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CHIRAL CATALYSTS FOR ENANTIOSELECTIVE INTERMOLECULAR CYCLOPROPANATION REACTIONS WITH METHYL PHENYLDIAZOACETATE. ORIGIN OF THE SOLVENT EFFECT IN REACTIONS CATALYZED BY HOMOCHIRAL DIRHODIUM(II) PROLINATES

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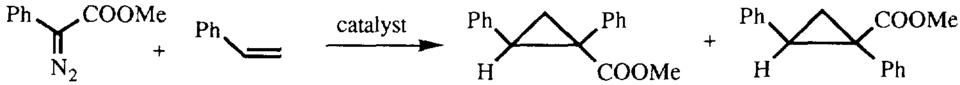
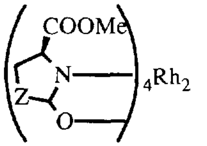
Summary: *The highest levels of enantiocontrol in intermolecular cyclopropanation reactions of methyl phenyldiazoacetate have been achieved with homochiral dirhodium(II) prolinates in pentane, the solvent effect for which (0.8 ± 0.2 kcal/mol) is associated with ligand alignment.* Copyright © 1996 Elsevier Science Ltd

Investigations of enantioselectivity and diastereoselectivity in intermolecular cyclopropanation reactions have principally focused on diazoacetate derivatives.[1] Exceptional enantiocontrol (>90% ee) has been achieved in reactions of diazoacetates with a limited number of alkenes using chiral salicylaldimine,[2] semicorrinato-,[3] and bis-oxazoline-ligated[4] copper(I) catalysts, as well as by *trans*-$RuCl_2$(Pybox-*ip*)(ethylene).[5] Diastereocontrol has been more elusive, generally requiring that the diazoacetate be derived from a sterically demanding alcohol or phenol.[4,6] Significantly, reports of stereoselective intermolecular cyclopropanation with other diazo compounds, particularly those with two functional attachments to the diazomethane core, have been virtually nonexistent.[1] Generally, high enantiocontrol is believed to be dependent on the relative size of the diazomethane attachments so that enantioselectivity decreases as the two diazomethane substituents become closer in size and electronic character.[7,8] An exception is the recent reports by Davies and coworkers,[9] already applied by Corey and Grant in the synthesis of *sertraline*,[10] that vinyldiazoacetates undergo highly enantioselective and diastereoselective cyclopropanation of certain alkenes catalyzed by homochiral dirhodium(II) prolinate derivatives; chiral dirhodium(II) carboxamidates were reported to be inactive for these applications.[5] In order to evaluate the significance of this discovery within the composite of chiral catalysts known to be effective for cyclopropanation, we have investigated stereocontrol in reactions of methyl phenyldiazoacetate and now report that homochiral dirhodium(II) prolinate catalysts, initially developed by McKervey and coworkers,[11] are uniquely suited to highly enantioselective and diastereoselective intermolecular cyclopropanation of selected alkenes with aryldiazoacetates. In the accompanying communication, Davies and coworkers report that this high stereocontrol can be generally achieved in cyclopropanation reactions with monosubstituted alkenes.

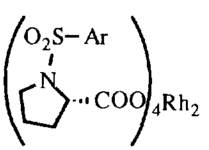
Reactions between methyl phenyldiazoacetate and styrene were performed with representative chiral dirhodium(II) and copper(I) catalysts in order to compare enantiocontrol and diastereocontrol in this cyclopropanation reaction (eq 1). Chiral dirhodium(II) carboxamidates (2) having the (2,2-*cis*)-geometry with two nitrogens and two oxygens



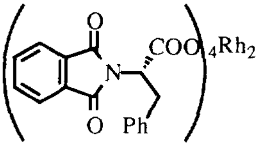
1E **1Z** (1)



2a: Z = CH_2, $Rh_2(5S\text{-}MEPY)_4$
2b: Z = O, $Rh_2(4S\text{-}MEOX)_4$
2c: Z = NCOPh, $Rh_2(4S\text{-}MBOIM)_4$
2d: Z = $NCOC_6H_4Bu^t\text{-}p$, $Rh_2(4S\text{-}TBOIM)_4$



3a: Ar = Ph
3b: Ar = $p\text{-}Bu^tC_6H_4$



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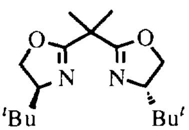

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bound to each rhodium,[12-14] including the previously unreported dirhodium(II) tetrakis[methyl 1-benzoyl-2-oxoimidazolidin-4(*S*)-carboxylate], $Rh_2(4S\text{-}MBOIM)_4$ (**2c**), and its 1-(*p*-*tert*-butylbenzoyl)-derivative $Rh_2(4S\text{-}TBOIM)_4$ (**2d**), McKervey's homochiral dirhodium(II) *N*-benzenesulfonyl derivative (**3a**)[11] and the *tert*-butylbenzenesulfonyl analog (**3b**) prepared by Davies,[9] the homochiral dirhodium(II) carboxylate developed by Hashimoto, Ikegami, and coworkers[16] with the *N*-phthalimide derivatives of L-phenylalanine (**4**), and Evans' chiral bis-oxazoline (**5**) ligand for copper(I)[4b] constituted the set of catalysts for which stereocontrol in eq 1 was evaluated (Table 1).

Table 1. Catalyst-Dependent Stereocontrol in the Cyclopropanation of Styrene with Methyl Phenyldiazoacetate[a]

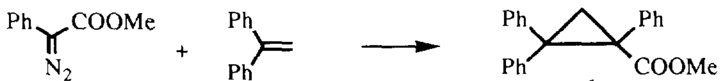
catalyst/ solvent	yield, %[b]	**1E**:**1Z**	**1E** ee, %[c]	catalyst/ solvent	yield, %[b]	**1E**:**1Z**	**1E** ee, %[c]
2a/CH_2Cl_2	27	97:3	49	**3a**/CH_2Cl_2	45	97:3	60
2b/CH_2Cl_2	57	96:4	41	**3b**/CH_2Cl_2	77	97:3	61
2c/CH_2Cl_2	73	96:4	48	**3b**/pentane	73	96:4	85
2d/CH_2Cl_2	63	95:5	77	**4**/CH_2Cl_2	95	98:2	34[d]
2d/pentane	69	94:6	75	**4**/pentane	82	96:4	16[d]
$Rh_2(cap)_4$/CH_2Cl_2	37	97:3	-	**5**/CuOTf/$CHCl_3$	54	99:1	8

[a]Reactions performed using 1.0 mol % of catalyst by controlled addition of methyl phenyldiazoacetate (1.0 mmol) in 5 mL of CH_2Cl_2 to styrene (10 mmol) in 5 mL of CH_2Cl_2. With pentane, 10 mL + 15 mL, respectively, was used. [b]Isolated yield of 1. [c](1*R*,2*S*)-Enantiomer; % ee values were determined by capillary GC with baseline resolution on a Chiraldex B-Ph column. [d](1*S*,2*R*)-Enantiomer.

As is evident from the Table, dirhodium(II) carboxamidates give virtually identical enantioselectivities for the formation of **1E**; other dirhodium(II) analogs of **2b** including those in which the COOMe group is replaced by benzyl, $Rh_2(4R\text{-BNOX})_4$,[12] or phenyl, $Rh_2(4R\text{-PHOX})_4$,[13] give similar results (42 and 52% ee, respectively). The exception is $Rh_2(4S\text{-TBOIM})_4$ (**2d**) whose *p-tert*-butylbenzoyl substituent increases selectivity from less than 50% (compare with **2c**) to greater than 75% ee. Among catalyst/ligands **3-5**, the highest level of enantiocontrol is provided by the homochiral dirhodium(II) prolinate **3b** from a reaction performed in pentane. The composite results suggest that methyl phenyldiazoacetate/styrene is a useful model with which to assess chiral catalyst effectiveness; the controlling features in this system are significantly different from those of the universally employed ethyl diazoacetate/styrene.[1-7] The diastereocontrol observed with dirhodium(II) caprolactamate, $Rh_2(cap)_4$, as well as with other catalysts in the Table, demonstrates that the **1E**:**1Z** ratio is a function of the reacting carbene and styrene rather than from the chiral ligands of the catalysts.

As previously established by Davies and coworkers in cyclopropanation reactions with vinyldiazoacetates catalyzed by **3b**,[9] the use of pentane as the solvent provides a dramatic increase in enantiocontrol. A similar increase is observed for the cyclopropanation of styrene with methyl phenyldiazoacetate (61 → 85% ee). However, the positive influence of pentane on enantiocontrol appears to be specific to **3b** since with **4** a reversal in % ee is observed with the use of pentane, and there is no effect of pentane on enantiocontrol with $Rh_2(4S\text{-TBOIM})_4$ (**2d**). Pentane appears to influence the alignment of prolinate ligands on dirhodium(II) to increase enantiocontrol; the more rigid structural arrangement of chiral dirhodium(II) carboxamidates prevents a similar solvent effect.

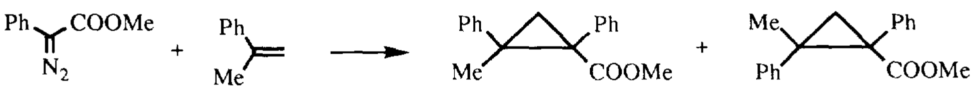
The capabilities of homochiral dirhodium(II) prolinate catalysts for high stereocontrol in intermolecular cyclopropanation reactions were further evaluated with the use of alkenes other than styrene. Exceptional enantiocontrol was achieved with 1,1-diphenylethene (eq 2)[17] and, curiously, the enhancement in enantiocontrol with the use of pentane



6 (2)

	yield, %	ee, %
3a/CH_2Cl_2	57	91
3b/pentane	83	97
3b/CH_2Cl_2	61	86

here (corresponding to 0.9 kcal/mol) is similar to that for the cyclopropanation of styrene (0.7 kcal/mol, Table 1) as well as for the cyclopropanation of styrene with (*E*)-2-diazo-4-phenyl-3-butenoate.[9a] With α-methylstyrene the methyl esters of both (*E*)- and (*Z*)-1,2-diphenyl-2-methylcyclopropanecarboxylates were formed (eq 3) with low diastereo-



7E **7Z** (3)

	yield, %	**7E**:**7Z**	% ee **7E**	% ee **7Z**
3a/CH_2Cl_2	86	61:39	63	73
3b/pentane	88	60:40	85	81
2d/CH_2Cl_2	91	69:31	36	14

control but with enantiocontrol from reactions catalyzed by **3b** (85% ee for **7E**) which was virtually identical to that achieved with styrene (Table 1). Further investigations of stereocontrol in cyclopropanation reactions of aryldiazoacetates using these and modified homochiral dirhodium(II) prolinate catalysts are underway.

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