Pergamon

Tetrahedron Letters, Vol. 38, No. 25, pp. 4367-4370, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00930-1

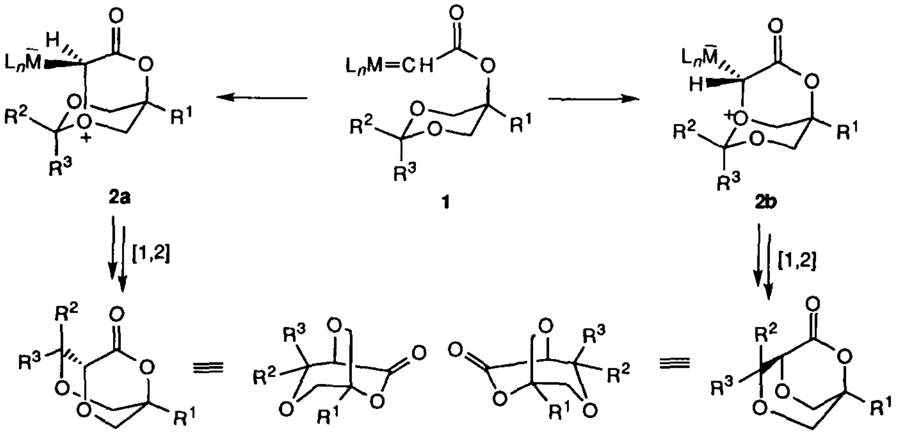
Highly Enantioselective Oxonium Ylide Formation and Stevens Rearrangement Catalyzed by Chiral Dirhodium(II) Carboxamidates

Michael P. Doyle*, Doina G. Ene, David C. Forbes, and Jason S. Tedrow

Department of Chemistry, Trinity University, San Antonio, Texas 78212 (U.S.A.)

Summary: *1,3-Dioxan-5-yl diazoacetates undergo conformation dependent oxonium ylide generation catalyzed by chiral dirhodium(II) carboxamidates, and Stevens rearrangement product(s) are formed with high chemoselectivity and with enantioselectivities reaching 88% ee.*

Oxonium ylides have been made synthetically viable as a result of their catalytic generation from diazocarbonyl compounds.[1,2] Their most useful transformations have been [2,3]-sigmatropic rearrangements of allyl or propargyl ethers and [1,2]-insertions (Stevens rearrangements),[3-6] and several reports have recently described moderate levels of enantiocontrol or enantiomer differentiation in oxonium ylide reactions with the use of chiral dirhodium(II) or copper(I) catalysts.[7,8] We have taken an alternative approach to those previously used to achieve enantioselection by employing symmetrical 1,3-dioxan-5-yl diazoacetates wherein diastereotopic association of the metal carbene at one of the two ether oxygens is the source of enantiocontrol (Scheme 1). [1,2]-

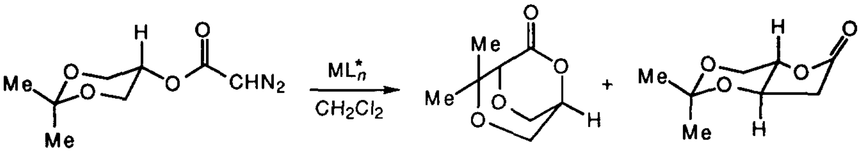


Scheme 1

*E-mail: MDoyle@trinity.edu FAX: +1-210-736-7569

Insertion will occur by migration of carbon-2 to the carbenic center either after or during dissociation of the ligated metal.

Diazo decomposition of 1,3-dioxane **4** in refluxing CH_2Cl_2 containing 1.0 mol % of chiral catalyst formed products from ylide generation/[1,2]-insertion (**5**) and carbon-hydrogen insertion (**6**) in moderate yield (eq 1). Product yields were subject to fluxuations, dependent on trace impurities.

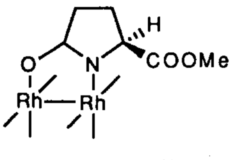


(1)

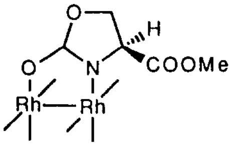
4	yield, %	5, %	6, %
$Rh_2(5S\text{-MEPY})_4$	53[a]	22 (55% ee)	78 (85% ee)
$Rh_2(4S\text{-MEOX})_4$	46	42 (66% ee)	58 (98% ee)
$Rh_2(4R\text{-MEOX})_4$	42	41 (64% ee)	59 (99% ee)
$Rh_2(4S\text{-MPPIM})_4$	52	63 (65% ee)	37 (96% ee)

[a] In refluxing $ClCH_2CH_2Cl$

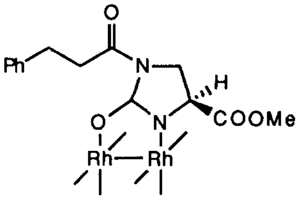
Chemoselectivity was dependent on the catalyst employed, but enantiocontrol was relatively unchanged through the catalyst series. However, the product from C-H insertion, which is the dimethyl ketal of 2-deoxyribonolactone,[9] was formed as the (*S,S*)-enantiomer from *S*-configured catalysts with enantiocontrol up to 99% ee, and the ylide rearrangement product **5** was obtained in 65±1% ee and could be enriched to 98% ee by a single crystallization (10:1 hexanes: EtOAc).[10] Obviously, ylide generation occurred from the metal carbene in the axial conformation while C-H insertion operated from the equatorial conformation.



$Rh_2(5S\text{-MEPY})_4$[11]

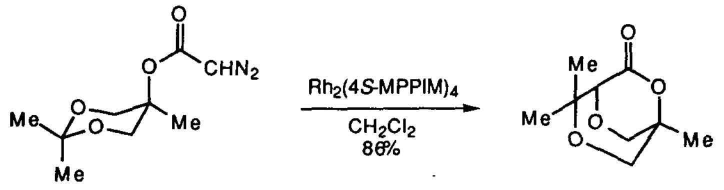


$Rh_2(4S\text{-MEOX})_4$[12]



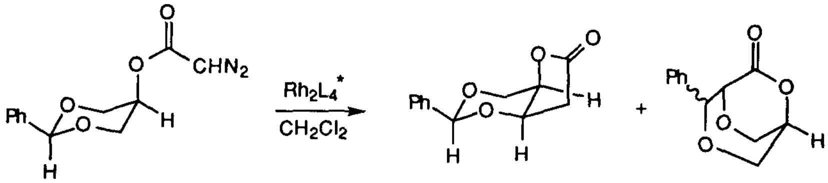
$Rh_2(4S\text{-MPPIM})_4$[13]

Since **5** could only be formed from the conformation (1) in which the carbenic carbon was projected onto the ether oxygens from the axial position, 1,3-dioxane derivative **7** was constructed in order to favor this conformation. Diazo decomposition of **7** catalyzed by $Rh_2(4S\text{-MPPIM})_4$ gave the ylide-derived product **8** virtually exclusively in high yield and in 81% ee (eq 2). The only by-product was that from C-H insertion into the equatorial ring methylene C-H bond (2% of total). With other chiral dirhodium(II) catalysts, C-H insertion was more pronounced, and trace amounts of the spirolactone product from insertion into a methyl C-H bond were also observed, but the sum of these products was <15% and enantioselectivity for **8** was 80±1% ee.



7 → **8**: 81% ee (2)

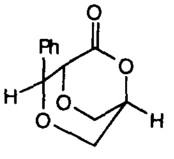
In order to confirm the conformational requirement for chemoselective ylide formation, benzylidine derivative **9** was prepared and treated with the selection of chiral catalysts. As expected, the dominant reaction process was that from ylide formation (eq 3), but we were surprised

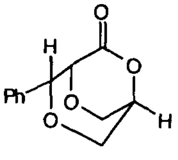


(3)

9	*yield, %*	**10**, %	**11**, %
Rh$_2$(4S-MEOX)$_4$	72	31	69
Rh$_2$(5S-MEPY)$_4$	78	12	88
Rh$_2$(4S-MPPIM)$_4$	74	12	88

to find that the [1,2]-insertion product consisted of two diastereoisomers, one of which having enantiomeric excesses that were dependent on the catalyst (***exo*-11**) and the other with % ee values that were relatively independent of the catalyst (***endo*-11**). The formation of ***exo*-11** is

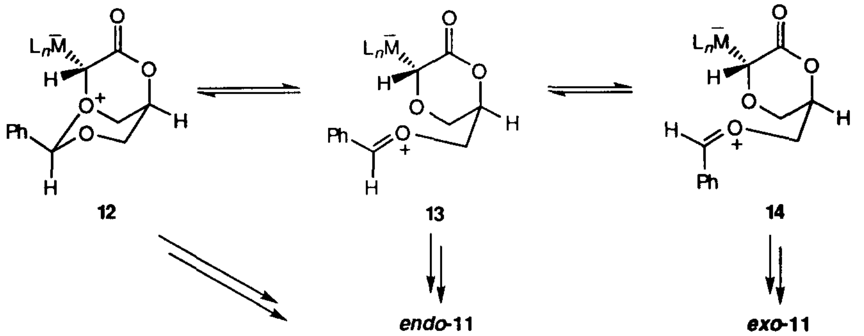




***endo*-11**, %		***exo*-11**, %
67 (39% ee)	Rh$_2$(4S-MEOX)$_4$	33 (33% ee)
60 (42% ee)	Rh$_2$(5S-MEPY)$_4$	40 (52% ee)
56 (40% ee)	Rh$_2$(4S-MPPIM)$_4$	44 (88% ee)

consistent with a pathway for ylide rearrangement involving the production of **13** and rotation of the attached benzaldehyde to **14** (Scheme 2), the driving force for which is steric interaction between phenyl and the catalyst in **12**. That rearrangement occurs through catalyst-associated ylides is suggested by catalyzed-dependent enantiocontrol in the formation of ***exo*-11**.

The facility with which oxonium ylides are formed, and evidence that the chiral metal catalyst remains attached to the ylide during rearrangement, suggests a new role for chiral dirhodium(II) carboxamidates in catalytic asymmetric syntheses. We are investigating the uses of these catalysts



Scheme 2

for other ylide transformations.

Acknowledgment. Support for this research from the National Science Foundation and the National Institutes of Health (GM 46503) is gratefully acknowledged. We are grateful to A. Dyatkin for his results in this area.

References and Notes

1. Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263.
2. Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S. Ed.; Pergamon Press, New York, 1995; Vol. 12, Chapter 5.2.
3. Doyle, M. P.; Bagheri, V.; Claxton, E. E. *J. Chem. Soc., Chem. Commun.* **1990**, 46.
4. West, F. G.; Naudu, B. N.; Tester, R. W. *J. Org. Chem.* **1994**, *59*, 6892.
5. Clark, J. S.; Dossetter, A. G.; Whittingham, W. G. *Tetrahedron Lett.* **1996**, *37*, 5605.
6. Brogan, J. B.; Bauer, C. B.; Rogers, R. D.; Zercher, C. K. *Tetrahedron Lett.* **1996**, *37*, 5053.
7. McCarthy, N.; McKervey, M. A.; Ye, T.; McCann, M.; Murphy, E.; Doyle, M. P. *Tetrahedron Lett.* **1992**, *33*, 5983.
8. (a) Ito, K.; Yoshitake, M.; Katsuki, T. *Tetrahedron* **1996**, *52*, 3905. (b) Ito, K.; Yoshitake, M.; Katsuki, T. *Heterocycles* **1996**, *42*, 305.
9. This derivative is not available through direct reaction of 2-deoxyribonolactone with acetone: Han, S.-Y.; Joullié, M. M.; Petasis, N. A.; Bigorra, J.; Corbera, J.; Font, J.; Ortuno, R. M. *Tetrahedron* **1993**, *49*, 349.
10. All new products were identified from their characteristic spectra, and elemental analyses confirmed their composition. Enantiomeric excesses were obtained from GC analyses on Chiraldex columns with baseline resolution; for example, both **5** and **6** were analyzed on a 30-m Chiraldex B-PH column with enantiomer separations of 5 and 8 min, respectively.
11. Doyle, M. P.; Winchester, W. R.; Hoorn, J. A.; Lynch, V.; Simonsen, S. H.; Ghosh, R. *J. Am. Chem. Soc.* **1993**, *115*, 9968.
12. Doyle, M. P.; Dyatkin, A. B.; Protopopova, M. N.; Yang, C. I.; Miertschin, C. S.; Winchester, W. R. *Rec. Trav. Chim. Pays-Bas* **1995**, *114*, 163.
13. Doyle, M. P.; Zhou, Q.-L.; Raab, C. E.; Roos, G. H. P.; Simonsen, S. H.; Lynch, V. *Inorg. Chem.* **1996**, *118*, 8837.

(*Received in USA* 26 *March* 1997; *accepted* 5 *May* 1997)