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CO Assistance in Ligand Exchange of a Ruthenium Racemization Catalyst: Identification of an Acyl Intermediate

Jenny B. Åberg, Jonas Nyhlén, Belén Martín-Matute, Timofei Privalov, and Jan-E. Bäckvall*

Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, SE-106 91 Stockholm, Sweden

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Mechanistic studies of hydrogen transfer reactions with ruthenium catalysts have recently attracted considerable interest,[1] and these catalysts have found extensive applications in hydrogenations, dehydrogenations, and racemizations.[1a,2] For example, cyclopentadienylruthenium catalysts **1**−**4** have successfully been employed as racemization catalysts in dynamic kinetic resolution (DKR) of *sec*-alcohols (Figure 1).[3] The racemization catalyst is used in combination with an enzyme and an acyl donor to afford enantiopure acetates in high yields.

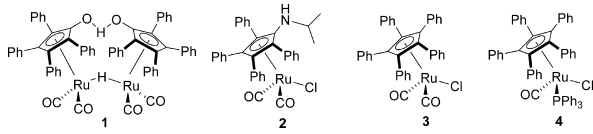
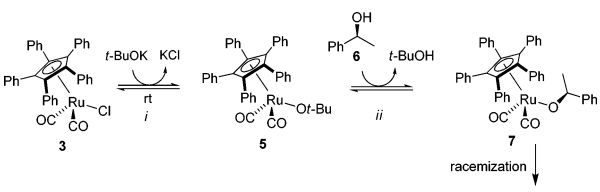


Figure 1. Ruthenium catalysts employed in dynamic kinetic resolution.

Ruthenium catalyst **3** is very efficient in racemizing *sec*-alcohols via fast DKR reactions at room temperature,[3a,b] and we have previously studied the racemization mechanism for this catalyst.[3b,4] Complex **3** is activated by *t*-BuOK to give ruthenium *tert*-butoxide complex **5** (Scheme 1, step *i*). In the subsequent alcohol−alkoxide exchange, *sec*-alkoxide complex **7** is formed (Scheme 1, step *ii*). Racemization via β-hydride elimination requires a free coordination site, and this could be formed by either $\eta^5 \rightarrow \eta^3$ ring slippage[4] or loss of a carbon monoxide ligand.[5] *tert*-Butoxide complex **5** and *sec*-alkoxide complex **7** were characterized by ^{1}H and ^{13}C NMR spectroscopy.[3a,4] In addition, we showed that the ketone formed from the β-hydride elimination is coordinated to ruthenium throughout the racemization cycle and that the hydride $(Ph_5Cp)Ru(CO)_2H$ is not an active catalytic intermediate.[3b,4]

An interesting question is how the catalyst is activated and how the ligand exchange takes place.[4] Recent computational studies in our group suggested that the ligand exchange takes place via participation of a CO ligand, leading to an acyl intermediate.[5] In the present communication, we provide experimental evidence for such an acyl intermediate by in situ FT-IR measurements and NMR spectroscopy.

Scheme 1. Proposed Mechanism of Racemization of *sec*-Alcohols by Ruthenium Catalyst **3**



Reaction of ruthenium chloride **3** with *t*-BuOK at room temperature resulted in a color change from yellow to orange-red. In situ FT-IR monitoring showed the immediate disappearance of the two CO bands of **3** at 2049 and 2001 cm^{-1} (symmetric and asymmetric stretch, respectively) with the concomitant appearance of a new peak at 1933 cm^{-1} (Figure 2). After ∼1 min, the two CO bands of the *tert*-butoxide complex **5**[6] began to appear, and the intensity of the peak at 1933 cm^{-1} decreased and disappeared in another 1−2 min. The single peak at 1933 cm^{-1} indicates that there is only one CO ligand in the intermediate. The new intermediate (1933 cm^{-1}) was assigned as acyl intermediate **A**.[7]

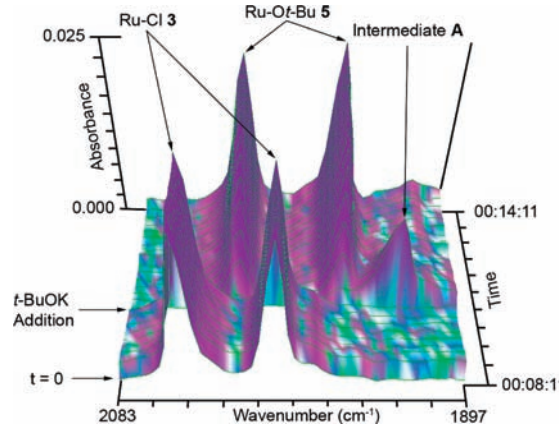


Figure 2. Surface view of in situ FT-IR measurements at room temperature, showing the peak for acyl intermediate **A**.

Acyl intermediate **A** has a lifetime of <3 min at room temperature, and in addition to the IR band at 1933 cm^{-1} (CO), there is another band at 1596 cm^{-1} (acyl). The acyl peak could be detected only under very dry conditions,[8] and it correlates well with similar structures in the literature.[9] The shift toward lower wavenumber of the remaining CO ligand (1933 cm^{-1} vs 2049 and 2001 cm^{-1}) is consistent with its anionic structure.[9a] The ruthenium center is more electron-rich, and the stronger back-donation from the metal makes the C═O bond weaker. At lower temperatures, intermediate **A** was still formed very rapidly but was stable for a longer time: at −70 °C, intermediate **A** was formed within 3 min and was stable for more than 3 h, while at −55 °C, it was formed within 2 min and was stable for at least 3 h (Figure S2 in the Supporting Information).

As soon as the temperature was increased to room temperature, *tert*-butoxide complex **5** was formed. The transformation into **5** occurred slowly at −20 °C ($t_{1/2} \approx 100$ min) and more rapidly at 0 °C ($t_{1/2} = 26$ min).

We also studied intermediate **A** by ^{1}H and ^{13}C NMR spectroscopy. In our previous NMR studies of alkoxides **5** and **7**, intermediate **A** was not observed.[3a,4] This is not surprising, since catalyst **3** and *t*-BuOK were mixed at room temperature before they were put into the NMR spectrometer, and the lifetime of **3** at this temperature is <3 min. One problem with studying this reaction

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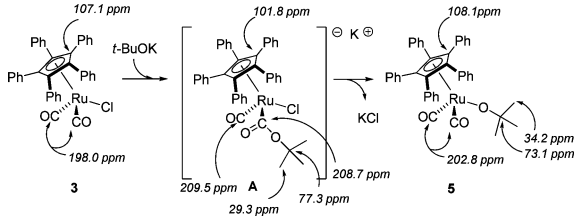
by NMR spectroscopy is the poor solubility of ruthenium chloride **3** in toluene and the high viscosity of toluene at low temperature. Sample preparation was performed by quick transfer of a −78 °C preformed solution of the intermediate to an NMR tube via a cannula. The sample was then frozen (−196 °C) and quickly transferred to the precooled probe of the NMR spectrometer. The low solubility and therefore low concentration made it difficult to run ^{13}C NMR experiments, since it was not possible to get a reasonable signal-to-noise ratio for the carbonyl peaks. This problem was solved by employing ^{13}CO-labeled catalyst **3** (for its preparation, see the Supporting Information). With the ^{13}CO-enriched ruthenium chloride **3**, it was possible to monitor the reaction by ^{13}C NMR at low temperature. Acyl intermediate **A** was studied and characterized at −32 °C (Scheme 2).

Scheme 2. Detection of Acyl Intermediate **A** by ^{13}C NMR in Toluene-d_8 at −32 °C



Acyl intermediate **A** has CO peaks at 209.5 (CO) and 208.7 ppm (acyl).[10] The peak of the CO ligand is shifted downfield. This is comparable to the chemical shifts reported for other anionic complexes (e.g. 208.1 ppm for $[PPN]^+[Ru_3(CO)_{11}(CO_2CH_3)]^-$ (**8**) in THF-d_8).[11] The acyl peak of **A** appears at an unusually high chemical shift compared with those of similar structures in the literature.[9b,d,11] For example, the acyl peak of **8** appears at 189 ppm, and the neutral cyclopentadienylruthenium complexes [Cp*Ru(CO)$_2$(COOMe)] and [Cp^Ru(COOMe)(CO)$_2$][12] also have acyl peaks in this region [191.3 ppm (C_6D_6)[9d] and 193.7 ppm (CD_2Cl_2),[9b] respectively]. However, none of these structures has a chloride bound to ruthenium. We estimated the ^{13}C NMR shifts of intermediate **A** using density functional theory (DFT) calculations and found that they are in agreement with the expected values for this structure.[13] When the temperature was raised to 0 °C, the peaks at 209.5 and 208.7 ppm for intermediate **A** slowly disappeared, and the peak at 202.8 ppm for the CO groups of *tert*-butoxide complex **5** appeared. At room temperature, this transformation was rapid.

In addition, we studied the alcohol−alkoxide exchange (Scheme 1, step *ii*), which also should occur via CO assistance.[5] However, no acyl intermediate similar to **A** has been detected to date by in situ FT-IR measurements at room temperature and below (Figure S1). At room temperature, the alcohol−alkoxide exchange was very rapid (<1 min), but at −78 °C the *tert*-butoxide ligand of complex **5** was not exchanged by phenylethanol for at least 1 h. However, at −50 °C, the reaction slowly took place ($t_{1/2}$ = 15 min) and the CO peaks of *sec*-alkoxide complex **7** at 2026 and 1971 cm^{-1} (symmetric and asymmetric stretch, respectively) appeared. The rate of disappearance of *tert*-butoxide complex **5** was the same as the rate of formation of *sec*-alkoxide complex **7**, and the reaction was complete within 2.5 h. The ruthenium concentration in this experiment was 12 mM, which is ∼5 times lower than in our previous NMR studies of the alkoxide exchange,[4] and therefore, the reaction was slower here than in the previous experiments. The failure to detect an intermediate in the alcohol−alkoxide exchange is in accordance with the low computed barrier of activation for this reaction via CO participation (12 kcal/mol).[5,14]

In conclusion, we have provided experimental evidence for CO ligand participation in the exchange of chloride for *tert*-butoxide in η^5-(Ph$_5$Cp)Ru(CO)$_2$Cl (**3**). An acyl intermediate, **A**, was observed by in situ FT-IR measurements and low-temperature NMR spectroscopy prior to formation of *tert*-butoxide complex **5**. This shows how high-energy intermediates (produced via ring slip or dissociation) can be avoided in ligand exchange[15] and that this may be common in complexes bearing CO ligands.

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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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(6) The CO bands of **5** appear at 2021 and 1964 cm^{-1}. For experimental details, see the Supporting Information.
(7) The reaction mixture containing intermediate **A** also showed characteristic peaks in the area of C−O stretching vibrations (*t*-BuO). However, the mixture possibly contained *t*-BuOH (and *t*-BuOK), and the peaks in this area were not easy to assign.
(8) H_2O vapor in the system absorbed in the region of 1600 cm^{-1}, and a background spectrum was automatically subtracted from the collected data. If the amount of H_2O vapor was not constant (which it seldom is), a peak in this region might not be visible. Indeed, in our first experiments, the system contained so much humidity that a lot of noise in this region made it difficult to detect the acyl peak.
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(10) The shifts were too close to allow a definite assignment, and they may be reversed (DFT calculations indicated that $\delta_{CO} > \delta_{acyl}$; see note 13). Even if the shifts are reversed, the structural conclusions remain the same.
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(12) Cp* = Me$_5$Cp; Cp^ = 1-MeO-2,3,4-tris(neopentyl)Cp.
(13) The estimated ^{13}C NMR shifts were 205.3 (acyl) and 211.4 ppm (CO). For experimental details, see the Supporting Information.
(14) The computed barrier for the corresponding exchange of chloride for *tert*-butoxide in **3** is 16.7 kcal/mol (see ref 5).
(15) For a discussion of avoiding high-energy pathways in ligand exchange, see: Casey, C. P.; Vosejpka, P. C.; Underiner, T. L.; Slough, G. A.; Gavney, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 6680.

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