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Cooperative Catalysis: Large Rate Enhancements with Bimetallic Rhodium Complexes

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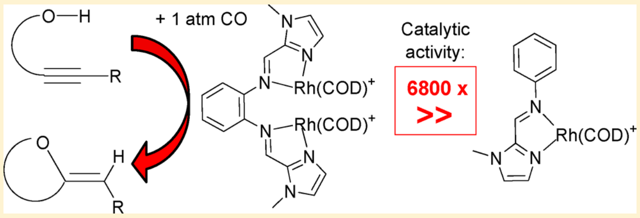
Ⓢ *Supporting Information*

ABSTRACT: A large increase in reaction rate was observed for the catalyzed mono- and dihydroalkoxylation of alkynes when structurally constrained bimetallic Rh(I) catalysts with imidazolyl-imine ligands were compared to their monometallic analogues. The "cooperative" enhancement was vastly improved by restricting the conformational freedom of the bimetallic structure and minimizing the intermetallic Rh···Rh distance.



Bimetallic complexes have the potential to yield remarkable reaction efficiencies in homogeneous catalysis.[1] In certain instances the bimetallic catalyst is significantly more active than the related monometallic catalyst with a similar structure at the metal center. This increase in catalytic activity is attributed to a "cooperative" interaction of the two metal centers in the bimetallic catalyst. One of the more versatile approaches to bimetallic catalyst design is to link two discrete metal complexes by a covalently bound tether.[1e] Such an approach has been used with great effect for a number of diverse reactions such as the Co_2, Cu_2, or Zn_2 catalyzed hydrolysis of phosphate esters,[2−4] the use of Cr_2, Al_2, or Co_2 catalysts for the asymmetric ring opening of epoxides[5] and various Ni_2, Ti_2, and Zr_2 polymerization catalysts.[6,7]

We have recently demonstrated that bimetallic Rh_2 and Ir_2 bis(1-pyrazolyl)methane (bpm) complexes are highly effective catalysts for the dihydroalkoxylation of alkynediols.[8] The degree of cooperative rate enhancement observed was found to be highly dependent on the structure of the linking group, with the highest catalytic activity obtained when the two metal centers were supported on a 1,8-anthracenyl scaffold (Figure 1a). Despite the rigidity of the aromatic linking group, these complexes still contain a high degree of conformational flexibility due to rotation about the bpm−arene bond and a fluxional pseudoboat conformation of the bpm metallacycle. As a result, the intermetallic distances are poorly defined.

In an effort to develop more effective bimetallic catalysts, we report here a series of new bis-rhodium(I) complexes containing structurally rigid imidazolyl-imine chelates attached directly to a linking scaffold via the imine nitrogen donor (Figure 2). This arrangement significantly reduces the degree of conformational freedom and allows for a shorter intermetallic distance through alignment of the complex planes (Figure 1b). The resulting bimetallic complexes achieved an enormous increase in reaction rate when used as catalysts to promote the addition of OH bonds to alkynes relative to that obtained using an analogous monometallic catalyst.

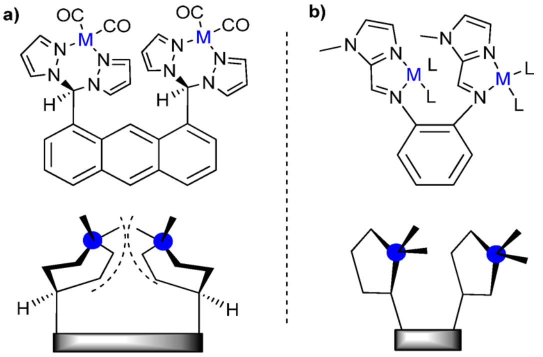


Figure 1. Bimetallic catalyst design: from a fluxional bpm ligand scaffold (a) to a rigid imidazolyl-imine chelate (b, this work) that allows a closer metal−metal separation.

Catalyst Synthesis. A series of three bimetallic ligand scaffolds were synthesized with two imidazolyl-imine donors connected by either a rigid phenylene linker via the meta (*m*-diimine, **2a**) and ortho (*o*-diimine, **3a**) positions or a more flexible ethylene linker (Et-diimine, **4a**) (Figure 2). For comparison the monometallic ligand Ph-imine (**1a**) was also prepared. The corresponding mono- and bimetallic rhodium(I) 1,5-cyclooctadiene (COD) complexes (**1b**−**4b**, Figure 2) were formed by reaction of the ligands **1a**−**4a** with $[Rh(COD)_2]$-BArF (where BArF = tetrakis[3,5-bis(trifluoromethyl)phenyl]-borate) in THF at room temperature. In the ^1H NMR spectra of **2b**−**4b** only a single set of resonances was observed for the imidazolyl-imine chelate, indicating equivalent rhodium complex environments.

Introducing a CO atmosphere to a DCM solution of the COD complexes **1b**, **2b**, and **4b** gave the carbonyl complexes **1c**, **2c**, and **4c** (Figure 2), which were identified in situ using ^1H NMR spectroscopy as the sole products of the reaction. Initial

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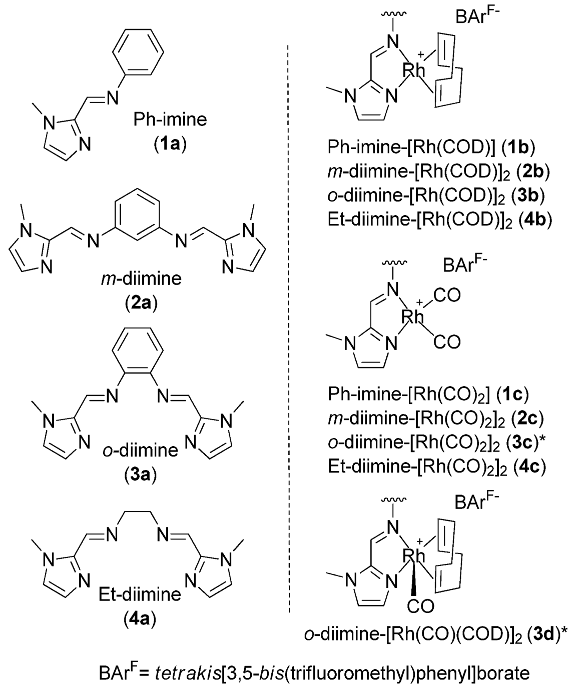


Figure 2. Imidazolyl-imine ligands (**1a**−**4a**) and their corresponding Rh(COD) (**1b**−**4b**), $Rh(CO)_2$ (**1c**−**4c**), and Rh(CO)(COD) (**3d**) complexes. (*) Complexes **3c,d** were formed as an inseparable mixture in a ca. 1:1 ratio.

attempts to isolate **1c**, **2c**, and **4c** by either crystallizing the complexes through the slow addition of pentane or removing the volatiles in vacuo led to a complex mixture of decomposition products. These decomposition products appeared to contain recoordinated COD, indicating a high lability of the CO ligand in the absence of a CO atmosphere. Isolation of the desired products **1c**, **2c**, and **4c** could be achieved cleanly in high yield by rapidly crystallizing the complexes from a CO-saturated solution. This was done by adding the reaction solution to a vast excess of pentane and collecting the resulting pale yellow powders. Once isolated, **1c**, **2c**, and **4c** appeared to be stable in solution over prolonged periods with no CO atmosphere present.

Introducing a CO atmosphere to a solution of the *o*-phenylene-linked complex **3b** gave a mixture of the expected product *o*-diimine-$[Rh(CO)_2]_2$ (**3c**) and the partially carbonylated complex *o*-diimine-$[Rh(CO)(COD)]_2$ (**3d**) in a ca. 1:1 ratio. Adding the reaction solution to a vast excess of pentane gave an inseparable mixture of the two products **3c,d**. A fortuitous crystal of **3c** was grown over 1 month from a CO-saturated solution of the complex in DCM layered with pentane; X-ray diffraction analysis gave the solid-state structure shown in Figure 3. The two metal centers in **3c** can be seen to lie on opposite sides of the phenylene plane; however, an inward twist of the complex planes (C_{PhN}-C_{Ph}−N−C = 137.1(6) and 140.4(6)°) results in a relatively short Rh···Rh distance of 3.325(1) Å. An intermolecular contact of 3.325 ± 0.1 Å is not uncommon between Rh complexes containing π-basic carbonyl or isonitrile ligands and a sterically flat coordination sphere.[9] This distance is consistent with a weak metal−metal interaction between the two Rh centers in **3c**, as described previously by Mann et al.[10]

The ^1H and ^{13}C NMR spectra of the bimetallic carbonyl containing complexes **2c**, **3c,d**, and **4c** indicated that the two

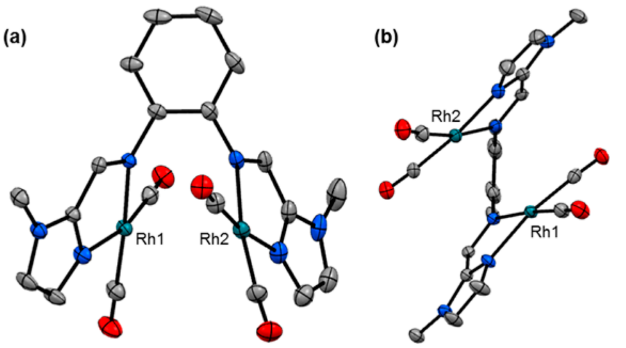


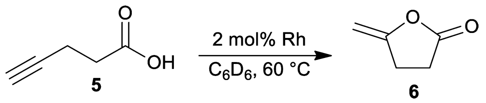
Figure 3. ORTEP depictions of *o*-diimine-$[Rh(CO)_2]_2$ (**3c**) viewed perpendicular (a) and parallel (b) to the phenylene axis.

Rh centers have equivalent coordination environments. ^1H NMR spectra were also acquired in the temperature range 203−323 K for both **2c** and the mixture **3c,d**. The spectra showed no significant changes and retained narrow line widths as the temperature was lowered from 323 K to 223 K. At temperatures below 223 K a slight broadening of the resonances was observed. The consistency of the spectra over a wide range of temperatures indicates that the complex structure is not fluxional on the NMR time scale at these temperatures and that the distance between the Rh atoms is well-defined.

Catalysis. We have long been interested in using rhodium(I) catalysts for the synthesis of oxygen-containing heterocycles via the intramolecular cyclization of alkynoic acids and alkyne diols.[11] The resulting lactone and spiroketal products are prevalent in a wide range of biologically active natural products, and the development of tools that can facilitate their efficient and selective synthesis is of broad significance.[12]

To explore the utility of our new bimetallic catalyst design for hydroalkoxylation reactions, we first investigated the cyclization of 4-pentynoic acid (**5**) to α'-angelica lactone (**6**), a monohydroalkoxylation reaction, using the Rh(COD) complexes **1b**−**4b** as catalysts. The reactions were carried out in benzene-d_6 at 60 °C using 2 mol % of the monometallic catalyst **1b** or 1 mol % of the bimetallic catalysts **2b**−**4b** to give an equivalent metal loading in all systems (Table 1). The monometallic catalyst Ph-imine-[Rh(COD)] (**1b**) and the *m*-phenylene-linked bimetallic catalyst *m*-diimine-$[Rh(COD)]_2$ (**2b**) were both found to be largely inactive for this transformation, achieving less than 4% conversion after 24 h (entries 1 and 2). Conversely, the *o*-phenylene-linked bimetallic

Table 1. Catalyzed Cyclization of 4-Pentynoic Acid (5) to α'-Angelica Lactone (6) using 1b−4b[a]



entry	catalyst	conversion, %[b] (time)
1	Ph-imine-[Rh(COD)] (**1b**)	<4 (24 h)
2	*m*-diimine-$[Rh(COD)]_2$ (**2b**)	<4 (24 h)
3	*o*-diimine-$[Rh(COD)]_2$ (**3b**)	99 (2.3 h)
4	Et-diimine-$[Rh(COD)]_2$ (**4b**)	48 (24 h)

[a] Conditions: 4-pentynoic acid (**5**) (0.310 mmol), 6.2 μmol of Rh (2 mol %), and C_6D_6 (0.5 mL). [b] Determined by a comparison of product and substrate integrals in the ^1H NMR spectrum.

complex *o*-diimine-[Rh(COD)]$_2$ (**3b**) was a highly active catalyst for this reaction, achieving quantitative conversion of the substrate within 2.3 h (entry 3). Clearly the shorter Rh⋯Rh separation that is possible in complex **3b**, in comparison to the similar phenylene-linked complex **2b**, is essential to achieve a cooperative bimetallic enhancement of the reaction rate. The catalyst Et-diimine-[Rh(COD)]$_2$ (**4b**), which contains a short ethylene linker, was also considerably more reactive than its monometallic counterpart **1b**, achieving 48% conversion after 24 h (entry 4). Notably the reactivity of **4b** is slower than that of the *o*-phenylene-linked catalyst **3b**. While both catalysts contain a short two-carbon linking group, the flexible ethylene chain in **4b** would allow the two metal centers to adopt a more remote conformation. The population of these remote states would therefore limit effective cooperation between the metal centers.

Encouraged by these results, we investigated the dihydroalkoxylation of the alkyne diol substrate **7** to yield the spiroketal products **8a,b** (Figure 4). We have previously shown that Rh(CO)$_2$ complexes are much more effective catalysts for this reaction than Rh(COD) complexes when using bidentate N,N′-donor ligands.[9e] We therefore began our investigation using the isolated CO-containing complexes **1c**, **2c**, and **4c** (Figure 4, top). The reaction was performed with a total rhodium loading of 2 mol % in 1,1,2,2-tetrachloroethane-d_2 (TCE-d_2) at 25 °C, with reported conversions indicating the sum of both regioisomers **8a,b**. Both the monometallic complex Ph-imine-[Rh(CO)$_2$] (**1c**) and the *m*-phenylene-linked complex *m*-diimine-[Rh(CO)$_2$] (**2c**) achieved high conversions after 3.5 h, 88% and 99%, respectively, with the bimetallic complex **2c** slightly more active than its monometallic congener **1c**. The bimetallic ethylene-linked complex Et-diimine-[Rh(CO)$_2$] (**4c**) was a much poorer catalyst for this reaction, showing a rapid initial reaction rate followed by deactivation of the catalyst.

In an alternative approach to studying the catalytic activity of the complexes with CO coligands, the dihydroalkoxylation of **7** was performed under 1 atm of CO with the Rh(COD) complexes **1b**–**4b** (Figure 4, bottom), thereby generating the CO-containing complexes in situ. Under these conditions the activity of all bimetallic catalysts was dramatically enhanced relative to the monometallic catalyst **1b**. The bimetallic cooperativity was observed to increase as both the separation between metal centers decreased (**3b** (+CO) ≫ **2b** (+CO)) and the flexibility of the linking scaffold decreased (**3b** (+CO) ≫ **4b** (+CO)), consistent with our observations above on the catalyzed cyclization of 4-pentynoic acid (**5**) using the Rh(COD) complexes **1b**–**4b** without CO present. The *o*-phenylene-linked complex **3b** was in fact an exceptionally reactive catalyst in the presence of a CO atmosphere, achieving quantitative conversion of the substrate within 12 min.

The level of intermetallic cooperativity observed for the dihydroalkoxylation of **7** using the *o*-phenylene-linked complex **3b** under 1 atm of CO is remarkably high. The turnover frequency calculated at 50% conversion (TOF$_{50}$) for **3b** (1370 h^{-1}) is over 6800 times greater than that obtained with the monometallic complex **1b** (0.2 h^{-1}) under identical conditions (Table 2, entries 2 and 4). The high catalytic activity obtained with **3b** is even more extraordinary when comparing the efficiency of the other in situ generated catalysts **1b**, **2b**, and **4b** (+CO) with that of the isolated catalysts **1c**, **2c**, and **4c**. Such a comparison reveals the reaction to be normally impeded by a CO atmosphere. For example, quantitative conversion of the substrate was achieved within 5 h using the isolated complex **1c**, whereas the in situ generated catalyst **1b** (+CO) obtained a maximum conversion of only 60% after 143 h (Table 2, entries 1 and 2). The *o*-phenylene-linked bimetallic catalyst **3b** (+CO) is still 98 times faster than the isolated monometallic catalyst **1c**

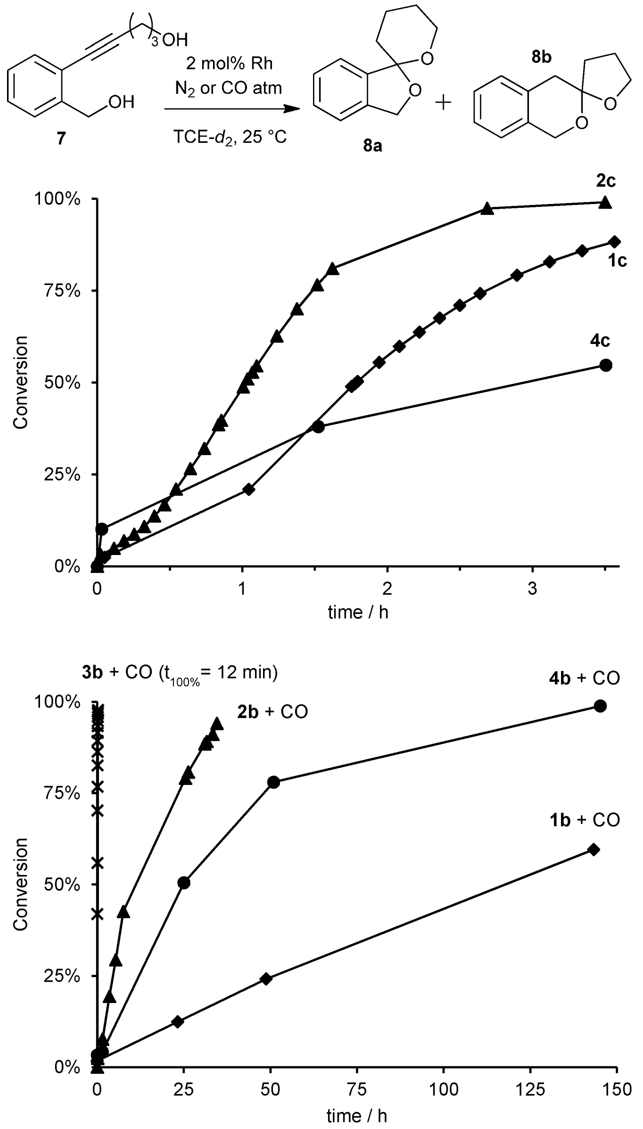


Figure 4. Catalyzed dihydroalkoxylation of **7** to yield spiroketals **8a**,**b**: (top) reactions performed under N$_2$ for the preformed CO-containing complexes **1c**, **2c**, and **4c**; (bottom) carbonylated complexes generated in situ using complexes **1b**–**4b** under a CO atmosphere.

Table 2. Catalyzed Dihydroalkoxylation of 7 using 1c under N$_2$ or 1b–4b under 1 atm of CO[a]

entry	catalyst	conversion, %[b] (time)	8b/8a	TOF$_{50}$ (h^{-1})
1	**1c**	99 (5 h)	0.10	13.9
2	**1b** + CO	60 (143 h)	0.23	0.2
3	**2b** + CO	99 (35 h)	0.36	2.2
4	**3b** + CO	99 (12 min)	0.25	1370
5	**4b** + CO	99 (145 h)	0.35	1.0

[a] Conditions: diol (**7**) (0.200 mmol), 4.0 μmol of Rh (2 mol %), and TCE-d_2 (0.6 mL). For reactions performed under CO, a solution of the catalyst was degassed and 1 atm of CO added prior to addition of **7**. [b] Determined by a comparison of product and substrate integrals in the ^{1}H NMR spectrum.

(TOF_{50} = 13.9 h^{-1}). The regioselectivity of the reaction was found to be independent of the catalyst rate and did not vary significantly between catalysts. In all reactions the spiroketal **8a** was formed as the most favored regioisomer (Table 2).

The dramatic increase in reaction efficiency reported here using the *o*-phenylene-linked bimetallic catalyst **3b** is rarely observed in bimetallic catalysis. Our previous best result obtained with a bpm-ligated dirhodium complex linked by a 1,8-anthracenyl scaffold (Figure 1a, M = Rh) was found to be only 34 times faster than its monometallic analogue for the dihydroalkoxylation of **7**.[8] Complex **3b** appears uniquely structured to facilitate such massive levels of cooperative rate enhancement. The principles of minimizing conformational flexibility and intermetallic distance have led to a highly cooperative system for the addition of OH bonds to alkynes. We have previously proposed a mechanism for the rhodium-catalyzed dihydroalkoxylation of **7** which involves attack of the benzylic alcohol on the π-coordinated alkyne as the first step.[11d] A more detailed investigation of how this mechanism applies to a bimetallic-catalyzed process is ongoing.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text, figures, a table, and CIF files giving experimental procedures for the synthesis of all compounds, the preparation of catalytic reactions, and crystallographic data for compounds **1b**,**c** and **3c**. This material is available free of charge via the Internet at http://pubs.acs.org. Crystallographic data for the structures reported in this paper have also been deposited with the Cambridge Crystallographic Data Centre (CCDC) as supplementary publication nos. 944983–944985.

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Notes

The authors declare no competing financial interest.

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