{IV}}$ and the ligand.[§]

In contrast, the 3,4,5-trihydroxy ligand produces a dark red solution with $\mathrm{V^{III}}$ in methanol/water. This material has a prominent band in the visible region at 470 nm which is characteristic of oxo bridged $\mathrm{V^{III}}$ dimers.[10] The formation of such a dimer would be consistent with the inability of (**2**) to encapsulate the metal. This is also obvious from the oxidation of the $\mathrm{V^{III}}$ complex which yields, not an intense blue 'tris' complex, but rather a pale violet 'bis' vanadyl species.[¶] However, reaction of (**2**) with vanadate yields a $\mathrm{V^{IV}}$ product very similar to that formed by (**1**). Thus as is seen with the tunichromes both (**1**) and (**2**) will rapidly reduce $\mathrm{V^V}$ to $\mathrm{V^{IV}}$ although even the use of a large excess of the ligand with respect to the metal does not result in further reduction.

Our present results suggest the following. First, although the tunichromes can be expected to reduce $\mathrm{V^V}$ to $\mathrm{V^{IV}}$ they probably cannot reduce $\mathrm{V^{IV}}$ to $\mathrm{V^{III}}$. Of course it is possible that the $\mathrm{V^{IV}}$ formed in the initial reduction becomes ligated in such a way as to lower its redox potential. Secondly while the tunichromes should be good ligands for $\mathrm{V^{III}}$ in neutral solutions, based on their stereochemistry they would be expected to yield oxo bridged dimers which are not consistent with the reported EXAFS spectra.[11] This observation would support the notion that the tunichromes and the vanadium(III) are not located in the same cell types.[12] Further work on these and other model systems is in progress and should provide us with a better understanding of the role of tunichromes in acsidians.

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[†] Both compounds gave satisfactory elemental analyses, mass spectra, ^{1}H and ^{13}C n.m.r., u.v., and i.r. data.

[‡] The $\mathrm{V^{III}}$ complex displays a broad featureless absorbtion in the visible spectrum and is e.s.r. silent at 77 K. For the $\mathrm{V^{IV}}$ complex, $\lambda_{max.}$ 600 and 725 nm, $\varepsilon_m{}^{600}$ ~3100, $g_\perp$ 1.955, $g_\parallel$ 1.926, $A_\perp$ 73 × 10^{-4}, $A_\parallel$ 180 × 10^{-4} cm^{-1}.

[§] λ 590 (640 sh) nm ε_m ~6500, $g_\perp$ 2.002, $g_\parallel$ 1.965, $A_\perp$ 30 × 10^{-4}, $A_\parallel$ 100 × 10^{-4} cm^{-1}. Based on quantitation of the e.s.r. spectrum and solid state magnetic moments it appears that 75—80% of the starting $\mathrm{V^V}$ has been reduced to $\mathrm{V^{IV}}$.

[¶] $\lambda_{max.}$ 540 and 750 nm, $\varepsilon_m{}^{540}$ ~50, $g_\perp$ 1.982, $g_\parallel$ 1.935, $A_\perp$ 70 × 10^{-4}, $A_\parallel$ 185 × 10^{-4} cm^{-1}.