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Chemoselectivity and enantiocontrol in catalytic intramolecular metal carbene reactions of diazo acetates linked to reactive functional groups by naphthalene-1,8-dimethanol

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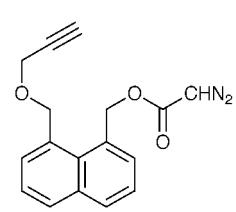
The use of chiral dirhodium(II) carboxamidate catalysts for metal carbene transformations of diazo acetates linked to a reactive functionality through naphthalene-1,8-dimethanol produces chemoselective and enantioselective reaction either at the remote functionality or by addition to the 1,2-position of the naphthalene ring; enantioselectivities up to 84% ee have been obtained for the Büchner reaction.

Considerable mechanistic and synthetic interest has been directed recently to the Büchner reaction.[1,2] Catalytic intramolecular cycloaddition has been pursued with vigor since dirhodium(II) catalysts were employed,[3,4] but there have been few reports that provided evaluation of the Büchner reaction in competitive processes.[5,6] Similarly, only two reports have documented enantiocontrol in this transformation from the use of chiral catalysts.[3,7] In our ongoing investigations of enantiocontrol in catalytic intramolecular metal carbene transformations, we have discovered two reacting systems that offer catalyst-controlled chemoselectivity and the highest levels of enantiocontrol yet achieved in aromatic cycloaddition reactions.

We investigated the influence of catalyst on the partitioning of the metal carbene derived from **1** between products **2** and **3**. The diazo acetate linked to a propargyl group through a naphthalene-1,8-dimethanol (**1**) was prepared by standard methods in good overall yield. Consistent with recently reported results for macrocyclic cyclopropenation,[8] treatment of **1** with $Rh_2(OAc)_4$ produced macrocyclic cyclopropene **2** in 69% isolated yield. However, the application of chiral catalysts to this system resulted not only in **2** but also in the aromatic cycloaddition product **3**. Indeed, use of $Rh_2(4R\text{-MEOX})_4$ gave **3** in 66% overall yield and in 73% ee. The norcaradiene structure for **3** was confirmed spectrally and is consistent with results obtained with a structurally analogous diazo ketone.[9] Results obtained with a representative selection of chiral catalysts are presented in Table 1.

As is evident in these data, the catalyst has a definite but, in this system, unpredictable influence on chemoselectivity. The selectivity achieved with chiral dirhodium(II) carboxamidate catalysts is not uniform. Also, since reactivity of the catalysts generally finds $CuPF_6$–**4** to be comparable to $Rh_2(S\text{-TBPRO})_4$, with both of them much more reactive than the chiral dirhodium(II) carboxamidates, chemoselectivity appears to respond here to a subtle combination of electronic and steric effects. In any case, proper choice of catalyst allows the selection of either **2** or **3**.

The competition between ylide formation and aromatic cycloaddition was also evaluated. By investigating the design potential of the naphthalene-1,8-dimethanol linker for ylide formation–[2,3]-sigmatropic rearrangement,[10] we discovered similar results to those reported in Table 1. The synthesis of **5** was accomplished in good yield. Treatment with $Rh_2(S\text{-TBPRO})_4$ caused the sole production of [2,3]-sigmatropic rearrangement (Scheme 1) product **7** in 82% yield (6% ee).[11] In contrast, use of $Rh_2(4S\text{-MEOX})_4$ gave aromatic cycloaddition product **8** exclusively in 55% isolated yield (84% ee). The use of $CuPF_6$–**4** gave a 20:80 mixture of **7** (44% ee) and **8** (76% ee).



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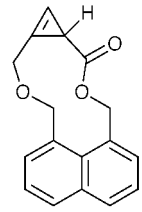

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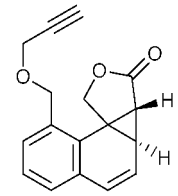

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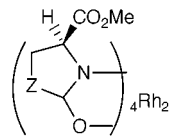
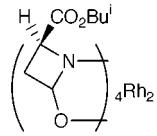
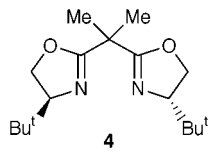


$Rh_2(4S\text{-MEOX})_4$ Z = O
$Rh_2(5S\text{-MEPY})_4$ Z = CH_2
$Rh_2(4S\text{-MPPIM})_4$ Z = $NCOCH_2CH_2Ph$



$Rh_2(4S\text{-IBAZ})_4$



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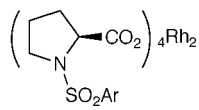


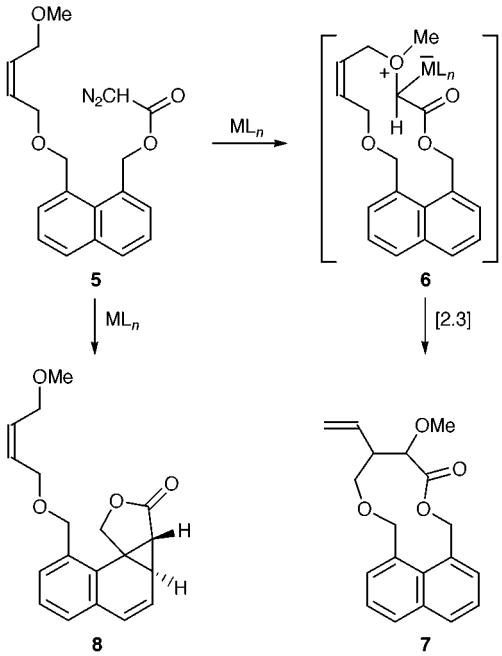
$Rh_2(S\text{-TBPRO})$
(Ar = *p*-$Bu^tC_6H_4$)

To determine the effectiveness of these catalysts for aromatic cycloaddition on the basic naphthalene system, **9** was treated with a selection of catalysts from Table 1. Aromatic cycloaddition product **10** was produced[12] in high isolated yield in each case (% **10**, % ee): $Rh_2(4R\text{-MEOX})_4$ (76% yield, 56% ee); $Rh_2(5S\text{-MEPY})_4$ (72% yield, 42% ee); $Rh_2(4S\text{-IBAZ})_4$ (87% yield, 81% ee); $Cu(MeCN)_4PF_6$–**4** (83% yield, 42% ee). Thus,

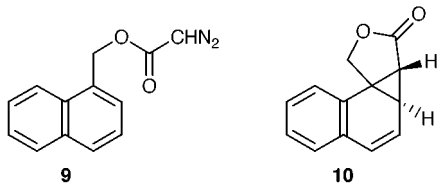
Table 1 Products from catalytic diazo decomposition of **1**[a]

Catalyst	Isolated yield (%)[b]	Relative yield (%)		Ee (%)	
		2	**3**	**2**	**3**
$Rh_2(OAc)_4$	69	100	0	—	—
$Rh_2(4R\text{-MEOX})_4$	66	0	100	—	73
$Rh_2(5S\text{-MEPY})_4$	74	54	46	62	10
$Rh_2(4S\text{-MPPIM})_4$	74	83	17	15	—
$Rh_2(4S\text{-IBAZ})_4$	74	68	32	51	65
$Cu(MeCN)_4PF_6$–**4**	72	14	86	—	59
$Rh_2(S\text{-TBPRO})_4$	72	98	2	11	—

[a] Reactions were performed in refluxing CH_2Cl_2 using 1.0 mol% catalyst. [b] Yield of **2** + **3** after chromatography.



Scheme 1



in this case, $Rh_2(4S\text{-IBAZ})_4$ is superior even to $Rh_2(MEOX)_4$ catalysts for highly enantioselective aromatic cycloaddition.

The composite of results demonstrates that the more reactive catalysts favor reactions that occur at remote functional groups rather than at the nearby naphthalene. This selectivity characterizes alkyne addition and ylide formation and should also be evident in other addition and association reactions. Furthermore, the enantiomeric excess for aromatic cycloaddition in these naphthalene systems is the highest yet reported.

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Notes and references

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11 Only one product was observed by GC and NMR analyses and, based on results reported in ref. 10, this product is assumed to be the *erythro* isomer.

12 Enantiomeric excesses for **3**, **8** and **10** were determined with baseline separation on a WHELK-O column operated at 2 ml min^{-1} in hexanes–Pr^iOH (9 : 1). *Selected data* for **10**: δ_H(300 MHz, $CDCl_3$) 7.51 (d, *J* 7.1, 1H), 7.39–7.22 (m, 3H), 6.53 (d, *J* 9.5, 1H), 6.34 (dd, *J* 9.5, 4.6, 1H), 5.13 (d, *J* 9.5, 1H), 4.35 (d, *J* 9.5, 1H), 2.45 (dd, *J* 4.6, 2.4, 1 H), and 1.08 (d, *J* 2.4, 1H); δ_C(75 MHz, $CDCl_3$) 176.5, 133.1, 130.7, 128.9, 128.3, 128.2, 127.5, 124.7, 124.1, 69.2, 34.2, 30.9 and 21.2; $\nu_{max}(CHCl_3)$/cm^{-1} 1789 and 1752; mp 82–84 °C (Calc. for $C_{13}H_{10}O_2$: C, 78.77; H, 5.08. Found: C, 77.95; H, 5.14%).

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