Stereospecific coordination of L-hydroxyproline esters with triosmium clusters

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The reactions of cluster $(\mu\text{-H})Os_3(CO)_{10}(\mu\text{-OH})$ with ethyl and isopropyl esters of L-oxyproline were studied. In the presence of Me_3NO intermediate complex $(\mu\text{-H})Os_3(CO)_9(\mu\text{-OH})L$ (L — isopropyl ester of L-oxyproline) is formed, which slowly converts to the more stable cluster $(\mu\text{-H})Os_3(CO)_9\{\mu,\eta^2\text{-}O\overline{CHCH_2CH(COOPr^i)NHCH_2}\}$. Cluster complexes containing chelate-bridging heterocycles were also obtained by heating $(\mu\text{-H})Os_3(CO)_{10}(\mu\text{-OH})$ with esters of L-oxyproline. In both cases, only one of the possible diastereomeric complexes $(\mu\text{-H})Os_3(CO)_9\{\mu,\eta^2\text{-}O\overline{CHCH_2CH(COOPr^i)NHCH_2}\}$ (R = Et, Pr^i) is formed, which indicates that the reactions are stereospecific. Based on analysis of Dreiding's models, an attempt to determine the absolute configuration of the obtained clusters was made.

Key words: triosmium clusters, L-hydroxyproline esters, stereospecific coordination.

We have previously shown[1,2] that amino alcohols and thioamino alcohols (ethanolamine, L-α-serine, and L-α-cysteine ethylates) react at room temperature and in the presence of Me_3NO with cluster $(\mu\text{-H})Os_3(CO)_{10}(\mu\text{-OH})$ (**1**) to form new cluster complexes with bidentate chelate-bridging coordination of the ligands, $(\mu\text{-OH})Os_3(CO)_9\{\mu\text{-}\eta^2\text{-}XCH_2CHRNH_2\}$ (X = O, S; R = H, CO_2Et).[1,2] In the case of optically active serine and cysteine esters, the pairs of diastereomers are formed in virtually equal proportions. The heating of cluster **1** with ethanolamine, an amino alcohol whose structure is comparatively simple, gives a complex with chelate-bridging coordination of the amino alcohol, along with cluster $(\mu\text{-H})Os_3(CO)_{10}(\mu\text{-}NHCH_2CH_2OH)$,[2] in which the organic ligand is symmetrically coordinated *via* the bridging NH group. Based on the data obtained, it was proposed[2] that the replacement of one CO group of the $Os(CO)_3$ fragment with the amino group of the NH_2CH_2CHROH ligand results in chelate bridging coordination of amino alcohols, whereas the attack of the amino group at one of the two osmium atoms bonded with the bridging ligands ("bridging" osmium atoms) is accompanied by substitution of the μ-OH group to produce μ-NH-coordination of the organic ligand.

This work deals with the reactions of **1** with L-hydroxyproline ethylates and isopropylates both with and without the use of Me_3NO. These reactions are of special interest from stereochemical point of view, because the esters of L-hydroxyproline are bulky optically active amino alcohols containing a rather rigid heterocycle. Stereochemical analysis based on Dreiding's models showed that the coordination of the esters of L-hydroxyproline to the $Os_3(CO)_{10}$ fragment *via* the bridging oxygen atom was the most favorable. Nevertheless, μ-coordination *via* nitrogen atom of the heterocycle would hardly cause serious steric hindrances. Both modes of chelate-bridging coordination (μ(O), η^2(O,N) or μ(N), η^2(N,O)) of L-hydroxyproline to an Os_3 metallocycle with the bridging oxygen or nitrogen atom are possible. However, in the latter case, terminal coordination of either a nitrogen or oxygen atom due to steric reasons seems to be possible only to one of the two closest osmium atoms to give a single diastereomer in each case.

The reaction of cluster **1** with L-hydroxyproline isopropylate involving the participation of Me_3NO occurs in three stages. At the first stage, when introducing Me_3NO to the solution, unstable complex $(\mu\text{-H})Os_3(CO)_9(\mu\text{-OH})L$ (**2**) (L is L-hydroxyproline isopropylate) is formed. Its IR spectrum in the region of CO stretching vibrations is almost identical to the IR spectrum of previously prepared[2] complex $(\mu\text{-H})Os_3(CO)_9(\mu\text{-OH})\{NH_2(CH_2)_2OH\}$ with terminally coordinated ethanolamine. After 3 h the starting complex completely converts to **2**, which is unstable in solution

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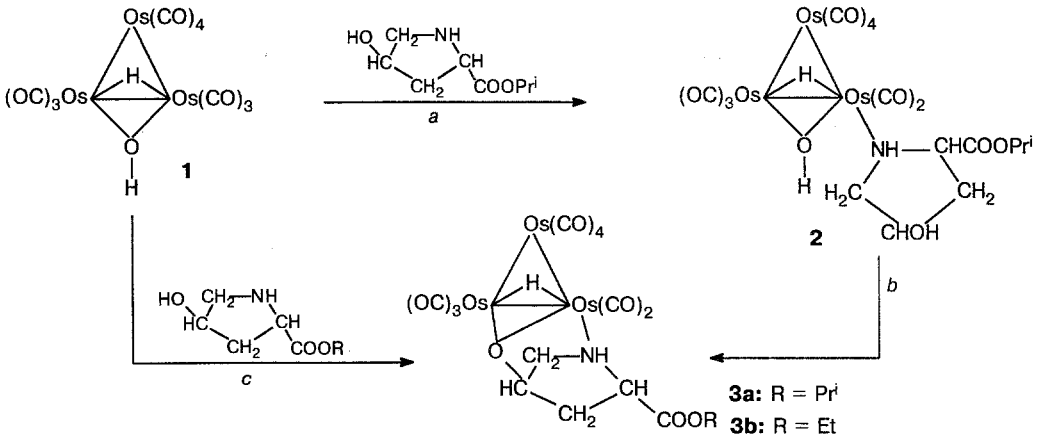
Scheme 1



Reagents and conditions: *a*. Me_3NO, dioxane, 20 °C, 3 h; *b*. 20 °C, 6 days; *c*. dioxane, 101 °C, 20—30 h.

in the absence of excess organic ligand and was not adequately characterized. In contrast to the analogous complex with triethanolamine,[2] this cluster complex very slowly converts to a new product at ambient temperature. An attempt to accelerate the process by increasing the temperature leads to the decomposition of complex **2**. The decomposition also proceeds, though to the less extent, at ambient temperature. This is most probably induced by the presence of an excess of Me_3NO in the solution, which is necessary for the first stage of the reaction to occur. After storing the reaction mixture for 6 days at ambient temperature, about 10 % of a new product and ~15 % of unreacted intermediate cluster **2** were isolated. The same new product was obtained in 73 % yield by boiling the mixture of cluster **1** with L-hydroxyproline isopropylate in dioxane for 20 h. The change of the isopropyl ester of L-hydroxyproline with the ethyl ester does not has much effect on the rate of the reaction and the yield (65 %) of the corresponding product. Contrary to ethanolamine,[2] no indications of the formation of the cluster containing a monodentate-coordinated ligand were found.

The IR spectra of the new products and of the corresponding clusters with the chelate-bridging coordination of amino alcohols[1,2] are virtually identical in the areas of stretching vibrations of carbonyl ligands. Besides, the spectra contain no bands of the alcohol and bridging OH groups, whereas a downfield shift of the NH vibration bands (up to ~3310 cm^{-1}) is indicative of the coordination of the ligands to the amino group. The IR data, the *m/z* values for the molecular ions (994 and 981 for **3a** and **3b**, respectively), and the character of fragmentation in mass spectra indicate that the molecular formula is $Os_3(CO)_9L$ (L is L-hydroxyproline ethylate or isopropylate) and make it possible to suggest the following scheme for the reactions studied (Scheme 1).

The proposed structure of the complexes is in agreement with the ^1H NMR spectral data of the isolated compounds (see Fig. 1 and Experimental). Bidentate coordination of the hydroxyproline esters leads to disappearance of the signal of the alcohol group and to an ~0.8 ppm downfield shift of the NH group signal. The similar downfield shift (0.3—0.6 ppm) of the signals of the protons of the O—CH< and N—CH< fragments is also in agreement with coordination of a ligand by the oxygen and nitrogen atoms. There is one upfield signal in the spectrum of each complex, *viz.*, −11.14 ppm for **3a** and −11.08 ppm for **3b**. These chemical shifts are close to those of μ-H ligands in clusters $(\mu\text{-H})Os_3(CO)_9\{\mu\text{-}\eta^2\text{-}OCH_2CHRNH_2\}$ (−11.75 ppm, R = H; −10.71 ppm, R = CO_2Et).[2] The upfield shift of ~1 ppm of one of the protons of the CH_2 group in the O—CH—CH_2—NH fragment is worth noting. The analysis of Dreiding's model for cluster **3** (see the sketch of this model over the ^1H NMR spectrum of **3** in Fig. 1) showed that one of the CH_2 protons (H(7)) is in the vicinity of the CO group of the equatorially coordinated $Os(CO)_3$ fragment and is positioned in the area of the shielding effect of the triple C≡O bond.

The both cluster complexes obtained have very high values of molecular optical rotation: $[M]_D^{20}$ +1611° (CH_2Cl_2, *c* 0.35) for **3a** and $[M]_{578}^{16}$ +1092° (CH_2Cl_2, *c* 5.54) for **3b**.

Taking into account all of the experimental data, one may conclude that, in the case of both heating and using Me_3NO, the reaction of cluster $(\mu\text{-H})Os_3(CO)_{10}(\mu\text{-OH})$ (**1**) with L-hydroxyproline esters leads to a single diastereomeric complex. This is in agreement with the results of the analysis of Dreiding's models and indicates a stereospecific character of the reactions under study.

It should also be noted that, unlike the triosmium complexes with bidentately coordinated serine and cysteine esters,[3] coordination of L-hydroxyproline esters on the $Os_3(CO)_9$-fragment does not lead to the epimirization of the ligand even at high temperature. Otherwise, according to Scheme (1), each of the hydroxyproline esters

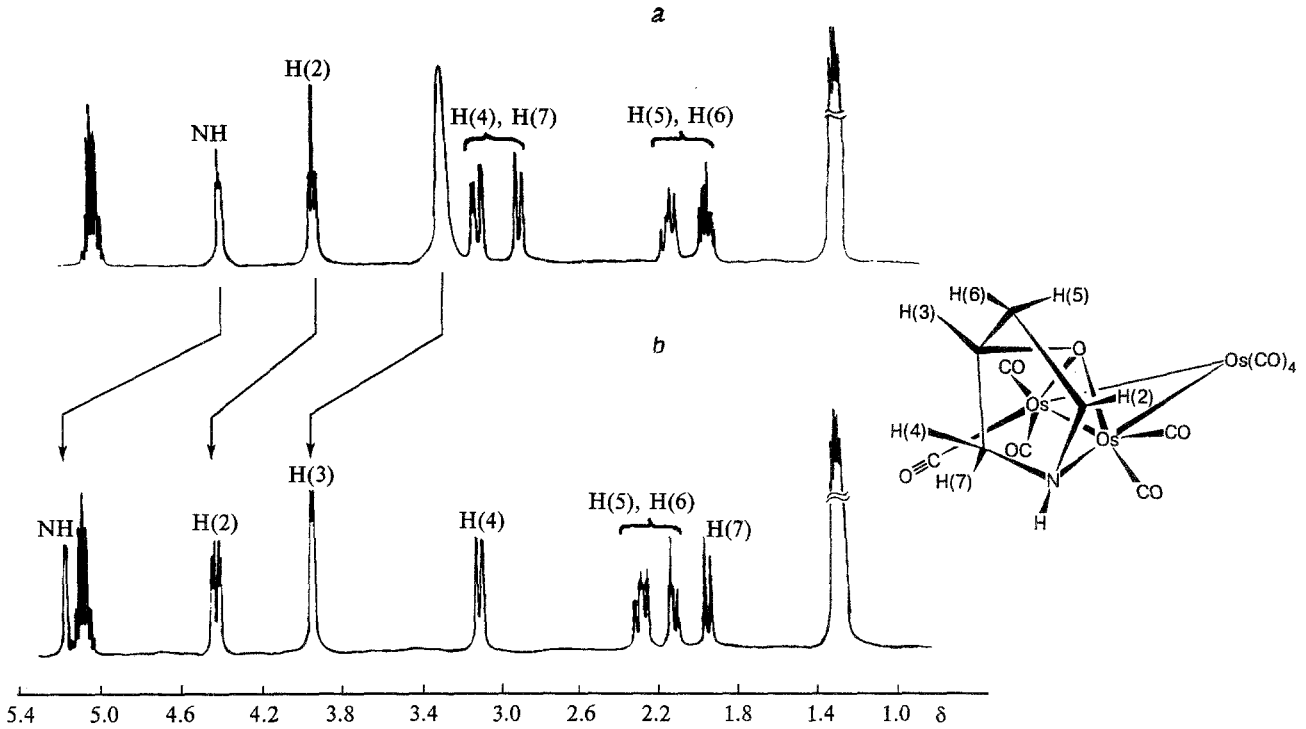


Fig. 1. Low field area of the ^{1}H NMR spectra ($CDCl_3$, 22 °C) of the isopropyl ester of L-hydroxyproline (*a*) and the cluster $(\mu\text{-H})Os_3(CO)_9\{\mu,\eta^2\text{-}OCHCH_2CH(COOPr^i)NHCH_2\}$ (**3b**) (*b*). A fragment of Dreiding's model for **3** is shown above the spectrum of **3b** (the ester group and μ-H-ligand are not depicted, for simplification).

would form a pair of diastereomeric clusters, which could be detected in the ^{1}H NMR spectra even without separation of these diastereomeric complexes (by chromatography or recrystallization).

Compounds **3a** and **3b** were isolated from the reaction mixtures as oils that could not be crystallized, which made it impossible to determine their structures and absolute configurations.

We attempted to determine probable absolute configuration of the complexes obtained, taking into account the fact that coordination of L-hydroxyproline esters on the triosmium cluster leads in each case to a single optical isomer, whereas using Dreiding's models one can rather validly determine, to which of the two bridging osmium atoms is the nitrogen atom of the heterocycle coordinated. We found that no stereochemical nomenclature is available for the description of absolute configuration of chiral trinuclear cluster metal cycles.

Exchanging one of the axial CO groups for X in the case of $M_3(CO)_{12}$ (M = Os, Ru), which have D_{3h} symmetry, makes the molecule prochiral, while the exchange of the second CO group at the adjacent metal atom for Y leads to a planar chirality of the cluster complex $M_3(CO)_{10}XY$ (*e.g.*, cluster **A**, Fig. 2). In this molecule, all three of the metal atoms have different ligand environment.

In principle, two systems based on the conventional Cahn—Ingold—Prelog *R,S* nomenclature[4] can be used for description of such metal cycles with planar chirality. According to one of these systems, each atom of the metal cycle that conditionally has an octahedral environment should be regarded as a chiral center, wherein the substituents are two adjacent metal atoms and its own ligands. The metal atoms are numerated, and the individual configurational index is assigned to each metal atoms of the metal cycle using the existing rules for determination of the consecutive order of the ligands for octahedral structures.[5] However, this system exhibits significant drawbacks when used for the chiral cluster metal cycles. First, in the most of the trinuclear metal cycles not all of the metal atoms have, as a rule, octahedral ligand environments. The presence of bridging ligands in these metal cycles often increases the coordination number to nine.[6—8] Therefore, for such compounds, it is very difficult to use the stereochemical nomenclature designed for octahedral complexes. The other disadvantage of this system is the fact that it is impossible to regard a planar chiral cluster as a whole.

We believe that these drawbacks can be eliminated by applying to planar chiral metal cycles a stereochemical *R,S* nomenclature, which resembles the nomenclature widely used for chiral ferrocene derivatives.[9,10] For this purpose, one should determine the consecutive order of the coordination centers of the metal cycle according to known rules. For heterometal clusters, the order of metal atoms is determined first; those having the greater

atom numbers are considered to be more significant. If several metal atoms of the same type are present, the total significance of the ligand environment for each metal atom is determined by the rules used for organic ligands. In the case of homometal clusters, the total significance of the ligand environment for each metal atom is determined directly. For ligands with the same donor atoms but different dentality, a ligand with a lower dentality is regarded as more significant. For example: $PR_3 > \mu\text{-}PR_2 > \mu_3\text{-}PR > SR_2 > \mu\text{-}Sr > \mu\text{-}OR > NR_3 > \mu\text{-}NR_2 > CR_2$ and so on. If one looks along the main axis of the molecule, which goes through the center of the metal cycle, from the side with the greatest number of axial carbonyl ligands, and the shortest way from the most significant coordinative center to the least significant one is clockwise, the *R* configuration is assigned to this chiral fragment. In the opposite case, the *S* configuration is assigned. If the numbers of axial ligands on both sides of the metal cycle are equal, the direction of the main axis of the molecule should be determined so that the beginning is at the side where the total significance of the axial ligands is higher. If the ligands have their own chiral centers, they are marked by the usual *R,S* nomenclature for organic compounds.

Figure 2 shows examples of using the stereochemical nomenclature proposed by us for some planar chiral trinuclear cyclic clusters.

One can see from the Fig. 2 that, according to our nomenclature, *S* configuration should be assigned to clusters **3a** and **3b** taking into account the experimental data and the analysis of their structure with Dreiding's models (see Fig. 2, *d*).

At present, in order to confirm the absolute configuration of clusters **3a** and **3b** by an independent approach, we are making attempts at synthesizing their crystal derivatives by the replacement of one or several CO groups with another ligands.

Experimental

The syntheses of clusters **3a,b** were carried out in an argon atmosphere using freshly distilled solvents. Cluster $(\mu\text{-}H)Os_3(CO)_{10}(\mu\text{-}OH)$ was synthesized by a known procedure.[11] IR spectra were recorded on a Specord IR-75 instrument. The ^1H NMR spectra of the ethyl ester of L-oxyproline and cluster **3a** were registered on a Tesla BS-567 spectrometer, and those of the isopropyl ester of L-oxyproline and cluster **3b** were obtained on a Bruker MSL-400 instrument using TMS as

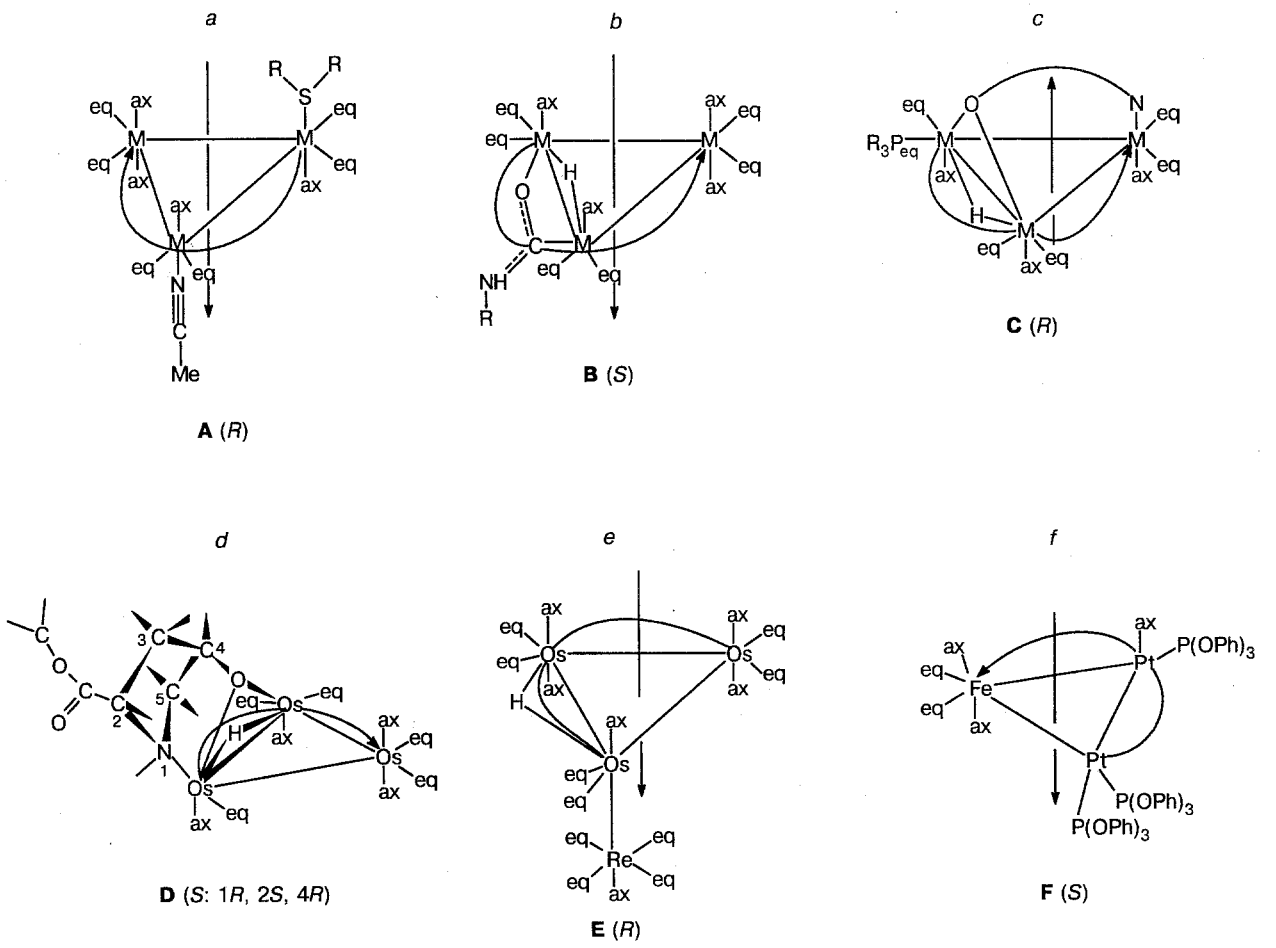


Fig. 2. Stereochemical *R,S* nomenclature suggested in the present work for a series of three nuclear planar chiral complexes (*a—f*); "ax" and "eq" are axial and equatorial carbonyl groups.

the internal standard. The assignment of the ^{1}H NMR signals was performed by the method of double homonuclear resonance. The mass spectra were recorded on an MKh-1310 mass spectrometer using ionizing irradiation of 70 eV. The values of the optical rotation were determined on Perkin-Elmer and Palomat A polarimeters (Carl Zeiss, Jena).

Synthesis of L-oxyproline ethers. A flow of dry HCl was passed through a solution of L-hydroxyproline in ethyl or isopropyl alcohol (~7 g per 250 mL) at ambient temperature until saturation. Then, without stopping the HCl flow, the solution was refluxed for 2 h. The reaction mixture was concentrated at reduced pressure, and the solid residue was dissolved in 25 mL of an alcohol (ethyl or isopropyl, respectively). A flow of NH_3 was passed through the solution for 1 h with cooling (acetonitrile/liquid nitrogen). The NH_4Cl that precipitated was filtered off, and the filtrate was evaporated. The isopropyl ester was a solid product, while the ethyl ester was obtained as an oil, which was than distilled *in vacuo* (5 Torr, 146 °C). ^{1}H NMR of the ethyl ester of L-hydroxyproline ($CDCl_3$), δ: 4.24 (m, 1 H, NH); 4.05 (q, 2 H, $OC\underline{H}_2CH_3$); 3.95 (m, 1 H, H(2)); 3.66 (m, 2 H, H(3)+OH); 2.91 (d.d, 1 H); 2.75 (d, 1 H, H(4,7)); 1.59 (m, 2 H, H(5,6)); 0.92 (t, 3 H, $OCH_2C\underline{H}_3$). ^{1}H NMR of isopropyl ester of L-hydroxyproline ($CDCl_3$), δ: 4.95 (hept, 1 H, $C\underline{H}(CH_3)_2$); 4.34 (br, 1 H, NH); 3.87 (t, 1 H, H(2)); 3.26 (br, 2 H, H(3)+OH); 3.13 (d.d, 1 H); 3.08 (d.t, 1 H, H(4,7)); 2.12 (m, 1 H); 1.93 (m, 1 H, H(5,6); 1.23 (d.d, 6 H, $CH(C\underline{H}_3)_2$).

Synthesis of $(\mu\text{-H})Os_3(CO)_9\{\mu,\eta^2\text{-}\overline{OCHCH_2CH(COOEt)NHCH_2}\}$ (3a). A mixture of 146 mg ($1.68\cdot10^{-4}$ mol) of $(\mu\text{-H})Os_3(CO)_{10}(\mu\text{-OH})$ and 150 mg ($9.44\cdot10^{-4}$ mol) of ethyl ester of L-hydroxyproline was refluxed for 30 h. The solution was evaporated to 8—10 mL and fractionated by chromatography on silica gel (μ 40/100) (hexane : diethyl ether : benzene, 6 : 3 : 1). A second, intensely yellow colored fraction was isolated. 107 mg (64.9 %) of **3a** was obtained. IR (CH), ν/cm^{-1}: 2099 m, 1056 s, 1017 v.s, 1997 s, 1980 pl, 1974 s, 1931 m (C≡O); 1738 w (C(O)OEt); 3310 w (NH). ^{1}H NMR ($CDCl_3$), δ: 5.18 (br, s, 1 H, NH); 4.40 (d.d, 1 H, H(2); 4.18 (qu, 2 H, O—$C\underline{H}_2$—CH_3); 3.91 (d, 1 H, H(3)); 3.06 (d, 1 H, H(4)); 2.15 (m, 2 H, H(5,6); 1.9 (d.d, 1 H, H(7)); 1.25 (t, O—CH_2—$C\underline{H}_3$); −11.14 (s, 1 H, μ-H). Mass spectrum, *m/z*: 987 [M$^+$] (^{192}Os); 987−28*n*, [M−*n*CO]$^+$ (*n* = 1÷9). Found (%): C, 20.14; H, 1.62; Os, 58.21. $C_{16}H_{13}NO_{12}Os_3$. Calculated (%): C, 19.56; H, 1.32; Os, 58.13. $[M]_D^{20}$ = +1621° (CH_2Cl_2, *c* 0.35).

Synthesis of $(\mu\text{-H})Os_3(CO)_9\{\mu,\eta^2\text{-}\overline{OCHCH_2CH(COOPr^i)NHCH_2}$ (3b).

A. A mixture of 167 mg ($1.91\cdot10^{-4}$ mol) of $(\mu\text{-H})Os_3(CO)_{10}(\mu\text{-OH})$ and 166 mg ($1.15\cdot10^{-3}$ mol) of isopropyl ester of L-hydroxyproline was refluxed for 20 h in 20 mL of dioxane. The solution was evaporated to 8—10 mL and fractionated by chromatography on silica gel (μ 40/100) (hexane : diethyl ether : benzene, 6 : 3 : 1). The fractions were isolated in the following order: $Os_3(CO)_{12}$ (1.5 mg, pale yellow); unreacted $(\mu\text{-H})Os_3(CO)_{10}(\mu\text{-OH})$ (5.5 mg, yellow); $(\mu\text{-H})Os_3(CO)_9\{\mu,\eta^2\text{-}OCHCH_2CH(COOPr^i)NHCH_2\}$ (**3b**) (136 mg, bright yellow, 73.7 % with respect to the reacted **1**).

IR (CCl_4), ν/cm^{-1}: 1099 m, 1056 s, 1017 v.s, 1996 s, 1971 s, 1917 m (C≡O); 1738 w (C(O)OEt); 3310 w (NH).

^{1}H NMR ($CDCl_3$), δ: 5.16 (br. s, 1 H, NH); 5.07 (hept, 1 H, H(1)); 4.43 (d.d, 1 H, H(2)); 3.94 (d, 1 H, H(3)); 3.1 (d.d, 1 H, H(4)); 2.28 (m, 1 H); 2.12 (m, 1 H, H(5,6)); 1.95 (d, 1 H, H(7)); 1.29 and 1.26 (both d, 6 H, $CH(C\underline{H}_3)_2$); −11.08 (s, 1 H, μ-H).

Mass spectrum, *m/z*: 1001 [M$^+$] (^{192}Os); 1001−28*n*, [M−*n*CO]$^+$ (*n* = 1÷9).

B. A solution of 16 mL ($1.34\cdot10^{-4}$ mol) of $Me_3NO\cdot2H_2O$ in 6 mL of alcohol was added dropwise to a solution of 119.5 mg ($1.49\cdot10^{-4}$ mol) of $(\mu\text{-H})Os_3(CO)_{10}(\mu\text{-OH})$ and 100 mg ($5.81\cdot10^{-4}$ mol) of the isopropyl ester of L-hydroxyproline in 20 mL of dioxane over a period of 3 h with stirring at ambient temperature. The reaction mixture was stored for 6 days at ambient temperature, evaporated to 10 mL, and separated by chromatography on Silufol (hexane : benzene : acetone, 4 : 1 : 1). Two pure intensely yellow colored fractions were isolated. 31 mg (10.5 %) of $(\mu\text{-H})Os_3(CO)_9(\mu\text{-OH})$ $\{\overline{NHCH(COOPr^i)CH_2CH(OH)CH_2}\}$ (**2**) and 19 mg (19.6 %) of **3b** were obtained. IR of compound **2** (CCl_4), ν/cm^{-1}: 1093 m, 1051 s, 1014 v.s, 1998 m, 1986 sh, 1915 m (C≡O); 1738 w (C(O)OEt). After registration of the IR spectrum, the product was analyzed by chromatography to reveal that, when stored in solution, **2** decomposes to a series of compounds, in which starting cluster **1** predominates.

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