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LETTERS

Chiral catalyst enhancement of diastereocontrol for O–H insertion reactions of styryl- and phenyldiazoacetate esters of pantolactone

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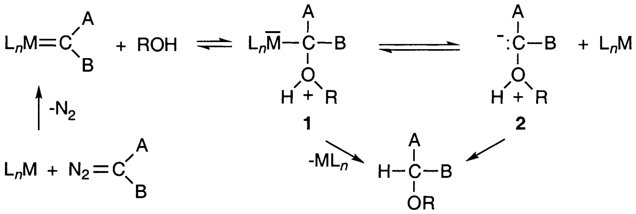
Abstract—The chiral dirhodium(II) catalyst $Rh_2(MEAZ)_4$ increases diastereocontrol for intermolecular O–H insertion reactions of diazo esters having a chiral auxiliary over that achieved with $Rh_2(OAc)_4$. © 2002 Elsevier Science Ltd. All rights reserved.

Efficient, highly stereoselective oxygen–hydrogen insertion has long been sought in catalytic reactions of diazo compounds.[1–3] Two pathways for these reactions were thought possible. The first, a direct insertion reaction analogous to the concerted C–H insertion,[4] was deemed to be improbable because of the absence of similar reactivity/selectivity outcomes between the two processes. The second, and most likely, pathway was ylide formation followed by rapid 1,2-hydrogen shift (Scheme 1).[3,5] Here two conditions arise: (1) that the metal-associated ylide (**1**) undergoes concerted hydrogen shift/metal dissociation and (2) that free ylide (**2**) formation precedes hydrogen shift. Although ylide reactions were long believed to proceed through the free ylide, there is now considerable evidence that the former pathway may account for product formation in favorable instances.[6] However, there have been no reports of enantioselective O–H insertion reactions from the use of chiral catalysts.[1–3,7]

Moody investigated diastereoselectivity in the O–H insertion reactions of water and alcohols with phenyldiazoacetates of several chiral alcohols with dirhodium(II) acetate as the catalyst.[8] Chiral auxiliaries from (−)-borneol, (+)- and (−)-menthol, (+)-8-phenylmenthol, (+)- and (−)-2-phenylcyclohexanol, and (−)-10-(dichlorohexylsulfamoyl)-10-isoborneol were used, and reactions with water, methanol, 2-propanol, and *tert*-butyl alcohol were studied. However, selectivities were highly variable, and the highest diastereomer ratios achieved (with 8-phenylmenthol and MeOH) were less than 77:23. Landais has provided an example with the styryldiazoacetate pantolactone ester and water where 75:25 dr was realized using $Rh_2(OAc)_4$ as the catalyst.[9] We have investigated the O–H insertion reactions of (*R*)-(−)-pantolactone esters of phenyldiazoacetate and *trans*-styryldiazoacetate with and without the use of chiral dirhodium(II) catalysts. We report here that there is significant enhancement of diastereoselectivity with



Scheme 1.

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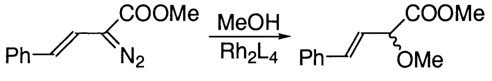
chiral dirhodium(II) carboxamidate catalysts, and there is a special role for pantolactone in these reactions.

Methyl *trans*-styryldiazoacetate undergoes facile O–H insertion in reactions with methanol catalyzed by $Rh_2(OAc)_4$ to form only **3** (Eq. (1)).[10] With the chiral catalyst $Rh_2(4S\text{-MEAZ})_4$ (**4**), previously shown to be highly effective for diazo decomposition of vinyldiazoacetates,[11] **3** was formed in high yield but with only 5% ee. The pantolactone esters of *trans*-styryldiazoacetate (**5**) prepared in high yield by standard methods, were similarly treated. With $Rh_2(OAc)_4$ a 54:46 diastereomer ratio was realized, but with $Rh_2(4S\text{-MEAZ})_4$ and its enantiomer, $Rh_2(4R\text{-MEAZ})_4$, diastereomer ratios were 42:58 and 24:76, respectively, indicating not only a significant catalyst influence on stereoselectivity but also significant characteristics of match/mismatch in diastereoisomer selection. The dominant stereoisomer was dependent on the configuration of the pantolactone auxiliary rather than on the configuration of the catalyst ligands. The absolute configuration of the major diastereoisomer was based on that previously reported for methyl 2-hydroxy-4-phenylbutanoate.[12]



(1)

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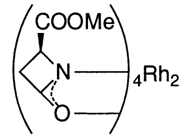

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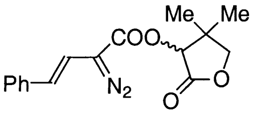

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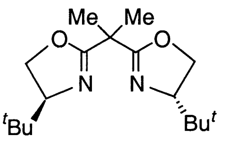
The O–H insertion product from reactions of *R*-**5** with MeOH catalyzed by $CuPF_6$/**6**, $Rh_2(5S\text{-MEPY})_4$ (**7**) and $Rh_2(4S\text{-MPPIM})_4$ (**8**) was not observed. However, diazo decomposition of **5** occurred readily in the presence of catalysts **9**–**12**, and these results are reported in Table 1. The most suitable catalyst for O–H insertion into methanol is $Rh_2(MEAZ)_4$, and there is no obvious advantage from this catalyst's ligand ester group. The use of $Rh_2(4R\text{-MEAZ})_4$ with *R*-**5** and $Rh_2(S\text{-DOSP})_4$ (**9**) with *S*-**5** give complementary results, the former favoring the *S*-enantiomer by more than 3:1 and the latter favoring the *R*-enantiomer by more than 2:1. Variation of the alcohol in reactions of *R*-**5** catalyzed by $Rh_2(4R\text{-MEAZ})_4$ gave similar results: H_2O (dr = 18:82), PhOH (dr = 24:76), $PhCH_2OH$ (dr = 21:79), $H_2C{=}CHCH_2OH$ (dr = 27:73). Neither isopropyl alcohol nor *tert*-butyl alcohol gave even moderate yields of O–H insertion products. Reactions of menthyl and 8-phenylmenthyl esters of *trans*-styryldiazoacetate with **4** as the catalyst and both H_2O and MeOH as nucleophiles were also investigated. However, enhancements (Δ) were much lower (1–16) than those reported in Table 1.

With the pantolactone ester of phenyldiazoacetate (**13**) the influence of catalyst was even more pronounced than that reported in Table 1 (Eq. (2)). $Rh_2(4R\text{-MEAZ})_4$ inverts the diastereomer preference of $Rh_2(OAc)_4$ in reactions with MeOH and substantially enhances the diastereomer preference in reactions with H_2O (Table 2). Consideration was given to intramolecular entrapment of the intermediate carbene as a carbonyl ylide (**15**), but attempts to trap this species by dipolar cycloaddition (DMAD) were not successful.

Table 1. Diastereocontrol in O–H insertion reactions of **5** with methanol[a]

Diazo compound	Catalyst	O–H insertion product Yield (%)[b]	dr[c]	Δ[d]
R-**5**	$Rh_2(OAc)_4$	55	54:46	0
R-**5**	$Rh_2(4S\text{-MEAZ})_4$ (**4**)	52	42:58	12
R-**5**	$Rh_2(4R\text{-MEAZ})_4$ (**4**)	74	24:76	30
R-**5**	**9**	80	39:61	15
S-**5**	**9**	83	71:29	17
S-**5**	**10**	83	75:25	21
R-**5**	**11**	57	44:56	10
S-**5**	**11**	80	76:24	22
R-**5**	**12**	44	45:55	9
S-**5**	**12**	83	77:23	23

[a] Reactions were performed at room temperature in CH_2Cl_2 using 0.5 mol% of catalyst and 2.0 equiv. of methanol.
[b] Weight yield of product after chromatography.
[c] Diastereoisomer ratio = 2*R*:2*S*.
[d] Change in dr from result with $Rh_2(OAc)_4$.



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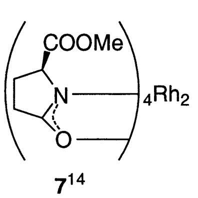

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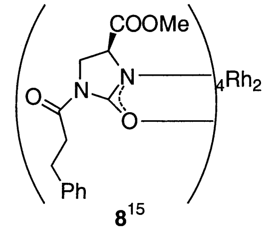
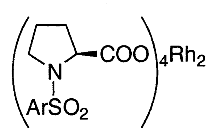
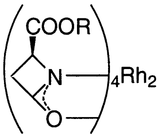


8[15]



9 (Ar = $C_{12}H_{25}C_6H_4$)[16]



10:[17] R = ^{i}Bu [$Rh_2(S\text{-IBAZ})_4$]

11:[18] R =  [$Rh_2(S,S\text{-MenthAZ})_4$]

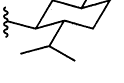
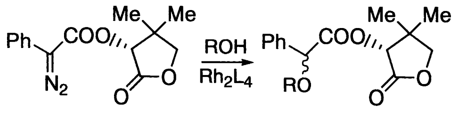
12:[18] R =  [$Rh_2(S,R\text{-MenthAZ})_4$]

Table 2. Diastereocontrol in O–H insertion reactions of **13**[a]



(2)

13 **14**

Catalyst	ROH, R=	O–H insertion product		
		Yield (%)[b]	dr[c]	Δ[d]
$Rh_2(OAc)_4$	Me	82	70:30	0
$Rh_2(4S\text{-MEAZ})_4$	Me	76[e]	51:49	19
$Rh_2(4R\text{-MEAZ})_4$	Me	86[e]	30:70	40
$Rh_2(OAc)_4$	H	85	57:43	0
$Rh_2(4S\text{-MEAZ})_4$	H	69	74:26	17
$Rh_2(4R\text{-MEAZ})_4$	H	82	85:15	18

[a] Reaction conditions were the same as those reported in Table 1.

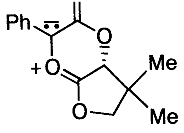
[b] Weight yield of product after chromatography.

[c] Diastereomer ratio: *R*:*S*.[8]

[d] Change in dr from result with $Rh_2(OAc)_4$.

[e] Reaction performed in refluxing CH_2Cl_2.

Still the overall results demonstrate that diastereoselectivity enhancement can be achieved with the use of a chiral catalyst, and future investigations of ylide-based transformations should take this into account.



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Acknowledgements

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