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Enantiocontrol in the Generation and Diastereoselective Reactions of Catalytically Generated Oxonium and Iodonium Ylides. Metal-Stabilized Ylides as Reaction Intermediates

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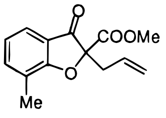
The reactions of ylides generated by catalytic diazo decomposition in the presence of Lewis bases (B:) are generally believed to occur from the free ylide rather than from the metal-associated ylide (Scheme 1).[1−5] As a result there has been a reluctance to investigate methodologies for ylide formation that employ chiral catalysts because the free ylide will produce racemic product. Recently there have been indications that metal-associated ylides could be the product-forming intermediates in selected transformations. McKervey, McCann, and co-workers have reported that **1** could be formed in up to 60% ee by [2,3]-sigmatropic rearrangement of the oxonium ylide formed in an intramolecular reaction of diazoketoester **2** with a chiral dirhodium(II) carboxylate catalysts,[6] and Hodgson has expanded upon this methodology with results at the 53% ee level.[7] Uemura has recently communicated that a chiral copper(I) bis-oxazoline and a dirhodium(II) carboxamidate were successful in intermolecular ylide generation/[2,3]-sigmatropic rearrangement with a sulfonium or selenonium ylide leading to **3**, where ee values of 13−41% were described (diastereomeric ratio < 2:1).[8] Katsuki found up to 64% ee with a similar system using a chiral cobalt(III) salen catalyst,[9] and Clark reported asymmetric induction up to 56% ee in intramolecular oxonium ylide formation from **4** followed by [2,3]-sigmatropic rearrangement.[10] However, in each of these cases the asymmetric transformation could have arisen from the free ylide after dissociation of the metal but before configurational inversion at the onium center. Jacobsen has reported asymmetric induction up to 67% ee for Cu(I)L*-catalyzed aziridine formation with benzylideneanilines and ethyl diazoacetate (EDA) from proposed azomethine ylides,[11] where a free ylide intermediate is improbable. Our investigations have focused on oxygen and halonium ylides, and we now present results which require that metal associated ylides are the primary product-forming intermediates in [2,3]-sigmatropic rearrangements.



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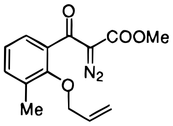

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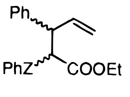
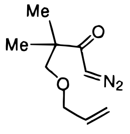


3 (Z = S, Se)



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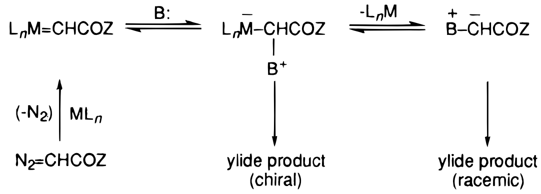
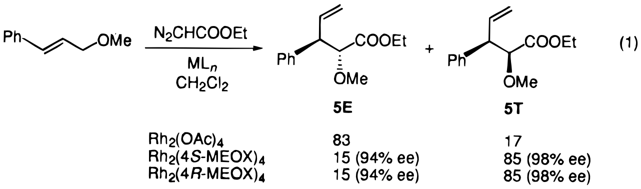
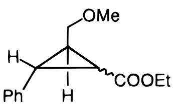
Scheme 1



Allylic oxonium ylides, generated by dirhodium(II) acetate catalyzed decomposition of diazocarbonyl compounds in the presence of allyl methyl ethers, undergo [2,3]-sigmatropic rearrangement with a high degree of diastereocontrol.[12] With cinnamyl methyl ether and ethyl diazoacetate (EDA), the predominant ylide-derived product is the erythro isomer **5E** (eq 1, relative stereochemistry is indicated); intermolecular cyclopropanation is competitive, and the ratio of products derived from ylide rearrangement (**5**) to cyclopropanation (**6**) is 73:27. However, with the use of the chiral catalysts dirhodium(II) tetrakis[methyl 2-oxooxazolidine-4 (*R* and *S*)-carboxylate], Rh$_2$(4*R*-MEOX)$_4$ and Rh$_2$(4*S*-MEOX)$_4$ (**7**),[13] diastereoselectivity is reversed, competition from cyclopropanation is diminished (5:6 = 89:11 with **7**) and each of the ylide-derived diastereoisomers is formed with exceptionally high enantiocontrol, independent of the molar ratio of reactants.[14] Using Cu(CH$_3$CN)$_4$PF$_6$/chiral bis-oxazoline **8**,[15] diastereoselectivity was like that with CuPF$_6$ alone or Rh$_2$(OAc)$_4$, but enantioselectivity was low (<5% ee **5E**, 27% ee **5T**). Intermediate selectivities were found with other dirhodium(II) catalysts. Isolated yields of **5** are lower in reactions catalyzed by Rh$_2$(MEOX)$_4$ (32%) or CuPF$_6$/**8** (38%) than in those catalyzed by Rh$_2$(OAc)$_4$ (67%) when performed under the same conditions.[16]





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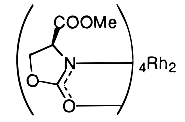

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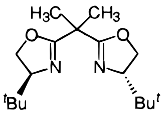

8

Enantiocontrol in intramolecular ylide formation/[2,3]-sigmatropic rearrangement is exemplified by results with **9** (eq 2). In reactions catalyzed by Cu(CH$_3$CN)$_4$PF$_6$/**8** a 13-membered ring oxonium ylide is formed with high chemoselectivity (8:1 ylide: cyclopropanation) and undergoes stereocontrolled internal [2,3]-

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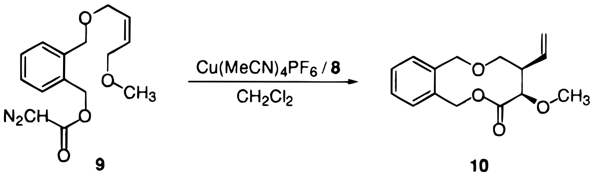
(16) Reactions were performed by addition of EDA in CH$_2$Cl$_2$ over 10 h to a refluxing CH$_2$Cl$_2$ solution of 0.5 equiv of cinnamyl methyl ether and 1.0 mol % of catalyst.

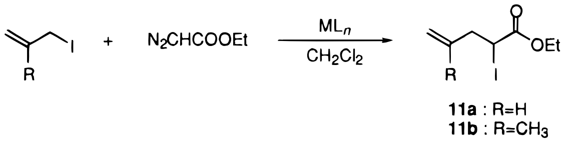
S0002-7863(97)02095-7 CCC: $15.00



9 **10** (2)

sigmatropic rearrangement[17] to form **10**, solely as the cis stereoisomer, in 35% isolated yield and 65% ee.[18] The use of **7** in place of $CuPF_6$/**8** did not produce **10** in significant amounts.

As in prior evaluations of enantiocontrol for catalytic ylide generation and [2,3]-sigmatropic rearrangement,[6,8–10] the possibility exists that even the extraordinary enantiocontrol achieved with $Rh_2(MEOX)_4$ catalysts in eq 1 could have arisen from the free ylide that possessed a memory for its source. This would not be the case if asymmetric induction could be achieved from allyl iodide, which is highly selective for ylide generation in reactions catalyzed by $Rh_2(OAc)_4$,[19] and whose "free" ylide is achiral. Consequently, we have treated allyl iodide with EDA in the presence of chiral dirhodium(II) and copper(I) catalysts and have obtained the expected ylide rearrangement product **11**[20] (eq 3) in catalyst-dependent % ee values (Table 1).



11a : R=H
11b : R=CH3

(3)

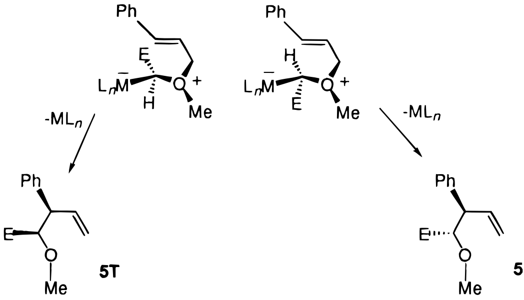
Isolated yields of 11 were low with chiral dirhodium(II) carboxamide catalysts $Rh_2(4S\text{-MEOX})_4$, $Rh_2(4R\text{-MEOX})_4$, and $Rh_2(4S\text{-MPPIM})$ (12–15% yield after distillation), but the only detectable byproducts were those from carbene dimer formation. Isolated yields improved with the use of chiral dirhodium(II) *tert*-butylbenzenesulfonyl-prolinate catalyst, $Rh_2(^t\text{Bu-}(S)\text{-Pro})$[4,21] but enantiocontrol was considerably diminished (4% ee). However, with $CuPF_6$/**8** both the isolated yield of **11** (62% after distillation) and enantiocontrol (69% ee) were sufficiently high to be conceptionally significant and synthetically meaningful. Similarly, $CuPF_6$/**8** caused the formation of **11b** in 67% isolated yield with 37% ee, and the factors that influence this selectivity are under investigation.

Table 1. Enantiocontrol in Catalytic Ylide Generation/[2,3]-Sigmatropic Rearrangement with Allyl Iodide/Ethyl Diazoacetate

catalyst	[allyl iodide]:[EDA]	**11a**:dimer[a]	**11a** (% ee)[b]
$Rh_2(OAc)_4$	4:1	98:2	
$Rh_2(t\text{Bu-}(S)\text{–Pro})_4$	2:1	67:33	4
$Rh_2(4S\text{-MEOX})_4$	4:1	20:80	39
$Rh_2(4R\text{-MEOX})_4$	4:1	18:82	39
$Rh_2(4S\text{-MPPIM})_4$	4:1	17:83	12
$CuPF_6$/**8**	4:1	100:0	69

[a] Ratio of **11a** to carbene dimers maleate and fumarate. [b] Determined by GC on a Chiraldex B–PH column.

Scheme 2



Catalyst-dependent diastereoselectivity implicates a metal-associated ylide in the product forming step.[22] The [2,3]-sigmatropic rearrangement occurs on the metal-associated ylide, presumably during metal dissociation in what is formally a backside displacement reaction that involves inversion of configuration (Scheme 2, E = COOEt). The enantiocontrol achieved with $Rh_2(MEOX)_4$ or $CuPF_6$/**8** catalysts indicates the extent to which these chiral catalysts control the approach of the nucleophilic reactant onto the carbene center. These results suggest that asymmetric induction in ylide-derived processes can now be actively pursued using chiral catalyst methodologies.

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Supporting Information Available: Full experimental details including tables of product distributions as a function of catalyst and reactant ratios, stereochemical determination of **5**, and spectral and analytical data for **9** and all reaction products, including analysis of % ee (9 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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