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ENHANCEMENT OF STEREOSELECTIVITY IN CATALYTIC CYCLOPROPANATION REACTIONS

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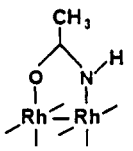
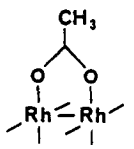
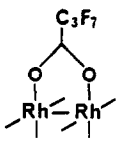
Summary: Significant enhancement of trans(anti) stereoselectivity is achieved in rhodium(II) acetamide catalyzed cyclopropanation reactions of 2,3,4-trimethyl-3-pentyl diazoacetate (ODA) and diazoacetamides.

The synthetic usefulness of catalytic cyclopropanation reactions has been limited by their low stereoselectivities.[1] Preferential trans selectivity is observed in reactions of olefins with diazo esters,[2] but few examples have been reported in which the relative yield of the trans isomer exceeds 80 percent. Although there is general recognition that the transition metal catalyst and the diazo compound exert control on cyclopropanation selectivity,[3,4] the combinations of catalyst and diazo compound that could achieve high trans selectivity have not previously been identified.

Rhodium(II) carboxylates are recognized as the catalysts of choice for cyclopropanation reactions.[5] Although stereochemical preferences from some modifications in the carboxylate ligands have been reported,[6] none have appeared to strongly enhance trans(anti) cyclopropanation stereoselectivities. However, two potential rhodium(II) catalysts, dirhodium perfluorobutyrate[7] and dirhodium acetamide,[8] whose ligands provide significant opposing electronic







influences relative to rhodium acetate, have not previously been utilized. Similarly, diazocarbonyl compounds possessing carbonyl attachments that are substantially different from ethoxy have rarely been employed. We now report the spectrum of stereoselectivities that can be achieved with simple modifications of catalyst and diazocarbonyl compound.

The trans/cis product ratios for cyclopropanation of styrene using three rhodium(III) catalysts and four diazocarbonyl compounds are reported in Table 1.

Table 1. Stereoselectivity Enhancement in Catalytic Cyclopropanation of Styrene

	trans/cis (yield, %)			
Catalyst	$N_2CHCOOEt$	$N_2CHCOOCMe(\underline{i}\text{-}Pr)_2$	$N_2CHCONMe_2$	$N_2CHCON(\underline{i}\text{-}Pr)_2$
$Rh_2(OOCC_3F_7)_4$	1.1 (81)	1.1 (83)	1.5 (67)	12 (51)
$Rh_2(OAc)_4$	1.6 (95)	2.4 (95)	2.2 (74)	64 (53)
$Rh_2(NHCOCH_3)_4$	2.1 (89)	4.4 (87)	2.4 (70)	114 (47)

These reactions were performed at room temperature using previously described methods for addition[5b] with a 10-fold excess of styrene and 1.0 mol percent of catalyst based on diazo compound. Except for reactions with N,N-diisopropyldiazoacetamide, where carbene dimer formation and intramolecular carbon-hydrogen insertion[9] were in competition with olefin addition, product yields were remarkably high. Isomer identifications and stereoisomer ratios were obtained as previously described[2a] and, in some cases, cyclopropane products were also converted by transesterification or by hydrolysis/esterification to the known ethyl ester for further confirmation.

The data in Table 1 describe the broadest spectrum of cyclopropanation stereoselectivities that has been reported for any olefin. Rhodium(II) perfluorobutyrate obviously offers minimum stereochemical preference and, as is evident from the trans/cis isomer ratios obtained with both ethyl diazoacetate (EDA) or 2,3,4-trimethyl-3-pentyl diazoacetate (ODA),[10] there is little steric bias in the transition state for cyclopropanation with this reactive catalyst. In contrast, rhodium(II) acetamide has a remarkable facility for preferential trans orientation, even in reactions with EDA. For comparison, the corresponding trans/cis product ratios for reactions of EDA with styrene were 1.5 with rhodium(II) pivalate and 0.9 with iodorhodium(III)mesotetraphenylporphyrin (RhTPPI).[11] Rhodium(II) trifluoroacetamide gave results that were nearly identical with those achieved with $Rh_2(OAc)_4$, and rhodium(II) trifluoroacetate provided stereoselectivities that were intermediate between $Rh_2(OAc)_4$ and $Rh_2(OOCC_3F_7)_4$. Copper catalysts that included $CuCl\cdot P(O\text{-}\underline{i}\text{-}Pr)_3$, $Cu(OTf)_2$, and $Cu(acac)_2$ gave lower trans selectivities than rhodium(II) acetamide.

Stereoselectivities for catalytic cyclopropanation reactions of representative alkenes by EDA and ODA are reported in Table 2. Clearly, stereoselectiv-

Table 2. Stereoselectivity Enhancement in Catalytic Cyclopropanation of Representative Alkenes[a]

	trans/cis (anti/syn)					
	$Rh_2(OOCC_3F_7)_4$		$Rh_2(OAc)_4$		$Rh_2(NHCOCH_3)_4$	
Alkene	EDA	ODA	EDA	ODA	EDA	ODA
1-Hexene	1.2	1.4	1.4	2.5	1.7	3.5
n-Butyl vinyl ether	1.3	1.4	1.7	2.1	2.8	3.8
Ethyl vinyl ether	1.3	1.5	1.6	2.3	2.8	4.4
Bicyclo[2.2.1]hept-2-ene	1.5	2.0	2.0	3.2	3.6	5.0
3,3-Dimethyl-1-butene	1.5	1.8	2.9	5.9	5.0	8.0
Cyclohexene	2.0	4.1	3.8	9.5	10	11

[a]Product yields ranged from 60 to 93 percent with an average yield of 84% for reactions with EDA. With ODA the range in product yields was from 62 to 99 percent with an average yield of 85%.

ities are responsive to the catalyst and the size of the alkoxy substituent on the diazoester as well as to olefinic substituents, and these changes are in accord with mechanistic predictions.[1a] Because of the ease of its preparation,[12] its reactivity towards each of the catalysts employed, and the high product yields obtained from its use, ODA is preferred over the diazoacetamides.[13] The stereoselectivities obtained with ODA are comparable to or greater than those resulting from the use of N,N-dimethyldiazoacetamide (eg., 12 from cyclohexene with $Rh_2(OAc)_4$ catalysis but only 1.7 from ethyl vinyl ether with the same catalyst).

In each of the reported examples, the change in the relative percentage of the trans(anti) isomer from $Rh_2(OOCC_3F_7)_4$ catalysis of cyclopropanation with EDA to $Rh_2(NHCOCH_3)_4$ catalysis of cyclopropanation with ODA is greater than 20 and with 3,3-dimethyl-1-butene is as high as 29. The anti-isomer from cyclopropanation of cyclohexene is produced in greater than 90 percent relative yield, and even ethyl vinyl ether affords the trans-cyclopropane isomer in greater than 80 percent yield.[14] Clearly, substantial enhancement of trans(anti) stereoselectivity can be achieved with simple structural modifications of the catalyst and diazo compound.[15]

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