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Unexpected Formation of a Cyclopentadienylruthenium Alkoxycarbonyl Complex with a Coordinated C=C Bond

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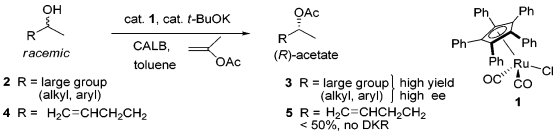
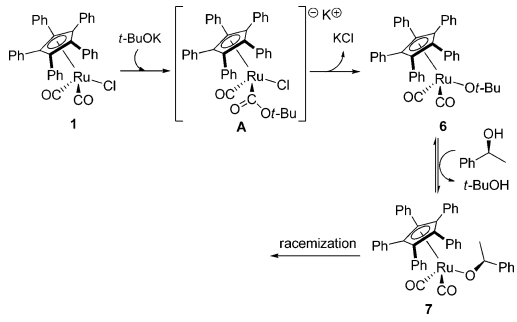
Ruthenium catalyst **1** has successfully been used in combination with lipases to convert racemic *sec*-alcohols **2** into enantiopure acetates **3** in high yields and excellent ee's via dynamic kinetic resolution (DKR) (Scheme 1).[1] In connection with our work on chiral diols,[2] one strategy involved DKR of 5-hexen-2-ol (**4**) followed by transformation of the double bond into a chlorohydrin and subsequent DKR of the chlorohydrin alcohol.[1c] However, DKR of olefinic alcohol **4** has not been successful to date because of very slow racemization, which suggests that the double bond may coordinate to ruthenium and inhibit racemization. In the present work, we have studied the reaction of Ru catalyst **1** with olefinic alcohol **4** by NMR spectroscopy and in situ FT-IR measurements and obtained evidence for the formation a novel (alkoxycarbonyl)Ru olefin complex.

Scheme 1. DKR of *sec*-Alcohols (CALB = *Candida antarctica* Lipase B)



Various ruthenium catalysts have been successfully employed in (transfer) hydrogenation and racemization.[3,4] We have previously studied the racemization mechanism of *sec*-alcohols by Ru catalyst **1**.[5] Complex **1** is activated by *t*-BuOK to give *tert*-butoxide complex **6**. We recently demonstrated that this ligand exchange takes place via assistance of coordinated CO with the formation of an acyl intermediate **A** (Scheme 2),[6] which undergoes rapid alkoxide migration from carbon to ruthenium at room temperature to give complete conversion to *tert*-butoxide complex **6** within a few minutes. Complex **6** subsequently undergoes an alcohol−alkoxide exchange to give a *sec*-alkoxide complex **7**. Racemization via β-hydride elimination requires a free coordination site, which could be formed by either $\eta^5 \rightarrow \eta^3$ ring slippage[5] or loss of CO.[7]

Scheme 2. Mechanism of the Racemization of *sec*-Alcohols by **1**



The reaction between alcohol **4** and complex **6** was first studied at room temperature. Complex **6** was mixed with **4** (1.1 equiv) in toluene-d_8 in an NMR tube. ^{1}H NMR analysis showed the disappearance of **6** and the formation of a 1:1 mixture of two diastereomers[8] that have the C=C bond coordinated to ruthenium. Initially, three possible structures, **8a**−**b** (only one CO), **9a**−**b** (η^3-Ph_5C_5), and **10a**−**b** (acyl compound) were considered (Figure 1). We argued that the olefin may coordinate to the open site on Ru required for β-hydride elimination, which would dramatically slow the racemization. For simplicity, the two diastereomers that are formed are herein designated as **a** and **b**.

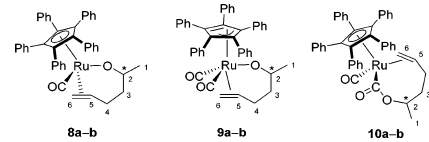


Figure 1. Possible structures of the two diastereomers having a coordinated double bond.

From the ^{1}H NMR spectrum, it is clear that the double bond is coordinated to ruthenium. The proton at the internal carbon of the double bond (H5) appears at 4.52 and 4.28 ppm for **a** and **b**, respectively. This corresponds to an upfield shift of 1.2−1.5 ppm relative to the corresponding proton of **4** (5.74 ppm) and can be compared to the 0.6 ppm upfield shift of the double-bond protons of *trans*-3-hexene upon coordination to ruthenium.[9] The terminal double bond protons (H6 and H6′) of both complexes appear as a multiplet at 2.22−2.37 ppm, which corresponds to an upfield shift of ∼2.6 ppm relative to the analogous protons of **4** (5.01 and 4.93 ppm). An upfield shift of similar magnitude upon coordination to ruthenium has previously been reported in the literature.[10] Also, the ^{13}C NMR (toluene-d_8) signals of the double-bond carbons are shifted upfield. The internal olefin carbon (C5) is shifted from 139.0 ppm (free alcohol) to 85.6 and 84.5 ppm for **b** and **a**, respectively. This is in agreement with the literature values for similar complexes.[9] The terminal carbon (C6) is shifted even further upfield, from 114.5 ppm (**4**) to 1.9 (**a**) and 19.4 (**b**) ppm.

The α-CH protons (H2) of the diastereomers **a** and **b** appear at 4.21 and 3.90 ppm, respectively, i.e., they are shifted ∼0.5 ppm downfield relative to the free alcohol (3.49 ppm).[11] This is similar to the downfield shift of the α-CH proton of the 1-phenylethoxide ligand of **7** (Scheme 2) and would seem to support structures **8** and **9** (Figure 1). However, a downfield shift for the α-CH protons is also expected for structures **10**. In addition, the ^{13}C NMR peaks of the α-carbon (C2) are shifted downfield from 67.1 ppm to 75.1 and 74.1 ppm for **b** and **a**, respectively.

Since $\eta^5 \rightarrow \eta^3$ ring slippage[1b,5] or loss of CO[7] is suggested in the racemization, we were eager to find out whether **a** and **b** had one or two CO groups remaining on Ru. The ^{13}C NMR spectrum showed three peaks in a 2:1:1 ratio between 203 and 204 ppm (Figure 2).

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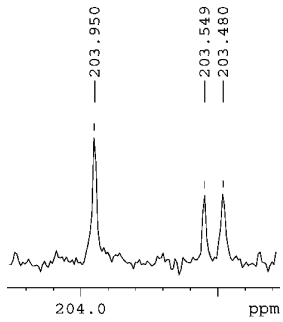


Figure 2. ^{13}C NMR spectrum of complexes **a** and **b** from the reaction between *tert*-butoxide complex **6** and olefin alcohol **4**.

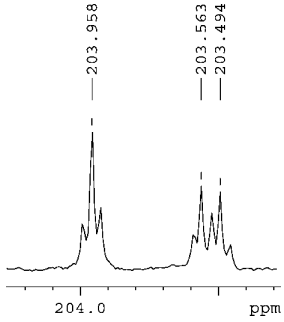


Figure 3. Carbonyl signals of ^{13}CO-labeled complexes **a** and **b** (55% ^{13}CO).

These results could be interpreted in different ways, but we were able to understand the appearance of the ^{13}C NMR spectrum when ^{13}CO-enriched *tert*-butoxide complex **6** (55% ^{13}C) was used in the reaction with olefinic alcohol **4**. The ^{13}C NMR spectrum shows a coupling ($J_{CC} \approx 8.2$ Hz) between the ^{13}CO groups. In addition to these doublets, singlets from the ^{13}CO groups having a neighboring ^{12}CO group were observed. Overall this made the signals look like triplets (Figure 3). The coupling between two CO groups indicates that the alkene complexes have two CO groups each. The signal at lower field (204.0 ppm) corresponds to two overlapping CO groups. The observation of two carbonyl groups in each of compounds **a** and **b** rules out structure **8** as a possible structure for the alkene complexes. Furthermore, no free CO could be detected at 184.7 ppm.[12]

This was further confirmed by 2D NMR spectroscopy. Thus, the HMBC spectrum[13] of the ^{13}C-labeled diastereomers **a** and **b** clearly showed cross-peaks between the olefin protons and two CO groups each (Figure 4).

Of the remaining structures for alkene complexes **a** and **b**, acyl compounds **10** are expected to be more stable than η^3-coordinated compounds **9** (Figure 1). The only argument against complexes **10**

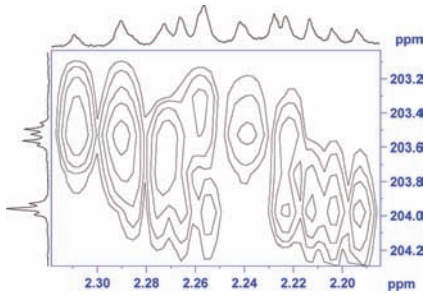


Figure 4. Cross-peaks in the HMBC spectrum additionally confirm that each of the diastereomers **a** and **b** must have two coordinated CO groups.

is that the acyl carbon is expected to shift further upfield than the peaks observed for **a** and **b**.[14] Since only one signal was detected in the ^{13}C NMR spectrum for the cyclopentadienyl carbons (at 108.0 ppm for both complexes), the ligand can be η^3-coordinated only if there is a fast equilibrium between the five carbons of the cyclopentadienyl ring. This would make these five carbons equivalent at room temperature. Therefore, we studied the diasteromeric complexes **a** and **b** at low temperature. At 0 °C, the peak at 108.0 ppm splits into two peaks in a 1:1 ratio. At lower temperatures, these peaks are further separated: e.g., at −55 °C they appear at 107.71 and 107.74 ppm, respectively, and at −78 °C they appear at 107.42 and 107.46 ppm, respectively. There is no significant change in the line width in the low-temperature ^{13}C NMR spectra, which rules out exchange at low temperature and makes the η^3-coordinated structures **9** unlikely. The observed data are therefore best explained by the two diastereomers **a** and **b** having η^5-coordinated cyclopentadienyl ligands, coincidently appearing at the same chemical shift at room temperature and separating at lower temperatures. Therefore, structures **10** seem to be the only possibility for alkene complexes **a** and **b**. The ^{13}C NMR shifts of the acyl carbon (203.48 and 203.55 ppm, respectively) are further downfield than those for similar compounds in the literature.[14] However, a similar unexpected downfield shift in the signal of the acyl carbon of complex **A** was recently observed.[6]

The reaction between olefinic alcohol **4** and *tert*-butoxide complex **6** was also studied by in situ FT-IR measurements. The reaction of **4** with complex **6** was slow and could not be followed to completion, since decomposition started after ∼1 h. One CO peak (1982 cm^{-1}) in the 1900−2100 cm^{-1} region was formed at the same rate at which the CO peaks of complex **6** (2021 and 1964 cm^{-1}) disappeared. In addition, it was possible to detect a peak in the region where acyl peaks commonly appear (1644 cm^{-1}) (Figure 5).[6,14a,b,15]

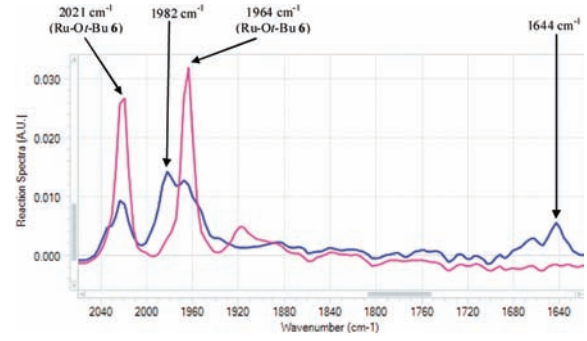


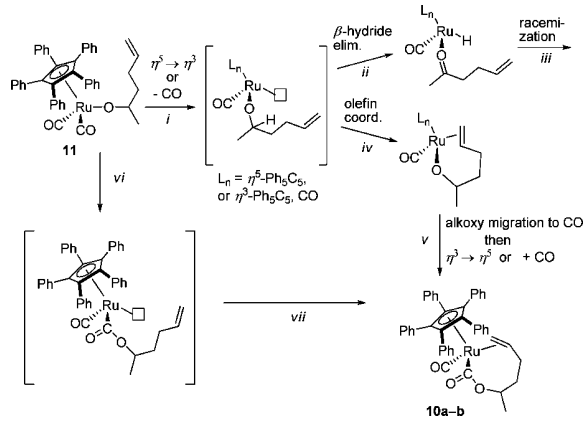
Figure 5. FT-IR spectra before (pink, $t = 0$ min) and after (blue, $t = 29$ min) the addition of 5-hexene-2-ol (**4**) to *tert*-butoxide complex **6**.

The peak at 1644 cm^{-1} was formed at the same rate as the CO peak at 1982 cm^{-1} (see the peak height analysis in Figure S4 in the Supporting Information), and this further supports the assignment of the diasteromeric complexes **a** and **b** as alkoxycarbonyl complexes **10a**−**b** (Figure 1).

Possible pathways for the formation of alkoxycarbonyl complexes **10a**−**b** are given in Scheme 3. The first step would be an alcohol−alkoxide exchange similar to that depicted in Scheme 2, which would produce alkoxide complex **11**. Racemization of *sec*-alcohols via alkoxide complexes has been proposed to proceed via β-hydride elimination, which requires the formation of a free coordination site on ruthenium.[16] This could be provided by either $\eta^5 \rightarrow \eta^3$ ring slippage[5] or dissociation of a CO ligand[7] (Scheme 3, step *i*). Two competing reactions may fill this free coordination site: in addition to β-hydride elimination (step *ii*), which would

lead to racemization of the alcohol (step *iii*), the double bond can coordinate to ruthenium (step *iv*). Complexes **10a**−**b** would then be formed via migration of the alkoxy moiety to the CO ligand (migratory insertion, step *v*), which would explain the easy formation of the large ring (**10a**−**b**).[17] An alternative pathway for formation of **10a**−**b** would be migration of the alkoxy group to CO in **11** (step *vi*) followed by coordination of the double bond (step *vii*).

Scheme 3. Possible Routes for the Formation of **10a**−**b**



The rate of racemization would be slow because ruthenium is held as inactive **10a**−**b**. In Scheme 3 we have assumed that the racemization occurs via β-hydride elimination. However, other racemization mechanisms are also possible, such as those involving CO participation.[16] In these alternative mechanisms, the rate of racemization would also be slowed by the formation of **10a**−**b**.

In conclusion, we have used ^{1}H and ^{13}C NMR spectroscopy and in situ FT-IR measurements to characterize two diastereomers (**10a** and **10b**)[18] of an alkoxycarbonyl complex having a double bond coordinated to ruthenium. IR peaks were observed at 1982 cm^{-1} (CO) and 1644 (acyl) cm^{-1}. These studies have provided further insight into the mechanism of the highly efficient racemization catalyst **1**.

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Supporting Information Available: Experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) Only two of the four possible diastereoisomers were observed [there are three stereogenic centers: the ruthenium, the α-carbon of the alcohol (C2), and one of the coordinated carbons of the alkene (C5)].

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(11) The assignments of the protons were made by conventional 2D NMR experiments (see the Supporting Information for further details).

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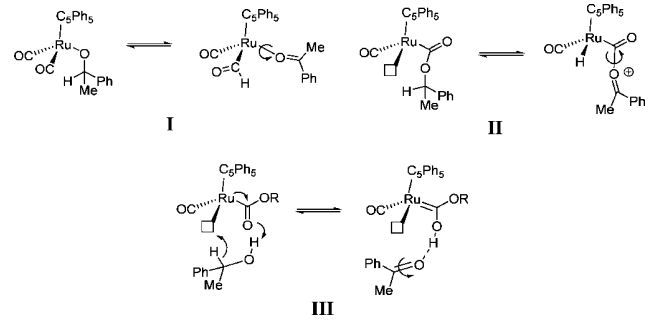
(16) Other mechanisms for racemization are also possible. These include a formyl intermediate (**I**), an acyloxy intermediate (**II**), and a hydroxyl carbene intermediate (**III**):



(17) The easy formation of a seven-membered ring from a six-membered ring via 1,2-migration is known in a number of rearrangements, e.g., the Beckman rearrangement and the Baeyer−Villiger oxidation.

(18) Only two of the four possible diatereomers were observed. Density functional theory calculations indicate that the change in the configuration at C5 relative to the configuration at Ru leads a significant energy change. This means that for a given Ru configuration, it is energetically favorable to coordinate one face of the alkene, whereas coordination of the other face is very unfavored. The two diastereoisomers observed must therefore have the same or opposite absolute configuration at C2 and C5 (2*R*,5*R*−2*S*,5*S*, or 2*R*,5*S*−2*S*,5*R*) (Nyhlén, J., unpublished results).

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