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# Nucleophilic Isomerization of Epoxides by Pincer-Rhodium Catalysts: Activity Increase and Mechanistic Insights

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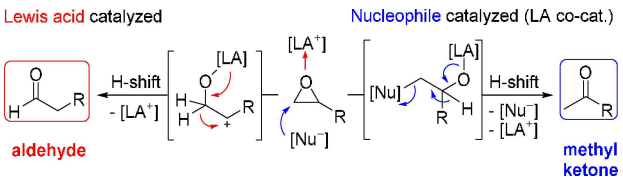
Herein, we present the efficient isomerization of epoxides into methyl ketones with a novel pincer-rhodium complex under very mild conditions. The catalyst system has an excellent functional group tolerance and a wide array of epoxides was tested. The corresponding methyl ketones were obtained in very high yields with excellent chemo- and regioselectivity. In addition, we investigated mechanistic details like the isomerization of the catalyst, and we obtained evidence that the catalytic cycle follows a β-hydride elimination-reductive elimination pathway after the nucleophilic ring opening of the epoxide.

## Introduction

In contrast to the common Lewis acid catalyzed isomerization of terminal epoxides (Meinwald reaction),[1] which leads to the formation of aldehydes via generation of the more stable carbenium intermediate,[2] the isomerization by nucleophilic catalysts is rare and results in the formation of methyl ketones (Scheme 1).[3] This pathway is very attractive because, in combination with the Corey-Chaykovsky reaction, it provides an oxidation-free route for the synthesis of methyl ketones from aldehydes or, together with the epoxidation of olefins, an alternative to the Wacker oxidation. Since the discovery of this opposite regioselectivity in 1962 by Eisenmann,[3a] it was evident that the catalysis is not only achieved by a nucleophilic catalyst on its own, but typically requires a Lewis acid co-catalyst [LA$^+$] which pre-activates the epoxide by coordination, but does not lead to ring opening under carbocation formation.

In case of the results of Eisenmann, the catalytic system **A** (Figure 1) most likely consists of the $[Co(CO)_4]^-$ nucleophile and the Lewis acid $[Co(CH_3OH)_6]^{2+}$ formed *in situ* by disproportionation of $[Co_2(CO)_8]$ in methanol that is required as a solvent. In 2015 we have reported on a selective ring opening using the nucleophilic Rh-catalyst **B** (5 mol%) along with 20 mol% of the Lewis acid co-catalyst $LiNTf_2$ at 60 °C.[3h] A more active system was reported by Coates using [Al(salen)][Co(CO)$_4$].[3i] While both systems were highly selective with terminal alkyl epoxides, the isomerization of phenyl oxirane led to a mixture of the aldehyde and the ketone in almost equal amounts. This prompted us to develop the more nucleophilic CO-free rhodium catalyst **D**, in which the highly reactive metal center is intramolecularly stabilized by coordination of both *N*-homoallyl substituents of the so-called bimca$^{Homo}$ (1,8-bis(imidazolin-2-ylidene)-3,6-di(*tert*-butyl)carbazolide) carbene-pincer-ligand.[3j] Due to its higher nucleophilicity, a mixture of the weak Lewis acids LiBr and LiCl (2:1), which are present from the synthesis of **D** in THF, is sufficient to act as a co-catalyst in benzene. With




**Scheme 1.** Lewis acid- (left) and nucleophile- (right) catalysed Meinwald reaction of terminal epoxides: formation of aldehydes versus methyl ketones.

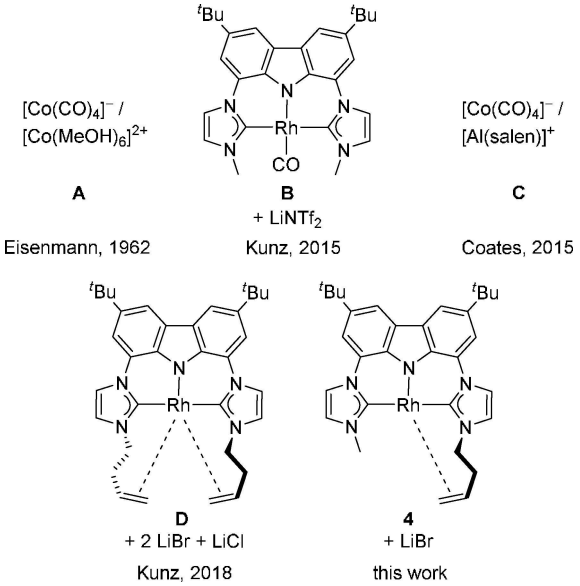



**Figure 1.** Rhodium pincer complexes and suitable Lewis acid co-catalysts for the nucleophilic Meinwald rearrangement.

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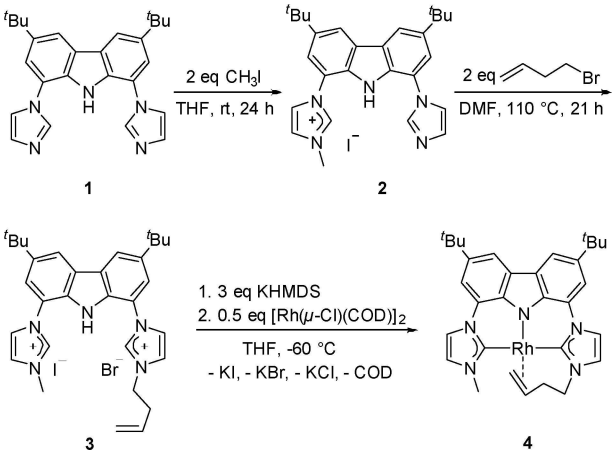
this system it was not only possible to achieve a selectivity of methyl ketone vs. aldehyde of 40:1 and 95% yield in the isomerization of phenyl oxirane after 2 h at room temperature (5 mol% **D**), but also to isomerize the highly sensitive *p*-methoxyphenyl oxirane to the corresponding ketone with a ratio of 10:1 and in 57% yield.

The functional group tolerance of catalyst **D** is very high, but sterically demanding substrates such as *tert*-butyloxirane, $-NH_2$, or –OH containing substrates, some *ortho*-substituted aryl oxiranes or internal epoxides required very long reaction times and/or elevated temperatures, which in some cases still led to low yields. Therefore, we were interested in developing our catalyst system further along with gaining more insight into the reaction mechanism.

As the 18 $e^-$ rhodium complex **D** requires the dissociation of one olefin moiety to react as a nucleophile, we envisaged the 16 $e^-$ complex **4** being an interesting target to fulfill our purpose: The complex would still be stabilized intramolecularly by one olefin moiety during catalysis but in addition exhibit a higher nucleophilicity and thus catalytic activity. However, an unsymmetrically *N*-substituted bimca ligand or related systems have hitherto not yet been reported. In the following, we will report on the synthesis of the unsymmetrical bimca ligand **bimca$^{Me,Homo}$** and its Rh complex **4** as well as the catalytic activity of **4** in the regioselective epoxide isomerization. In addition, more insight into the reaction mechanism and deactivation pathways will be provided.

## Results and Discussion

The synthesis of an unsymmetrically substituted bimca ligand requires the selective monoalkylation of bisimidazol **1**. Based on the observation that the monoalkylated product **2** was formed as a byproduct when reacting bisimidazol **1** with an excess methyl iodide in THF,[4] we investigated the monoalkylation further. In acetonitrile the reaction of equimolar amounts of bisimidazol **1** and methyl iodide or Meerwein's salt ($Me_3OBF_4$) leads to a 1:1 mixture of the dialkylated product and the starting material **1**. However, if the reaction is carried out with even a twofold excess of methyl iodide in THF at room temperature the desired product **2** is formed due to its precipitation under these conditions, which prevents further alkylation (Scheme 2). After workup by filtration, the imidazolium salt **2** was obtained in 90% yield as a yellow solid. The reduced symmetry leads to four signals for the carbazole moiety and six signals for the imidazolium moieties. The presence of only one NH signal with the same integral as the other aromatic peaks excludes a potential 1:1 mixture of **1** and the dimethylated product. The introduction of the *N*-homoallyl substituent was carried out with a twofold excess of 4-bromo-1-butene at 110 °C in dimethylformamide and the desired bisimidazolium salt **3** was isolated after workup in 95% yield. The 10 signals for the aromatic imidazolium and carbazole protons can be clearly assigned with the help of 2D NMR experiments including an NOE experiment to assign the peaks to the relative sides of the carbazole backbone.




**Scheme 2.** Synthesis of the unsymmetrical rhodium catalyst **4**.

The preparation of **4$^{LiX}$** was achieved by deprotonation of **3** with LiHMDS and subsequent addition of $[Rh(\mu\text{-Cl})(COD)]_2$. However, the generated COD and HMDS during the reaction cannot be removed *in vacuo* without decomposition of the complex, possibly due to the presence of the lithium salts. To obtain the pure complex **4**, we transmetalated the ligand from the potassium complex [K(bimca$^{Me,Homo}$)] generated *in situ* by deprotonation of **3** with KHMDS. The potassium halides formed could be readily removed by filtration and complex **4** isolated by removal of all volatiles *in vacuo*.

The structure of complex **4** could be identified by NMR experiments. Bonding of the terminal double bond to the rhodium centre is proven by the $^1J_{RhC}$ coupling constants of 13.2 Hz (C16) and 13.7 Hz (C17) in the $^{13}C$ NMR spectrum and the 4 signals for the diastereotopic hydrogen atoms at the two methylene groups of the homoallyl substituent. The *cis*/*trans* assignment of the olefinic signals at 3.50 ppm ($^3J = 7.7$ Hz, H-$17_{cis}$) and 2.94 ppm ($^3J = 11.5$ Hz, H-$17_{trans}$) is based on the vicinal coupling constants, which are smaller than those typically observed in non-coordinated olefins (e.g. in compound **3**: $^3J_{HH} =$ 17.2 Hz (*trans*) and 10.3 Hz (*cis*)), and can be explained with the lower s-character due to a rehybridization upon coordination of the metal ion. The relative assignment of axial and equatorial methylene signals is based on the Karplus equation. Finally, information on the relative conformation of the metallacycle were obtained with an NOE experiment, which confirmed the aforementioned assignments. Out of several minimum conformations of similar energy obtained by DFT-calculations, the NOE data is in accordance with the structure that is second lowest in energy ($\Delta = 1.5$ kJ/mol; Figure 2 and Supporting Information).

With the new rhodium complex **4** in hand, we were able to investigate the isomerization of phenyl oxirane (**5a**) as the model substrate. To our satisfaction, an initial test using 5 mol% of complex **4** together with 10 mol% LiBr (pre-activated with 5 $\mu$L THF-$d_8$) in $C_6D_6$ revealed full conversion at room temperature in a short time and demonstrated that the catalyst was more active than the previous catalyst **D** (Table 1, entry 1).

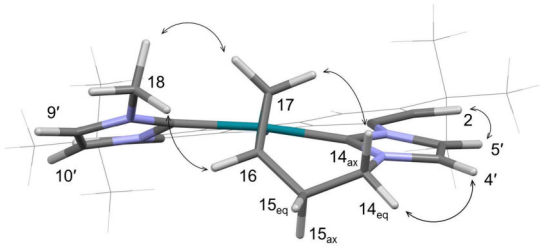
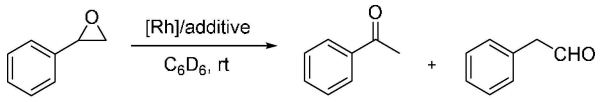



**Figure 2.** Minimum conformation of complex **4** based on DFT-D3 calculations (Turbomole: BP86/def2-TZVP) and observed NOE cross peaks (indicated with arrows). For clarity reasons, part of the carbazole backbone is depicted in wireframe style.

**Table 1.** Optimization of the reaction conditions for the isomerization of phenyl oxirane in presence of rhodium catalyst **4**.[a]




**5a** **6a** **7a**

| Entry | Catalyst [mol %] | Conc.**5a** [mol/L] | *t* | Yield [%][b] | Ratio (**6a**:**7a**) |
|---|---|---|---|---|---|
| 1 | 5 | 0.1 | 40 min | 84 | >99:1 |
| 2 | 3 | 0.1 | 70 min | 89 | >99:1 |
| 3 | 1 | 0.1 | 120 min | >99 | >99:1 |
| 4[c] | 1 | 0.1 | 24 h | 7 | 5:1 |
| 5[d] | 1 | 0.1 | 24 h | 6 | 10:1 |
| 6 | 1 | 0.2 | 60 min | 99 | >99:1 |
| 7 | 1 | 0.4 | 50 min | 95 | >99:1 |
| 8 | 1 | 0.8 | 40 min | 92 | >99:1 |
| 9 | – | 0.8 | 60 min | <5 | – |

[a] Carried out in *J. Young* NMR tubes and with 10 mol% LiBr and 5 $\mu$L THF-$d_8$. [b] Yield ($^1$H NMR) of **6a** calibrated to 1,3,5-trimethoxybenzene (internal standard). [c] Without LiBr. [d] THF-$d_8$ as the solvent.

Encouraged by this result, we tried to reduce the catalyst loading: 1 mol% of the catalyst was sufficient for a fast and quantitative rearrangement without influencing the excellent regioselectivity (Table 1, entries 2 and 3). To test whether lithium bromide was still necessary as a co-catalyst we applied the isolated catalyst **4** without adding any Lewis acids. The catalytic activity was reduced dramatically under these conditions (Table 1, entry 4). This indicates that a Lewis acid is essential for the pre-activation of the substrates. Low conversion was also obtained using THF-$d_8$ as the solvent which most likely stems from competitive binding between THF and the substrate to the Lewis acid co-catalyst (Table 1, entry 5). Afterward, the concentration of phenyl oxirane was studied. Epoxide concentrations of 0.2 mol/L (Table 1, entry 6) shortened the reaction time substantially and the reaction was 10 times faster compared to catalyst **D**. Further increase of the concentration led to a reduced reaction time whereas the yields decreased slightly (Table 1, entries 7 and 8). In addition, the need for catalyst **4** was also tested. Without rhodium catalyst **4** the yield remained below 5% (Table 1, entry 9). Thus, the optimized reaction conditions (1 mol% catalyst **4**, 0.2 M epoxide, $C_6D_6$, room temperature) were applied to investigate the generality of this protocol.

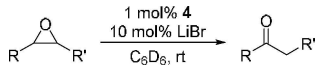
Using complex **4** as the catalyst, various functionalized epoxides were converted successfully into the desired methyl ketones (Table 2). Phenyl oxirane (**5a**) and aryl oxirane **5b** bearing the strong electron-withdrawing trifluoromethyl substituent were transformed regioselectively in excellent yield. To our delight, epoxides **5c** and **5d** possessing electron-donating groups (methyl or methoxy) were converted into **6c** and **6d** with still very good regioselectivities of 50:1 and 22:1 favoring the methyl ketones (**6c**, **6d**) over the aldehydes (**7c**, **7d**) in good to moderate yields. Even the *ortho*-substituted methyl ketone **6e** was obtained from **5e** in high yield and with excellent regioselectivity. Besides aryl ketones, epoxides bearing NH or OH groups like sulfonamide (**5f**) and hydroxyl groups (**5g**) were rearranged to the desired methyl ketones with 1 mol% catalyst loading in 83% (**6f**) and 90% (**6g**) yield, albeit at longer reaction time (24 h). The high nucleophilicity of complex **4** is also compatible with an ester group. The isomerization of epoxide **5h** afforded **6h** in moderate yield after 24 h at 60 °C and 5 mol% catalyst loading. As the extended reaction times may derive from competing coordination of LiBr at the Lewis basic centers of functional groups, we have increased the amount of LiBr to 50 mol% and achieved full conversion already after 1 h reaction time at moderate to excellent yield (entries 6–8) at room temperature. In the case of **5g**, the moderate yield resulted from unknown side products which will be studied further. Furthermore, the sterically demanding 2-(*tert*-butyl) oxirane (**5i**) can be also converted to the desired product **6i**, albeit with higher catalyst loading (5 mol%) and reaction temperature.

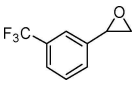
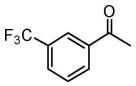
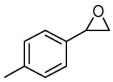
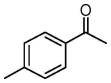
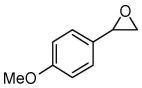
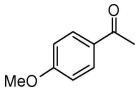
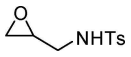
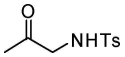
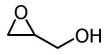
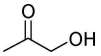
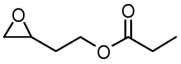
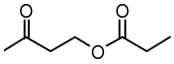
The internal epoxides **5j–l** react considerably faster compared with rhodium catalyst **D**. At 80 °C, 7-oxabicyclo[4.1.0] heptane (**5j**) was isomerized into cyclohexanone in almost quantitative yield. Furthermore, *cis*-2,3-epoxybutane (**5k**) was also compatible with the catalyst system and yielded 99% butan-2-one. In contrast, the conversion of *trans*-2,3-epoxybutane (**5l**) under otherwise identical conditions yielded only 7% of butan-2-one. This outcome is of considerable interest as it is contrary to the results from Coates and coworkers, who obtained less than 40% conversion with *cis*-2-hexene oxide but 98% yield with *trans*-2-hexene oxide applying $[(salcy)Al(THF)_2]^+$ $[Co(CO)_4]^-$ as the catalyst.[5]

**Mechanistic considerations**. When we tried to isolate catalyst **4** by chromatography at silica gel under argon, we isolated the isomerized complex **8** (Figure 3, top) as indicated by the characteristic substitution pattern in the NMR spectra. The signal at 1.17 ppm with an integral of 3H shows a $^3J$ (6.3 Hz) and a $^4J$ coupling to the olefinic signals at 4.56 (H-15) and 4.09 ppm (H-16). The *cis*-conformation of the double bond is not only confirmed by the $^3J$ coupling constant of 6.3 Hz, but also by the NOE between methyl signal H-17 and the signal H-14b of the methylene group. In addition, an NOE cross-peak is observed between the signals of both olefinic protons and the *N*-methyl signal. The assignment of the peaks of the imidazole moieties and carbazole backbone are based on the observed NOE cross peaks (Figure 3, bottom).

Complex **8** is of importance as it is also formed under the conditions applied for the catalysis. While the *in situ* prepared

**Table 2.** Substrate scope in the isomerization of epoxide catalysed by rhodium complex **4**.[a]




| Entry | Substrate | Product | *t* | Yield [%][b] | Ratio (**6**:**7**) |
|---|---|---|---|---|---|
| 1 | **5a**  | **6a**  | 1 h | 99 | >99:1 |
| 2 | **5b**  | **6b**  | 1 h | 98 | >99:1 |
| 3 | **5c**  | **6c**  | 1 h | 77 | 50:1 |
| 4 | **5d**  | **6d**  | 1 h | 42 | 22:1 |
| 5 | **5e**  | **6e**  | 24 h | 92 | 33:1 |
| 6 | **5f**  | **6f**  | 24 h<br>1 h | 83<br>94[e,g] | – |
| 7 | **5g**  | **6g**  | 24 h<br>1 h | 90<br>42[e,g] | – |
| 8 | **5h**  | **6h**  | 24 h<br>1 h | 67[c,e]<br>80[e,g] | – |
| 9[d–f] | **5i**  | **6i**  | 24 h | 99 | – |
| 10[d–f] | **5j**  | **6j**  | 24 h | 99 | – |
| 11[d–f] | **5k**  | **6k**  | 24 h | 99 | – |
| 12[d–f] | **5l**  | **6k**  | 24 h | 7 | – |

[a] Carried out in *J. Young* NMR tubes and with 10 mol% LiBr and 5 $\mu$L THF-$d_8$, 0.2 M concentration of epoxides. [b] Yield ($^1$H NMR) of **6a** calibrated to 1,3,5-trimethoxybenzene (internal standard). [c] At 60 °C. [d] 20 mol% $LiNTf_2$ instead of LiBr. [e] 5 mol% catalyst **4**. [f] At 80 °C. [g] 50 mol% LiBr.

complex $\mathbf{4}^{LiX}$ is stable in THF-$d_8$, isomerization takes place within one hour at room temperature when 2 eq of LiBr are added to a solution of the isolated complex **4** in benzene-$d_6$ without the presence of any amount of epoxide. Obviously, the Lewis acidity of the lithium cation in benzene is enhanced to such an extent that the isomerization of the double bond can occur.

To prove that complex **8** is an active catalyst itself, we have carried out the Meinwald reaction of phenyl oxirane with the isolated complex **8** under the general conditions (1 mol% **8**, 10 mol% LiBr, 5 $\mu$L THF-$d_8$, room temperature). The reaction rate is comparable to that when starting from complex **4**. We assume that the isomerization of complex **4** to **8** as well as the Meinwald reaction of phenyl oxirane catalyzed by complex **4** or **8** occurs at comparable reaction rates. Isomerizations of the double bond can also be observed using catalyst **D**. However, due to the two *N*-homoallyl moieties, mixtures are obtained, and the NMR spectra become very complex.

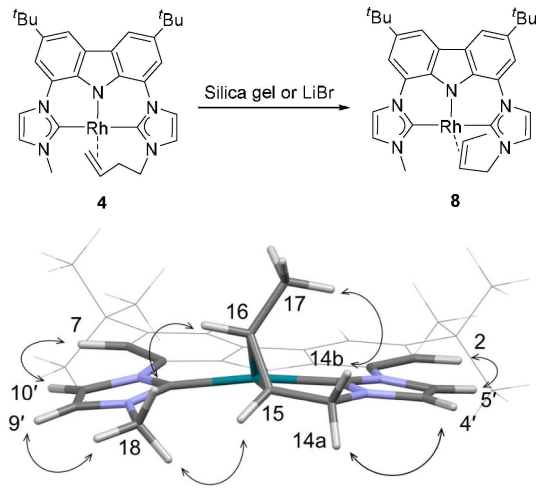
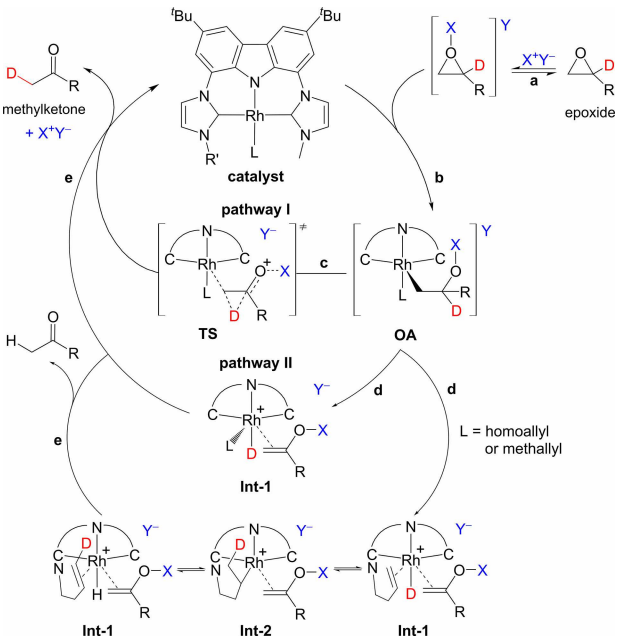
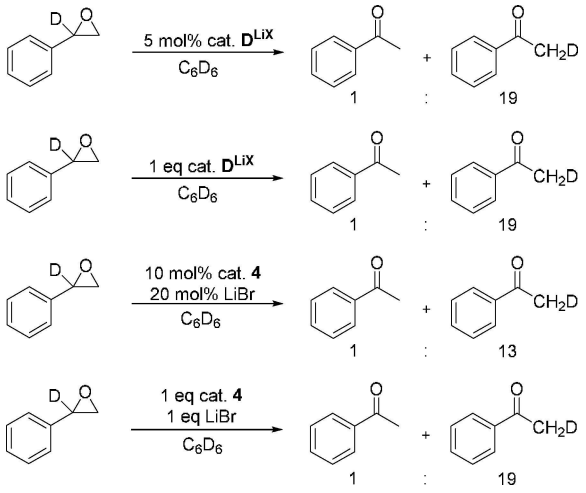



**Figure 3.** Top: Isomerization of the terminal double bond of complex **4** to an internal *cis*-double bond in complex **8** by Lewis acids. Bottom: Minimum conformation of the isomerized complex **8** based on DFT calculations (Turbomole: BP86/def2-TZVP) and observed NOE cross peaks (indicated with arrows). For clarity reasons, part of the carbazole moiety is depicted in wireframe style.




**Scheme 3.** Initially proposed catalytic cycle (pathway I and pathway II) for complex **B** (L = CO) and evidence for pathway II following the observed H/D exchange in the case of the homoallyl complexes **D** and **4** (*vide infra*).

Earlier, we had proposed a catalytic cycle for catalyst **B**, in which the oxidative addition product **OA** was confirmed by NMR spectroscopy (Scheme 3).[3h] From this intermediate two possible pathways can lead to the product: a concerted 1,2-H shift under reductive elimination of the catalyst (c) or β-hydride elimination (d) to form the Rh-hydride intermediate (**Int-1**), which subsequently undergoes reductive elimination (e) to release the product and the catalyst.




**Scheme 4.** D/H exchange during the isomerization of 1-D-phenyl oxirane with the *N*-homoallyl substituted catalysts **D** and **4** indicate a hydrido–Rh(III) intermediate **Int-1** in the catalytic cycle.

As the hydride intermediate (**Int-1**) was not observed during the catalysis with complex **B** (L = CO), we envisaged that the *N*-homoallyl moiety of catalyst **D** or **4** could insert into the Rh–H intermediate **Int-1** to give the rhodium alkyl intermediate **Int-2**, which could undergo a D/H exchange in case deuterated phenyl oxirane was used. To prove this hypothesis, we carried out catalytic experiments with 1-D-phenyl oxirane as substrate with both *N*-homoallyl-substituted catalysts **D** and **4** under catalytic as well as stoichiometric conditions (Scheme 4). In all cases, we found an exchange of the deuterium by hydrogen in the methylphenyl ketone of 5–7%. (deuteration degree of the phenyl oxirane: 98%).

Based on these observations, we favor pathway II for the catalytic cycle of the nucleophilic Meinwald reaction with our rhodium catalysts. This pathway is also supported by the observations by Milstein, who isolated hydrido-2-oxoalkyl complexes when reacting $RhCl(PMe_3)_3$ with neat methyl or phenyl oxirane.[3g] In this case, the reductive elimination to acetone or acetophenone is the rate limiting step.[6]

**Catalyst deactivation pathways**. In addition, we observed two deactivation products of the catalyst. We recognized the formation of red crystals after finishing a VT NMR experiment of catalyst **4** with 1.0 equiv. of phenyl oxirane at room temperature. The X-ray structure analysis reveals the formation of a bromido–Rh(III) complex, in which the *N*-homoallyl substituent is coordinated in a $\eta^3$-allyl coordination mode to the oxidized metal center (Figure 4). The allyl–Rh bonds measure 2.137 (Rh–C17), 2.114 (Rh–C16) and 2.220 Å (Rh–C15). As the isomerization of phenyl oxide **5a** is very fast, it is likely that the formation of complex **9** occurs after the catalysis. C–H activation at the allylic position to form an allylhydrido complex and subsequent substitution of the hydrido by a bromido ligand can explain its formation.

From the testing of *cis*-1,2-(diethoxycarboxyl)oxirane (5 mol% **4** (2.3 mg), 20 mol% $LiNTf_2$ (4.6 mg), *cis*-1,2-(diethoxy carboxyl)oxirane (15.1 mg) and 1,3,5-trimethoxybenzene

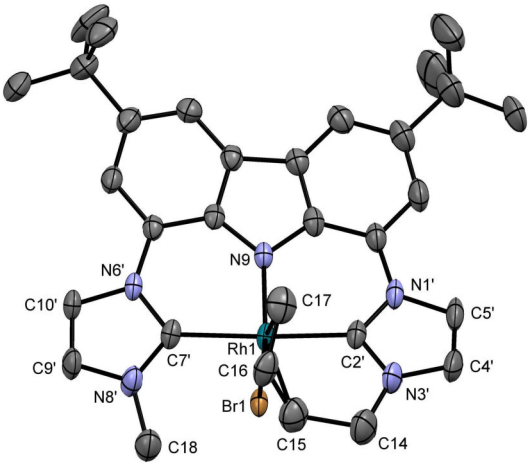



**Figure 4.** Molecular structure of the catalyst deactivation product **9**. Atoms are shown with anisotropic atomic displacement parameters at the 50% probability level. Hydrogen atoms as well as 3.5 co-crystallized benzene molecules are omitted for clarity.

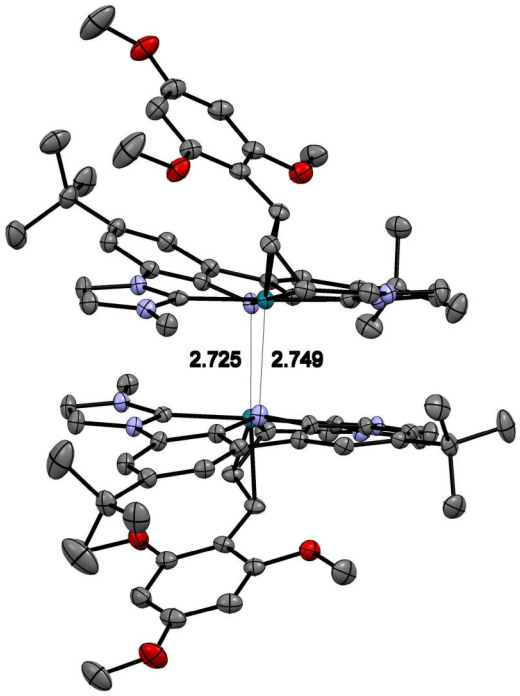



**Figure 5.** Molecular structure of the side product **10**. Atoms are shown with anisotropic atomic displacement parameters at the 50% probability level. Hydrogen atoms as well as the two $NTf_2^-$ counter ions and two co-crystallized benzene molecules are omitted for clarity.

(4.3 mg), 24 h at 80 °C and 24 h at 100 °C) we obtained red single crystals in the NMR tube after several days at room temperature. The X-ray structure analysis reveals that under the elevated temperature the internal standard 1,3,5-trimethoxybenzene has reacted with the *N*-homoallyl moiety of complex **4** in a formal dehydrogenation and C–C bond formation to the Rh(III)($\eta^3$-allyl) complex **10** (Figure 5). In the solid state the 16e$^-$ Rh-d$^6$ complex forms a Lewis-pair dimer between the rhodium and the carbazole nitrogen atoms with a mean distance of 2.74 Å. The allyl rhodium bonds measure 2.143 (Rh–C17), 2.124 (Rh–C16) and 2.243 Å (Rh–C15) (mean).

To avoid erroneous catalytic results in the NMR experiments, catalytic tests with substrates of low reactivity should be carried out either with an inert or without an internal standard.

## Conclusions

Herein, we have presented the most active and selective catalyst system for the nucleophilic Meinwald reaction of terminal epoxides so far. The reactivity enhancement of catalyst **4** was achieved by providing only one coordinating *N*-homoallyl substituent at the ligand scaffold. The isolated complex **4** can undergo isomerization of the double bond in the presence of weak Lewis acids and benzene as solvent to yield the *N*-methallyl complex **8**, which is itself a comparably active catalyst in the Meinwald reaction. D/H exchange experiments provide strong evidence for a β-hydride elimination/reductive elimination pathway via a hydrido–Rh intermediate for the Rh-catalyzed nucleophilic Meinwald reaction.

## Experimental Section

*General information.* Unless otherwise noted, all reactions were carried out under an argon atmosphere in dried and degassed solvents using Schlenk technique. Toluene, pentane, dichloromethane and tetrahydrofuran were purchased from Sigma Aldrich and dried using an MBraun SPS-800 solvent purification system. All lithium salts used were obtained from commercial suppliers, dried in vacuum and used without further purification. Chemicals from commercial suppliers were degassed through freeze-pump-thaw cycles prior to use. Rhodium complex **D** was synthesized according to the literature procedure.[3j] $^1$H and $^{13}$C NMR spectra were recorded using a Bruker ARX 250 or AVANCE II+400 spectrometer. Chemical shifts δ (ppm) are given relative to the solvent's residual proton and carbon signal respectively: THF-$d_8$: 3.58 ppm ($^1$H NMR) and 67.57 ppm ($^{13}$C{H} NMR); $C_6D_6$: 7.16 ppm ($^1$H NMR) and 128.39 ppm ($^{13}$C{H} NMR); DMSO-$d_6$: 2.50 ppm ($^1$H NMR) and 39.51 ppm ($^{13}$C{H} NMR). Coupling constants (*J*) are expressed in Hz. Signals were assigned as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet) and variations thereof; (br) refers to a broad signal. The assignment of peaks is based on 2D NMR correlation and NOE spectra.

**Synthesis of Hbimca$^{MeHomo}$·HI·HBr (3).** *a) Synthesis of 2:* To a suspension of **1** (0.74 g, 1.8 mmol) in 10 mL THF was added MeI (0.51 g, 3.6 mmol) dropwise. The reaction was stirred at room temperature for 24 h to form a pale precipitate. The mixture was filtered and dissolved in dichloromethane. After removal of solvent, product **2** was obtained as a light yellow solid (0.89 g, 1.6 mmol, yield: 90%). $^1$H NMR (250.13 MHz, DMSO-$d_6$) δ = 11.24 (s (br), 1H, NH), 9.69 (s (br), 1H, H-7′), 8.57 (d, $^4J_{HH}$ = 1.7 Hz, 1H, H-5), 8.42 (d, $^4J_{HH}$ = 1.7, 1H, H-4), 8.21 (s (br), 1H, H-2′), 8.19 (ps t, $^3J_{HH}$ = 1.8 Hz, 1H, H-10′), 7.98 (ps t, $^3J_{HH}$ = 1.7 Hz, 1H, H-9′), 7.73 (ps t, $^3J_{HH}$ = 1.3 Hz, 1H, H-5′), 7.66 (d, $^4J_{HH}$ = 1.7 Hz, 1H, H-7), 7.50 (d, $^4J_{HH}$ = 1.7 Hz, 1H, H-2), 7.22 (ps t, $^3J_{HH}$ = 1.0 Hz, 1H, H-4′), 3.99 (s, 3H, H-18), 1.45 (s, 18H, H-11 and H-13). $^{13}$C{H} NMR (62.90 MHz, DMSO-$d_6$) δ = 143.6 and 143.2 (C3 and C6), 138.0 (C7′), 137.2 (C2′), 132.7 (C8a), 132.1 (C1a), 129.1 (C4′), 125.7 (C4a), 125.0 (C5a), 123.7 (2x) (C10′ and C9′), 121.7 (C1), 121.0 (C7), 120.2 (C5′), 120.0 (C2), 119.1 (C5), 118.9 (C8), 116.7 (C4),

36.0 (C18), 34.78 and 34.70 (C10 and C12), 31.65 and 31.62 (C11 and C13). $C_{27}H_{32}N_5I$ (553.50): calcd C 58.59, H 5.83, N 12.65; found C 58.38, H 6.29, N 12.30. m.p.: 287 °C (dec.).

b) *Synthesis of* ***3****:* To a solution of the monomethylated product **2** (0.89 g, 1.6 mmol) in 10 mL DMF was added 4-bromobutene (0.43 g, 3.2 mmol) in one portion. The reaction was stirred at 110 °C for 21 h. The solvent was removed via oil pump and a good precipitate was achieved after adding a bit of ethanol and diethyl ether. The mixture was filtered, and the residue was resolved in dichloromethane. After removal of the solvent, the product **3** was obtained as a light yellow solid (1.0 g, 1.5 mmol, yield: 95%). $^1$H NMR (250.13 MHz, DMSO-$d_6$) δ = 11.63 (s (br), 1H, NH), 10.06 (s (br), 1H, H-2′), 10.01 (s (br), 1H, H-7′), 8.65 (s (br), 2H, H-4 and H-5), 8.32 (s (br), 1H, H-5′), 8.29 (s (br), 1H, H-10′), 8.17 (s (br), 1H, H-4′), 8.06 (s (br), 1H, H-9′), 7.76 (d, $^4J_{HH}$ = 1.3 Hz) and 7.75 (d, $^4J_{HH}$ = 1.4 Hz) (2H, H-2 and H-7), 5.92 (ddt, $^3J_{HH}$ = 17.2 Hz, $^3J_{HH}$ = 10.3 Hz, $^3J_{HH}$ = 6.8 Hz, 1H, H-16), 5.23 (dd, $^3J_{HH}$ = 17.2 Hz, $^2J_{HH}$ = 1.0 Hz, 1H, H-17$_{trans}$), 5.16 (d (br), $^3J_{HH}$ = 10.3 Hz, 1H, H-17$_{cis}$), 4.44 (t, $^3J_{HH}$ = 7.2 Hz, 2H, H-14), 4.03 (s, 3H, H-18), 2.78 (dt, $^3J_{HH}$ = 6.8 Hz, $^3J_{HH}$ = 7.2 Hz, 2H, H-15), 1.47 (s, 18H, H-11 and H-13). $^{13}$C{H} NMR (62.90 MHz, DMSO-$d_6$) δ = 143.7 (C3 and C6), 137.9 (C7′), 137.3 (C2′), 133.7 (C16), 132.3 and 132.2 (C1a and C8a), 125.5 and 125.4 (C4a and C5a), 123.9 (C9′), 123.3 (C5′), 123.2 (C10′), 122.9 (C4′), 120.92 and 120.89 (C2 and C7), 119.42 and 119.37 (C4 and C5), 119.0 (C1 and C8), 118.3 (C17), 48.4 (C14), 36.1 (C18), 34.9 (C10 and C12), 33.2 (C15), 31.6 (C11 and C13). m.p.: 263 °C.

**Preparation of catalysts 4$^{LiX}$.** *a) In situ generation of* **[Li(bimca$^{Me,Homo}$)]**: Lithium bis(trimethylsilyl)amide (7.3 mg, 44 μmol) was added to the suspension of **3** (10.0 mg, 14.5 μmol) in 0.5 mL of THF-$d_8$ at room temperature and a light yellow solution with blue fluorescence was formed. After 10 min, the quantitative formation of **[Li(bimca$^{Me,Homo}$)]** was confirmed by $^1$H NMR spectroscopy. $^1$H NMR (400 MHz, THF-$d_8$) δ = 7.99 (s (br), 2H, H-4 and H-5), 7.73 (s (br), 2H, H-5′ and H10′), 7.39 (s (br), 2H, H-2 and H-7), 7.21 and 7.15 (each s (br), each 1H, H-4′ and H-9′), 5.80–6.05 (m, 1H, H-16), 5.15 (d, $^3J_{HH}$ = 16.5 Hz, 1H, H-17$_{trans}$), 5.04 (d, $^3J_{HH}$ = 10.5 Hz, 1H, H-17$_{cis}$), 4.26–4.35 (m, 2H, H-14), 3.93 (s (br), 3H, H-18), 2.70–2.80 (m, 2H, H-15), 1.50 (s, 18H, H-11 and H-13).

*b) In situ generation of* **4$^{LiX}$**: [Rh(μ-Cl)(COD)]$_2$ (0.5 eq) was added to the previous prepared solution of **[Li(bimca$^{Me,Homo}$)]** (1.0 eq) at room temperature. The solution was stirred for 10 min. Catalyst **4$^{LiX}$** was obtained as an orange solution in quantitative yield as determined by NMR spectroscopy. $^1$H NMR (400 MHz, THF-$d_8$) δ = 8.17 (d, $^3J_{HH}$ = 2.2 Hz, 1H, H-10′), 8.10 (d, $^3J_{HH}$ = 2.3 Hz, 1H, H-5′), 8.08–0.09 (m, 2H, H-4 and H-5), 7.73 (d, $^4J_{HH}$ = 1.5 Hz, 1H, H-2), 7.70 (d, $^4J_{HH}$ = 1.5 Hz, 1H, H-7), 7.17 (d, $^3J_{HH}$ = 2.3 Hz, 1H, H-4′), 7.16 (d, $^3J_{HH}$ = 2.2 Hz, 1H, H-9′), 4.65–4.58 (m, 1H, H-16), 4.28 (ps td, $^{2/3}J_{HH}$ = 12.4 Hz, $^3J_{HH}$ = 2.2 Hz, 1H, H-14$_{ax}$), 4.09 (d ps t, $^2J_{HH}$ = 13.0 Hz, $^3J_{HH}$ = 3.6 Hz, 1H, H-14$_{eq}$), 3.92 (s, 3H, H-18), 3.50 (d, $^3J$ = 7.7 Hz, 1H, H-17$_{cis}$), 2.94 (d, $^3J$ = 11.5 Hz, 1H, H-17$_{trans}$), 2.67 (br dd, $^2J_{HH}$ = 15.1 Hz, $^3J_{HH}$ = 12.4 Hz, 1H, H-15$_{ax}$), 2.33–2.25 (m, 1H, H-15$_{eq}$) (overlap with COD signal), 1.53 and 1.52 (each s, 18H, H-11 and H13). $^{13}$C{H} NMR (101 MHz, THF-$d_8$) δ = 184.8 (d, $^1J_{RhC}$ = 43.3 Hz, C7′), 179.0 (d, $^1J_{RhC}$ = 45.7 Hz, C2′), 139.2 (C3), 139.1 (C6), 137.1 (C1a), 136.8 (C8a), 127.3 and 127.2 (C4a and C5a), 126.6 (C9′), 126.0 (C8), 125.7 (C1), 123.9 (C4′), 116.1 (C10′), 116.5 (C5′), 113.6 (C5), 113.4 (C4), 111.3 (C7), 110.2 (C2), 51.3 (d, $^1J_{RhC}$ = 13.2 Hz, C16), 47.5 (C14), 38.9 (C18), 37.0 (d, $^1J_{RhC}$ = 13.7 Hz, C17), 35.6 (C10 and C12), 32.8 (C11 and C13), 31.9 (C15).

**Preparation of catalyst 4**. Imidazolium salt **3** (100 mg, 145 μmol), potassium bis(trimethylsilyl)amide (86.9 mg, 436 μmol) and [Rh(μ-Cl)(COD)]$_2$ (35.8 mg, 72.6 μmol) were added to a dry flask at room temperature. The flask was cooled down to −60 °C for 30 min. Cold THF was injected into the flask and the reaction was stirred for another 30 min at −60 °C. After completion, the reaction was filtered to remove potassium halides. The collected filtrate was dried under vacuum and the residue was washed with pentane (3 × 5 mL). Pure catalyst **4** was obtained after removal of solvent as a yellow solid (43.6 mg, 75.0 μmol, yield: 52%). The NMR data (THF-$d_8$) correspond to the results obtained from using **[Li(bimca$^{Me,Homo}$)]**. $C_{31}H_{36}N_5Rh$ (581.56): calcd C 64.02, H 6.24, N 12.04; found C 61.70, H 6.02, N 11.36. Possibly contains residual KBr: $C_{31}H_{36}N_5Rh \cdot 0.2$ KBr: calcd C 61.51, H 5.99, N 11.57.

**Synthesis of the isomerized rhodium complex 8**. To a *J. Young* NMR tube containing LiBr (6.9 mg, 80 μmol) and 20 μL of THF-$d_8$, was added catalyst **4** (23.2 mg, 40.0 μmol) with $C_6D_6$ (0.8 mL). Catalyst **8** was generated at room temperature after 1 h in quantitative yield as determined by NMR spectroscopy. Another method for achieving complex **8** was to run a chromatography on silica gel with complex **4**. $^1$H NMR (400 MHz, THF-$d_8$) δ = 8.19 (d, $^3J_{HH}$ = 2.2 Hz, 1H, H-10′), 8.14 and 8.13 (each d, each $^4J_{HH}$ = 1.6 Hz, each 1H, H-5 and H-4), 8.02 (d, $^3J_{HH}$ = 2.2 Hz, 1H, H-5′), 7.81 (d, $^4J_{HH}$ = 1.6 Hz, 1H, H-7), 7.73 (d, $^4J_{HH}$ = 1.6 Hz, 1H, H-2), 7.27 (d, $^3J_{HH}$ = 2.0 Hz, 1H, H-4′), 7.17 (d, $^3J_{HH}$ = 2.0 Hz, 1H, H-9′), 4.56 (br ps t, 1H, $^3J_{HH}$ = 7.2 Hz, H-15), 4.45 (dd, $^2J_{HH}$ = 11.7 Hz, $^3J_{HH}$ = 6.8 Hz, 1H, H-14$_a$), 4.09 (d ps quint, $^3J_{HH}$ = 6.2 Hz, $^4J_{HH}$ = 2.3 Hz, 1H, H-16), 3.97 (br d, $^2J$ = 11.7 Hz, 1H, H-14$_b$), 3.71 (s, 3H, H-18), 1.55 and 1.54 (each s, 18H, H-11 and H-13), 1.17 (dd, $^3J_{HH}$ = 6.3 Hz, $^4J_{HH}$ = 0.6 Hz, 3H, H-17). $^{13}$C{H} NMR (101 MHz, THF-$d_8$) δ = 187.9 (d, $^1J_{RhC}$ = 42.4 Hz, C7′), 187.2 (d, $^1J_{RhC}$ = 44.3 Hz, C2′), 139.5 and 139.2 (C3 and C6), 137.5 (C1a), 136.3 (C8a), 127.9 and 127.6 (C4a and C5a), 126.4 (C1), 126.2 (C8), 124.6 (C9′), 118.3 (C4′), 116.5 (C10′), 114.8 (C5′), 114.1 (C5), 113.8 (C4), 111.4 (C7), 109.7 (C2), 57.3 (d, $^1J_{RhC}$ = 14.1 Hz, C16), 53.8 (d, $^1J_{RhC}$ = 12.7 Hz, C15), 50.0 (C14), 37.6 (C18), 35.72 and 35.65 (C10 and C12), 32.93 and 32.90 (C11 and C13), 20.9 (C17). $^1$H NMR (400 MHz, $C_6D_6$) δ = 8.46 (s, 2H), 7.67 (s, 1H), 7.59 (s, 1H), 7.49 (s, 1H), 7.23 (s, 1H), 6.36 (s, 1H), 6.14 (s, 1H), 4.48–4.40 (m, 1H, H-15), 4.31 (ps quint, $^3J_{HH}$ = 6.0 Hz, 1H, H-16), 4.09 (dd, $^2J_{HH}$ = 11.2 Hz, $^3J_{HH}$ = 6.8 Hz, 1H, H-14$_a$), 3.66 (br d, $^2J_{HH}$ = 11.7 Hz, 1H, H-14$_b$), 3.12 (s, 3H, H-18), 1.55 (br s, 18H, H-11 and H-13), 1.37 (br d, $^3J_{HH}$ = 6.0 Hz, 3H, H-17).

**DFT calculations**. Performed based on density functional theory at the BP86/def2-SVP and/or BP86/def2-TZVP[7] level implemented in Turbomole.[8] The RI-approximation[9] and the Grimme dispersion correction D3-BJ[10] were used all over. Several structures were optimized differing in the conformation of the rings formed by the coordination of the double bond. Minimum structures were verified at the BP86/def2-SVP level by calculating the Hessian matrix and ensuring that it has no imaginary frequency.

**X-ray structure analysis**. CCDC 1907047 (**9**) and 1907048 (**10**) contain the supplementary crystallographic data. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk/data_request/cif.

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## Conflict of Interest

The authors declare no conflict of interest.

**Keywords:** Rhodium · Homogenous catalysis · Epoxides · Isomerization · Carbene ligands

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# FULL PAPERS

**Finding the path**: The efficient isomerization of a wide range of epoxides into methyl ketones is achieved using a novel pincer-rhodium complex under very mild conditions with excellent chemo- and regioselectivity. Investigations on the mechanism reveal the concomitant isomerization of the catalyst and provide evidence for a β-hydride elimination-reductive elimination step in the catalytic cycle.