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A survey of the different roles of polyoxometalates in their interaction with amino acids, peptides and proteins

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One of the most attractive areas in inorganic chemistry is the synthesis of polyoxometalates (POMs) exhibiting new properties and applications. Since the impact of POMs in biochemistry and related fields of research has increased in the last few years, there has been a special interest in this topic. Significant progress in biological applications has been made where the interaction of POMs with amino acids, peptides and proteins is relevant. Versatile POMs play a series of different roles in the interaction with these biomolecules as described in this review. Various types of interactions are established, depending on the POM shape and charge, the amino acid side chain, peptide sequence or protein structure. Experimental conditions such as temperature, acidity, solvent, *etc*. are also important factors that influence the binding/reactivity of POM with biomolecules, as described herein. This understanding allows the adequate design of the POM-biomolecule couple for tailoring and controlling mechanisms of action such as catalysis, inhibition, and aggregation, or the crystallising agent.

Introduction

Polyoxometalates (POMs), often described as soluble oxide clusters, are a diverse and vast family of polynuclear oxo-bridged early transition metal compounds of (MO_x) polyhedrals, where M is generally W, Mo, V, Nb or Ta in their highest

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Mina Arefian

Mina Arefian was born in 1985 in Neyshabur, Iran. She received her B.Sc. degree in 2008 from Ferdowsi University of Mashhad and her M.Sc. degree from Shahrood University of Technology in 2011. In the same year, she started her Ph.D. in Ferdowsi University of Mashhad. Her main interest is in bio-inorganic chemistry, and she is now pursuing her Ph.D. thesis under the supervision of Hossein Eshtiagh-Hosseini and Masoud Mirzaei considering synthesis of inorganic–organic hybrid based polyoxometalates and biomolecules in order to investigate intermolecular interactions within their crystalline networks.

Masoud Mirzaei

Masoud Mirzaei was born in 1980 in Tehran, Iran. He received his B.Sc. degree from the IAU in 2003 and his M.Sc. and Ph.D. degrees from FUM in 2006 and 2010. He completed his doctoral thesis under the supervision of Hossein Eshtiagh-Hosseini and the late Hossein Aghabozorg. He started his career as an assistant professor at FUM in 2010 and was promoted to associate professor in 2013. His research interests focus on inorganic–organic hybrids based on polyoxometalates and coordination chemistry. He has published more than 120 papers, reviews and one book chapter in LAP so far. He has served as a reviewer for scientific journals from all continents, and has reviewed many manuscripts.

oxidation number. The three-dimensional structure of POMs is defined primarily by either corner sharing (one bridging μ_2-oxo group) or edge sharing (two bridging μ_2-oxo groups) of MO_6 octahedrals. Occasionally it can be also defined by sharing of three bridging μ_2-oxo groups (face sharing). Eventually connection of polyhedrals in different fashions leads to various structures.[1] POMs include two families of isopolyanions ($[H_xM_yO_z]^{n-}$) and heteropolyanions ($[X_xM_mO_y]^{q-}$) (X = heteroatom, *e.g.* B, P, Si and M = first-row transition metals in their highest oxidation numbers). Heteropolyanions, including hetero atoms, possess increased stability compared with isopolyanions.[2] They have been receiving growing attention in recent years due to the wide range of their applications extending from catalysis[3–11] to biological and pharmaceutical fields.[12]

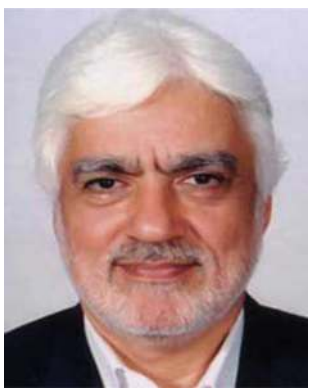
The first POMs were synthesized almost 200 years ago, but the structural identity of many species has been established only fairly recently.[13] Great advances in both instrumentation and single crystal X-ray diffraction methods in recent years has allowed the characterization of large clusters.[14]

POMs have a huge structural diversity with well-defined architectures and variable, but controlled shape and size in the nanometer range. Moreover, it is possible to tune the physical and chemical properties of POMs such as their redox and electronic activity and bioactivity. These capabilities enable the developing of desired properties and using them in different areas of research, for example, catalysis, drug discovery, imaging, crystal engineering *etc*. These versatile inorganic entities have been used as binding blocks for building functional solids. In particular, their promising biological activity has motivated a great deal of research.[15–17]

POMs are inorganic molecules with well-defined size, shape, configurable charge, and ability to interact with organic moieties. For more than two decades, it has been proven that the physical and chemical properties of POMs are adequate for biological applications; however, the main drawback is commonly related to their insufficient selectivity. Nevertheless, POMs are found to exhibit biological activity as antibacterial,[18,19] anticancer,[20] and antiviral[21] agents.

Although POMs are tuneable and easily accessible inorganic drug prototypes, their full potential can be optimized by enhancing their biocompatibility through organic functionalization with bioactive moieties.[13] Association between POMs and natural biomolecules (proteins, peptides and amino acids) is a good strategy to improve their properties by taking advantage of the different characteristics of both moieties. For this reason, studies on the interaction between POMs and biomolecules are attracting increasing attention. Progress in this field is difficult due to the complexity of both POMs and the protein, peptide or amino acid. It is also important to take into consideration the different binding/interaction mechanism of POMs with the biomolecules. The binding mode can be dominated by the non-covalent interactions such as electrostatic forces, hydrogen bonds, or van der Waals forces between the organic and the inorganic parts, therefore the understanding of these forces is also important. Moreover, the organic and inorganic moieties can be also linked *via* strong covalent or ion-covalent bonds.[22] The anionic character of polyoxometalates (POMs) facilitates their association with organic counter cations (basic amino acids) through non-directional electrostatic forces or more directional electrostatically enhanced H-bonding interactions. Regarding the covalent/coordination bonds, the POMs can be directly linked to a metallic center as a ligand or an electrophilic group of the biomolecule. Moreover, in metal substituted POMs (MS-POMs), the interaction can also occur with nucleophilic groups of the organic ligands.

During the last few years, the scientific world has witnessed great progress in POM chemistry and many reviews have been published dealing with different aspects such as synthetic

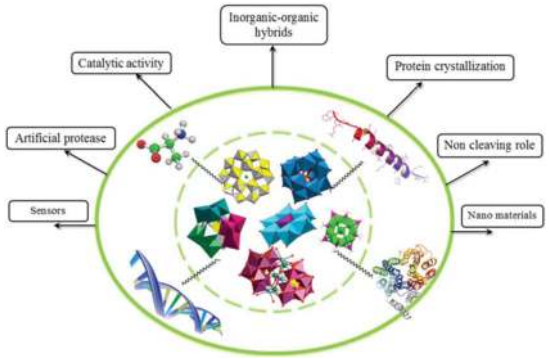


Hossein Eshtiagh-Hosseini

Hossein Eshtiagh-Hosseini was born in 1947 in Tabriz, Iran. He received his B.Sc. degree from Tabriz University in 1969 and his M.Sc., Ph.D., and postdoc degrees from the University of Sussex, England, in 1973, 1977, and 1979. He started his career as an assistant professor at FUM in 1979 and was promoted to associate professor in 2008 and full professor in 2012. His research interests focus on inorganic–organic hybrids based on polyoxometalates, coordination chemistry, and organometallic. He has published more than 130 papers, reviews and one book chapter in LAP so far.

Antonio Frontera

Prof. A. Frontera received his PhD from the Universitat de les Illes Balears (Spain) in 1994. During this period, he combined theory and experiment to propose a plausible mechanism for the direct lithiation of polyphenolic compounds. Moreover, he studied the mechanism of diotropic reactions. After two years of postdoctoral research in the laboratory of Prof. W. L. Jorgensen (Yale University, USA), 1995–1996, devoted to the OPLS force field parameterization of carbohydrates, he came back to Spain as a research scientist at the Universitat de les Illes Balears, where he is currently a professor working on noncovalent interactions.



Scheme 1 Different capabilities of POMs in interaction with essential biomolecules (amino acid, peptide, protein and DNA) as promising biological active species are represented.

approaches,[21–25] properties,[14,26] and applications.[27,28] Also two additional reviews provide further insights into POM chemistry: one surveys the coordination modes (0–12) of Keggin type POMs in inorganic–organic hybrid compounds[24] and the other describes the effect of various organic ligands on POM based inorganic–organic hybrids.[25]

In the present review, we highlight the most important investigations of compounds combining POMs with proteins (pro), peptides (pep) or amino acids (aa). This field of research reveals a great variety of POM roles that have not been previously reviewed, covering the three types of molecules (pro/pep/aa). For instance, modifications in the POM structure result in different behaviour in its interaction with proteins, peptides and amino-acids. Therefore, the aim of this review is to provide a comprehensive description of the different roles of POMs in their interaction with these relevant biological molecules (Scheme 1).

We have divided this review into the following sections. First we deal with the synthesis and characteristics of POM–aa hybrid materials. That is, we describe recent research in inorganic–organic hybrid or pseudo-hybrid materials and their role as catalyst in amino acid redox reactions. Secondly, we describe the different roles of POMs in their interaction with peptides and proteins: as sensors, hydrolysing agents to cleave peptide bonds (artificial proteases) and enzyme inhibitors. Finally, we describe the utilization of POMs as crystallizing agents in the field of protein crystallography.

POM–amino acid assemblies

Nature's building blocks, amino acids, as the basic units of proteins and peptides, are of great importance in biochemistry and life science. They are able to connect organic and inorganic groups because of their flexible coordination modes and variety of side chains. Amino acid ligands have at least two (N and O) coordination sites, which favours the coordination to transition metals (TMs) or Ln ions using various coordination fashions.[29] They are enantiopure compounds, water soluble, non-toxic and economically affordable. These advantages make them appropriate candidates in bio-inorganic applications, especially in combination with POMs. On the other hand, since it has been shown that some types of POMs have interesting therapeutic effects, the possibility of obtaining beneficial synergistic effects by combining them have caught scientists' attention.[13]

There are various types of natural amino acids considering their side chain properties: (i) amino acids with charged (positive or negative) side chains, (ii) with polar but uncharged side chains, and (iii) aromatic and aliphatic hydrophobic side chains. Negatively charged POMs can interact electrostatically with positively charged amino acid side chains and with proton donors by hydrogen bonding. For example, arginine, histidine and lysine are positively charged at physiological pH and are able to form both electrostatic and hydrogen bond interactions with POMs. In general, POM–aa compounds can be classified in two families as follows: (i) supramolecular assemblies in which POMs interact with amino-acids *via* non-covalent interactions, (ii) covalent binding of amino acids to POMs, metal-substituted POMs or lacunary POMs to form hybrid complexes *via* covalent/coordination bonding.

In the following sub-sections we provide some illustrative examples covering each family of the above mentioned categories. Comprehensive information is given in Table 1.

POM–amino acid based inorganic–organic hybrids

The First pioneering studies combining POMs and amino-acids were reported in the 1990s.[30–34] For instance, Yamase and coworkers[32] reported the coordination of a lysine ligand to γ-octamolybdate in 1995. After that, a dramatic growth of manuscripts devoted to the fabrication of hybrid complexes occurred.[35–43]

In 2002, Kortz *et al.*[13] described a series of lone pair containing Anderson type heteropolymolybdates, typically $[X^{n}Mo_6O_{21}]^{6-n}$ (X^{III} = As, Sb, Bi; X^{IV} = Se, Te), functionalized covalently by glycine ($HO_2CCH_2NH_2$), β-alanine ($HO_2C(CH_2)_2NH_2$), 4-aminobutyric acid ($HO_2C(CH_2)_3NH_2$), λ-alanine ($HO_2CCHCH_3NH_2$) and λ-lysine (HO_2CCH-{$(CH_2)_4NH_2$}NH_2). In the solid state architecture, three amino acids are bound to two edge-sharing Mo centers by their carboxylate group on the same side of the ring (see Fig. 1).

Some interesting reports have been published related to chirality, which is one of the most challenging and important aspects of polyoxometalate chemistry.[42–46] One of the first studies was published by Pope *et al.*[30] in 1996, where the synthesis and structural characterization of three chiral Sn-substituted complexes of the lacunary anions $[PW_9O_{34}]^{9-}$ and α-$[SiW_9O_{34}]^{10-}$ were reported. The formation of enantiomers upon interaction with L-lysine was demonstrated by ^{183}W NMR spectroscopy.

Several years later the same group isolated a sandwich type POM, $[Ce(\alpha_1\text{-}P_2W_{17}O_{61})(H_2O)_x]^{7-}$, in dimeric *meso* form (D,L), after addition of a series of enantiopure amino-acids. It was possible to distinguish between diastereomers using ^{31}P NMR spectroscopy. It was suggested that the amino acids interact with POM through coordination of the carboxylate to Ce^{3+} and

Table 1 A summary of POM-based materials interacting with aa/pep/pro/DNA. NC stands for non-covalent and C for covalent interaction between POM and aa/pep/pro/DNA

Entry	POM/MS-POM	aa/pep/pro	Year	Ref.
1 (NC)	$[V_{10}O_{28}]^{6-}$	Gly–Gly, Gly–His	1994	61
2 (NC)	$[Sn^{II}_3(R\text{-}PW_9O_{34})_2]^{12-}$, $[Sn^{II}_3(R\text{-}SiW_9O_{34})_2]^{14-}$, $[Sn^{II}_3(\alpha\text{-}SiW_9O_{34})_2]^{14-}$	Lys	1996	30
3 (NC)	Bis(acetato)dirhodium-11-tungstophosphate	L-Met), L-cysteine	1998	31
4 (NC)	$[V_{10}O_{28}]^{6-}$, $[H_2W_{12}O_{42}]^{10-}$	Cowpea chlorotic mottle virus	1998	107
5 (NC)	$H_6[P_2Mo_{18}O_{62}]\cdot 16H_2O$	Lys	2000	35
6 (NC)	$K_{10}H_3[Pr\text{-}(SiMo_7W_4O_{39})2]\cdot H_2O$	4-Aminobenzoic acid	2000	108
7 (NC)	Rh_2-Substituted $H_3[PW_{12}O_{40}]$	Meth, di/tri peptide containing meth	2000	109
8 (NC)	Keggin, Dawson and their derivatives	Envelope glycoprotein gp120 of HIV	2000	36
9 (NC)	$[Ce^{III}(\alpha_1\text{-}P_2W_{17}O_{61})(H_2O)_x]^{7-}$	D,L-Pro	2001	45
10 (NC)	$K_{10}[Cu_4(H_2O)_2(AsW_9O_{34})_2]$	β-Ala	2001	37
11 (NC)	$H_3PMo_{12}O_{40}$	Ala	2001	110
12 (C)	$[XnMo_6O_{21}]^{6-n}$ (X^{III} = As, Sb, Bi; X^{IV} = Se, Te)	L-Ala, L-Lys, Gly, 4-amino butyric acid	2002	13
13 (C)	V_6O_{24}	β-Ala	2002	38
14 (NC)	$H_3[PMo_{12}O_{40}]$	Hgly–Gly	2002	39
15 (NC)	$\{Mo_{57}V_6\}$	Mo-Storage model protein	2003	111
16 (C)	$[\alpha_2\text{-}P_2W_{17}O_{61}(SnR)]^{7-}$	R: amino acid	2003	112
17 (NC)	$H_3[PMo_{12}O_{40}]$	Gly	2003	40
18 (NC)	$[H_3PMo_{12}O_{40}]\cdot nH_2O$, $[H_4SiMo_{12}O_{40}]\cdot nH_2O$, $[H_4GeMo_{12}O_{40}]\cdot nH_2O$	Ornithine	2004	41
19 (NC)	Potassium dodecatungstato cobaltate(III)	BSA	2004	113
20 (NC)	Mo–O clusters, specially Mo_7O_{24}	Mo storage protein	2005	114
21 (C)	$[Cd_4(H_2O)_2(As_2W_{15}O_{56})_2]^{16-}$	4-Aminobenzoic acid	2005	115
22 (NC)	$[K_6SiNiW_{11}O_{39}]$, $[\alpha\text{-}K_8P_2NiW_{17}O_{61}(H_2O)]$, $[K_{10}P_2Zn_4(H_2O)_2W_{18}O_{68}]$	Basic fibroblast growth factor (bFGF)	2005	83
23 (NC)	$[SiW_{12}O_{40}]^{4-}$, $[BW_{12}O_{40}]$,[5] $[H_2W_{12}O_{40}]^{6-}$, $[Zn_4(H_2O)_2(PW_9O_{34})_2]^{10-}$, $[Zn_4(H_2O)_2(P_2W_{15}O_{56})_2]^{16-}$	Prp	2005	64
24 (NC)	$K_5[BW_{12}O_{40}]\cdot 15H_2O$	L-Pro, D-pro	2006	42
25 (NC)	$K_6[P_2W_{18}O_{62}]\cdot 14H_2O$, $K_4[SiMo_{12}O_{40}]\cdot 3H_2O$, $K_7[PTi_2W_{10}O_{40}]\cdot 6H_2O$	β-Lactam antibiotics	2006	116
26 (NC)	$Na_3[PW_{12}O_{40}]$	Prion protein	2006	117
27 (NC)	$[AlO_4\text{-}Al_{12}(OH)_{24}(H_2O)_{12}]^{7+}$ $[Al_{30}O_8(OH)_{56}(H_2O)_{24}]^{18+}$	BSA	2006	118
28 (NC)	$[As_2W_{18}(VO)_3O_{66}]^{11-}$	Cys	2006	52
29 (C)	$\{M(H_2O)_3(pro)Mo_4O_{13}\}_2$ (M = Co, Ni, Cu, Zn)	Pro	2006	43
30 (C)	$(H_3O)_3\{[Na_3(H_2O)_{13}][(Cu(Gly)_2)_2(H_2W_{12}O_{42})]\}$	Gly	2006	119
31 (NC)	$H_3[PMo_{12}O_{40}]$	Gly	2006	120
32 (NC)	$H_3[PW_{12}O_{40}]$	Albumin	2006	53
33 (NC)	$H_4[SiMo_{12}O_{40}]$	Gly	2006	121
34 (C)	$H_3[BW_{12}O_{40}]$	$Gly[Cu_6Na(Gly)_8]$	2007	122
35 (C)	$[PSn(Cl)W_{11}O_{39}]_4$	L-Phenylalanine and L-tyrosine	2007	123
36 (NC)	$[NaP_5W_{30}O_{110}]^{14-}$, $[H_2W_{12}O_{40}]^{6-}$	HSA	2007	69,124
37 (NC)	$[\alpha\text{-}PTi_2W_{10}O_{40}]^{7-}$	SARS-CoV 3CL (severe acute respiratory syndrome 3c like protease)	2007	125
38 (NC)	$H_4[SiW_{12}O_{40}]$	Gly	2007	126
39 (NC)	$K_6SiW_{11}Co(H_2O)O_{39}\cdot 10H_2O$	HSA	2007	127
40 (NC)	Mo cluster	Mo/W-Storage protein	2007	128
41 (NC)	Mo cluster	Mo/W-Storage protein	2008	129
42 (NC)	$[H_2V_{10}O_{28}]^{4-}$	Gelatine	2008	130
43 (NC)	$[P_2Mo_{18}O_{62}]^{6-}$	CK2	2008	91
44 (NC)	Europium decatungstate	BSA	2008	86
45 (NC)	Europium decatungstate	BSA	2008	86
46 (NC)	$R_2\text{-}[P_2W_{17}O_{61}]^{10-}$, $\alpha_2\text{-}[NiP_2W_{17}O_{61}]^{8-}$, $\alpha_2\text{-}[CuP_2W_{17}O_{61}]^{8-}$	HSA	2008	89
47 (NC)	$[P_2W_{18}O_{62}]^{6-}$	Cyt c (cytochrome c enzyme)	2008	131
48 (NC)	$[\alpha_1\text{-}Yb(H_2O)_4P_2W_{17}O_{61}]^{7-}$	Ser, *N*-phosphonomethyl-L-proline	2008	132
49 (NC)	$H_4[SiW_{12}O_{40}]$	Pro	2008	133
50 (C)	$[Al(OH)_6Mo_6O_{18}]\cdot 6H_2O$, $[Cr(OH)_6Mo_6O_{18}]\cdot 3H_2O$, $[Al(OH)_6Mo_6O_{18}]\cdot 9H_2O$	His	2009	48
51 (C)	$(TBA)_6[\alpha_1\text{-}P_2W_{17}O_{61}\{SnCH_2CH_2C(=O)\}]$	Tripeptide: (H_2N-Trp-Ala-Leu-CO_2Me)	2009	46
52 (NC)	$Ag_3PW_{12}O_{40}$	Prion protein (PrP)	2009	65
53 (NC)	$[V_{10}O_{28}]^{6-}$	Various proteins	2009	58
54 (NC)	$[Gd(\beta_2\text{-}SiW_{11}O_{39})_2]^{13-}$	HSA	2009	134
55 (C)	$[\gamma\text{-}XW_{10}O_{36}]^{8-}$ (X = Si, Ge)	Amino acid bonded P=O	2009	135
56 (NC)	Tungsten based POM	Glycoproteins	2009	136
57 (NC)	$[PW_{12}O_{40}]^{3-}$, $[SiW_{12}O_{40}]^{4-}$, $[BW_{12}O_{40}]^{5-}$, $[H_2W_{12}O_{40}]^{6-}$, $[As_4W_{40}O_{140}]^{28-}$, $[Zn_4(H_2O)_2(P_2W_{15}O_{56})_2]^{16-}$	Prion protein	2009	137
58 (NC)	$[V_{15}As_6O_{42}(H_2O)]^{6-}$	HSA (Trp residue)	2010	138

Table 1 *(Contd.)*

Entry	POM/MS-POM	aa/pep/pro	Year	Ref.
59 (NC)	$[EuW_{10}O_{36}]^{9-}$	HSA	2010	68
60 (NC)	$[\alpha\text{-}SiW_{12}O_{40}]^{4-}$	His	2010	139
61 (NC)	$H_3[PMo_{12}O_{40}]\cdot nH_2O$	Gly	2010	140
62 (NC)	$[EuW_{10}O_{36}]^{9-}$	Histone H1	2010	88
63 (NC)	$[TeMo_6O_{24}]^{6-}$, $[TeW_6O_{24}]^{6-}$	Gly	2010	141
64 (NC)	$H_3[PW_{12}O_{40}]$	H-Phe-Phe-NH_2 HCl	2010	142
65 (NC)	$K_6[P_2Mo_{18}O_{62}]$	CK2	2010	66
66 (NC)	$Na_8Co_3[Mo^{VI}_{126}Mo^{V}_{28}O_{462}H_{14}(H_2O)_{46}\ (HOC_6H_4CH_2CH(NH_3^+)COO^-)_{12}]\cdot$ *ca.* $200H_2O$	TrP	2010	143
67 (NC)	$H_3[PM_{12}O_{40}]$, $H_4[SiM_{12}O_{40}]$, M = Mo, W	Arg	2010	144
68 (NC)	$Na_9[Eu(W_{10}O_{36})]$, $Na_{22}Cs_3[CsCEu_6As_6W_{63}O_{218}(H_2O)_{14}(OH)_4]CsCl\cdot 76H_2O$, $Na_{21}Cs_4[CsCTb_6As_6W_{63}O_{218}(H_2O)_{14}(OH)_4]\cdot 76H_2O$	Serum albumin	2010	85
69 (NC)	Mo_8O_{26}	Gly	2011	145
70 (NC)	A series based Keggin and Dawson type tungstopolyanions	HIV-1-protease	2011	146
71 (NC)	$[NaP_5W_{30}O_{110}]^{14-}$, $[H_2W_{12}O_{40}]^{6-}$	Aβ1–40	2011	92
72 (NC)	$K_8[P_2CoW_{17}O_{61}]$, $\alpha\text{-}Na_9H[SiW_9O_{34}]$, $Na_5[IMo_6O_{24}]$	Aβ1–40	2011	93
73 (NC)	$H_3[PMo_{12}O_{40}]$, $H_3[PW_{12}O_{40}]$	Leu, Pro	2011	147
74 (NC)	$(n\text{Bu}_4)_3[PW_{11}O_{39}\{(SiC_6H_4NH_2)_2O\}]$ on gold surface		2012	148
75 (NC)	$[Nb_{10}O_{28}]^{6-}$, $[V_{10}O_{28}]^{6-}$	Ca^{2+}-ATPase, protein cysteine	2012	149
76 (NC)	Mo cluster	Mo-Storage protein	2012	150
77 (NC)	$K_{15}H[Zr(\alpha_2\text{-}P_2W_{17}O_{61})_2]$	Gly–Gly	2012	74
78 (NC)	$K_8[\alpha\text{-}SiW_{11}O_{39}]$	Cys	2012	54
79 (NC)	Decavanadate, vanadate, tungstate and niobate	Ca^{2+}-ATPase	2012	149
80 (NC)	$[PW_{12}O_{40}]^{3-}$	Ile	2012	151
81 (NC)	$K_5H_9[Na(H_2O)P_5W_{30}O_{110}]\cdot 45H_2O$, $K_6P_2W_{18}O_{62}$	Val, Gly, Pro	2012	47
82 (C)	$[P_2W_{18}O_{62}]^{6-}$	$\{Cu_2(2,2'\text{-bipy})_2(pz)(Gly)\}_2^{6+}$	2013	152
83 (NC)	$H_4SiW_{12}O_{40}$	Cys	2013	50
84 (NC)	$K_8P_2W_{16}V_2O_{62}\cdot 18H_2O$	Dopamine, ascorbic acid	2013	153
85 (NC)	$(Et_2NH_2)_8[\{\alpha\text{-}PW_{11}O_{39}Zr\text{-}(\mu\text{-}OH)(H_2O)\}_2]\cdot 7H_2O$	Gly–Gly, Gly–Ser	2013	78
86 (NC)	$K_{15}H[Zr(\alpha_2\text{-}P_2W_{17}O_{61})_2]\cdot 25H_2O$	Gly–Aa, Aa–Gly or Aa–Ser	2013	75
87 (NC)	Mo clusters: $[Mo_8O_{26}]^{4-}$	Mo storage protein	2012	150
88 (NC)	$(Me_4N)_2[W_5O_{18}Zr(H_2O)_3]$	(His–Ser)	2013	80
89 (NC)	$\gamma\text{-}[Mo_8O_{24}]^{4-}$	Lys, Pro	2013	154
90 (NC)	$H_3[PW_{12}O_{40}]$, $K_7[PW_{11}O_{39}]$, $K_4[EuPW_{11}O_{39}]$	HSA, BSA	2013	87
91 (NC)	$\{SiW_9Ni_4\}$ based POM	4-(Dimethylamino)butyrate	2013	155
92 (NC)	$[(W(OH)_2)_2(Mn(H_2O)_3)_2(Na_3(H_2O)_{14})(BiW_9O_{33})_2](Himi)_2\cdot 16H_2O$	Factor Kβ p65 protein in human gastric adenocarcinoma (SGC-7901)	2013	97
93 (NC)	$K_8[P_2CoW_{17}O_{61}]$	Aβ1–40	2013	156
94 (NC)	$K_{13}[Eu(SiW_{11}O_{39})_2]$, $Na_9[EuW_{10}O_{36}]$, $K_{12.5}Na_{1.5}[NaP_5W_{30}O_{110}]$, $K_9CoW_{12}O_{40}$, $Na_3(H_2O)_6[Al(OH)_6Mo_6O_{18}]$	Hemoglobin, BSA	2013	157
95 (NC)	$[Ce(\alpha\text{-}PW_{11}O_{39})_2]^{10-}$	HEWL	2013	81
96 (NC)	POM@P (POM = $K_8[P_2CoW_{17}O_{61}]$), (P = Aβ15–20)	Aβ1–40	2013	60
97 (NC)	$KCs_4[Gd(\alpha\text{-}SiW_{11}O_{39})]\cdot 25H_2O$, $K_{13}[Gd(\beta_2\text{-}SiW_{11}O_{39})_2]\cdot 27H_2O$	HSA	2013	158
98 (NC)	Tetrabutylammonium $[W_{10}O_{32}]^{4-}$	Valine and isoleucine derivatives	2014	159
99 (NC)	$\{Ni_6PW_9\}$-based tungstophosphates	Pro	2014	160
100 (C)	$[PW_{12}O_{40}]^{3-}$	$[KCu_4(Gly)_4(OH)_2(H_2O)_2Cl]$	2014	161
101 (NC)	$Na_6[TeW_6O_{24}]\cdot 22H_2O$	Tyrosinase	2014	162
102 (NC)	$[Ln(H_2O)_8]_2\text{-}[Fe_4(H_2O)_8(thr)_2][\beta\text{-}SbW_9O_{33}]_2\cdot 22H_2O$ [Ln = Pr^{III}, Nd^{III}, Sm^{III}, Eu^{III}, Gd^{III}, Dy^{III}, Lu^{III}]	Thr	2014	49
103 (NC)	Dawson POM	Amyloid-β peptide	2015	163
104 (NC)	$Fe^{III}AspPW_{12}$	Asp	2015	164
105 (NC)	$K_{15}H[Zr(\alpha_2\text{-}P_2W_{17}O_{61})_2]\cdot 25H_2O$	Tetraglycine	2015	165
106 (NC)	$\{(Mo)Mo_5\}\{Mo_1^{V}\}_5$	Aβ-peptide	2014	166
107 (NC)	$K_{15}H[Zr(\alpha_2\text{-}P_2W_{17}O_{61})_2]$	HSA	2014	167
108 (NC)	Molybdenum oxide based on $\{Mo_{132}\}$		2014	168
109 (C)	$[(CuO_6)Mo_6O_{18}(As_3O_3)_2]^{4-}$, $[TeMo_6O_{24}]^{6-}$	$[Cu(Arg)_2]_2$	2014	169
110 (C)	$[MnMo_6O_{18}(O(CH_2)_3C)_2]_3$	Integrate in peptide chain	2014	55
111 (NC)	$[Na(H_2O)P_5W_{30}O_{110}]^{14-}$, $K_6[P_2W_{18}O_{62}]$	Pro, Leu, Asp	2014	170
112 (NC)	$(n\text{Bu}_4N)_6[\{W_5O_{18}Zr(\mu\text{-}OH)\}_2]\cdot 2H_2O$, $(Et_2NH_2)_{10}[Zr(PW_{11}O_{39})_2]\cdot 7H_2O$, $(Et_2NH_2)_8[\{\alpha\text{-}PW_{11}O_{39}Zr(\mu\text{-}OH)(H_2O)\}_2]\cdot 7H_2O$, $K_{15}H\ [Zr(\alpha_2\text{-}P_2W_{17}O_{61})_2]\cdot 25H_2O$, $Na_{14}[Zr_4(P_2W_{16}O_{59})_2(\mu_3\text{-}O)_2(OH)_2\text{-}(H_2O)_4]\cdot 10H_2O$	HSA	2014	171
113 (NC)	$[K_{13}[Eu(SiW_{10}MoO_{39})_2]]$	Lys, Arg, His	2014	172

Table 1 *(Contd.)*

Entry	POM/MS-POM	aa/pep/pro	Year	Ref.
114 (NC)	Mo cluster	Mo-Storage protein	2014	173
115 (NC)	$H_3[PW_{12}O_{40}]$, $H_3[PMo_{12}O_{40}]$	Ile, Cys	2014	173
116 (NC)	$[Me_2NH_2]_{10}[Ce(PW_{11}O_{39})_2]$	HEWL	2014	174
117 (NC)	$K_8P_2NiW_{17}O_{61}$, $K_8P_2CoW_{17}O_{61}$	Aβ-40	2014	175
118 (NC)	$[Al_2O_8Al_{28}(OH)_{56}(H_2O)_{24}]^{18+}$	BSA	2014	176
119 (NC)	$K_{13}[Eu\text{-}(SiW_9Mo_2O_{39})_2]$	BSA	2015	177
120 (NC)	Based on $Mo_{72}Fe_{30}$	Heat-shock protein and histone protein	2015	67
121 (NC)	$(Et_2NH_2)_8[\{\alpha\text{-}PW_{11}O_{39}Zr\text{-}(\mu\text{-}OH)(H_2O)\}_2]\cdot 7H_2O$, $(Me_4N)_2[W_5O_{18}Zr(H_2O)_3]$, $Na_{14}[Zr_4(P_2W_{16}O_{59})_2(\mu_3\text{-}O)_2(OH)_2(H_2O)_4]\cdot 57H_2O$	Triglycine, tetraglycine, glycylglycylhistidine, and glycylserylphenylalanine	2015	178
122 (NC)	$H_3[PW_{12}O_{40}]$	Diphenylalanine	2015	179
123 (NC)	$K_4EuPW_{11}O_{39}$, $[Me_2NH_2]_{10}[Ce(PW_{11}O_{39})_2]$	HEWL, α-lactalbumin	2015	180
124 (NC)	$Na_6[TeW_6O_{24}]\cdot 22H_2O$	Hen egg-white lysozyme (HEWL)	2015	95
125 (NC)	$[Fe(C_4H_5NO_4)]_{3.5}H_{0.5}SiW_{12}O_{40}\cdot 14H_2O$	Asp	2015	181
126 (NC)	$(Me_4N)_2[W_5O_{18}Zr\text{-}(H_2O)_3]$, $(nBu_4N)_6[\{W_5O_{18}Zr(\mu\text{-}H)\}_2]\cdot 2H_2O$, $(Et_2NH_2)_{10}[Zr(PW_{11}O_{39})_2]\cdot 7H_2O$, $(Et_2NH_2)_8[\{\alpha\text{-}PW_{11}O_{39}Zr\text{-}(m\text{-}OH)(H_2O)\}_2]\cdot 7H_2O$, $(Et_2NH_2)7H_2[Zr_3(\mu\text{-}OH)_3(\alpha\text{-}PW_9O_{34})_2]\cdot 12H_2O$, $Na_{14}[Zr_4(P_2W_{16}O_{59})_2\text{-}(\mu_3\text{-}O)_2\ (OH)_2(H_2O)_4]\cdot 57H_2O$	Asp residue in myoglobin	2015	76
127 (NC)	$Na_9EuW_{10}O_{36}\cdot 32H_2O$@ PAA (PAA = polymerized acrylic acids)	Dmt-D-Arg-Phe-Lys-NH_2; (Dmt = dimethyltyrosine)	2015	182
128 (NC)	$[\{Cu^{II}(H_2O)_2\}\{Ca_4(H_2O)_4(HO_{0.5})_3(en)_2\}\{Ca\subset P_6Mo^{V}_4Mo^{VI}_{14}O_{73}\}]$, $(H_4bth)[\{Fe^{II}(H_2O)\}\{Ca\subset P_6Mo^{VI}_{18}O_{73}\}]$, $(H_2bih)_3[\{Cu^{II}(H_2O)_2\}\{Ca\subset P_6Mo^{V}_2Mo^{VI}_{16}O_{73}\}]$, $(H_2bib)_3\text{-}[\{Fe^{II}(H_2O)_2\}\{Ca\subset P_6Mo^{V}_2Mo^{VI}_{16}O_{73}\}]$	Amino acids	2015	183
129 (NC)	$Na_{14}[Zr_4(P_2W_{16}O_{59})_2(\mu_3\text{-}O)_2(OH)_2(H_2O)_4]\cdot 57H_2O$	Gly–Gly	2015	184
130 (NC)	$K_{15}H[Zr(\alpha_2\text{-}P_2W_{17}O_{61})_2]\cdot 25H_2O$	Insulin chain B	2015	185
131 (NC)	$Na_9[EuW_{10}O_{36}]\cdot 32H_2O$	Arg/Lys-rich peptide from HPV (human papillomavirus capsid protein)	201	142
132 (NC)	Keggin, Dawson, Preyssler	19 amino acids	2015	186
133 (NC)	$(TBA)_3[Fe\text{–}Mo_6O_{18}\{(OCH_2)_3CNHCOC_6H_5\}_2]\cdot 3.5ACN$, $(TBA)_3[FeMo_6O_{18}\{(OCH_2)_3CNHCOC_8H_7\}_2]\cdot 2.5ACN$, $(TBA)_3[Mn\text{–}Mo_6O_{18}\{(OCH_2)_3CNHCOC_6H_5\}_2]\cdot 3.5ACN$, $(TBA)_3[MnMo_6O_{18}\{(OCH_2)_3CNHCOC_8H_7\}_2]\cdot 2.5ACN$, (ACN = acetonitrile)	HSA, BSA	2015	187
134 (NC)	$K_{13}[Eu(SiW_{10}MoO_{39})_2]\cdot 28H_2O$	HPV16 L1 peptide	2015	188
135 (NC)	POM in protein crystallography	Lys-rich peptides of HPV-16 and HPV-18 capsid proteins	2015	23
136 (NC)	$[TBA]_3[GaMo_6O_{18}(OH)_3\{(OCH_2)_3CCH_2OH\}]$, $Na_3[FeMo_6O_{18}\{(OCH_2)_3CCH_2OH\}_2]$, $[TMA]_2[GaMo_6O_{18}(OH)_3\{(OCH_2)_3CNH_3\}]$, $Na[TMA]_2[FeMo_6O_{18}(OH)_3\{(OCH_2)_3CNH_3\}](OH)$	BSA	2015	71
137 (NC)	$H_{3-x}PW_{12}O_{40}$, (x = 1.0–3.0)	Gly	2015	51
138 (NC)	$Na_6[Mo_7O_{24}]$	Phosphodiester bond in DNA model: bis(p-nitrophenyl)phosphate	2008	101
139 (NC)	$K_6[P_2Mo_{18}O_{62}]$	Oncogene Sox2	2011	190
140 (NC)	$K_7[(Mn^{III}\cdot H_2O)(\alpha_2\text{-}P_2W_{17}O_{61})]\cdot 12H_2O$, $K_7[(Fe^{III}\cdot H_2O)(\alpha_2\text{-}P_2W_{17}O_{61})]\cdot 8H_2O$, $K_8[(Co^{II}\cdot H_2O)(\alpha_2\text{-}P_2W_{17}O_{61})]\cdot 16H_2O$, $K_8[(Ni^{II}\cdot H_2O)(\alpha_2\text{-}P_2W_{17}O_{61})]\cdot 17H_2O$, $K_8[(Cu^{II}\cdot H_2O)(\alpha_2\text{-}P_2W_{17}O_{61})]\cdot 16H_2O$, $K_{13}[Ln(H_2O)_{3,4}(\alpha_2\text{-}P_2W_{17}O_{61})]_2\cdot 26H_2O$, Ln = Y, La and Eu, $K_{15}H[Zr(\alpha_2\text{-}P_2W_{17}O_{61})_2]\cdot 25H_2O$	DNA models: 4-nitrophenyl phosphate, bis-4-nitrophenyl phosphate	2012	106
141 (NC)	$\{[Zn_3Na_2(\mu\text{-}OH)_2(bpdo)_6(H_2O)_{16}][PW_{12}O_{40}]_2\}\cdot(bpdo)_3\cdot C_2H_5OH\cdot 2H_2O$; bpdo = 4,4′-bis(pyridine-N-oxide)	Bis(p-nitrophenyl)phosphate (BNPP)	2013	103
142 (NC)	$\{[Cu(PPA)_2]_2[H_3PMo_{12}O_{40}]\}\cdot 8H_2O$, $\{[Zn(PPA)_2][H_3PMo_{12}O_{40}]\}\cdot[HPPA]\cdot 3H_2O$	CT-DNA	2013	191
143 (NC)	$K_7Na_3[Cu_4(H_2O)_2(PW_9O_{34})_2]\cdot 20H_2O$	Human osteosarcoma derived cell line, MG-63	2012	192
144 (NC)	$[Co^{II}(C_{19}FH_{22}N_3O_4)_3][C_{19}FH_{23}N_3O_4][HSiW_{12}O_{40}]\cdot 23H_2O$	CT-DNA	2014	193
145 (NC)	$(Et_2NH_2)_8[\{\alpha\text{-}PW_{11}O_{39}Zr(\mu\text{-}OH)(H_2O)\}_2]\cdot 7H_2O$	Bis(4-nitrophenyl) phosphate	2014	102
146 (NC)	$(Himi)_2[Bi_2W_{20}O_{66}(OH)_4Co_2(H_2O)_6Na_4(H_2O)_{14}]\cdot 17H_2O$ (imi = imidazole)	DNA of human colon carcinoma HT-29 cell	2014	99
147 (NC)	$[SiW_{11}O_{39}\{Sn(CH_2)_2CO\}]^{8-}$, $[P_2W_{17}O_{61}\{Sn(CH_2)_2CO\}]^{6-}$	5′-NH_2 terminated 21-merDNA	2015	194
148 (NC)	$Na_5[PMo_{10}V_2O_{40}]\cdot nH_2O$	CT-DNA	2015	195
149 (NC)	$(Et_2NH_2)_8[\{\alpha\text{-}PW_{11}O_{39}Zr(\mu\text{-}OH)\ (H_2O)\}_2]\cdot 7H_2O$	Bis(4-nitrophenyl)phosphate	2015	196
150 (NC)	$K_6[SiMo_{11}O_{39}Co(H_2O)]\cdot nH_2O$	CT-DNA	2016	100
151 (NC)	$Na_{14}[Zr_4(P_2W_{16}O_{59})_2(\mu_3\text{-}O)_2(OH)_2(H_2O)_4]\cdot 57H_2O$	4-Nitrophenyl phosphate	2016	104
152 (NC)	$[\{\alpha\text{-}PW_{11}O_{39}Zr(\mu\text{-}OH)(H_2O)\}_2]^{8-}$	pUC19DNA	2017	105
153 (NC)	$Na_{22}Cs_3[Cs(Eu/Tb)_6As_6W_{63}O_{218}(H_2O)_{14}(OH)_4]\cdot CsCl\cdot 76H_2O$	Serum albumin	2015	189

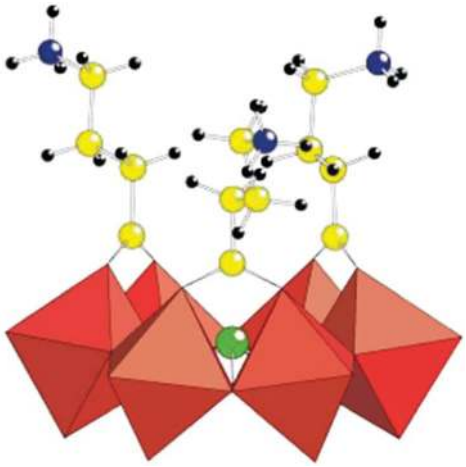


Fig. 1 Combined polyhedral/ball and stick representation of $[Se^{IV}Mo_6O_{21}\{O_2C(CH_2)_3NH_3\}_3]^{2-}$. Se green, C yellow, N blue and H black.[13] Reproduced with permission of the copyright holder.

hydrogen bonding of the ammonium cation to an adjacent oxygen atom of POM.[45]

As an example of non-covalent bonding, two inorganic–organic hybrid materials containing $K_5H_9[Na(H_2O)P_5W_{30}O_{110}]\cdot 45H_2O$ and $K_6[P_2W_{18}O_{62}]\cdot 10H_2O$ polyoxometalates with valine, glycine and proline, were reported in 2012 by our group.[47] The cationic amino acids were H-bonded to metal–oxide clusters establishing electrostatically enhanced H-bonding interactions with polyoxoanions and forming pseudo-organic–inorganic hybrid materials (see Fig. 2). The hydrogen bonds between $Hpro^+$ ions and crystallization water molecules led to a suitable hole, in which polyoxoanions are located. Those extensive non covalent interactions induce the formation of stable frameworks even in solution, thus presenting promising applications in solution phase.

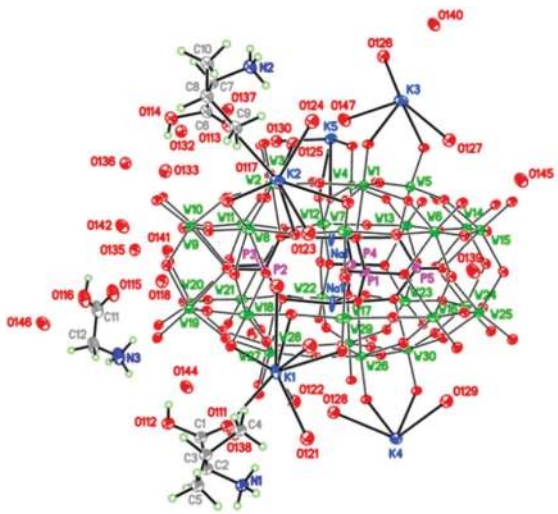


Fig. 2 ORTEP representation of $(Hval)_2(Hgly)(H_3O)_6K_5[Na(H_2O)P_5W_{30}O_{110}]\cdot 19.5H_2O$. C gray, N dark blue, O red, H light green, K blue, W green, P purple.[47] Reproduced with permission of the copyright holder.

In 2006 Wang and coworkers[42] induced chirality to a POM inorganic–organic hybrid, by using copper-D/L proline moieties. It was the first example of a homochiral 3D open-framework based on POMs and amino acids connected by means of covalent and noncovalent bonds. Copper complexes of D/L-proline and $[BW_{12}O_{40}]^{5-}$ formed a hybrid, in which proline molecules coordinate to two adjacent copper centers *via* carboxyl oxygen atoms and an N atom as a three dentate ligand. The Keggin clusters were also bounded to two Cu centers *via* terminal oxygen atoms as bidentate ligands (see Fig. 3 and 4).

Anderson type POMs have two extra terminal oxygen atoms with respect to Keggin type POMs, thus they have additional coordination sites. In this respect, the interaction of copper-His complex with Anderson type POM was investigated in 2009.[48] The Anderson POM is connected to the Na^+ center and also to the Cu-His complex *via* the histidine carboxyl oxygen atom. In the absence of the Na^+ center discrete structures are formed by means of hydrogen bonding interactions between Cu–His complexes and Anderson POMs (see Fig. 5).

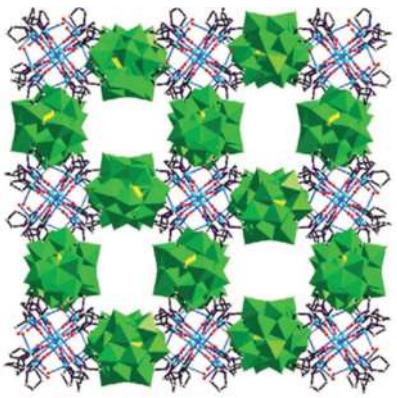


Fig. 3 The 3D open-framework structure of $D\text{-}KH_2[(D\text{-}C_5H_8NO_2)_4(H_2O)Cu_3][BW_{12}O_{40}]\cdot 5H_2O$, which is composed of copper-proline polymer chains covalently linked to Keggin polyoxoanions, viewed along the *c* axis.[42] Reproduced with permission of the copyright holder.

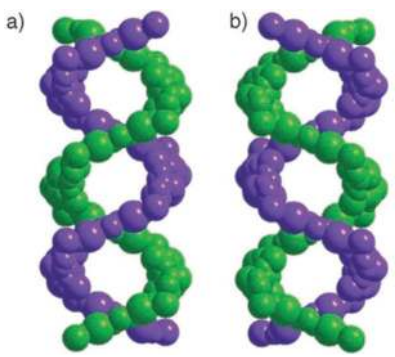


Fig. 4 Space-filling diagrams of (a) two intertwined right-handed $D\text{-}KH_2[(D\text{-}C_5H_8NO_2)4(H_2O)Cu_3][BW_{12}O_{40}]\cdot 5H_2O$, and (b) the two intertwined left-handed helices of $D\text{-}KH_2[(D\text{-}C_5H_8NO_2)_4(H_2O)Cu_3][BW_{12}O_{40}]\cdot 5H_2O$.[42] Reproduced with permission of the copyright holder.

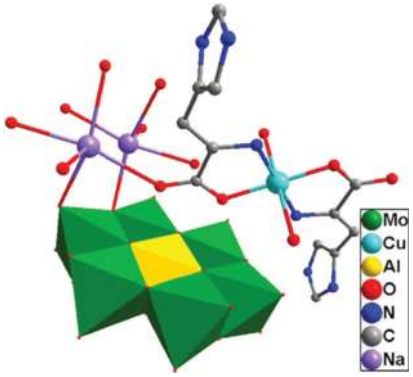


Fig. 5 Stick/polyhedral view of the asymmetric unit of the $[Cu(C_6H_8N_3O_2)(C_6H_9N_3O_2)(H_2O)_2][Na(H_2O)_2]_2[Al(OH)_6Mo_6O_{18}]\cdot 6H_2O$ complex.[48] The hydrogen atoms and crystal water molecules are omitted for clarity. Reproduced with permission of the copyright holder.

The utilization of lanthanide cations in these assemblies provides the opportunity to take advantage of their magnetic and luminescence properties. For instance, in 2014, a series of seven heterometallic inorganic–organic hybrids were reported.[49] These isomorph structures consist of iron transition metals, lanthanide metals {Ln = Pr^{III}, Nd^{III}, Sm^{III}, Eu^{III}, Gd^{III}, Dy^{III} and Lu^{III}} and threonine amino acid that organically functionalize the structures. Lanthanide ions provided luminescence and magnetic properties to these compounds (see Fig. 6).

POM catalysis related to amino acids is a very important application. In this respect, it has been reported that POMs can act as catalysts in redox reactions. For example, an inorganic–organic hybrid containing $H_4[SiW_{12}O_{40}]$ was used to prepare the chemically modified carbon paste electrode (CPE), that is able to simultaneously reduce iodate and oxidise cysteine.[50] In some cases amino-acids are incorporated in the POM-catalyst structures. For instance, the catalytic activity of a series of Gly-tungstophosphoric acids with different ratios of Gly showed catalytic activity for the esterification reaction of palmitic acid with methanol for the production of methyl palmitate.[51] In electrochemical approaches amino-acids are also utilized as electrode modifiers to improve catalytic activity.[52]

In addition to the above mentioned features of POMs, their nanometer range dimensions together with their surface charge open new windows to their applications. The use of phosphotungstic acid is a convenient method for solubilisation, purification and functionalization of carbon nanotubes (CNTs). Negatively charged polyanions prevent CNT aggregation through repulsion with graphite walls. On the other hand, POMs adsorbed to CNTs act as anchors, binding to albumin protein molecules through interactions between the HPW and the amine groups in aa side chains of albumin[53] (Fig. 7). Another remarkable feature of POMs in association with amino acid was reported in 2012. In this report, microtubes of tungstosilicate doped with L-cysteine amino acid were fabricated. The unique redox property of POMs was used in gas sensing since its colour changes from light purple to dark blue on exposure to ammonia gas.[54]

In 2014 [55] the term "inorganic amino acid" was used to describe the $[MnMo_6O_{18}(O(CH_2)_3C)_2]_3$ molecule. This POM can be conveniently integrated in a peptide chain (see Fig. 8), resulting in an "inorganic amino acid" with high charge

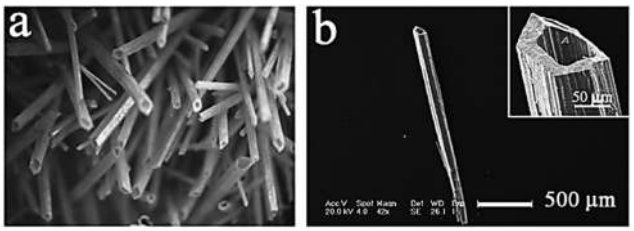


Fig. 7 Optical micrograph (a) and ESEM image (b) of the Lcys-SiW_{12} $(K_{3.3}(C_3H_7NO_2S)_{0.7}H_{0.7}SiW_{12}O_{40}\cdot 2H_2O)$ microtubes.[54] Reproduced with permission of the copyright holder.

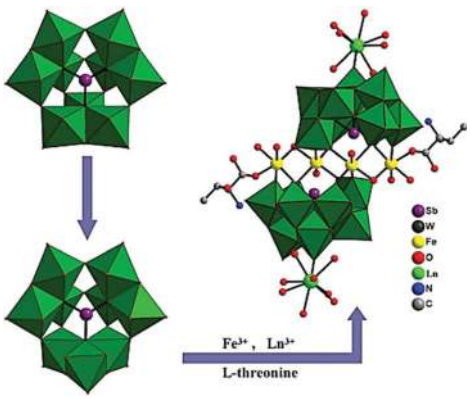


Fig. 6 Heterometallic inorganic–organic hybrids of Fe–Ln–POM functionalized with Thr $([Ln(H_2O)_8]_2[Fe_4(H_2O)_8(thr)_2][B\text{-}\beta\text{-}SbW_9O_{33}]_2\cdot 22H_2O$ [Ln = Pr^{III}, Nd^{III}, Sm^{III}, Eu^{III}, Gd^{III}, Dy^{III}, Lu^{III}, thr = threonine).[49] Reproduced with permission of the copyright holder.

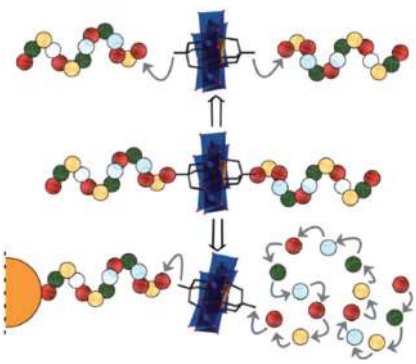


Fig. 8 Schematic representation of the two approaches that used[55] for the integration of POM clusters into peptide chains: solution-phase reaction with pre-synthesized peptides (top) and incorporation of the POM building block as an unnatural amino acid during stepwise peptide synthesis (bottom). Reproduced with permission of the copyright holder.

density, redox activity, and an additional coordination or catalytic site that can be incorporated in a protein. This may have promising new applications in protein biochemistry and medicinal chemistry.

Roles of POMs in association with peptides and proteins

Hill, Pope and co-workers have described POMs' potent biological activity and their promising utilization as inorganic bioactive materials, including antiviral and anti-HIV activity.[21,56,57] Moreover, the role of oxovanadates in biological systems as an insulin mimic has been reviewed in 2009.[58] Several oxometalates and POMs have been proposed as potential inhibitors of reverse transcriptase and other related enzymes.[59] It has been also shown that POMs show synergistic effects when forming hybrid materials with peptides in certain therapies.[60] These therapeutic effects of POMs are mainly due to interactions with proteins in the viral cell envelope, disease-causing proteins or inhibition of the enzymatic activity. In general, the mechanisms of action are not well known and they remain to be elucidated. Hence investigating these interactions (Fig. 10) on a molecular level is important for the characterization and the development of future compounds with the ability to act selectively. There are several reports[58,59,61–67] in which the interaction between POMs and proteins has been investigated at a molecular level and which reveal that diverse physicochemical factors are important in controlling the binding mechanism (Fig. 9).

The different types of POMs or their derivatives like MS-POMs, behave differently facing a peptide chain or protein molecules. Obviously their behaviour depends on multiple influencing parameters: (i) POM electrostatic charge, which is important for establishing electrostatic interactions; (ii) shape and size, which is crucial in host–guest interactions; (iii) type and composition, which affects, for instance, the number of terminal oxygen atoms that can participate in H-bonding interactions; (iv) redox potential, acid strength and metal ion

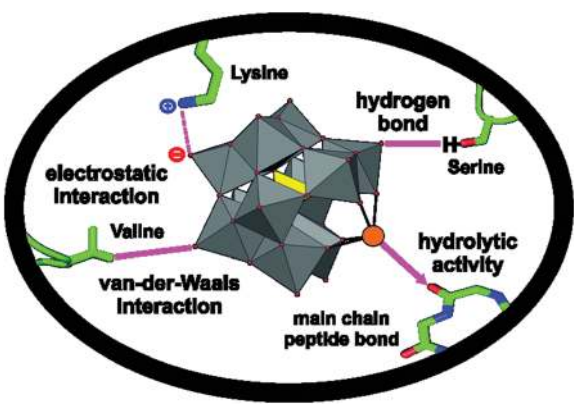


Fig. 9 Graphic showing the most frequent POM–protein interactions.[23] Reproduced with permission of the copyright holder.

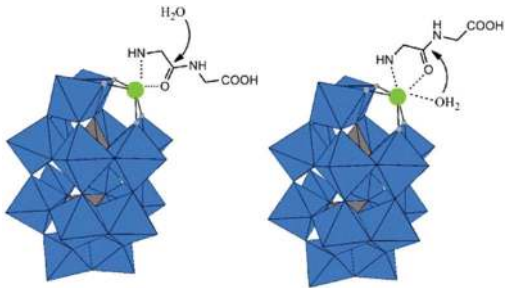


Fig. 10 Mechanism for the hydrolysis of GG in the presence of 1: nucleophilic attack of solvent water (left) and coordinated water (right); Zr green.[74] Reproduced with permission of the copyright holder.

embedded in the POM structure also influence their binding/coordination ability. On the other hand (biomolecule), amino acid side chain charge, volume and sequence in pep/pro chain and environmental parameters like temperature, pH and solution ionic strength are also important factors. The pioneering works studying interactions between peptides and POM, by Crans,[59,61] Petterson[62] and Yamase *et al.*[63] were carried out in the late 1980s and early 1990s. Years later, further attempts were made in order to analyse how POMs interact with peptides and proteins. Particularly relevant are those studies involving human serum albumin (HSA), bovine serum albumin (BSA), hen egg white lysozyme (HEWL)[58] and disease causing proteins, like prion proteins,[64,65] protein kinase CK2,[66] histone protein.[67]

In addition, nowadays the use of rare-earth metals which are environment sensitive luminescent species is of great interest. POM structures modified with these metal cations can be specifically used as optical labelling agents. The unique feature of POMs is their tunability (polarity, surface charge distribution, shape, *etc.*). Therefore, several properties can be adapted influencing their recognition and reactivity with target biological macromolecules.[21]

Furthermore, it has been generally accepted that the main factor of the biological activity of POMs arises from their capability to establish non-covalent interactions with biomolecules.[68,69] However, the coordination ability of diverse metal ions in MS-POM structures can modulate their behaviour in their interaction with pro/pep that is further described in the following sections. As an example of this diversity, certain POM-based compounds are able to react with peptides by cleaving peptide bonds as artificial proteases and others simply interact with pro/pep structures acting as diagnostic or therapeutic agents, without affecting the peptide bonds. Examples of both behaviours are further described below.

POMs as hydrolysing agents to cleave peptide bonds in peptides or proteins

Selective hydrolytic cleavage of the peptide bond in proteins is one of the most important procedures in analytical biochemistry and biotechnology applications. It is mostly used for protein structure analysis, protein engineering, and the design

of target-specific protein-cleaving drugs.[70] Natural proteases are expensive and only work in a limited range of temperature and pH. However, POM-based peptide bond cleaving agents are easy to handle, not expensive and usually work under mild conditions, so the pro/pep fragments remain usable. Therefore, their future as the new generation of artificial proteases is promising.

For being hydrolytically active POMs, the metal sites must be accessible, to effectively interact with the inert amide bond in pro/pep. In this way the combination of POMs with strong Lewis acid metals in their structure is necessary for exhibiting peptidase activity.[23,71] Investigation of several metal substituted Dawson type POMs with Mn^{III}, Fe^{III}, Co^{II}, Ni^{II}, Cu^{III}, Y^{III}, La^{III}, Eu^{III}, Yb^{III}, Zr^{IV} and Hf^{IV} hydrolytic activity toward Gly–Gly dipeptide revealed that only Zr^{IV} and Hf^{IV} substituted POMs, $K_{15}H[M(\alpha_2\text{-}P_2W_{17}O_{61})_2]\cdot 25H_2O$ (M: Zr^{IV} or Hf^{IV}), are active species. Kinetic and DFT studies revealed that in isopolyanion (oxovanadates[72] and oxomolybdates[73]) monomeric forms are the active ones. The problem is that near physiological pH values, these isopolyoxometalates are not in stable form, limiting their usage in wide application. This problem can be resolved using more stable heteropolyoxometalates. Zr^{IV} is an appropriate hydrolytically active metal cation due to its high Lewis acidity, redox inactive behaviour and oxophilicity. Moreover, it is a kinetically labile species, so it rapidly exchanges coordinated ligands and adopts various geometries and coordination numbers. Since Zr^{IV} itself has a tendency to form an insoluble gel, it is convenient to embed Zr^{IV} in a POM structure to take advantage of the beneficial properties of both POM and Zr^{IV}. It has been shown[74] that at least two potentially free coordination sites in the transition metal are needed for hydrolysis reaction (see Fig. 11).

Therefore, the absence of free coordination sites in POMs containing first row transition metals (Mn^{III}, Fe^{III}, Ni^{II}, Co^{II} and Cu^{III}) makes them inactive species. They have only six coordination sites and five of them are occupied by the pentadentate POM ligand and one by a water molecule. Other metal ions like Y^{III}, La^{III}, Eu^{III} and Yb^{III} can provide enough free coordination sites; however their low Lewis acidity and their marked tendency to create dimers in solution lead to very low activity. In some cases, the MS-POM shows activity apparently without the presence of free binding sites. For instance the Zr–POM compound (1 : 2) shown in Fig. 11 (top left) does not have any free coordination sites to bind to the peptide. However it is able to dissociate into two monomeric species $[Zr(H_2O)_3(P_2W_{17}O_{61})]$ and $[(P_2W_{17}O_{61})Zr(\mu\text{-}OH)(H_2O)_2]$ (see Fig. 11). The latter is able to form a new dimer $[(P_2W_{17}O_{61})Zr(\mu\text{-}OH)(H_2O)_2]_2$, in which two water molecules coordinate to Zr^{IV} ions. These water ligands can be easily replaced, thus explaining the catalytic activity of this new dimer.

Different aa side chains induced dramatic changes in the binding modes to Zr^{IV}-substituted Dawson type POM. A series of amino acids with different sizes and nature of side chain have been examined toward reacting with $K_{15}H[Zr(\alpha\text{-}P_2W_{17}O_{61})_2]\cdot 25\ H_2O$. ^{1}H-NMR measurements showed that a larger volume of the aa aliphatic side chain clearly decreases the Gly–aa peptide bond hydrolysis rate. For example the replacement of the H atom in Gly with the methyl group in Ala caused a six fold decrease in the hydrolysis rate, showing the profound effect of steric hindrance. The fast reaction rate of Ser and Thr containing peptides indicates the key role of the OH group in the side chain. The hydroxyl group assists in amide bond hydrolysis following the mechanism shown in Fig. 12.[75] The coordination mode is shown in Fig. 13.

Moreover, electrostatic interactions have a key role in the binding mechanism of POMs to pro/pep structures. The electrostatic attraction from positively charged aa side chains to POM anions enhances the hydrolysis rate. In contrast, the carboxylate side chain in Glu competes for coordination to the Zr^{IV} center and hinders the effective coordination of the peptide carbonyl group, strongly decreasing the reaction rate (see Fig. 14). These valuable findings are helpful to design a novel and selective class of artificial proteases.[74,75] Parac-Vogt and coworkers[76,77] have recently shown that Zr^{IV}-substituted Lindqvist, Keggin and Wells–Dawson type POMs selectively hydrolyse the horse-heart myoglobin (HHM). HHM has a high sequence of Asp and Glu content, including eight Asp

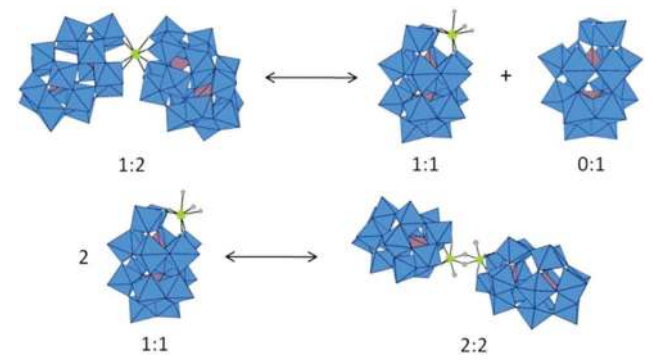


Fig. 11 Equilibrium between different forms of Zr–POM based compound: dimeric POM zirconium compounds and monomeric species; $[Zr(H_2O)_3(P_2W_{17}O_{61})]$ and $[(P_2W_{17}O_{61})Zr(\mu\text{-}OH)(H_2O)_2]$.[74] Reproduced with permission of the copyright holder.

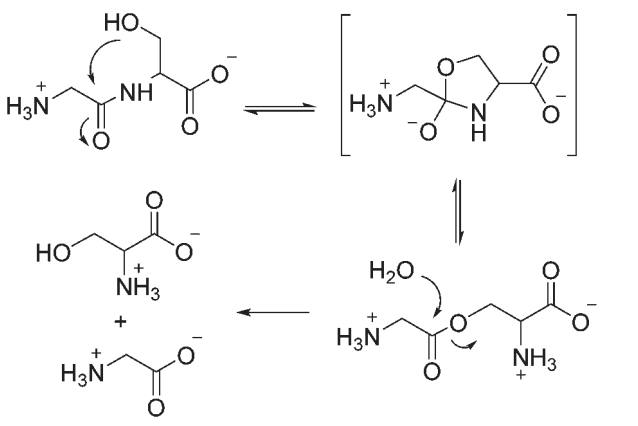


Fig. 12 N → O acyl rearrangement in Gly–Ser.

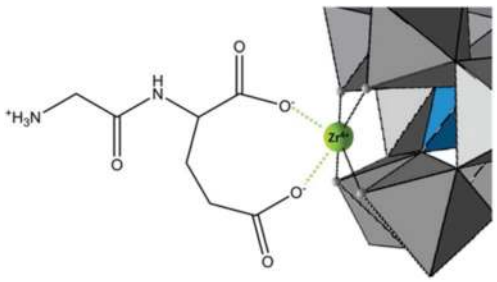


Fig. 13 Coordination of Gly–Glu to the Zr(IV)-substituted Wells–Dawson POM. The side chain and C-terminal carboxylic group mimic the structure of the inhibitor glutaric acid.[75] Reproduced with permission of the copyright holder.

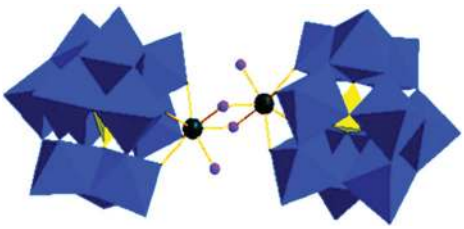


Fig. 14 Zr^{IV}-Keggin $(Et_2NH_2)_8[\{\alpha\text{-}PW_{11}O_{39}Zr\text{-}(\mu\text{-}OH)(H_2O)\}_2]\cdot 7H_2O$.[78] Reproduced with permission of the copyright holder.

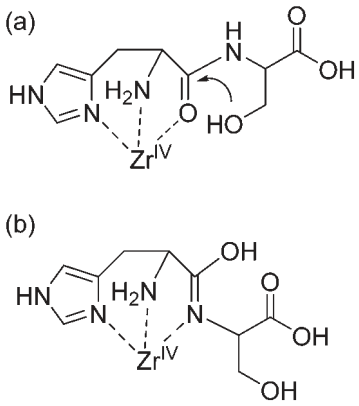


Fig. 15 Coordination of His–Ser to Zr^{IV} in $(Me_4N)_2[W_5O_{18}Zr(H_2O)_3]$. Hydrolytically active (a) and inactive (b) Zr^{IV}/His–Ser complex.[80]

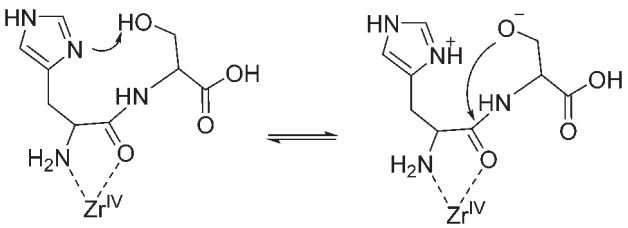


Fig. 16 Proposed mechanism for His–Ser hydrolysis in the presence of $(Me_4N)_2[W_5O_{18}Zr(H_2O)_3]$.[80]

and thirteen Glu residues. Among a set of Zr^{IV}-substituted POMs the Zr^{IV}-Keggin $(Et_2NH_2)_8[\{\alpha\text{-}PW_{11}O_{39}Zr\text{-}(\mu\text{-}OH)(H_2O)\}_2]\cdot 7H_2O$ (Fig. 14) displayed the highest reactivity.[78] The larger dimeric structures are not able to interact efficiently with Asp–X bonds. This POM shows a beneficial monomer/dimer equilibrium that explains its high activity. HHM hydrolysis specifically at Asp–X and less at Glu–X (X = any aa) peptide bonds proved the ability of selective hydrolysis of this POM. Both the attraction between negatively charged MS-POM and positive regions on HHM and the metal-coordination of the carboxylate group (Asp side chain) are responsible for cleaving the peptide bonds.[76] The coordination of the carboxylate group of the Glu side chain is less favourable relative to Asp, due to the formation of a less stable six membered chelate ring, thus decreasing the reaction rate.[77]

One of the most intriguing aspects of POMs applications is their inhibitory effect in the polymerization of amyloid β-peptides (Aβ) into amyloid fibrils, which is important in Alzheimer's disease research[79] as further described below.

In 2013, the first example of Lindqvist type POM, $(Me_4N)_2[W_5O_{18}Zr(H_2O)_3]$, capable of hydrolysing a series of peptides was reported. It is noteworthy that in these complexes Zr^{IV} possesses three available coordination sites, thus more than Zr-Dawson based compounds that have two available coordination sites. A series of dipeptides Ser–X residues were analysed and those dipeptides with aliphatic side chains were more reactive. Moreover, the His–Ser is the most active due to its unique interaction mode (see Fig. 15).

Intramolecular attack by the side-chain hydroxyl group on the amide carbonyl carbon atom produces a five-membered cyclic transition state, which rearranges to an acylated serine intermediate. Moreover, the imidazole N atom of His in His–Ser acts as an acceptor of the hydroxyl proton from the Ser residue, promoting the intramolecular attack of the Ser residue on the amide carbonyl carbon atom[80] (see Fig. 16).

The use of $[Ce(\alpha\text{-}PW_{11}O_{39})_2]^{10-}$ as an artificial nontoxic protease toward hen egg white lysozyme (HEWL) reported by Parac-Vogt and co-workers in 2013[81] is other example of protein hydrolysis promoted by MS-POMs. The $[Ce(\alpha\text{-}PW_{11}O_{39})_2]^{10-}$ POM presented selectivity for HEWL peptide bonds between Trp28–Val29, and Asn44–Arg45 at physiological pH and temperature. In contrast it was inert toward the hydrolysis of the HEWL homologous α-lactalbumin because the charge of this protein is the opposite, thus emphasizing the importance of the electrostatic attraction between the POM and protein.[81]

In general, it is difficult to establish an exact relationship between hydrolysis process and the POM nature, since many factors influence both the binding and reaction mechanisms such as size and charge of POMs and the amino acid side chain.

Non-cleaving role of POM (systems including pep/pro and POMs)

In 2004, the effective interaction of $K_5SiCoW_{11}O_{39}$[82] with human basic fibroblast growth factor (bFGF) was demon-

strated by fluorescence and CD spectroscopy. The binding of POM to bFGF causes conformational changes of bFGF. Remarkably, cell proliferation assays showed that in lower molar ratios, POM stimulates the mitogenic activity of bFGF and in higher molar ratios, POM inhibits the mitogenic activity of bFGF. One year later, related research analysed the binding ability of a series of POMs, the Keggin ($K_6SiNiW_{11}O_{39}$), the Wells–Dawson (α-$K_8P_2NiW_{17}O_{61}(H_2O)$), and Keggin-derived sandwich ($K_{10}P_2Zn_4(H_2O)_2W_{18}O_{68}$) to bFGF. It is a globular single-chain heparin-binding polypeptide that is synthesized by various cells and is one of the important pharmacologic therapy targets. The structure of POMs has a major effect in the recognition and binding ability to bFGF, thus preventing the interaction with endothelial cell surface receptors.[83] Another related investigation proposes the utilization of POMs as precipitating agents for prion proteins *via* multivalent electrostatic interactions. The aggregation mechanism strongly depends on the size and charge of POMs. That is, in a series of Keggin-POMs with similar size but different charge, the optimal concentration needed for aggregation is inversely proportional to POM charge density. In addition, examining a set of POMs with various sizes and structures and the same charge showed that very large POMs inhibit efficiently the sedimentation of PrPsc proteins. According to their results, a low concentration and charge density of POM anions induce the formation of larger aggregates (precipitation). In contrast, a high POM concentration and charge density lead to a saturation of the target sites on PrPsc, preventing protein chain aggregation and precipitation.[64]

Albumin proteins are widely studied proteins due to their known sequence and stability of structure in solution.[84] Therefore, they are ideal proteins to investigate interactions with POMs. In particular, human serum albumin (HSA) has been used to investigate interaction with POMs using tryptophan fluorescence quenching, taking advantage of the fact that it contains only one single tryptophan in position 214.[23,85]

In another study reported by Nadjo *et al.* in 2007 [69] the effect of POM size and charge in their interaction with pro/pep was also analysed. The interaction of $[H_2W_{12}O_{40}]^{6-}$ and $[NaP_5W_{30}O_{110}]^{14-}$, as examples of two completely different POMs, (in both charge and size) with HSA was studied by CD, fluorescence and isothermal titration calorimetry (ITC) experimental techniques. While $[H_2W_{12}O_{40}]^{6-}$ forms a 1 : 1 complex with a negligible effect on the protein structure, $[NaP_5W_{30}O_{110}]^{14-}$ binds to HSA in more than five different sites and destabilizes the HSA structure. It should be also mentioned that the pH value has a strong influence on the binding ability of POMs to proteins/peptides and their solubility.[69]

Another important and fascinating application of POMs in their association with proteins is the use of rare-earth metals thus acting as optical labelling agents. For instance, the luminescence of europium(III) is very sensitive to its environment (Fig. 17). In this respect, the interaction between POM and bovine serum albumin (BSA) has been proved by using time resolved luminescence and steady state measurements. The Eu^{III} luminescence increases in europium decatungstate

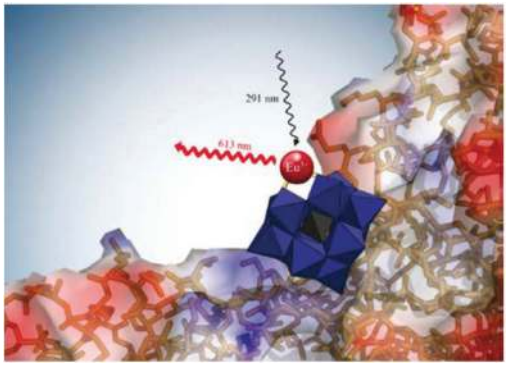


Fig. 17 Eu^{III} luminescence excitation scheme.[87] Reproduced with permission of the copyright holder.

POMs upon binding to BSA due to the ligand to metal charge transfer band.[86]

Following this interesting application, the interaction between Eu-decatungstate and HSA was also investigated in 2009 [88] and one year later the interaction between this POM and histone H1 protein was analysed.[68] In this latter example, the binding of POM to the protein structure caused some changes in its secondary structure, and a concomitant increase of the luminescence effect of the Eu-decatungstate up to 10 fold.[68] These studies underline the interesting application of Eu-decatungstate as a convenient luminescence bio-labelling agent.

Later in 2013 Parac-Vogt *et al.*[87] performed a more comprehensive study on Keggin, $H_3PW_{12}O_{40}$ and its derivatives $K_7PW_{11}O_{39}$ and $K_4EuPW_{11}O_{39}$, in association with HSA and BSA, using steady state and time resolved Eu^{III} luminescence in combination with Trp fluorescence spectroscopic measurements. Comparison between hydrolytically inactive POMs (Eu-substituted) and their active analogues (such as Zr^{IV}/Hf^{IV}-substituted Dawson or Ce^{IV}-substituted Keggins[77]) allowed obtaining valuable information regarding the interaction details and binding sites. The cavities with approximately 10 Å diameter that incorporate positively charged Arg and Lys amino acids are ideal for the interaction with the aforementioned anionic POMs.[87]

The binding ability of non-hydrolysing Dawson type POMs (P_2W_{17}, NiP_2W_{17} and CuP_2W_{17}) toward the HSA protein has been also investigated[88] and compared with Keggin and Preyssler POMs. This investigation reveals that other factors such as atomic composition, dimension and POM weight are also important in controlling the binding process. All these Dawson type POMs efficiently quench Trp fluorescence, having the following order: H_2W_{12} < P_2W_{17} < CuP_2W_{17} < NiP_2W_{17}. Therefore, MS-POMs have stronger ability to interact with HSA. Ni-Substituted Dawson is more effective than its Cu analogues. Isothermal titration calorimetry (ITC) experiments showed that the lacunary POM has two binding sites on HSA while NiP_2W_{17} has three and only one for CuP_2W_{17}. This is likely due to the difference in the coordination properties of Ni^{II} and Cu^{II} including Jahn–Teller effect.[89]

Protein kinase CK2 is a multifunctional kinase of medical importance that is regulated in many cancers. The inhibitory effect of POMs has been shown in the interaction with CK2 at nano-molar range concentration[90] in 2008 Hasenknopf and co-workers[91] studied the effects of structures (Preyssler, Dawson, Keggin) and composition/functionalization (lanthanides, organotin groups) and concluded that the structure has greater effect. That is, the inhibition effect of POMs, increases as their size and charge density also increase. That is, Keggin ions are inactive and larger Dawson types are moderately active. The highly charged and large Preyssler POM is the most active inhibitor of CK2. In addition, different activities were observed in several organotin substituted Dawson POMs.[91]

The interaction of Aβ1–40 peptide with two typical POMs; Preyssler $[NaP_5W_{30}O_{110}]^{14-}$ and Keggin $[H_2W_{12}O_{40}]^{6-}$ has also been studied to evaluate their ability to inhibit fibrillization of Aβ1–40 peptide, which is responsible for Alzheimer's disease (Fig. 18). The Aβ1–40 peptide has a high content of cationic residues (Arg5, His6, His13, His14 and Lys16) that provides favourable electrostatic interaction with negatively charged POMs. In addition, hydrogen bonding interactions are also involved in the binding mechanism encompassing both the amide backbone of the Aβ1–40 peptide and amino acid side chains. The large and highly charged P_5W_{30} occupies the positive patches on Aβ1–40 in a 1 : 1 complex (Fig. 19); however more stable complexes between smaller H_2W_{12} and Aβ1–40 are formed, acting as inorganic surfactant and preventing any aggregation of the peptide chains even after several months.[92]

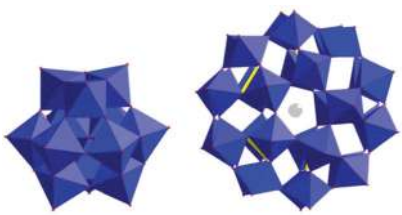


Fig. 18 Keggin structure $[H_2W_{12}O_{40}]^{6-}$ (H_2W_{12}) (left); the wheel-shaped structure $[NaP_5W_{30}O_{110}]^{14-}$ (P_5) (right).[92] Reproduced with permission of the copyright holder.

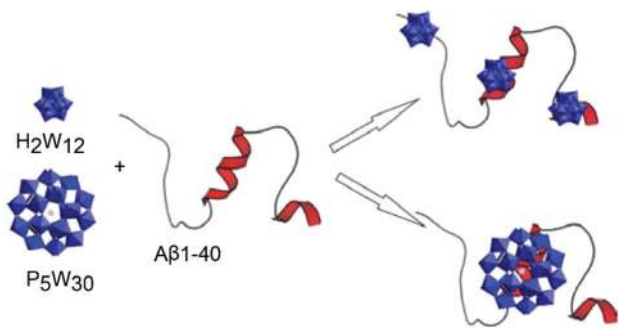


Fig. 19 The different binding patterns for the two POMs $[H_2W_{12}O_{40}]^{6-}$ (H_2W_{12}) and $[NaP_5W_{30}O_{110}]^{14-}$ (P_5W_{30}). The dimensions of the POMs and the peptide were taken into account in the scheme.[92] Reproduced with permission of the copyright holder.

The binding properties of POMs to Aβ peptides have been also reported by Wang's group. A number of Dawson, Keggin, and Anderson structures were studied and the results indicated that $K_8[P_2CoW_{17}O_{61}]$ has the best inhibitory effect. Also it is demonstrated that inhibition increases as POM size does. Binding to Aβ monomers or interactions between the large POM surface and Aβ oligomers seems to be the possible mechanism of inhibition. Several parameters influence the binding affinity to Aβ peptide chains, such as POM electrostatic charge, number of hydrogen bonding interactions and size. It is very important to gain knowledge on this topic to be able to improve the inhibition capability and, consequently, improve the therapeutic effect.[93] It has been demonstrated that the binding of $K_8[P_2CoW_{17}O_{61}]$ to the positively charged His13–Lys16 residue in Aβ inhibits its aggregation. Actually, $K_8[P_2CoW_{17}O_{61}]$ is the first example of POM that not only effectively inhibits Aβ aggregation but also degrades Aβ monomers and oligomers under photoirradiation conditions. Another strategy is to incorporate an Aβ fragment in the POM structure as bifunctional Aβ inhibitors in the form of spherical nanoparticles. In principle, this is a beneficial approach to take advantage of the selective binding process and to prevent oligomer-derived toxicity.[60]

It is clear that the interaction of pep/pro and POMs/MS-POMs is an interesting field of research and any little advance in the understanding of the binding mechanism with either discrete amino-acids, peptides or protein subunits may become crucial for the development of new POM or MS-POM species either as hydrolysing or non-hydrolysing agents. In addition, the possibility of fine tuning the properties of POMs is very important to be able to modify their reactivity/interaction with natural biomolecules, specially protein and peptides.

Protein crystallography

The accurate identification of protein structures on a molecular level is fundamental to gain knowledge into our understanding of protein functions and their interaction with other molecules. It also gives valuable information to understand enzymatic behaviour or simply to know the amino acid sequence. Moreover, it facilitates the design of new drugs and the identification of new targets. In this regard, X-ray crystallography is the most reliable approach since it enables visualization of the structure at the atomistic level. The challenge is obtaining suitable single crystals for X-ray crystallography. There are several compounds that are used as additives for protein crystallization. These compounds or crystallizing agents stabilize protein structures through creating intermolecular non-covalent interactions, thus promoting the formation of crystal lattices.

Zhang *et al.* have reported that the crystallization of bovine β lactoglobulin protein can be promoted by the addition of Y^{III} salts.[94] Since the anionic charge and shapes of POMs can be tuned, they are good candidates as additives for basic proteins,

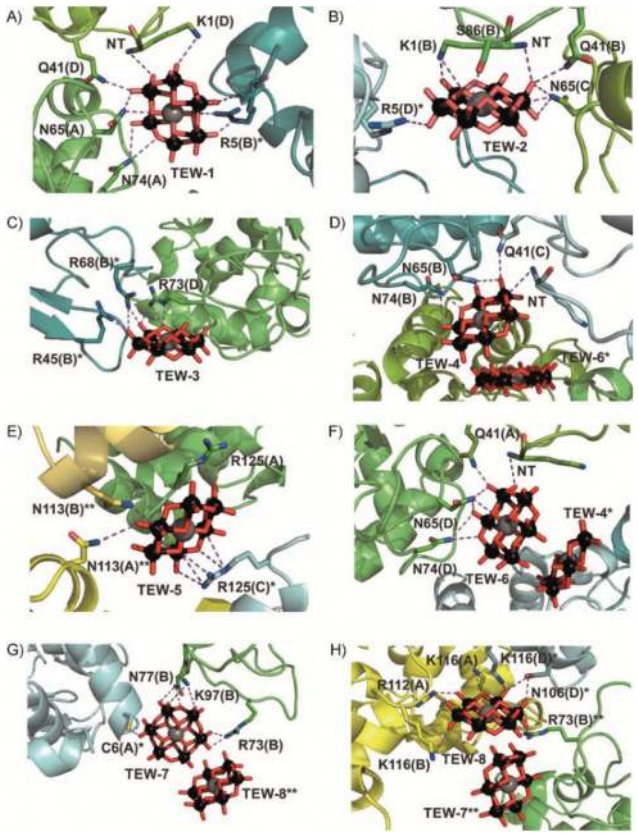


Fig. 20 $Na_6[TeW_6O_{24}]\cdot 22H_2O$ (TEW), binding sites. (A–H) Binding modes of all TEW molecules.[95] Reproduced with permission of the copyright holder.

similarly to Y^{III} for acidic ones. Actually, their application as crystallization agents has been recently reviewed[23] by Rompel and Bijelic. They described the different roles of POMs in protein crystallization. Apart from their ability to promote protein crystallization, POMs are able to stabilize enzyme conformations, rigidify flexible protein regions and enhance crystal stability and packing. A typical example[95] of the use of POMs as crystallization agents is the HEWL co-crystallization with $Na_6[TeW_6O_{24}]\cdot 22H_2O$ where the HEWL binds to POM *via* electrostatic and hydrogen bonds (see Fig. 20). Moreover, tyrosinase crystals were also obtained successfully using the same POM agent.[96]

Finally, Anderson–Evans POM is a very special structure compared with other kinds of POMs, because its roughly disc shape has been used to interact with narrow protein clefts or channels in order to reach protein parts inaccessible for other POMs and induce precipitation.[23]

POM assemblies with DNA

Although it is not the main topic of this review, we include a brief section where we highlight some important studies devoted to the interaction of POMs with DNA. For instance, it has been reported that some POMs exhibit prominent antiviral and antitumor activity since they are capable of efficiently inducing cancer cell apoptosis.[18,20,97] In addition, POMs are also able to inhibit both cell proliferation[97,98] and DNA damage.[99,100] However the exact mechanism of their interaction with DNA remains to be elucidated. It is worth mentioning that there are several studies where the use of POMs and functionalized POMs as therapeutic compounds is analysed (summarized in Table 1). Nevertheless, most of these works do not pay attention either to the interaction mechanism or the features of POMs that provide them the therapeutic effect. Therefore, it is not feasible to establish a relationship between the type of POM and its DNA binding ability. Finally, there are some promising studies that show the ability of POMs and POMs hybrids catalysing the cleavage of the phosphodiester bond in DNA model substrates.[101–106]

Concluding remarks

The importance of POMs as relevant inorganic biological active species has been proved by the research described in this review. Among many numerous challenges, POMs interaction with essential biomolecules has interesting applications. First POMs interaction with discrete amino acid units is useful for the fabrication of new functionalized materials. Moreover, their role as inhibitors and anti-aggregation agents is also important in their interaction with peptides and proteins. Another interesting aspect described herein is their role as catalysers (proteases) and also crystallizing agents. A bright future for these compounds in relevant biological systems can be anticipated. The most challenging issue is how to fine tune POMs and their derivatives for accomplishing the desired role. Focusing on POM, important factors are the shape, size, electrostatic charge, and nature of the metal cation in MS-POMs including number of coordination sites, size, monomer–dimer equilibrium and Lewis acidity strength. Obviously, the biological counterpart (aa/pep) can be also tuned to improve the properties of the final assembly.

Acknowledgements

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Notes and references

1 A. Müller, F. Peters, M. T. Pope and D. Gatteschi, *Chem. Rev.*, 1998, **98**, 239–272.
2 A. Blazevic and A. Rompel, *Coord. Chem. Rev.*, 2016, **307**, 42–64.
3 S. Sadjadi and M. Heravi, *Curr. Org. Chem.*, 2016, **20**, 1404–1444.

4 M. M. Heravi, G. Rajabzadeh, F. F. Bamoharram and N. Seifi, *J. Mol. Catal. A: Chem.*, 2006, **256**, 238–241.
5 M. M. Heravi, S. Sadjadi, N. M. Haj, H. A. Oskooie and F. F. Bamoharram, *Catal. Commun.*, 2009, **10**, 1643–1646.
6 M. M. Heravi and S. Sadjadi, *J. Iran. Chem. Soc.*, 2009, **6**, 1–54.
7 M. M. Heravi, M. Vazin Fard and Z. Faghihi, *Green Chem. Lett. Rev.*, 2013, **6**, 282–300.
8 M. M. Heravi, S. Sadjadi, H. A. Oskooie, R. H. Shoar and F. F. Bamoharram, *Catal. Commun.*, 2008, **9**, 504–507.
9 M. M. Heravi, S. Sadjadi, H. A. Oskooie, R. H. Shoar and F. F. Bamoharram, *Catal. Commun.*, 2008, **9**, 470–474.
10 S. Sadjadi, M. M. Heravi and M. Daraie, *J. Mol. Liq.*, 2017, **231**, 98–105.
11 S. Sadjadi, M. M. Heravi and M. Daraie, *Res. Chem. Intermed.*, 2017, **43**, 2201–2214.
12 F. Carn, N. Steunou, M. Djabourov, T. Coradin, F. Ribot and J. Livage, *Soft Matter*, 2008, **4**, 735.
13 U. Kortz, M. G. Savelieff, F. Y. A. Ghali, L. M. Khalil, S. A. Maalouf and D. I. Sinno, *Angew. Chem., Int. Ed.*, 2002, **41**, 4070–4073.
14 D.-L. Long, E. Burkholder and L. Cronin, *Chem. Soc. Rev.*, 2007, **36**, 105–121.
15 P. Gouzerh and A. Proust, *Chem. Rev.*, 1998, **98**, 77–112.
16 E. Coronado and C. J. Gómez-García, *Chem. Rev.*, 1998, **98**, 273–296.
17 (*a*) P. R. Marcoux, B. Hasenknopf, J. Vaissermann and P. Gouzerh, *Eur. J. Inorg. Chem.*, 2003, **13**, 2406–2412; (*b*) S. She, S. Bian, J. Hao, J. Zhang, J. Zhang and Y. Wei, *Chem. – Eur. J.*, 2014, **20**, 16987–16994; (*c*) S. She, S. Bian, R. Huo, K. Chen, Z. Huang, J. Zhang, J. Hao and Y. Weiet, *Sci. Rep.*, 2016, **6**, 33529.
18 T. Yamase, *J. Mater. Chem.*, 2005, **15**, 4773–4782.
19 H. K. Daima, P. R. Selvakannan, A. E. Kandjani, R. Shukla, S. K. Bhargava and V. Bansal, *Nanoscale*, 2014, **6**, 758–765.
20 D. Menon, R. T. Thomas, S. Narayanan, S. Maya, R. Jayakumar, F. Hussain, V.-K. Lakshmanan and S. V. Nair, *Carbohydr. Polym.*, 2011, **84**, 887–893.
21 J. T. Rhule, C. L. Hill, D. A. Judd and R. F. Schinazi, *Chem. Rev.*, 1998, **98**, 327–358.
22 A. Dolbecq, E. Dumas, C. R. Mayer and P. Mialane, *Chem. Rev.*, 2010, **110**, 6009–6048.
23 A. Bijelic and A. Rompel, *Coord. Chem. Rev.*, 2015, **299**, 22–38.
24 M. Mirzaei, H. Eshtiagh-Hosseini, M. Alipour and A. Frontera, *Coord. Chem. Rev.*, 2014, **275**, 1–18.
25 S. Taleghani, M. Mirzaei, H. Eshtiagh-Hosseini and A. Frontera, *Coord. Chem. Rev.*, 2016, **309**, 84–106.
26 N. V. Izarova, M. T. Pope and U. Kortz, *Angew. Chem., Int. Ed.*, 2012, **51**, 9492–9510.
27 D. E. Katsoulis, *Chem. Rev.*, 1998, **98**, 359–388.
28 P. Gao, Y. Wu and L. Wu, *Soft Matter*, 2016, **12**, 8464–8479.
29 L. Chen, F. Zhang, X. Ma, J. Luo and J. Zhao, *Dalton Trans.*, 2015, **44**, 12598–12612.
30 F. Xin and M. T. Pope, *J. Am. Chem. Soc.*, 1996, **118**, 7731–7736.
31 M. E. Tess and J. A. Cox, *Electroanalysis*, 1998, **10**, 1237–1240.
32 M. Inoue and T. Yamase, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 3055–3063.
33 M. Cindric, N. Strukan, M. Devcic and B. Kamenar, *Inorg. Chem. Commun.*, 1999, **2**, 558–560.
34 A. Müller, S. K. Das, C. Kuhlmann, H. Bögge, M. Schmidtmann, E. Diemann, E. Krickemeyer, J. Hormes, H. Modrow and M. Schindler, *Chem. Commun.*, 2001, 655–656.
35 J. Liu, J. Peng, E. Wang, L. Bi and S. Guo, *J. Mol. Struct.*, 2000, **525**, 71–77.
36 M. Witvrouw, H. Weigold, C. Pannecouque, D. Schols, E. De Clercq and G. Holan, *J. Med. Chem.*, 2000, **43**, 778–783.
37 E.-B. Wang, Y. Xing, Y.-H. Wang and C.-W. Hu, *Chem. J. Chin. Univ.*, 2001, **22**, 362–366.
38 C. H. Ng, C. W. Lim, S. G. Teoh, H.-K. Fun, A. Usman and S. W. Ng, *Inorg. Chem.*, 2002, **41**, 2–3.
39 Z. Han, E. Wang, G. Luan, Y. Li, H. Zhang, Y. Duan, C. Hu and N. Hu, *J. Mater. Chem.*, 2002, **12**, 1169–1173.
40 Z.-B. Han, Y.-P. Chang, H.-Y. An and E.-B. Wang, *Chem. Res. Chin. Univ.*, 2003, **19**, 15–19.
41 J. Li, Y. Qi, J. Li, H. Wang, X. Wu, L. Duan and E. Wang, *J. Coord. Chem.*, 2004, **57**, 1309–1319.
42 H.-Y. An, E.-B. Wang, D.-R. Xiao, Y.-G. Li, Z.-M. Su and L. Xu, *Angew. Chem., Int. Ed.*, 2006, **45**, 904–908.
43 X. Wu and C. Lu, *Bull. Korean Chem. Soc.*, 2006, **27**, 1206–1210.
44 Y. Wang, H. Li, C. Wu, Y. Yang, L. Shi and L. Wu, *Angew. Chem., Int. Ed.*, 2013, **52**, 4577–4581.
45 M. Sadakane, M. H. Dickman and M. T. Pope, *Inorg. Chem.*, 2001, **40**, 2715–2719.
46 K. Micoine, B. Hasenknopf, S. Thorimbert, E. Lacôte and M. Malacria, *Angew. Chem., Int. Ed.*, 2009, **48**, 3466–3468.
47 H. Eshtiagh-Hosseini and M. Mirzaei, *J. Cluster Sci.*, 2012, **23**, 345–355.
48 P.-P. Zhang, J. Peng, A.-X. Tian, J.-Q. Sha, H.-J. Pang, Y. Chen, M. Zhu and Y.-H. Wang, *J. Mol. Struct.*, 2009, **931**, 50–54.
49 J.-W. Zhao, J. Cao, Y.-Z. Li, J. Zhang and L.-J. Chen, *Cryst. Growth Des.*, 2014, **14**, 6217–6229.
50 S. Kakhki and E. Shams, *J. Electroanal. Chem.*, 2013, **704**, 249–254.
51 X.-X. Han, K.-K. Chen, W. Yan, C.-T. Hung, L.-L. Liu, P.-H. Wu, K.-C. Lin and S.-B. Liu, *Fuel*, 2016, **165**, 115–122.
52 B. Keita, R. Contant, P. Mialane, F. Secheresse, P. Deoliveira and L. Nadjo, *Electrochem. Commun.*, 2006, **8**, 767–772.
53 B. Fei, H. Lu, Z. Hu and J. H. Xin, *Nanotechnology*, 2006, **17**, 1589–1593.
54 Y. Shen, J. Peng, H. Zhang, C. Meng and F. Zhang, *J. Solid State Chem.*, 2012, **185**, 225–228.

55 C. Yvon, A. J. Surman, M. Hutin, J. Alex, B. O. Smith, D.-L. Long and L. Cronin, *Angew. Chem., Int. Ed.*, 2014, **53**, 3336–3341.
56 S. G. Sarafianos, U. Kortz, M. T. Pope and M. J. Modak, *Biochem. J.*, 1996, **319**, 619–626.
57 D. A. Judd, J. H. Nettles, N. Nevins, J. P. Snyder, D. C. Liotta, J. Tang, J. Ermolieff, R. F. Schinazi and C. L. Hill, *J. Am. Chem. Soc.*, 2001, **123**, 886–897.
58 M. Aureliano and D. C. Crans, *J. Inorg. Biochem.*, 2009, **103**, 536–546.
59 D. C. Crans, *Comments Inorg. Chem.*, 1994, **16**, 35–76.
60 M. Li, C. Xu, L. Wu, J. Ren, E. Wang and X. Qu, *Small*, 2013, **9**, 3455–3461.
61 D. C. Crans, M. Mahroof-Tahir, O. P. Anderson and M. M. Miller, *Inorg. Chem.*, 1994, **33**, 5586–5590.
62 M. Fritzsche, K. Elvingson, D. Rehder and L. Petterson, *Acta Chem. Scand.*, 1997, **51**, 483–491.
63 T. Yamase, M. Inoue, H. Naruke and K. Fukaya, *Chem. Lett.*, 1999, **28**, 563–564.
64 I. S. Lee, J. R. Long, S. B. Prusiner and J. G. Safar, *J. Am. Chem. Soc.*, 2005, **127**, 13802–13803.
65 W. Liang, C. Huang and L. Ma, *Sci. China, Ser. B: Chem.*, 2009, **52**, 2156–2160.
66 R. Prudent, C. F. Sautel and C. Cochet, *Biochim. Biophys. Acta, Proteins Proteomics*, 2010, **1804**, 493–498.
67 I. G. Danilova, I. F. Gette, S. Y. Medvedeva, E. A. Mukhlynina, M. O. Tonkushina and A. A. Ostroushko, *Nanotechnol. Russ.*, 2015, **10**, 820–826.
68 L. Zheng, Y. Ma, G. Zhang, J. Yao, B. Keita and L. Nadjo, *Phys. Chem. Chem. Phys.*, 2010, **12**, 1299–1304.
69 G. Zhang, B. Keita, C. T. Craescu, S. Miron, P. De Oliveira and L. Nadjo, *J. Phys. Chem. B*, 2007, **111**, 11253–11259.
70 M. K. K. B. Grant, *Curr. Org. Chem.*, 2006, 1035–1049.
71 A. Blazevic, E. Al-Sayed, A. Roller, G. Giester and A. Rompel, *Chem. – Eur. J.*, 2015, **21**, 4762–4771.
72 P. H. Ho, T. Mihaylov, K. Pierloot and T. N. Parac-Vogt, *Inorg. Chem.*, 2012, **51**, 8848–8859.
73 P. H. Ho, K. Stroobants and T. N. Parac-Vogt, *Inorg. Chem.*, 2011, **50**, 12025–12033.
74 G. Absillis and T. N. Parac-Vogt, *Inorg. Chem.*, 2012, **51**, 9902–9910.
75 S. Vanhaecht, G. Absillis and T. N. Parac-Vogt, *Dalton Trans.*, 2013, **42**, 15437.
76 H. G. T. Ly, G. Absillis, R. Janssens, P. Proost and T. N. Parac-Vogt, *Angew. Chem., Int. Ed.*, 2015, **54**, 7391–7394.
77 L. Min, *Organic Chemistry of Drug Degradation*, RSC Publishing, Cambridge, UK, 2012.
78 H. G. T. Ly, G. Absillis and T. N. Parac-Vogt, *Dalton Trans.*, 2013, **42**, 10929–10938.
79 G. Yamin, K. Ono, M. Inayathullah and D. Teplow, *Curr. Pharm. Des.*, 2008, **14**, 3231–3246.
80 H. G. T. Ly, G. Absillis, S. R. Bajpe, J. A. Martens and T. N. Parac-Vogt, *Eur. J. Inorg. Chem.*, 2013, **2013**, 4601–4611.
81 K. Stroobants, E. Moelants, H. G. T. Ly, P. Proost, K. Bartik and T. N. Parac-Vogt, *Chem. – Eur. J.*, 2013, **19**, 2848–2858.
82 S. B. S. Takano, S. Gately, M. E. Neville, W. F. Herblin, J. L. Gross, H. Engelhard, M. Perricone and K. Eidsvoog, *Cancer Res.*, 1994, **54**, 2654–2660.
83 Q. Wu, J. Wang, L. Zhang, A. Hong and J. Ren, *Angew. Chem., Int. Ed.*, 2005, **44**, 4048–4052.
84 A. Farrugia, *Transfus. Med. Rev.*, 2010, **24**, 53–63.
85 G. Hungerford, F. Hussain, G. R. Patzke and M. Green, *Phys. Chem. Chem. Phys.*, 2010, **12**, 7266.
86 G. Hungerford, K. Suhling and M. Green, *Photochem. Photobiol. Sci.*, 2008, **7**, 734–737.
87 V. Goovaerts, K. Stroobants, G. Absillis and T. N. Parac-Vogt, *Phys. Chem. Chem. Phys.*, 2013, **15**, 18378.
88 L. Zheng, Z. Gu, Y. Ma, G. Zhang, J. Yao, B. Keita and L. Nadjo, *J. Biol. Inorg. Chem.*, 2010, **15**, 1079–1085.
89 G. Zhang, B. Keita, C. T. Craescu, S. Miron, P. de Oliveira and L. Nadjo, *Biomacromolecules*, 2008, **9**, 812–817.
90 M. T. Pope, *Introduction to Polyoxometalate Chemistry*, Springer, Netherlands, Dordrecht, 2003.
91 R. Prudent, V. Moucadel, B. Laudet, C. Barette, L. Lafanechère, B. Hasenknopf, J. Li, S. Bareyt, E. Lacôte, S. Thorimbert, M. Malacria, P. Gouzerh and C. Cochet, *Chem. Biol.*, 2008, **15**, 683–692.
92 Y. Zhou, L. Zheng, F. Han, G. Zhang, Y. Ma, J. Yao, B. Keita, P. de Oliveira and L. Nadjo, *Colloids Surf., A*, 2011, **375**, 97–101.
93 J. Geng, M. Li, J. Ren, E. Wang and X. Qu, *Angew. Chem., Int. Ed.*, 2011, **50**, 4184–4188.
94 F. Zhang, G. Zocher, A. Sauter, T. Stehle and F. Schreiber, *J. Appl. Crystallogr.*, 2011, **44**, 755–762.
95 A. Bijelic, C. Molitor, S. G. Mauracher, R. Al-Oweini, U. Kortz and A. Rompel, *ChemBioChem*, 2015, **16**, 233–241.
96 S. G. Mauracher, C. Molitor, R. Al-Oweini, U. Kortz and A. Rompel, *Acta Crystallogr., Sect. D: Biol. Crystallogr.*, 2014, **70**, 2301–2315.
97 L. Wang, B.-B. Zhou, K. Yu, Z.-H. Su, S. Gao, L.-L. Chu, J.-R. Liu and G.-Y. Yang, *Inorg. Chem.*, 2013, **52**, 5119–5127.
98 Y. Take, Y. Tokutake, Y. Inouye, T. Yoshida, A. Yamamoto, T. Yamase and S. Nakamura, *Antiviral Res.*, 1991, **15**, 113–124.
99 L. Wang, K. Yu, B.-B. Zhou, Z.-H. Su, S. Gao, L.-L. Chu and J.-R. Liu, *Dalton Trans.*, 2014, **43**, 6070.
100 S. Dianat, A. K. Bordbar, S. Tangestaninejad, S. H. Zarkesh-Esfahani, P. Habibi and A. Abbasi Kajani, *J. Iran. Chem. Soc.*, 2016, **13**, 1895–1904.
101 E. Cartuyvels, G. Absillis and T. N. Parac-Vogt, *Chem. Commun.*, 2008, 85–87.
102 T. K. N. Luong, G. Absillis, P. Shestakova and T. N. Parac-Vogt, *Eur. J. Inorg. Chem.*, 2014, **2014**, 5276–5284.
103 J. Li, Y. Huang and Q. Han, *J. Coord. Chem.*, 2013, **66**, 2405–2412.
104 T. K. N. Luong, P. Shestakova and T. N. Parac-Vogt, *Dalton Trans.*, 2016, **45**, 12174–12180.

105 T. K. N. Luong, I. Govaerts, J. Robben, P. Shestakova and T. N. Parac-Vogt, *Chem. Commun.*, 2017, **53**, 617–620.
106 S. Vanhaecht, G. Absillis and T. N. Parac-Vogt, *Dalton Trans.*, 2012, **41**, 10028.
107 T. Douglas and M. Young, *Nature*, 1998, **393**, 152–155.
108 J. Liu, L. Cheng, B. Liu and S. Dong, *Langmuir*, 2000, **16**, 7471–7476.
109 J. Cox, *Talanta*, 2000, **52**, 1081–1086.
110 Z.-B. Han, E.-B. Wang, G.-Y. Luan, C.-W. Hu, Y.-P. Chang, J. Li, N.-H. Hu and H.-Q. Jia, *Chem. Res. Chin. Univ.*, 2001, **17**, 356–361.
111 A. Nicoara, A. Patrut, D. Margineanu and A. Müller, *Electrochem. Commun.*, 2003, **5**, 511–518.
112 S. Bareyt, S. Piligkos, B. Hasenknopf, P. Gouzerh, E. Lacôte, S. Thorimbert and M. Malacria, *Angew. Chem., Int. Ed.*, 2003, **42**, 3404–3406.
113 A.-K. Bordbar, N. Sohrabi and S. Tangestaninejad, *Phys. Chem. Liq.*, 2004, **42**, 127–133.
114 D. Fenske, M. Gnida, K. Schneider, W. Meyer-Klaucke, J. Schemberg, V. Henschel, A.-K. Meyer, A. Knöchel and A. Müller, *ChemBioChem*, 2005, **6**, 405–413.
115 L. Bi, Y. Shen, J. Jiang, E. Wang and S. Dong, *Anal. Chim. Acta*, 2005, **534**, 343–351.
116 M. Inoue, T. Suzuki, Y. Fujita, M. Oda, N. Matsumoto and T. Yamase, *J. Inorg. Biochem.*, 2006, **100**, 1225–1233.
117 J. G. Safar, H. Wille, M. D. Geschwind, C. Deering, D. Latawiec, A. Serban, D. J. King, G. Legname, K. H. Weisgraber, R. W. Mahley, B. L. Miller, S. J. DeArmond and S. B. Prusiner, *Proc. Natl. Acad. Sci. U. S. A.*, 2006, **103**, 11312–11317.
118 O. Deschaume, K. L. Shafran and C. C. Perry, *Langmuir*, 2006, **22**, 10078–10088.
119 X.-Y. Wu, Q.-Z. Zhang, X. He, S.-M. Chen, W.-B. Yang and C.-Z. Lu, *Chin. J. Inorg. Chem.*, 2006, **8**, 1511–1516.
120 Y. Kong, L. Pan, J. Peng, B. Xue, J. Lu and B. Dong, *Mater. Lett.*, 2007, **61**, 2393–2397.
121 S.-Y. Gao, R. Cao, X. Li and Z.-Z. Lin, *Chin. J. Struct. Chem.*, 2006, **25**, 305–311.
122 H. An, E. Wang, Y. Li, Z. Zhang and L. Xu, *Inorg. Chem. Commun.*, 2007, **10**, 299–302.
123 I. Bar-Nahum, J. Ettedgui, L. Konstantinovski, V. Kogan and R. Neumann, *Inorg. Chem.*, 2007, **46**, 5798–5804.
124 G. Zhang, B. Keita, J.-C. Brochon, P. de Oliveira, L. Nadjo, C. T. Craescu and S. Miron, *J. Phys. Chem. B*, 2007, **111**, 1809–1814.
125 D. Hu, C. Shao, W. Guan, Z. Su and J. Sun, *J. Inorg. Biochem.*, 2007, **101**, 89–94.
126 J. Liu, Y. Li, E. Wang, D. Xiao, L. Fan, Z. Zhang and Y. Wang, *J. Mol. Struct.*, 2007, **837**, 237–244.
127 D. Ajloo, H. Behnam, A. A. Saboury, F. Mohamadi-Zonoz, B. Ranjbar, A. A. Moosavi-Movahedi, Z. Hasani, K. Alizadeh, M. Gharanfoli and M. Amani, *Bull. Korean Chem. Soc.*, 2007, **28**, 730–736.
128 J. Schemberg, K. Schneider, U. Demmer, E. Warkentin, A. Müller and U. Ermler, *Angew. Chem., Int. Ed.*, 2007, **46**, 2408–2413.
129 J. Schemberg, K. Schneider, D. Fenske and A. Müller, *ChemBioChem*, 2008, **9**, 595–602.
130 F. Carn, M. Djabourov, T. Coradin, J. Livage and N. Steunou, *J. Phys. Chem. B*, 2008, **112**, 12596–12605.
131 K. Jiang, H. Zhang, C. Shannon and W. Zhan, *Langmuir*, 2008, **24**, 3584–3589.
132 C. Boglio, B. Hasenknopf, G. Lenoble, P. Rémy, P. Gouzerh, S. Thorimbert, E. Lacôte, M. Malacria and R. Thouvenot, *Chem. – Eur. J.*, 2008, **14**, 1532–1540.
133 M. H. Alizadeh, R. Tayebee and M. Mirzaei, *Cryst. Res. Technol.*, 2008, **43**, 214–217.
134 L. Zheng, Y. Ma, G. Zhang, J. Yao, B. S. Bassil, U. Kortz, B. Keita, P. de Oliveira, L. Nadjo, C. T. Craescu and S. Miron, *Eur. J. Inorg. Chem.*, 2009, 5189–5193.
135 M. Carraro, G. Modugno, A. Sartorel, G. Scorrano and M. Bonchio, *Eur. J. Inorg. Chem.*, 2009, 5164–5174.
136 A. Seko, T. Yamase and K. Yamashita, *J. Inorg. Biochem.*, 2009, **103**, 1061–1066.
137 H. Wille, M. Shanmugam, M. Murugesu, J. Ollesch, G. Stubbs, J. R. Long, J. G. Safar and S. B. Prusiner, *Proc. Natl. Acad. Sci. U. S. A.*, 2009, **106**, 3740–3745.
138 R. K. Mitra, P. K. Verma, D. Wulferding, D. Menzel, T. Mitra, A. M. Todea, P. Lemmens, A. Müller and S. K. Pal, *ChemPhysChem*, 2010, **11**, 389–393.
139 P. Wu, J. Zhang, X. Xu, J. Hao, Z. Xiao, C. Lv and F. Xiao, *J. Cluster Sci.*, 2010, **21**, 173–179.
140 D. Fan, Y. Deng and J. Hao, *Amino Acids*, 2010, **39**, 1363–1367.
141 D. Dutta, A. D. Jana, M. Debnath, A. Bhaumik, J. Marek and M. Ali, *Dalton Trans.*, 2010, **39**, 11551.
142 T. Zhang, H.-W. Li, Y. Wu, Y. Wang and L. Wu, *J. Phys. Chem. C*, 2015, **119**, 8321–8328.
143 L. Zhang, Y. Li and Y. Zhou, *J. Mol. Struct.*, 2010, **969**, 69–74.
144 F. M. Santos, P. Brandão, V. Félix, A. M. V. Cavaleiro, E. de Matos Gomes and M. S. Belsley, *J. Mol. Struct.*, 2010, **963**, 267–273.
145 X. Y. Jiang, X. Y. Wu, R. M. Yu, D. Q. Yuan and W. Z. Chen, *Inorg. Chem. Commun.*, 2011, **14**, 1546–1549.
146 A. Flütsch, T. Schroeder, M. G. Grütter and G. R. Patzke, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 1162–1166.
147 H. E.-H. Mohammad Yousefi, M. Mirzaei, A. R. Salimi and M. Nikpour, *Indian J. Chem.*, 2011, **50**, 51–54.
148 D. Mercier, S. Boujday, C. Annabi, R. Villanneau, C. M. Pradier and A. Proust, *J. Phys. Chem. C*, 2012, **116**, 13217–13224.
149 G. Fraqueza, L. A. E. Batista de Carvalho, M. P. M. Marques, L. Maia, C. A. Ohlin, W. H. Casey and M. Aureliano, *Dalton Trans.*, 2012, **41**, 12749–12758.
150 B. Kowalewski, J. Poppe, U. Demmer, E. Warkentin, T. Dierks, U. Ermler and K. Schneider, *J. Am. Chem. Soc.*, 2012, **134**, 9768–9774.
151 M. P. A. Raissi Shabari and N. Heidari, *X-Ray Struct. Anal. Online*, 2012, **28**, 67–68.
152 Y. Xu, K. Yu, B. Zhou, Z. Su and J. Wu, *J. Coord. Chem.*, 2013, **66**, 1303–1310.

153 C. Zhou, S. Li, W. Zhu, H. Pang and H. Ma, *Electrochim. Acta*, 2013, **113**, 454–463.
154 Z. Chen, H. An, H. Zhang and Y. Hu, *CrystEngComm*, 2013, **15**, 4711.
155 G. Rousseau, E. Rivière, A. Dolbecq, J. Marrot, O. Oms and P. Mialane, *Eur. J. Inorg. Chem.*, 2013, 1793–1798.
156 M. Li, C. Xu, J. Ren, E. Wang and X. Qu, *Chem. Commun.*, 2013, **49**, 11394.
157 J. Liang, Y. Ma, H. Sun, W. Li and L. Wu, *J. Colloid Interface Sci.*, 2013, **409**, 80–87.
158 D. Kong, B. Wei, S. Zhou, H. Yang and Y. Jiang, *Chem. Res. Chin. Univ.*, 2013, **29**, 1055–1058.
159 S. D. Halperin, H. Fan, S. Chang, R. E. Martin and R. Britton, *Angew. Chem., Int. Ed.*, 2014, **53**, 4690–4693.
160 B. Cai, B.-F. Yang, H. He, J.-W. Zhao and G.-Y. Yang, *J. Cluster Sci.*, 2014, **25**, 1283–1293.
161 J. Zhang, Q. Lan, Z. M. Zhang, Z. J. Liu, Y. Liang and E. B. Wang, *J. Cluster Sci.*, 2014, **25**, 253–259.
162 S. G. Mauracher, C. Molitor, R. Al-Oweini, U. Kortz and A. Rompel, *Acta Crystallogr., Sect. F: Struct. Biol. Commun.*, 2014, **70**, 263–266.
163 N. Gao, H. Sun, K. Dong, J. Ren and X. Qu, *Chemistry*, 2015, **21**, 829–835.
164 L. Zhang, H. Zeng, Y. Zeng, Z. Zhang and X. Zhao, *J. Mol. Catal. A: Chem.*, 2014, **392**, 202–207.
165 K. Stroobants, G. Absillis, P. S. Shestakova, R. Willem and T. N. Parac-Vogt, *J. Cluster Sci.*, 2014, **25**, 855–866.
166 Q. Chen, L. Yang, C. Zheng, W. Zheng, J. Zhang, Y. Zhou and J. Liu, *Nanoscale*, 2014, **6**, 6886–6897.
167 K. Stroobants, V. Goovaerts, G. Absillis, G. Bruylants, E. Moelants, P. Proost and T. N. Parac-Vogt, *Chem. – Eur. J.*, 2014, **20**, 9567–9577.
168 M. Barboiu, Z. Mouline, M. Silion, E. Licsandru, B. C. Simionescu, E. Mahon and M. Pinteala, *Chem. – Eur. J.*, 2014, **20**, 6678–6683.
169 J.-W. Zhao, J.-L. Zhang, Y.-Z. Li, J. Cao and L.-J. Chen, *Cryst. Growth Des.*, 2014, **14**, 1467–1475.
170 B. Chahkandi, M. Mirzaei, M. Chahkandi, A. Shokrollahi, F. Zarghampour and M. Shamsipur, *J. Iran. Chem. Soc.*, 2014, **11**, 187–198.
171 K. Stroobants, G. Absillis, E. Moelants, P. Proost and T. N. Parac-Vogt, *Chem. – Eur. J.*, 2014, **20**, 3894–3897.
172 H.-W. Li, Y. Wang, T. Zhang, Y. Wu and L. Wu, *ChemPlusChem*, 2014, **79**, 1208–1213.
173 J. Poppe, E. Warkentin, U. Demmer, B. Kowalewski, T. Dierks, K. Schneider and U. Ermler, *J. Inorg. Biochem.*, 2014, **138**, 122–128.
174 K. Stroobants, D. Saadallah, G. Bruylants and T. N. Parac-Vogt, *Phys. Chem. Chem. Phys.*, 2014, **16**, 21778–21787.
175 N. Gao, H. Sun, K. Dong, J. Ren, T. Duan, C. Xu and X. Qu, *Nat. Commun.*, 2014, **5**, 3422.
176 Y.-X. Yan, H.-B. Yao, S. E. Smart, L.-B. Mao, W. Hu, S. Yuan, L. Du-Thumm, J. G. Masters, S.-H. Yu and L. Pan, *Langmuir*, 2014, **30**, 5248–5255.
177 P.-F. Gao, S. Zhang, H.-W. Li, T. Zhang, Y. Wu and L. Wu, *Langmuir*, 2015, **31**, 10888–10896.
178 H. G. T. Ly, G. Absillis and T. N. Parac-Vogt, *Eur. J. Inorg. Chem.*, 2015, **2015**, 2206–2215.
179 Z. Ma, Y. Qiu, H. Yang, Y. Huang, J. Liu, Y. Lu, C. Zhang and P. Hu, *ACS Appl. Mater. Interfaces*, 2015, **7**, 22036–22045.
180 V. Goovaerts, K. Stroobants, G. Absillis and T. N. Parac-Vogt, *J. Inorg. Biochem.*, 2015, **150**, 72–80.
181 H. Chen, L. Zhang, H. Zeng, D. Yin, Q. Zhai, X. Zhao and J. Li, *J. Mol. Catal. A: Chem.*, 2015, **406**, 72–77.
182 Z. Zhang, L. Zhou, Y. Zhou, J. Liu, X. Xing, J. Zhong, G. Xu, Z. Kang and J. Liu, *Biomaterials*, 2015, **65**, 56–65.
183 H. Zhang, K. Yu, J. Lv, L. Gong, C. Wang, C. Wang, D. Sun and B.-B. Zhou, *Inorg. Chem.*, 2015, **54**, 6744–6757.
184 H. G. T. Ly, T. Mihaylov, G. Absillis, K. Pierloot and T. N. Parac-Vogt, *Inorg. Chem.*, 2015, **54**, 11477–11492.
185 A. Sap, G. Absillis and T. N. Parac-Vogt, *Dalton Trans.*, 2015, **44**, 1539–1548.
186 M. Mirzaei, H. Eshtiagh-Hosseini, M. Arefian, F. Akbarnia, F. Miri, S. Edalatkar-Moghadam and M. Shamsipur, *J. Iran. Chem. Soc.*, 2015, **12**, 1191–1198.
187 E. Al-Sayed, A. Blazevic, A. Roller and A. Rompel, *Chem. – Eur. J.*, 2015, **21**, 17800–17807.
188 T. Zhang, H.-W. Li, Y. Wu, Y. Wang and L. Wu, *Chem. – Eur. J.*, 2015, **21**, 9028–9033.
189 A. S. Holmes-Smith, J. Crisp, F. Hussain, G. R. Patzke and G. Hungerford, *ChemPhysChem*, 2016, **17**, 418–424.
190 K. Narasimhan, S. Pillay, N. R. Bin Ahmad, Z. Bikadi, E. Hazai, L. Yan, P. R. Kolatkar, K. Pervushin and R. Jauch, *ACS Chem. Biol.*, 2011, **6**, 573–581.
191 J. Sha, T. Zheng, E. Zhang, H. Qiu, M. Liu, H. Zhao and H. Yuan, *J. Coord. Chem.*, 2013, **66**, 977–985.
192 I. E. León, V. Porro, S. Astrada, M. G. Egusquiza, C. I. Cabello, M. Bollati-Fogolin and S. B. Etcheverry, *Chem.-Biol. Interact.*, 2014, **222**, 87–96.
193 H. Liu, Y.-L. Zou, L. Zhang, J.-X. Liu, C.-Y. Song, D.-F. Chai, G.-G. Gao and Y.-F. Qiu, *J. Coord. Chem.*, 2014, **67**, 2257–2270.
194 A. M. Debela, M. Ortiz, V. Beni, S. Thorimbert, D. Lesage, R. B. Cole, C. K. O'Sullivan and B. Hasenknopf, *Chem. – Eur. J.*, 2015, **21**, 17721–17727.
195 S. Dianat, A.-K. Bordbar, S. Tangestaninejad, B. Yadollahi, R. Amiri, S.-H. Zarkesh-Esfahani and P. Habibi, *J. Inorg. Biochem.*, 2015, **152**, 74–81.
196 T. K. N. Luong, P. Shestakova, T. T. Mihaylov, G. Absillis, K. Pierloot and T. N. Parac-Vogt, *Chem. – Eur. J.*, 2015, **21**, 4428–4439.