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Stereoisomerism in polyoxometalates: structural and spectroscopic studies of bis(malate)-functionalized cluster systems†

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Pure enantiomers of a polytungstate cluster $[(\alpha\text{-}P_2W_{16}O_{59})Zr_2(\mu_3\text{-}O)(mal)]_2^{18-}$ (mal = malate) have been obtained and their conversion to *meso* diastereomers was observed by ^{31}P NMR.

Asymmetric synthesis in inorganic chemistry remains an area of considerable focus due to recent developments in enantioselective catalysis[1] as well as in bio-inorganic[2] and supramolecular chemistry.[3] In contrast to the highly developed nature of asymmetric synthesis in organic chemistry, the variability of coordination geometry and the higher coordination numbers of the d-block elements makes it difficult to control chirality in metal centers.[4,5] This is especially true in polyoxometalates (POMs)[6] which contain multiple metal centers that are subject to rapid racemization *via* water exchange, partial hydrolysis, or fluxional rearrangements.[7] As a result, it is often challenging to discriminate between enantiomers and/or diastereomers, and even more formidable to achieve partial or complete resolution.

Recently, we described the stereoselective synthesis of a POM complex through the use of chiral C_2-symmetric tartrate ligands,[8] following previous and concurrent work by the groups of Pope, Kortz, and others.[9–14] The Zr(IV) ions transmit carbon-centered tetrahedral chirality from a single L- or D-tartrate unit (tart) to the large polyoxoanion unit, therefore creating metal–oxide frameworks with a predetermined propeller-like chirality. In these complexes, $\{[\alpha\text{-}P_2W_{15}O_{55}(H_2O)]Zr_3(\mu_3\text{-}O)(H_2O)(\text{L- or D-tartH})[\alpha\text{-}P_2W_{16}O_{59}]\}^{15-}$ (L- or D-**1**), significant induced circular dichroism was observed in the absorption region of the POM chromophore. By increasing the number of controllable stereogenic centers, specific enantiomers and diastereomers are now possible by manipulating the configuration of the individual chiral inducers in one molecular unit. Herein we report such a family of stereoisomers containing two malate ligands coordinated to a nearly centrosymmetric metal–oxide framework, $[(\alpha\text{-}P_2W_{16}O_{59})Zr_2(\mu_3\text{-}O)(C_4O_5H_3)]_2^{18-}$ (**2**).

The reaction of $Na_{12}[\alpha\text{-}P_2W_{15}O_{56}]\cdot 18H_2O$ with a refluxed slurry of zirconyl nitrate and L- or D-malic acid leads to the enantiomerically pure complexes L,L-**2** and D,D-**2**, respectively. Both enantiomers crystallize in the acentric space group *P*1.‡ The absolute configurations of the chiral crystals of **2** are determined from the Flack parameter $x(u)$,[15] which is 0.109(8) and 0.122(9) for L,L-**2** and D,D-**2**, respectively. Despite the strong inversion-distinguishing power of the data, indicated by the small standard uncertainty ($u < 0.01$), the values of x are relatively large (compared to an ideal value of 0) and beyond the statistical fluctuations $|x| \leqslant 3u$.[16] However, the enantiopurity of both complexes was confirmed indirectly by ^{31}P NMR because the simultaneous presence of both L,L-**2** and D,D-**2** leads to the rapid formation of new species (with distinguishable ^{31}P signals) discussed below. The less than ideal x values are thus attributed, in part, to the disordered solvent water molecules present in the crystal lattice, which contribute little or no information about the absolute configuration of **2**. In addition, the pseudo-centrosymmetric arrangement of the dispersive heavy-atom scatterers (W and Zr), which dominate the diffraction data, makes determination of the absolute configurations more difficult.

The structures of L,L-**2** and D,D-**2** consist of a Zr-substituted polytungstate ligating two malates of the same handedness (Fig. 1a). The polytungstate assembly consists of two divacant $[\alpha\text{-}P_2W_{16}O_{59}]^{12-}$ anions linked by four Zr cations and is constitutionally similar to the centrosymmetric complex, $[Zr_4(\mu_3\text{-}O)_2(\mu_2\text{-}OH)_2(H_2O)_4(P_2W_{16}O_{59})_2]^{14-}$ (**3**), reported by May, Pope

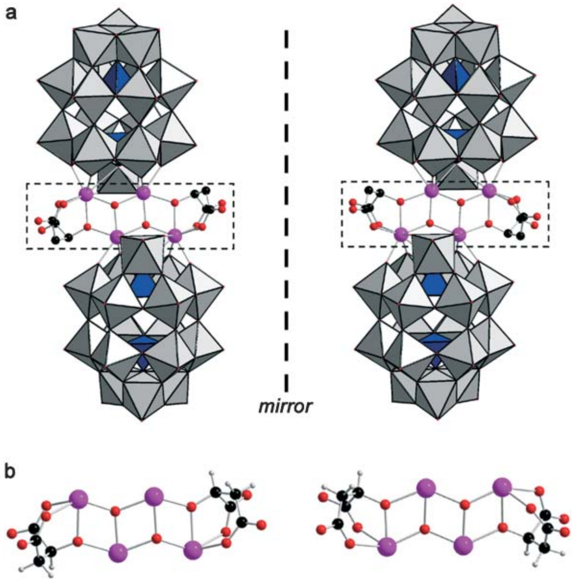

Fig. 1 (a) Crystal structures of the enantiomeric pair of **2**: L,L-**2** (left) and D,D-**2** (right); hydrogen atoms have been omitted for clarity. The W, P, Zr, C and O atoms are shown in gray, blue, pink, black and red, respectively. (b) A perspective view of the central units (indicated by dashed rectangles above) of L,L-**2** (left) and D,D-**2** (right), showing the loss of the center of symmetry. Small gray balls represent H atoms on the malate ligands.

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† Electronic supplementary information (ESI) available: Experimental details, thermal ellipsoid plots, circular dichroism spectra of L,L-**2** and D,D-**2** and diagrams of a complete set of 10 stereoisomers. See http://dx.doi.org/10.1039/b508468g

et al.[17] In **2**, the μ_2-OH and terminal aqua ligands in **3** are replaced by the oxygens of the ligating malates (from carboxylate and hydroxo moeities). Compound **3** crystallizes in the centrosymmetric space group $P\bar{1}$,[17] with the inversion center sitting at the center of the $[Zr_4O_4]^{8+}$ group, giving the molecule overall C_i symmetry. The presence of the two same-handed malate ligands in **2** adds two "left hands" or "right hands", one on each side of the polytungstate, and lowers the point group of the molecule to C_1 because the center of symmetry is broken (Fig. 1b). The bond lengths within the two malates and Zr–O_{mal} distances (2.145(8) Å to 2.276(7) Å) are all in the normal range. The most pronounced difference is found in the torsion angles of the two malate moieties [C(1)–C(2)–C(3)–C(4)], which are −55.3(1.2)° and −64.0(1.0)° for L,L-**2** and 57.4(1.6)° and 64.5(1.1)° for D,D-**2** (see ESI for numbering†), indicating that the unsymmetrical environment of the complex is a result of the loss of the inversion center present in **3**.

Solution NMR studies confirm that the solid-state structure is retained in solution. The ^{31}P NMR spectra of each of the two enantiomers of **2** (Fig. 2a) display four peaks at −6.36, −6.46, −13.86, and −13.87 ppm while **3** has only two peaks at −6.45 and −13.8 ppm.[17] The splitting for the two P atoms proximal to the Zr-ligated malates (P1) is quite pronounced (0.10 ppm), whereas the splitting for the distal P atoms (P2) is more subtle (0.01 ppm).§ Both of the enantiomers are obtained as alkaline salts (K^+ and Na^+), and they are reasonably soluble and thermally stable in water. This allows for the acquisition of NMR data on the unenriched ^{13}C nuclei, despite the long acquisition period (~20 h). The ^{13}C NMR spectra (^1H decoupled) of L,L-**2** and D,D-**2** have eight peaks grouped into four pairs (Fig. 2b) for the eight unique carbon atoms, corresponding to the two nonequivalent malate ligands, and also indicating that these enantiomeric complexes are configurationally stable in solution. As expected, the signals for the coordinated malates are shifted downfield with respect to the free ligand.[18]

Optical rotation measurements give positive and negative values for L,L-**2** and D,D-**2**, respectively. In addition, circular dichroism (CD) studies show that they are optically active in the metal–oxide absorption region and provide approximately mirror-image CD spectra of each other. Comparison of the CD spectra of the enantiomers of **2** and **1** reveals a correlation between the intensity of the signals and the chirality of the metal–oxide framework (Fig. S2, see ESI†). The intensities for L,L-**2** and D,D-**2** ($\Delta\varepsilon_{max}$ ~2.3 dm^3 mol^{-1} cm^{-1}) are much weaker than those observed for L-**1** and D-**1** ($\Delta\varepsilon_{max}$ ~35 dm^3 mol^{-1} cm^{-1}) despite the fact that the former species contain more chiral organic ligands than the latter, a clear response to the nearly-centrosymmetric metal–oxide framework of **2** in contrast to that of **1**. Therefore, the data confirm that the Cotton effects in the 250–350 nm region do indeed originate from the POM chromophore and demonstrate that even subtle differences in the nature of the chiral inducer, including geometrical preference, can affect POM chirality (*i.e.* tartrate *versus* malate).

One interesting aspect of having multiple stereogenic centers in **2** is that it increases the number of possible isomers present, depending on the symmetry of the POM framework. The description of the stereochemistry of **2** might be comparable to that of the linear tetraknotane[19,20] or hexaric acid.[21] Thus, in principle, **2** can have up to 10 different isomeric forms (4 enantiomeric pairs and 2 *meso* forms, see ESI†).[21] However, 6 of the 10 stereoisomers put the two $[P_2W_{16}O_{59}]^{12-}$ units into a cisoid arrangement with respect to the Zr_4 plane, instead of the transoid arrangement observed in the crystal structures of L,L-**2**, D,D-**2** and **3**. Internal steric and stereo-electronic effects make the observation of cisoid isomers very unlikely. Therefore, only the 4 energetically favorable transoid forms, whose diagrams are shown in Scheme 1, are considered for **2**.

Despite the fact that L,L-(+)-**2** and D,D-(−)-**2** are configurationally stable in solution, as indicated by NMR and chiroptical data, cross-over experiments monitored by ^{31}P NMR suggest that L- and D-malate are quite labile. Upon mixing L,L-(+)-**2** and D,D-(−)-**2** in a 1 : 1 ratio, the characteristic four-line ^{31}P signals quickly diminish and are replaced by a new set of signals at −6.39 and −13.85 ppm (Fig. 3, only the well-separated P1 peaks are shown), which are quite different from those observed for the centrosymmetric compound **3**.[17] The equilibrium is reached after

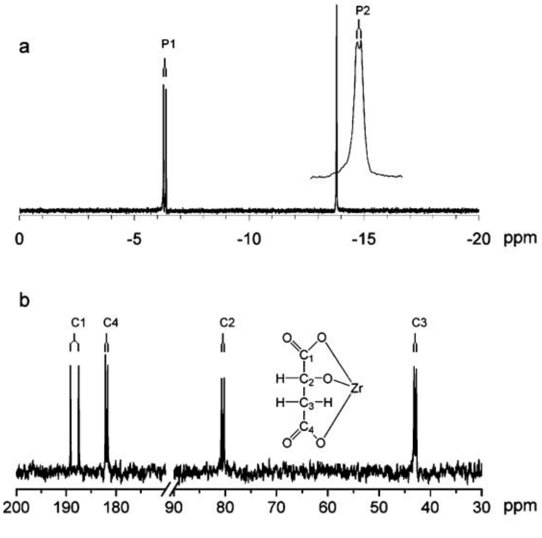
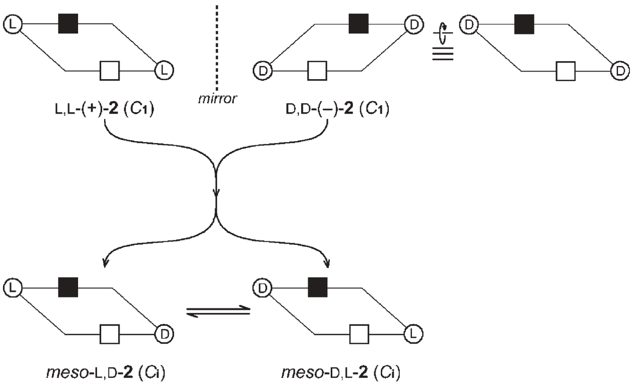


Fig. 2 (a) ^{31}P NMR and (b) ^{13}C NMR spectra for L,L-**2** and D,D-**2**.



Scheme 1 The relationships of the stereoisomers of **2**. A parallelogram represents the $[Zr_4O_4]^{8+}$ unit, whereas labeled open circles represent L- and D-malate ligands. The two $[\alpha\text{-}P_2W_{16}O_{59}]^{12-}$ units are in a transoid arrangement with respect to the plane of the Zr_4 parallelogram, with the inward-oriented unit represented by a filled square and the outward counterpart represented by an open square. The point group for each species is indicated in parentheses.

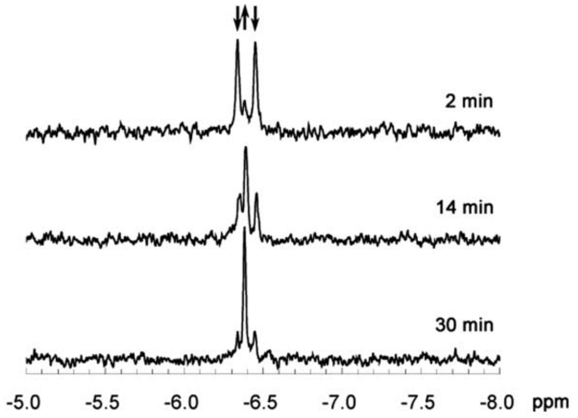


Fig. 3 ^{31}P NMR spectral changes of a 1 : 1 mixture of L,L-(+)-**2** and D,D-(−)-**2** with time (in D_2O, at 10 °C); only the signals for the proximal phosphorous atoms (P1) are shown.

approximately 30 min at 10 °C. The fact that the peaks for the enantiomeric forms disappear rapidly indicates that the new species is/are more thermodynamically stable relative to L,L-(+)-**2** and D,D-(−)-**2**. Replacement of one of the malate ligands in L,L-(+)-**2** or D,D-(−)-**2** with its optical counterpart will restore the center of symmetry since the complexes can now be related by the same inversion center as that in **3**. Therefore, a two-line ^{31}P NMR spectrum is expected on this basis. However, two *meso* complexes with C_i symmetry (Scheme 1), *meso*-L,D-**2** and *meso*-D,L-**2**, are both possible products and should be present in equimolar amounts, based on the fact the metal–oxide moiety is centrosymmetric and the two Zr coordination sites should have no particular preference for L- or D-malate. The two *meso* forms are diastereomers of each other and to the enantiomeric species, L,L-(+)-**2** or D,D-(−)-**2**. The observation of only a single pair of P resonances instead of two (*i.e.* one pair of signals for each of the two possible *meso* diastereomers), therefore, can most likely be rationalized by the spontaneous interconversion of the two *meso* forms in solution (Scheme 1), which is consistent with the lability of the malate ligands shown in the enantiomeric forms of **2**. The equilibrium constant (K, in H_2O, 10 °C) for eqn (1), evaluated by ^{31}P NMR, is *ca.* 85.

$$\text{L,L-(+)-}\mathbf{2} + \text{D,D-(}-\text{)-}\mathbf{2} \xrightleftharpoons{K} \textit{meso}\text{-L,D-}\mathbf{2} + \textit{meso}\text{-D,L-}\mathbf{2} \qquad (1)$$

Attempts to distinguish the two *meso* forms have been unsuccessful so far. Because these two compounds are extremely similar, conventional spectroscopic techniques, such as solid-state NMR, have been unsuccessful due to the broad signals. Low-temperature solution ^{31}P NMR was also attempted, but it did not lead to a noticeable broadening or splitting of the signals at the lowest possible temperature one can reasonably achieve in D_2O (4 °C). The introduction of a bulky group to the malate ligands might slow down the exchange process, however, and make differentiation of the two *meso* diastereomers possible.

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Notes and references

‡ Crystal data for D,D-**2**, $C_8H_{106}K_8Na_{10}O_{180}P_4W_{32}Zr_4$, M = 9997.59, space group $P1$, a = 13.817(1), b = 14.292(1), c = 26.318(2) Å, α = 92.816(2), β = 96.781(2), γ = 118.451(1)°, V = 4504.3(6) Å^3, T = 173(2) K, Z = 1, $2\theta_{\max}$ = 56.60°. The refinement converges with $R1$ = 0.0421 and w$R2$ = 0.1127 for 43 635 reflections with $I > 2\sigma(I)$. The Flack parameter $x(u)$ = 0.122(9). CCDC 276269. Crystal data for L,L-**2**, $C_8H_{114}K_8Na_{10}O_{184}P_4W_{32}Zr_4$, M = 10069.65, space group $P1$, a = 13.826(1), b = 14.309(1), c = 26.334(2) Å, α = 92.871(1), β = 96.639(1), γ = 118.518(1)°, V = 4513.8(5) Å^3, T = 173(2) K, Z = 1, $2\theta_{\max}$ = 56.56°. The refinement converges with $R1$ = 0.0480 and w$R2$ = 0.1267 for 43 605 reflections with $I > 2\sigma(I)$. The Flack parameter $x(u)$ = 0.109(8). CCDC 276270. The positions of the hydrogen atoms on the malate ligands were calculated for idealized positions. The structures were solved and refined using SHELXTL V6.12 software.[22] See http://dx.doi.org/10.1039/b508468g for crystallographic data in CIF or other electronic format.

§ One needs to increase the number of points and decrease the line broadening in the spectrum in order to observe the splitting in ^{31}P NMR. ^{31}P NMR data were collected at 161.9 MHz on a Varian Inova 400 MHz instrument with chemical shifts reported relative to 85% H_3PO_4. A total of 144064 data points were used with a spectral resolution of 1.2 Hz per data point; the line broadening parameter was set at 0.3; delay time, 10 s; acquisition time, 1.2 s.

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