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## Rational Synthesis of Tetranuclear Ruthenium Polyhydride Clusters and Their Mixed-Ligand Analogues**

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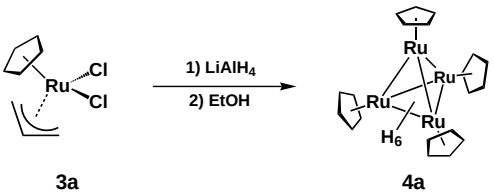
The reactivity of transition-metal cluster complexes has recently been attracted considerable attention because of their potential applicability to organic synthesis.[1] There have been a number of examples of unique reaction modes, such as successive cleavage of the carbon–hydrogen bond of alkanes,[2] the cleavage of the carbon–carbon double bond of 1,1′-disubstituted alkenes,[3] and the catalytic hydrogenation of aromatic compounds in aqueous media,[4] originating from the cooperative action of the metal centers. The advantageous properties of a multimetallic system over a monometallic one in the substrate activation step are its ability to *multiply coordinate* the substrate and the *multielectron transfer* between the substrate and the cluster. Such unique reactivity of the cluster likely comes from these two remarkable properties. The reactivity is most probably affected by the nuclearity of the cluster because the reactivity strongly depends on the number of transferable electrons: the more nuclei in the cluster, the more effectively electrons are transferred.[5] It is well established for mononuclear transition-metal complexes that the auxiliary ligand allows control over the reactivity of the complex through electronic and steric perturbation of the reaction site. Thus, the development of a rational method for the synthesis of clusters with higher nuclearity and a variety of auxiliary ligands seems to be essential for the application of such clusters to organic synthesis.

Recently, we have established the high and unique reactivity of the di- and trinuclear ruthenium polyhydride complexes $[\{(\eta^5\text{-}C_5Me_5)Ru\}_2(\mu\text{-}H)_4]$ (**1**) and $[\{(\eta^5\text{-}C_5Me_5)Ru\}_3(\mu\text{-}H)_3(\mu_3\text{-}H)_2]$ (**2**).[6] As an extension of the chemistry of "*trimetallic activation*", we tackled the development of a rational method for the synthesis of a tetranuclear ruthenium polyhydride cluster. We report herein, to the best of our knowledge, the first example of a rational synthesis of a series of tetranuclear polyhydride complexes having several combinations of the auxiliary cyclopentadienyl ligands.

Treatment of $[CpRuCl_2(\eta^3\text{-}C_3H_5)]$ (**3a**)[7] ($Cp = \eta^5\text{-}C_5H_5$) with $LiAlH_4$ in tetrahydrofuran followed by workup with ethanol [Eq. (1)] gave a new complex which was identified as the tetranuclear ruthenium hexahydride $[(CpRu)_4H_6]$ (**4a**) by $^1H$ and $^{13}C$ NMR spectroscopy and an X-ray diffraction study. In a similar manner, tetranuclear clusters $[\{(\eta^5\text{-}C_5H_4Me)Ru\}_4H_6]$ (**4b**) and $[\{(\eta^5\text{-}1,3\text{-}Me_2C_5H_3)Ru\}_4H_6]$ (**4c**) were derived from the corresponding $Ru^{IV}$ precursors, $[(\eta^5\text{-}C_5H_4Me)RuCl_2(\eta^3\text{-}C_3H_5)]$ (**3b**) and $[(\eta^5\text{-}1,3\text{-}Me_2\text{-}C_5H_3)RuCl_2(\eta^3\text{-}C_3H_5)]$ (**3c**),[8] respectively. Although the yields of **4a** and **4c** were not high (ca. 40%), the $^1H$ NMR spectra of the crude products obtained after removal of the aluminum salt showed that the tetranuclear hydride complexes **4a** and **4c** were formed exclusively. In the reaction of **3b** with $LiAlH_4$, however, the formation of **4b** was accompanied by a significant amount (ca. 40%) of the corresponding pentanuclear hydride complex, which was readily separated by column chromatography on alumina.




**3a** **4a** **(1)**

The $^1H$ NMR spectrum of the cluster **4a** exhibited two resonance signals assignable to Cp and hydride ligands at $\delta =$ 4.45 ppm (20H) and $\delta = -8.59$ ppm (6H), respectively. The

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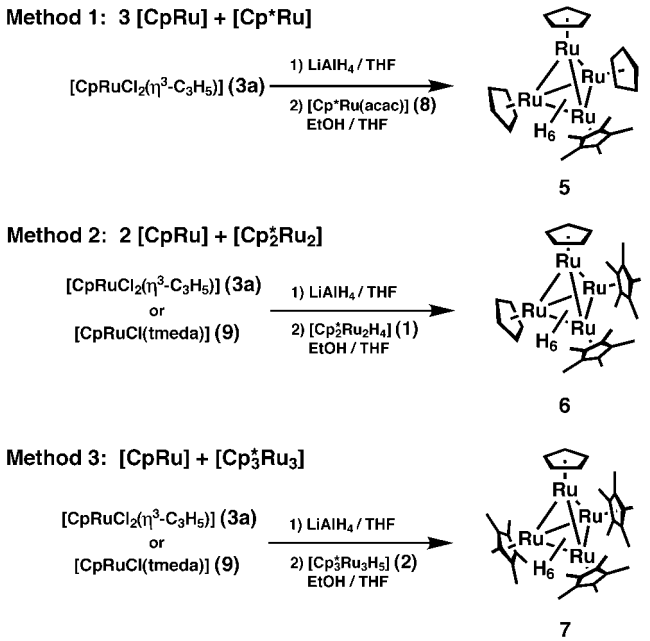
inversion-recovery ($T_1$) measurement for the hydride resonance signal was performed at 400 MHz at various temperatures. The observed $T_1$ value of 319 ms at −80 °C is deemed to be sufficient to characterize the complex as a classical metal hydride with no bonding interaction between the hydrogen atoms.[9] This contrasts with the related hexahydride tetraruthenium cluster $[H_6Ru_4(C_6H_6)_4]^{2+}$, which has been identified to contain nonclassical hydride ligands on the basis of spectroscopic, crystallographic, and theoretical investigations.[10] A significant upfield shift of the hydride signal is observed for **4a–c**; the signal moves further upfield as the number of methyl groups on the cyclopentadienyl ligand increases and is most probably due to the associated increase in the electron density at the metal center.

A series of tetranuclear ruthenium hexahydride complexes having several different combinations of the Cp ($C_5H_5$) and Cp* ($C_5Me_5$) ligands, were systematically synthesized as shown in Scheme 1.

When the $LiAlH_4$ adduct of **3a** was quenched with ethanol in the presence of 1/3 molar equivalent of the coordinatively unsaturated mononuclear complex **8**,[11] the [3:1] mixed-ligand cluster $[Cp_3Cp^*Ru_4H_6]$ (**5**) was formed (Method 1, Scheme 1).




Scheme 1. Methods for synthesizing mixed-ligand complexes **5**–**7**.

The most important criterion for the synthesis of the mixed-ligand clusters is the stoichiometry of the precursors. The [2:2] mixed-ligand cluster that has two Cp and two Cp* ligands, $[Cp_2Cp^*_2Ru_4H_6]$ (**6**), was prepared by the reaction of two molar equivalents of the precursor of the "CpRu" fragment with **1** (Method 2, Scheme 1). Both **3a** and [CpRuCl(tmeda)] (**9**; tmeda = tetramethylethylenediamine)[12] are applicable as the precursor of the "CpRu" fragment. In a similar manner the [1:3] mixed-ligand cluster was selectively synthesized by the reaction of the $LiAlH_4$ adduct of **3a** or **9** with an equimolar amount of **2** (Method 3, Scheme 1). The mixed-ligand clusters **5**–**7** were identified on the basis of the $^1H$ and $^{13}C$ NMR spectral data. The $^1H$ NMR spectra revealed the hydride ligands in **5**–**7** were equivalent in each complex, as observed for **4a–c**; this is probably due to the rapid exchange of their coordination sites. There is significant correlation between the chemical shifts for the hydride ligands in clusters **4**–**7** and the number of the methyl groups on the cyclopentadienyl ligands, $\delta = -8.59$ for **4a**, −8.69 for **4b**, −8.75 for **5**, −8.90 for **4c**, −8.94 for **6**, and −9.84 ppm for **7**. Thus, the electron density at the metal centers of the tetranuclear cluster complex is most probably controllable by changing the number of methyl groups on the $C_5$ rings.

The molecular structures of **4a–c**, **6**, and **7** were determined by X-ray diffraction studies (Figure 1).[13] All of the clusters **4a–c**, **6**, and **7** adopt a pseudo-tetrahedral structure and the corresponding bond lengths within each of the clusters are similar. The six Ru–Ru bonds in **4a** are classified into two groups, namely, four long bonds (2.8952(4)–2.938(1) Å) and two short bonds (2.683(2), 2.6897(4) Å). The two short bonds Ru1–Ru2 and Ru3–Ru4 skew each other. The low-temperature analyses of **4a–c** allowed us to determine and refine the positions of the metal-bound hydrogen atoms. Four of the six hydride ligands triply bridge each of the $Ru_3$ faces; the other two hydride ligands bridge the two short Ru–Ru bonds (Figure 2). The presence of the bridging hydride ligands is likely responsible for the shortening of the two

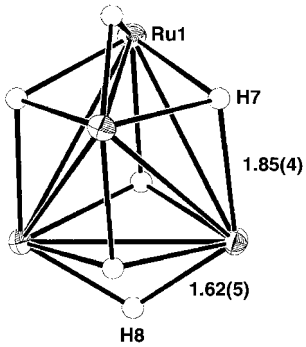



Figure 2. The $Ru_4H_6$ core of **4b**. $C_5H_4Me$ groups are omitted for clarity.

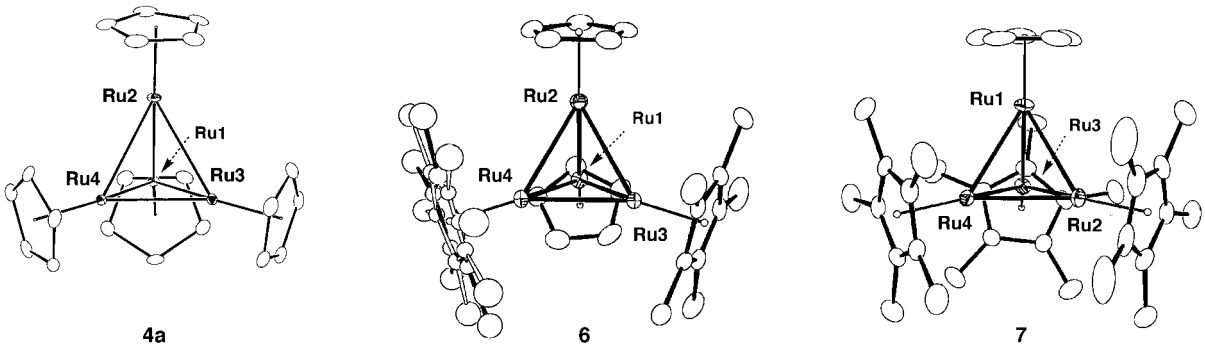



Figure 1. Molecular structures of **4a**, **6**, and **7**, with thermal ellipsoids at 30 % probability level.

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Ru–Ru bonds. Although the structural properties for **4a** are also common to the clusters **6** and **7**, the bond lengths of **6** and **7** are slightly elongated, probably due to the increased steric repulsion among the $C_5R_5$ (R = H or Me) ligands. The mean values of the distance between a ruthenium center and the centroid of the affiliated $\eta^5$-$C_5H_5$ (Cp) ring are in the order of **4a** > **6** > **7**. This result suggests that the increase in electron density at the metal centers arising from the introduction of methyl groups into the Cp ring enhances the back donation from the ruthenium center to the Cp group.

We have developed the first rational synthesis of a series of tetranuclear polyhydride complexes containing several different combinations of auxiliary cyclopentadienyl ligands and demonstrated that the electron density at the metal centers and the size of the reaction site of the tetranuclear cluster complex is most probably controllable by changing the number of methyl groups on the $C_5$ rings.

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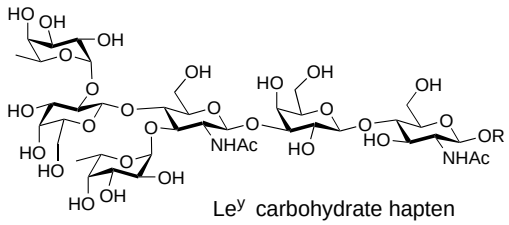
[13] X-ray structure analysis for **4a**: Measurement performed on a AFC-7R four-circle diffractometer equipped with graphite-monochromated $Mo_{K\alpha}$ radiation at −180 °C; crystal dats: triclinic, $P\bar{1}$, $a = 9.541(6)$, $b = 14.134(3)$, $c = 9.222(4)$ Å, $\alpha = 94.37$, $\beta = 104.64(4)$, $\gamma = 101.30(3)°$, $V = 1096.1(10)$ Å$^3$, $Z = 2$, $\rho_{calcd} = 2.172$ g cm$^{-1}$; 5346 unique reflections ($6° \le 2\theta \le 55°$), 4507 observed with $F > 3\sigma(F)$, 347 parameters; $R = 0.025$, $R_w = 0.034$. X-ray structure analysis for **4b**: Measurement performed on a RAXIS-2 imaging plate area detector at −50 °C; crystal data: tetragonal, $I\bar{4}$, $a = 12.6317(9)$, $c = 7.3590(3)$ Å, $V = 1174.2(1)$ Å$^3$, $Z = 2$, $\rho_{calcd} = 2.056$ g cm$^{-1}$; 724 reflections ($6° \le 2\theta \le 55°$), 701 observed with $F > 3\sigma(F)$, 70 parameters; $R = 0.017$, $R_w = 0.017$.X-ray structure analysis for **4c**: Measurement performed on an AFC-7R four-circle diffractometer at −100 °C; crystal data: monoclinic, $P2_1/n$, $a = 13.798(2)$, $b = 16.663(2)$, $c = 12.148(3)$ Å, $\beta = 98.60(1)°$, $V = 2761.6(7)$ Å$^3$, $Z = 4$, $\rho_{calcd} = 1.883$ g cm$^{-1}$; 6846 reflections ($6° \le 2\theta \le 55°$), 5606 observed with $F > 3\sigma(F)$, 422 parameters; $R = 0.022$, $R_w = 0.024$. X-ray structure analysis for **6**: Measurement performed on a RAXIS-2 imaging plate area detector at −80 °C; crystal data: monoclinic, $P2_1/n$, $a = 18.217(5)$, $b = 16.475(9)$, $c = 9.772(6)$ Å, $\beta = 90.87(3)°$, $V = 2932(3)$ Å$^3$, $Z = 4$, $\rho_{calcd} = 1.837$ g cm$^{-1}$; 8976 reflections ($6° \le 2\theta \le 55°$), 5691 observed with $F > 2\sigma(F)$, 282 parameters; $R_1 = 0.039$, $wR_2 = 0.108$. X-ray structure analysis for **7**: Measurement performed on an AFC-7R four-circle diffractometer at −80 °C; crystal data: monoclinic, $P2_1/a$, $a = 24.026(3)$, $b = 16.699(2)$, $c = 17.388(3)$ Å, $\beta = 90.37(1)°$, $V = 6955(1)$ Å$^3$, $Z = 8$, $\rho_{calcd} = 1.683$ g cm$^{-1}$; 16893 reflections ($5° \le 2\theta \le 60°$), 10387 observed with $F > 3\sigma(F)$, 703 parameters; $R = 0.039$, $R_w = 0.043$. CCDC-177793 (**4a**), CCDC-177794 (**4b**), CCDC-177795 (**4c**), CCDC-177796 (**6**), and CCDC-177797 (**7**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).


## Reactivity-Based One-Pot Synthesis of a Lewis Y Carbohydrate Hapten: A Colon–Rectal Cancer Antigen Determinant**

Kwok-Kong T. Mong and Chi-Huey Wong*

Lewis Y ($Le^y$) is part of a type 2 blood group antigen that carries a carbohydrate hapten containing two α-linked fucosyl moieties, one at the C-2 hydroxy group of the terminal galactose and the other at the C-3 hydroxy group of subterminal *N*-acetylglucosamine (Scheme 1).[1] As a tumor-related glycoconjugate, it is expressed on the tumor cell surface in 96% of colon–rectal adenocarcinoma and 46% of hepatocellular carcinoma.[2] Therefore, it is important to understand its pathological roles and to explore its antigenic properties to allow the development of cancer diagnostic and immunotherapeutic agents.[3] Recently, the $Le^y$ hapten has been synthesized by Danishefsky's group as part of a multiantigenic glycopeptide to exploit its potential as a carbohydrate-based anticancer vaccine.[4]




Scheme 1. The structure of a $Le^y$ carbohydrate hapten.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