

Catalysts with Mixed Ligands on Immobilized Supports. Electronic and Steric Advantages

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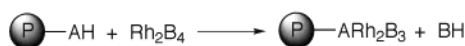
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ABSTRACT



Immobilized dirhodium(II) catalysts having mixed chiral ligands enhance reactivity (AH = azetidinone) and influence stereoselectivity in cyclopropanation and carbon–hydrogen insertion reactions.

The synthesis and applications of immobilized metal catalysts are receiving increasing attention because of their advantages for separation and reuse.^{1–3} However, attachment of a transition metal to a polymer through a bound ligand adds several reaction variables beyond those with uses of homogeneous catalysts. The structure of the polymer, the point of attachment of the ligand to the polymer, and the nature and strength of the metal–ligand association can affect turnover numbers and rates, recovery and reuse, and intrinsic catalyst selectivities.^{4–7} We have recently shown that immobilization of chiral dirhodium(II) tetrakis(methyl 2-oxa-

pyrrolidine-(5*S*)-carboxylate), Rh₂((5*S*)-MEPY)₄, could be achieved on the NovaSyn Tentagel (TG) hydroxy resin and the Merrifield resin through an ester linkage to one of the pyrrolidinone (PY) ligands with yields and selectivities for cyclopropanation reactions comparable to those with the homogeneous catalyst (Scheme 1).⁸

Structurally, neither **2** nor **3** are identical to the homogeneous Rh₂((5*S*)-MEPY)₄ because one of the ligands is bound to the polymer, making one rhodium face different from the other, but the enantioselectivity in cyclopropanation reactions does not appear to be affected significantly by the alkyl ester attachment,⁹ even to recovery and reuse eight times.

Immobilized dirhodium(II) catalysts offer an advantage beyond the conveniences of recovery and reuse that has not been previously reported. Mixed ligand systems prepared by substitution with the use of the polymer-bound ligand (eq

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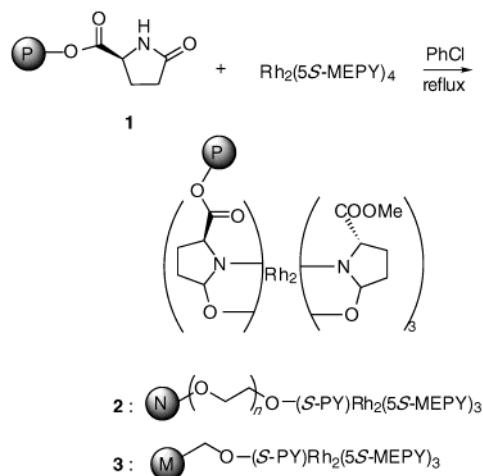
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Scheme 1. Preparation of Immobilized Chiral Dirhodium Carboxamides

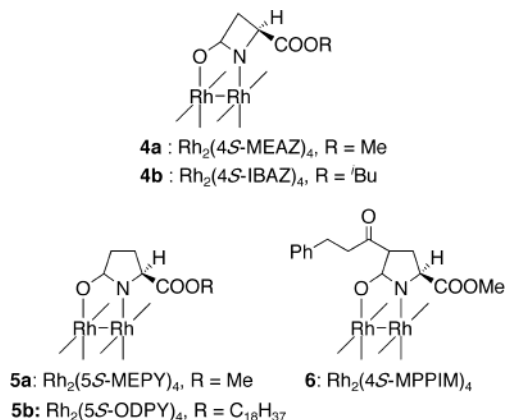


1) are conveniently accessible compared to replacement with “free ligand,” which gives mixtures, and the steric and electronic factors imparted on the catalyst with mixed ligands should be considerably different from those of catalysts with one ligand structure.



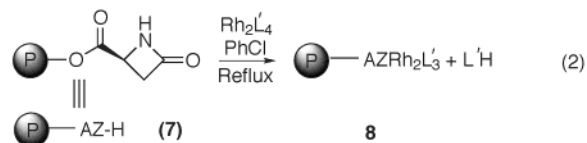
Would only one azetidinone ligand, for example, lengthen the rhodium–rhodium bond distance to enhance reactivity? Could the mixed ligand catalyst exhibit selectivities higher than those of its homogeneous counterparts? The answers to these questions are definitely yes as demonstrated by results from the following experiments.

Azetidinone-ligated dirhodium(II) catalysts (e.g., **4**) exhibit high reactivity for diazo decomposition relative to their counterparts that are constructed from five-membered ring heterocycles (e.g., **5** and **6**).¹⁰

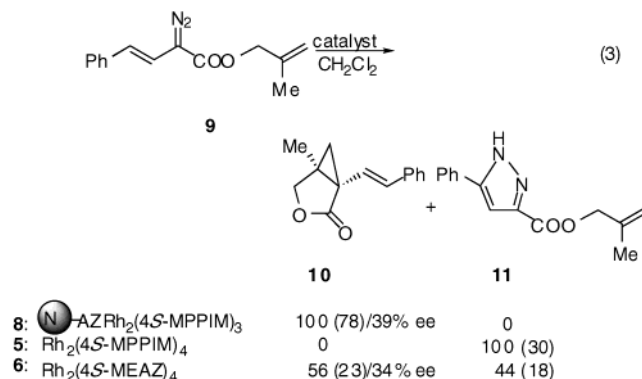


The reason for this is the longer Rh–Rh bond distance for azetidinone-ligated catalysts, whose origin is the wider bite-angle of the NCO dirhodium bridge.¹¹ Only these catalysts cause diazo decomposition of methyl phenyldiazoacetate and

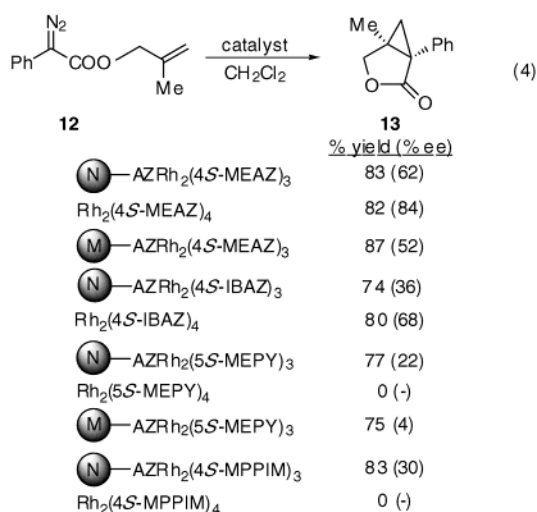
methyl styryldiazoacetate, for example, under mild conditions. The azetidinone-ligated resins were prepared by standard methods⁸ and then used to replace one of the ligands of the homogeneous $\text{Rh}_2((5S)\text{-MEPY})_4$, $\text{Rh}_2((4S)\text{-MPPIM})_4$, $\text{Rh}_2((4S)\text{-MEAZ})_4$, or $\text{Rh}_2((4S)\text{-IBAZ})_4$ catalysts (eq 2).



Styryldiazoacetates are notably resistant to catalytic diazo decomposition with dirhodium(II) carboxamides.¹² With catalysts that include **5** and **6**, only the intramolecular dipolar addition product (e.g., **11**) is observed, and this process does not involve dirhodium catalysis. The exception is catalysts such as **4** with azetidinone ligands.¹⁰ Consequently, we were surprised when the mixed-ligand catalyst **8** caused rapid conversion of **9** to **10** without forming **11** (eq 3), whereas



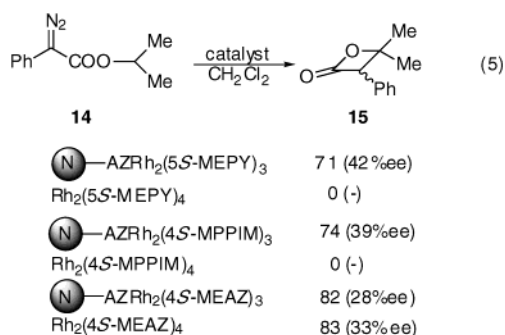
11 was the sole product with $\text{Rh}_2((4S)\text{-MPPIM})_4$ and even evident with $\text{Rh}_2((4S)\text{-MEAZ})_4$ (percent isolated yields are in parentheses). With the analogous phenyldiazoacetate (**12**), however, enantioselectivities were lower with **8** than with either $\text{Rh}_2((4S)\text{-MEAZ})_4$ or $\text{Rh}_2((4S)\text{-IBAZ})_4$ alone (eq 4).¹³



Neither **5** nor **6** caused diazo decomposition of **12** under these conditions, and unreacted starting material was recovered. Recovery and reuse of the polymer-linked catalyst through four cycles afforded the same product yields and selectivities as those reported ($\pm 2\%$). Catalyst loadings as low as 0.2 mol % were effective for complete conversion. Reactions in benzene or cyclohexane gave lower enantioselectivities than those in dichloromethane.

Catalyst loading was determined from % Rh elemental analyses and was 0.1 mmol/g for **8**. Coverage of polymer sites for ligand attachment was 60–90%, and dirhodium(II) attachment was more complete on the NovaSyn resin than on the Merrifield resin. However, the factor primarily responsible for lower yields and irreproducible results was water inclusion within the immobilized catalyst. Heating the catalyst at 50 °C under reduced pressure was effective in conditioning the catalyst for optimum use and reuse.

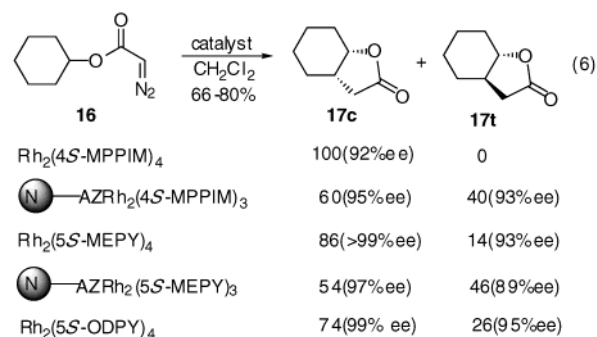
Another process for which azetidinone-ligated dirhodium(II) catalysts are uniquely suited is carbon–hydrogen insertion. In the case of 2-propyl phenyldiazoacetate (**14**), enantioselectivities in the range of 24–33% characterized five homogeneous azetidinone-ligated catalysts (eq 5).¹⁴



With **8**, where $L' = (5S)\text{-MEPY}$, however, selectivity was increased to a level beyond that with the most selective azetidinone-ligated homogeneous catalyst, suggesting another advantage of this catalyst methodology. Similar features of reaction were observed in reactions with cyclohexyl phenyldiazoacetate, which also resulted in exclusive formation of β -lactone product.

Homogeneous chiral dirhodium(II) carboxamidates have a characteristic diastereoisomeric preference for intramolecular C–H insertion of diazoacetates resulting in cis-

disubstituted lactones. The classic system is insertion reactions of cyclohexyl diazoacetate (**16**) for which high % ee values are common, but diastereoselectivities can vary (eq 6).¹⁵



Similar product yields and selectivities were obtained with the Merrifield resin-linked dirhodium catalyst **3** (**17c:17t** = 61:31, % ee **17c** > 99, % ee **17t** = 81) and with those where, in eq 1, B = (4S)-MPPIM (**17c:17t** = 52:48, % ee **17c** = 92, % ee **17t** = 57) and B = (4S)-MEAZ (**17c:17t** = 53:47, % ee **17c** = 97, % ee **17t** = 88). Application of the immobilized catalysts provides results that show no meaningful decrease in enantiocontrol, but diastereoselectivities for the trans isomer are clearly increased. To ascertain the cause of this change in diastereocontrol, we prepared the octadecyl ester analogue of $\text{Rh}_2((5S)\text{-MEPY})_4$, $\text{Rh}_2((5S)\text{-ODPY})_4$ (**4b**). When this catalyst, which is soluble in hydrocarbon solvents, was used, the **17c:17t** composition changed to 76:24, a value between those of $\text{Rh}_2((5S)\text{-MEPY})_4$ and the immobilized support. Thus, increasing the hydrocarbon content of the catalyst ester linkage increases diastereoselection for the trans isomer. This was confirmed in C–H insertion reactions of 1,3-dimethoxy-2-propyl diazoacetate¹⁶ where the cis:trans product ratio decreased from 93:7 with **5a** to 90:10 with **5b** and then to 82:18 with **8** ($L' = (5S)\text{-MEPY}$). As an example of the effectiveness of these immobilized catalysts for recovery/reuse, we conducted diazo decomposition of cyclohexyl diazoacetate with **8** ($L' = (4S)\text{-MPPIM}$) through three cycles without diminution in product yield or stereoselectivity. Further enhancements with these immobilized catalysts are currently under investigation.

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Supporting Information Available: Immobilized resin-catalyst preparation and characterization. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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