Rational Synthesis of Elusive Organic-Inorganic Hybrid Metal-oxo Clusters: Formation and Post-functionalization of Hexavanadates

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Paving the way towards new functional materials relies increasingly on the challenging task of forming organic-inorganic hybrid compounds. In that regard, discrete atomically-precise metal-oxo nanoclusters have received increasing attention due to the wide range of organic moieties that can be attached onto them through functionalization reactions. The Lindqvist hexavanadate family of clusters ([V₆O₁₆(OCH₂R)₃C-R]³⁺; V₆-R) is particularly interesting due to its magnetic, redox, and catalytic properties. However, compared to other metal-oxo cluster types it has been less extensively explored, which is mainly due to poorly understood synthetic challenges and the limited number of viable post-functionalization strategies. In this work, we present an in-depth investigation of the factors that influence the formation of hybrid hexavanadates (V₆-R HIPOMs) and leverage this knowledge to develop [V₆O₁₆(OCH₂R)₃CNHOCH₂Cl]₃⁺ (V₆-Cl) as a new and tunable platform for the facile formation of discrete hybrid structures based on metal-oxo clusters in high yields. Moreover, we showcase the versatility of the V₆-Cl platform through its facile post-functionalization via nucleophilic substitution with various carboxylic acids of differing complexity and with functionalities that are relevant in multiple disciplines of chemistry, such as supramolecular chemistry and biochemistry. Hence, V₆-Cl was shown to be a straightforward and versatile starting point for the formation of functional supramolecular structures or other hybrid materials, thereby enabling their exploration in various fields.

Introduction

Over the years, the ability to synthesize increasingly complex chemical structures has begun to blur the line between organic and inorganic materials. The formation of organic-inorganic hybrid materials that synergistically combine the properties of both organic and inorganic components has become increasingly interesting for the formation of functional materials. Thus, in recent years, metal-oxo clusters have emerged as valuable building-blocks for the formation of a variety of discrete organic-inorganic hybrid structures. Of the multiple possible hybrid structures, hybrid polyoxometalates (HIPOMs) have particularly attracted significant interest due to their applications in catalysis, materials science, energy storage, medicine and supramolecular chemistry. HIPOMs are a diverse family of discrete anionic metal-oxo clusters, commonly known as polyoxometalates (POMs), that can be covalently grafted with a wide range of organic molecules through the replacement of a metal centre by organosilanes or organosilicate species or through replacement of the bridging oxo ligands by alkoxides or amines. Such functionalization of metal-oxo clusters with various moieties has already proven beneficial, for example, in enhancing catalytic activity and efficiency. Additionally, organic derivatization has been recently demonstrated as a valuable strategy for addressing important challenges in renewable energy and energy storage. Moreover, these hybrid clusters can be regarded as analogues for MOF hybrid materials such as Metal Organic Frameworks (MOFs) and functionalized metal oxide nanoparticles or surfaces, due to similarities in their structure and electronic delocalization. In fact, several MOFs based on HIPOM building units have been reported showing the close connection between such hybrid frameworks and HIPOMs. However, the discrete atomically-precise structures of HIPOMs and their solubility in many different solvents makes them easier to study, thereby providing insights about metal-oxo based materials in general. Moreover, the synthetic challenges faced in the formation of MOF hybrid materials are more easily tackled at the scale of HIPOMs. Hence, the synthesis of increasingly more complex novel HIPOMs is likely to drive progress in many different fields.

Although hybrid metal-oxo clusters have been attracting increased attention in recent years, the factors that influence their formation in solution are still not well understood. As a result, there is a rather limited selection of HIPOMs that can be easily functionalized with various organic moieties. This is particularly the case for the Lindqvist hexavanadate HIPOM ([V₆O₁₆(OCH₂R)₃C-R]³⁺; V₆-R), which due to its interesting chemical and redox properties has been investigated in several fields such as catalysis, memory devices, energy conversion/storage, supramolecular self-assembly and host-guest chemistry, among others. Moreover, these V₆-R HIPOMs have a great structural versatility, since they can be mono-, bis-, tris- or tetra- functionalized with tris(alkoxo) ligands, depending on the composition and oxidation state of the metal centers. However, although V₆-R HIPOMs are one of the relatively limited literature available on V₆-R HIPOMs is likely due to the poor yields often obtained during their synthesis and the limited amount of V₆-R HIPOMs that can be easily derivatized with a wide range of organic species. Hence, elucidating the formation mechanism of such clusters is essential to address the issues typically encountered during their synthesis.
In general, the synthesis of metal-oxo hybrids with complex organic moieties attached to the inorganic core is often achieved by starting from a relatively simple building unit with a reactive terminal group that can then be modified through a post-functionalization reaction. Therefore, \([V_6O_{15}((OCH_3)_2CH(CHOH))_2]^{12-}\) \((V_6-OH)\), which can be easily obtained from decavanadate \((H_3[V_10O_{28}]^{8-}; V_{10})\) and pentaerythritol \((HOCH_2)_2CH(CHOH))^{29,30}\) is typically used for forming more complex \(V_6-R\) HPOMs with various organic moieties through esterification reactions with carboxylic acids and acid anhydrides but is not reactive towards many substrates \((\text{Scheme 1})\). An alternative route is to use \([V_6O_{15}((OCH_3)_2CNH)])^{22,33,34}\) \((V_6-NH_2)\) as a post-functionalization platform due to its more reactive amine terminal group but its synthesis from \(V_{10}\) and triacetoxymethylaminomethane \(((HOCH_2)_2CNH); Tris-NH_2\) typically results in very low yields \((\text{Scheme 1})\). In contrast, other metal-oxo clusters that have been successfully functionalized with Tris-NH_2 in high yields, thereby driving the formation of hybrid metal-oxo clusters is still necessary. Hence, by investigating the key factors in the synthesis of \(V_6-R\) HPOMs, a novel post-functionalization platform was developed, and this new HPOM was functionalized with multiple carboxylic acids of differing complexity to demonstrate the versatility of this platform in making the formation of hybrid polyoxovanadates more accessible compared to existing platforms.

### Results and discussion

The low yields often obtained in the synthesis of \(V_6-R\) HPOMs are typically attributed to the ease of reduction of the \(V^{5+}\) centers. However, to the extent of our knowledge, this has not been experimentally confirmed. Nevertheless, previously reported literature procedures suggest that the solvent and the nature of the functional groups on the tris(alkoxo) ligand have a significant influence on the outcome of the reaction. \(V_6-OH\) can be easily synthesized in acetonitrile (ACN) and water while \(V_6-NH_3-H\) can only be obtained in dimethylacetamide (DMA) and even in DMA the yield is typically less than 10% unless protecting groups are used. In order to understand what happens in solution during the synthesis of \(V_6-R\) HPOMs, we set out to study the reactions between \(V_{10}\) and triol ligands by \(H^1\) and \(^{51}V\) NMR and IR. Furthermore, the reaction of \(V_{10}\) with \((HOCH_2)_2C-NHCOCH_2Cl\) (Tris-Cl) was investigated in detail, since this triol ligand can be easily synthesized in high yields at the gram-scale. Moreover, the highly electrophilic chloroacetamide functionality of Tris-Cl can be exploited for nucleophilic substitution with a wide variety of carboxylic acids, amines, and thiols, as has been previously demonstrated by our group with other hybrid metal-oxo clusters. The high electrophilicity of the chloroacetamide carbon, and the \(S_N2\) mechanism favoured under polar aprotic conditions, allow for substitution reactions with relatively bulky or less nucleophilic substrates than with \(V_6-OH\) and its derivatives. Hence, the insights gained from following the reaction of \(V_{10}\) with the triol ligands were used to optimize the procedure for the synthesis of \(\text{TB}_{12}[V_6O_{15}((OCH_3)_2CNHCOCH_2Cl)]\) \((V_6-Cl)\) from Tris-Cl as a novel post-functionalization platform (Scheme 1).

#### Elucidating the impact of ligand functionalities

The reactions of two triol ligands, Tris-NH_3 and \((HOCH_2)_2C-CH_2\) \((\text{Tris-CH}_3)\), with \(V_{10}\) in ACN-D_2 were followed by \(H^1\) and \(^{51}V\) NMR to determine the role of the terminal group of the Tris ligand on the synthesis of the corresponding \(V_6-R\) HPOM. Although Tris-CH_3 and Tris-NH_3 have very similar structures, simply switching the methyl group for an amine has a major effect on the speciation of vanadates in solution (Scheme 2). The \(H^1\) and \(^{51}V\) NMR spectra of the reaction mixture consisting of \(V_{10}\) with Tris-CH_3 showed the appearance of peaks characteristic of \([V_6O_{15}((OCH_3)_2CCH)]^{2+}\) \((V_6-CH_3)\) after just 0.5 h of mixing at 80 °C (Figure S1;S3). Over time these peaks continued to grow while the peaks corresponding to \(V_{10}\) disappeared. In contrast, when \(V_{10}\) was reacted with Tris-NH_3, several peaks appeared in the \(^{51}V\) NMR spectrum within 0.5 h of heating (Figure S1), indicating that multiple vanadate species formed, with the main species being \([V_6O_{15}((OCH_3)_2CCH)]^{2+}\) \((V_6-CH_3)\) after just 0.5 h of heating (Figure S1), indicating that multiple vanadate species formed, with the main species being \([V_6O_{15}((OCH_3)_2CCH)]^{2+}\) \((V_6-CH_3)\) after just 0.5 h of heating. The formation of \(V_{12}\) and \(V_{13}\) was also observed to occur when \(V_{10}\) was heated at 80 °C on its own in ACN (Scheme 2), and over time \(V_{12}\) became the main species in solution based on \(^{51}V\) NMR. This can also be seen from the IR spectrum of \(V_{10}\) alone and with Tris-NH_3, both of which gave rise to the characteristic peaks of \(V_{12}\) in the fingerprint region after heating (Figure S9). The formation of \(V_{12}\) and \(V_{13}\) in the presence of Tris-NH_2 may be due to its poor solubility in ACN, which is much lower than that of Tris-CH_3 as also evidenced from the relative integration of the peak ca. 3.75 ppm due to the \(-OCH_2-\) groups of the free ligand (Figure S3-S4). As a result, only a small amount of Tris-NH_2 is present in solution at any given time, which reacts with \(V_{10}\) to form other vanadate species that give rise to several peaks around 5 ppm in the \(^1H\) NMR spectrum (Figure S4) along with additional peaks in the \(^{51}V\) NMR spectrum. These are likely caused by Tris-NH_2 reacting with \(V_{10}\) through both the \(-OH\) and \(-NH_2\) groups.
However, over time the peaks observed by $^{51}$V NMR gradually disappear, which is likely due to reduction of the $V^{5+}$ centres to form reduced species that cannot be observed by NMR. Interestingly, the peak at -498 ppm, which may correspond to $V_5$-NH$_2$, eventually becomes the only peak in the $^{51}$V NMR spectrum over the course of 120 h. This peak as well as the expected peak at around 5 ppm in the $^1$H NMR spectrum, remain very weak at all times, indicating that $V_5$-NH$_2$ is only present in low concentration, if at all. This is also evidenced from the IR spectrum recorded after 120 h which does not display the expected peaks of the $V_5$ core. Consequently, the poor yields typically obtained for $V_5$-NH$_2$ are not just due to the reduction of $V^{5+}$ centres, but also due to the poor solubility of the triol and side reactions with the more reactive amine group.

The reaction of $V_{10}$ with Tris-Cl in ACN-d$_3$ was also followed by $^1$H and $^{51}$V NMR and it displayed changes in speciation that were more comparable to Tris-CH$_3$ than Tris-NH$_2$ (Scheme 2). In contrast to Tris-NH$_2$, $V_{12}$ and $V_{13}$ were not formed in the presence of Tris-Cl, which may be due to the slightly higher solubility of Tris-Cl in ACN with respect to Tris-NH$_2$. Interestingly, two broad peaks were observed to appear at -228 and -294 ppm in the $^{51}$V NMR spectrum of the reaction mixture (Figure S1), which correspond to V environments that are more deshielded than expected for fully oxidized vanadates with oxo or alkoxo ligands. Hence, these new peaks may be due to paramagnetic shifting of $V^{5+}$ centres in mixed valence vanadates or due to coordination of the ligand to $V^{5+}$ centres through nitrogen. Mixed valence vanadates do indeed seem to form in the presence of Tris-Cl since the solution changes colour over time from orange/yellow (typical of $V^{5+}$) to dark green, which is indicative of reduction of some of the $V^{5+}$ centres to form a mixture of $V^{5+}$ and $V^{4+}$ or $V^{3+}$. This colour change was also observed to occur with Tris-NH$_2$ but not with Tris-CH$_3$. Therefore, the reduction of $V^{5+}$ may be due to N-H$$-$$O-V interactions that could lead to protonation of the POM core since the transfer of the N-H proton onto the oxo ligands of the vanadate species would likely result in reduction, and a similar process has been proposed to result in the photoinduced reduction of alkylammonium salts of molybdates. Furthermore, as the ligand reacts with the vanadate species, more $V^{5+}$ centres get reduced until eventually the vanadate species cannot be observed by $^{51}$V NMR. The ligand also seems to partially decompose over time, resulting in the appearance of a peak at -364 ppm belonging to VO$_2$Cl$_2$ (Figure S1), which was formed from the release of the chloride of Tris-Cl. Hence, the main product for the reaction of Tris-Cl and Tris-NH$_2$ with $V_{10}$ in ACN is not the desired $V_6$-R HPOM, as also evidenced by following the reaction of $V_{10}$ with Tris-Cl by IR spectroscopy (Figure S10), which after 120 h at 80 °C showed weak peaks corresponding to $V_6$-Cl along with peaks corresponding to another vanadate species. This is due to the poor solubility of the triol ligands as well as side reactions of these ligands with $V_{10}$. Moreover, this indicates that the yield of $V_6$-R HPOMs depends mainly on how the speciation of vanadates in solution is affected by the ligand through its concentration in solution and the reactivity of its functional groups.

### Investigating the role of the solvent

Since DMA has also been previously reported as a solvent in optimized procedures, in this work the impact of the solvent on the formation of $V_6$-Cl was investigated further. In doing so, the use of DMA as the solvent for the synthesis of $V_6$-Cl was determined to be crucial for obtaining the product in high yields, since the attempted synthesis in ACN or in water following the typical procedures used for the formation of hexavanadates resulted in many side products hindering the isolation of $V_6$-Cl. Differences in the reaction of $V_{10}$ with Tris-Cl in ACN vs in DMA can be seen from the $^1$H and $^{51}$V NMR spectra of aliquots obtained over 20 h, which showed more intense peaks corresponding to $V_6$-Cl when the reaction was conducted in DMA. This means that the formation of $V_6$-Cl is more favourable in DMA, which may be in part due to the higher solubility of Tris-Cl in this solvent. Furthermore, when $V_{10}$ is heated at 80 °C on its own in DMA, the speciation is quite different from that in ACN (Figure S6). While the $V_{12}$ structure is highly favoured in ACN, $V_{13}$ is the main species in DMA along with multiple other vanadate species of lower nuclearity, ranging from $V_1$ to $V_6$, which gradually disappear over time. This suggests that compared to ACN, the vanadate structures are more labile and prone to interconversion in DMA, which may also facilitate the formation of hexavanadates in DMA.

It was also observed that changing the solvent had an impact on the ability of $V^{5+}$ centres to be reduced. The cyclic voltammogram (CV) of $V_6$-Cl in either ACN or DMA (Figure 2(a)) shows a similar one-electron reversible reduction/oxidation wave due to the $V^{5+}/V^{4+}$ redox couple in both solvents, but the half-wave potential ($E_{1/2}$) is more negative in DMA compared to ACN (-1.08 and -1.01 V vs Fc/Fc⁺). This indicates that the reduction of $V^{5+}$ occurs more easily in ACN, which may be linked to the N-H$$-$$O-V interactions that could lead to protonation of the POM core since the transfer of the N-H proton onto the oxo ligands of the vanadate species would likely result in reduction, and a similar process has been proposed to result in the photoinduced reduction of alkylammonium salts of molybdates. Furthermore, as the ligand reacts with the vanadate species, more $V^{5+}$ centres get reduced until eventually the vanadate species cannot be observed by $^{51}$V NMR. The ligand also seems to partially decompose over time, resulting in the appearance of a peak at -364 ppm belonging to VO$_2$Cl$_2$ (Figure S1), which was formed from the release of the chloride of Tris-Cl. Hence, the main product for the reaction of Tris-Cl and Tris-NH$_2$ with $V_{10}$ in ACN is not the desired $V_6$-R HPOM, as also evidenced by following the reaction of $V_{10}$ with Tris-Cl by IR spectroscopy (Figure S10), which after 120 h at 80 °C showed weak peaks corresponding to $V_6$-Cl along with peaks corresponding to another vanadate species. This is due to the poor solubility of the triol ligands as well as side reactions of these ligands with $V_{10}$. Moreover, this indicates that the yield of $V_6$-R HPOMs depends mainly on how the speciation of vanadates in solution is affected by the ligand through its concentration in solution and the reactivity of its functional groups.

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interactions observed in the crystal structure obtained by crystallization in ACN (Figure 2(c)) since protonation of oxo ligands in the vanadate clusters has been shown to result in shifts towards lower potentials.\textsuperscript{29} In contrast, the crystal structure of a similar V\textsubscript{5}R HPOM with an amide group obtained by Bamba et al in DMA shows that DMA forms H-bonding interactions between its C=O group and the NH group of the ligand, thereby preventing N-H---O-V interactions from occurring.\textsuperscript{49} Therefore, reduction of V\textsuperscript{5+} induced by transfer of the proton from the ligand is less likely to occur in DMA than in ACN, making it overall a more suitable solvent. However, some side reactions resulting in the reduction of V\textsuperscript{5+} do still occur in DMA, as evidenced by the colour change of the solution. This results in the formation of mixed valence V\textsubscript{5-6}Cl which can be converted back to the fully oxidized form by the addition of 35 wt% H\textsubscript{2}O\textsubscript{2} at the beginning of the purification procedure. This oxidation step is important for the successful isolation of the desired fully oxidized species in high yields through the purification process. Overall, the combination of using DMA and oxidizing the crude product with H\textsubscript{2}O\textsubscript{2} results in a significantly improved yield.

Isolation and characterisation of V\textsubscript{5-6}Cl

Through optimization of the synthesis and purification procedures based on the insights obtained by following the reactions of the triols by NMR and IR, it was possible to obtain V\textsubscript{5-6}Cl directly from V\textsubscript{5}O\textsubscript{10} and Tris-Cl with a 60% yield after reacting in DMA at 80 °C under an argon atmosphere for 5 days. The formation of V\textsubscript{5-6}Cl was confirmed by NMR and ESI-MS (Figure 3). ESI-MS gave a peak at m/z = 1144.1 in negative mode, corresponding to V\textsubscript{5-6}Cl with only one TBA counter cation ([V\textsubscript{5-6}Cl\textsuperscript{+}TBA\textsuperscript{+}]; calcd. 1145.3) while in positive mode a peak at m/z = 1630.1 was obtained due to the POM with three TBA counter ions ([V\textsubscript{5-6}Cl\textsuperscript{+}3TBA\textsuperscript{+}]; calcd. m/z = 1630.2). Furthermore, \textsuperscript{1}H NMR showed a downfield shift from 3.57 to 5.11 ppm corresponding to the -CH\textsubscript{3}O- group of the tris(alkoxo) ligand becoming attached to V\textsubscript{5-6}Cl POM core. The peak at -494.47 ppm in \textsuperscript{31}V NMR further confirmed the formation of V\textsubscript{5-6}Cl since it is characteristic of trans-functionalized hexavanadates.\textsuperscript{34,49} Furthermore, the peaks in the IR spectrum in the range 700-1000 cm\textsuperscript{-1} are characteristic of ν V=O and ν V-O-V vibrations of the V\textsubscript{5-6}Cl POM core, while the peaks at 1114 and 1063 cm\textsuperscript{-1} due to ν C-O vibrations indicate attachment of the triol ligand onto the POM core.\textsuperscript{30,50} The exact structure of V\textsubscript{5-6}Cl was further confirmed by single crystal X-ray diffraction (SC-XRD) analysis. V\textsubscript{5-6}Cl crystallized in the triclinic space group P-1 with half of one POM and one TBA cation in the asymmetric unit. The obtained crystal structure (Figure 2(b)) shows a classical Lindqvist structure composed of six edge sharing (VO\textsubscript{4}) octahedra in an octahedral arrangement. Moreover, two Tris-Cl moieties are attached on opposite faces of the V\textsubscript{5-6}Cl POM core via three double-bridged oxygens (μ\textsubscript{2}-O) each. In addition, V\textsubscript{5-6}Cl was observed to form a 1D H-bond network due to H-bonding interactions between the NH group of the amide and a terminal oxygen of the V\textsubscript{5-6}Cl POM core with N---O distances of 2.91 Å (Figure 2(c)). Overall, the crystal structure together with the complementary spectroscopic techniques unambiguously confirms the formation of this novel post-functionalization platform.

Post-functionalization of V\textsubscript{5-6}Cl

The potential of V\textsubscript{5-6}Cl as a valuable post-functionalization platform was evaluated via nucleophilic substitution reactions with different carboxylic acids: valeric acid, phenylacetic acid, adamantane carboxylic acid, and biotin (Scheme 3). These carboxylic acids were selected to showcase the applicability of...
this post-functionalization strategy to yield compounds with widely different functionalities. Furthermore, functionalities that are of interest in supramolecular chemistry were chosen since HPOMs have been shown to produce new dynamic supramolecular structures that often result in enhanced properties. Consequently, four novel $V_6$-R HPOMs were synthesized from $V_6$-Cl and the aforementioned carboxylic acids: TBA$_2$[V$_{13}$O$_{33}$[O(CH$_2$)$_3$CNHC(O)CH$_2$-R)$_2$] where $R = -$ OOC(CH$_2$)$_3$CH$_3$ ($V_6$-Val), -OOCCH$_2$CH$_5$ ($V_6$-Ph), -OCC$_6$H$_5$ (V$_6$-Ad), and -OCC$_6$H$_5$OS (V$_6$-Biot).

The nucleophilic substitution reactions were performed by mixing $V_6$-Cl with tetrabutylammonium iodide (TBA-I), a carboxylic acid and a base in dry DMA for 2-5 h at 80 °C. Either Na$_2$CO$_3$ or tetrabutylammonium hydroxide (TBA-OH) were used as the base and both successfully promoted the nucleophilic substitution reaction. Na$_2$CO$_3$ was found to be more suitable for post-functionalization of $V_6$-Cl since, when using TBA-OH, hydrolysis of the ester bond after post-functionalization was observed by ESI-MS if the solution was left stirring for too long (Figure S12-S14). As a result, the yield and the purity of the product when using Na$_2$CO$_3$ were generally higher than with TBA-OH. For example, the synthesis of $V_6$-Ad gave a yield of 41.77% with TBA-OH while with Na$_2$CO$_3$ the yield was 50.39%. Nevertheless, when using Na$_2$CO$_3$, a small amount of the Na salt of the HPOM or mixed salts were sometimes obtained, but these could be easily converted back to the desired TBA salt by the addition of excess tetrabutylammonium bromide (TBA-Br). Hence, once the reaction conditions were optimized, post-functionalization of $V_6$-Cl resulted in yields of around 50% or higher overall.

It is worth noting that the post-functionalization of $V_6$-Cl with all selected carboxylic acids was possible despite their differences in steric hindrance and functionality. However, the nature of the organic species being used can have an impact on the outcome of the reaction. This was observed during the synthesis of $V_6$-Ph since the solution turned green due to the formation of $V_6$-Ph with mixed valence V centres. Hence, in order to obtain the desired fully oxidized $V_6$-Ph, an additional oxidation step with H$_2$O$_2$ was required. The higher propensity of $V_6$-Ph towards reduction over the other $V_6$-R HPOMs reported in this study is likely due to the ability of the aromatic ring to donate electrons to the POM. This resulted in a slightly lower yield for $V_6$-Ph compared to other $V_6$-R HPOMs. In contrast, $V_6$-Biot was successfully obtained in relatively high yield, even when using TBA-OH as the base. This is significant because the attempted post-functionalization of $V_6$-OH with biotin via esterification – using N,N'-dicyclohexylcarbodiimide (DCC) as the coupling agent and 4-dimethylaminopyridine (DMAP) to promote the reaction – was unsuccessful, and the previously reported esterification with stearic acid only gave a relatively low yield (10%). This shows the limitations of $V_6$-OH as a post-functionalization platform and highlights the versatility of $V_6$-Cl for the derivatization of hexavanadates with a wide range of different species to obtain new $V_6$-R HPOMs in reasonable yields.

Successful post-functionalization of $V_6$-Cl to form and isolate $V_6$-Val, $V_6$-Ph, $V_6$-Ad, and $V_6$-Biot was confirmed by $^1$H NMR (Figure S8) from the disappearance of the peak at around 12 ppm due to the -COOH environment and a downfield shift in the chemical shift of the -COCH$_3$ group from 4 ppm to around 4.45 ppm due to the chloro (-Cl) functionality being substituted by the carboxylate (-OOC-). The chemical shift and integration of the other peaks in the spectra of each compound were also consistent with the attachment of the carboxylate moieties to both tripodal anchors on the $V_6$ HPOM. Furthermore, $^{31}$V NMR (Figure S8) showed that the $V_6$ POM core structure remained intact after the post-functionalization, giving rise to a single peak at around -495 ppm for all compounds. This was further confirmed from the characteristic peaks at around 700-1000 cm$^{-1}$ in the IR spectra of the compounds due to the ν V=O and ν V–O–V vibrations (Figure S11). Peaks in positive ion mode due to the POM with extra TBA counter cations ([M+3TBA]$^+$) were also observed for the POMs with molecular weights within the measurement range. Moreover, the crystal structure of $V_6$-Val (Figure 4), obtained from crystals formed by slow evaporation of a solution of $V_6$-Val in CHCl$_3$, matched that of $V_6$-Cl with Cl replaced by the carboxylate. Unlike $V_6$-Cl, $V_6$-Val crystallized in the monoclinic P2$_1$/c space group, but it also formed a 1-D H-bond network.
due to H-bonding interactions between the NH group of the amide bond and a terminal oxygen of the hexavanadate POM core with N---O distances of 2.88 Å (Figure 4(b)). Furthermore, aside from having two TBA molecules per hexavanadate unit as expected, two chloroform molecules per hexavanadate unit were also present in the unit cell (Figure 4(a)). Overall, this confirms the successful post-functionalization of V₆-Cl with carboxylic acids.

Conclusions

In this work, an in-depth investigation of the factors that affect the synthesis of hexavanadates was leveraged to develop V₆-Cl as a novel post-functionalization platform. The study showed that the low yields often observed in the synthesis of hexavanadates are linked to the solution properties of the ligand and the reactivity of its functional groups, both of which affect the speciation of vanadates in solution. In general, the formation of a suitable post-functionalization platform requires a ligand with a reactive terminal group, however this may also cause undesired side reactions. This insight was crucial for the facile, one-step synthesis of V₆-Cl in high yields from decavanadate cluster and Tris-Cl with DMA as the solvent. In general, the key factors influencing the synthesis of hybrid hexavanadate clusters are: (i) the reactivity of the terminal group of organic ligand with respect to vanadate species in solution, (ii) the solubility of the organic ligand, (iii) the interactions of the solvent with the ligand which prevent side reactions, and (iv) the half-wave potential of V⁶⁺ centers in a chosen solvent, which makes the formation of mixed valence or fully reduced species less favorable. We also showed that V₆-Cl could be easily post-functionalized with a wide range of carboxylic acids that differ significantly in composition and complexity. The formation of such (bio)organic hybrids with biomolecules (e.g. biotin) may have potential as antitumor, antiviral, anticancer and anti-amyloid agents, while adamantane derivatives could be used for drug carrier systems in combination with cyclodextrin, among many other possible applications. Furthermore, this post-functionalization strategy can be extended to functionalization with other organic moieties, resulting in novel hybrid metal-oxo clusters for potential use in catalysis, medicine and molecular magnetism. Hence, through the successful synthesis of V₆-Cl as a novel, accessible, and versatile starting core with N---O distances of 2.88 Å (Figure 4(b)). Furthermore, aside from having two TBA molecules per hexavanadate unit as expected, two chloroform molecules per hexavanadate unit were also present in the unit cell (Figure 4(a)). Overall, this confirms the successful post-functionalization of V₆-Cl with carboxylic acids.

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Data availability

Crystallographic data for compounds V₆-Cl and V₆-Val has been deposited at The Cambridge Crystallographic Data Centre (CCDC) and allocated the deposition numbers CCDC2217991 and 2217992, respectively. This supplementary crystallographic data can be obtained free of charge via www.ccdc.cam.ac.uk/structures. All other data supporting the results discussed in this work is available within the paper and its ESI.

Author Contributions

D.E.S.M. and G.K. performed the synthesis and characterisation of all compounds with the assistance of M.A.M. K.Y.V.H. solved the crystal structures. T.N.P.V. and M.A.M. helped with the design and interpretation of the experiments. The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

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