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Enantioselective dirhodium(II)-catalyzed cyclopropanations with trimethylsilylethyl and trichloroethyl aryldiazoacetates

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This paper is dedicated to the memory of Professor Alan R. Katritzky, an inspirational leader in the field of heterocyclic chemistry

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ABSTRACT

Highly functionalized cyclopropanecarboxylates were readily prepared by rhodium-catalyzed cyclopropanation of alkenes with aryldiazoacetates and styryldiazoaceates, in which the ester functionality is either trimethylsilylethyl (TMSE) or trichloroethyl (TCE). By having labile protecting groups on the ester, chiral triarylcyclopropane carboxylate ligands were conveniently prepared. The asymmetric induction during cyclopropanation is dependent on the nature of the ester group and the chiral dirhodium tetracarboxylate catalyst. The prolinate catalyst Rh_2(*S*-DOSP)$_4$ was the optimum catalyst for asymmetric intermolecular cyclopropanation of TMSE diazoesters with styrene, while Rh_2(*R*-BPCP)$_4$ was the optimum catalyst for TCE diazoesters.

1. Introduction

Cyclopropanes are a common motif in natural products and medicinal targets, and are useful building blocks in complex molecule synthesis.[1–4] Therefore, the development of methods for their enantioselective synthesis has been of general interest.[5–11] Cyclopropanation between metal carbenes and alkenes is recognized as a classic reaction for the synthesis of cyclopropanes.[12] We have previously shown that the cyclopropanation reaction of aryldiazoacetates proceeds with high diastereoselectivity even under thermal conditions.[13] When cyclopropanation with donor/acceptor carbenoids is catalyzed by chiral dirhodium(II) tetracarboxylates, the reaction can proceed with high levels of enantioselectivity.[14–18] The reaction is even effective for electron deficient alkanes with the appropriate catalyst.[18] Mechanistic studies have suggested that these rhodium-catalyzed cyclopropanation reactions proceed by means of a concerted-asynchronous process.[19]

In a comparative study of different catalysts, Rh_2(DOSP)$_4$ was found to be the optimal catalyst for a broad range of methyl aryldiazoacetates (Fig. 1).[20] In addition, the two other chiral dirhodium(II) catalysts studied, Rh_2(*S*-PTAD)$_4$ and Rh_2(*R*-BNP)$_4$, were shown to have enantioselectivity profiles complementary to that of Rh_2(DOSP)$_4$. The former provided high levels of enantioinduction when the acceptor of the aryldiazoacetate precursor was varied. Whereas Rh_2(*R*-BNP)$_4$ was well suited for catalyzing highly enantioselective cyclopropanation of alkoxy-substituted methyl aryldiazoacetates. A drawback of Rh_2(DOSP)$_4$, however, is that high levels of enantioselectivity are typically achieved only when the

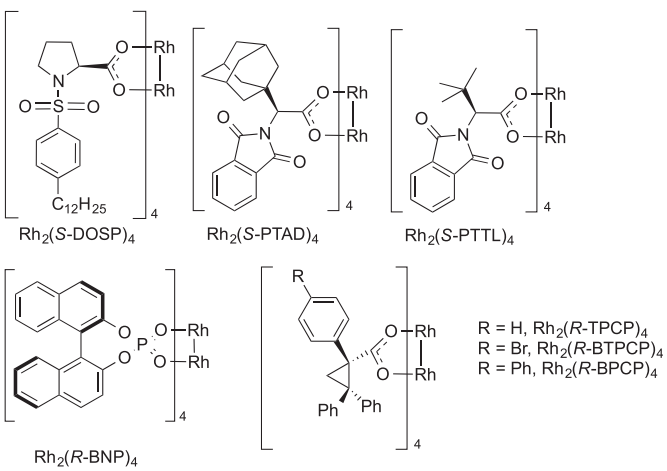

Fig. 1. Dirhodium(II) catalysts.

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acceptor group is a methyl ester as opposed to larger alkyl esters.[14] Additionally a model was developed to predict the stereochemistry of the Rh_2(*S*-DOSP)$_4$-catalyzed cyclopropanation.[21]

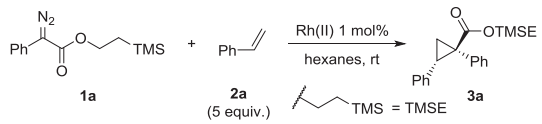
A new generation of chiral D_2-symmetric dirhodium(II) catalysts has emerged from the Davies group that employs chiral triarylcyclopropane carboxylates as ligands.[22] These ligands are derived from Rh_2(*R*-DOSP)$_4$ catalyzed cyclopropanation of 1,1-disubstituted olefins with aryldiazoacetates, followed by ester hydrolysis. The first member of this class was Rh_2(*R*-BTPCP)$_4$, which was found to catalyze classic reactions of donor/acceptor carbenoids such as cyclopropanation, tandem cyclopropanation/Cope rearrangement and combined C–H functionalization/Cope rearrangement/retro-Cope rearrangement. Furthermore, it was employed in the enantioselective synthesis of 2-arylbicyclo[1.1.0]butane carboxylates.[23] These catalysts also show promise in controlling the reactivity of rhodium-stabilized carbenoids derived from vinyldiazoacetates, which traditionally react at the carbene site with the benchmark catalysts, Rh_2(*R*-DOSP)$_4$ and Rh_2(*S*-PTAD)$_4$. A related analogue, Rh_2(*R*-TPCP)$_4$ was employed for the generation of [3+2] cycloaddition products derived from initial attack at the vinylogous position of the rhodium vinylcarbene.[24] Most recently, the biphenyl derivative Rh_2(*R*-BPCP)$_4$ has shown promise for site selective C–H functionalization. It was applied to the selective functionalization of activated primary C–H bonds, such as allylic and benzylic sites.[25] Furthermore, in combination with the more sterically hindered 2,2,2-trichloroethyl aryldiazoacetates, site selective and enantioselective C–H functionalization of methyl ethers was achieved.[26]

Given the important role that different ester groups play in the reactivity and selectivity of carbenoid C–H functionalization reactions, we undertook a study to uncover the role of 2-(trimethylsilyl)ethyl (TMSE) and 2,2,2-trichloroethyl (TCE) esters in cyclopropanation reactions. Previously, we had shown that the TMSE esters are prone to intramolecular reactions,[27] but we anticipated that this ester functionality would be compatible with intermolecular reactions of reactive alkenes. The TCE group appears to be very robust for rhodium carbene reactions, and so we expected donor/acceptor carbenes bearing TCE ester acceptor group would be very effective in intermolecular cyclopropanations. Both ester groups would be more easily removed than the corresponding methyl ester, which would expand the range of useful carbene transformations for the preparation of novel chiral carboxylate ligands. Herein we report the results of our efforts to develop asymmetric cyclopropanation reactions of TMSE aryldiazoacetates and TCE aryldiazoacetates.

2. Results and discussion

The study began with the reaction of TMSE phenyldiazoacetate **1a** and styrene **2a** to determine the optimal chiral dirhodium(II) catalyst for the formation of cyclopropane **3a** as a single diastereomer with high levels of enantioselectivity. Of the catalysts screened, Rh_2(*S*-DOSP)$_4$ provided the highest yield and level of enantioinduction, producing **3a** in 87% yield and 87% ee (Table 1, entry 1). Rh_2(*S*-BTPCP)$_4$ afforded the desired cyclopropane in moderate yield but low enantioselectivity, 67% yield and 43% ee, respectively (Table 1 entry 2). Both the phthalimido dirhodium(II) catalysts Rh_2(*S*-PTAD)$_4$ and Rh_2(*S*-NTTL)$_4$ provided low yields and enantioselectivity in the reaction.

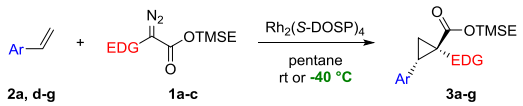
Table 1
Chiral dirhodium(II)-catalyzed cyclopropanation of TMSE phenyldiazoacetate and styrene

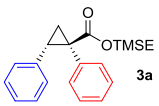
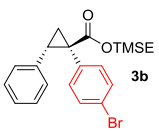
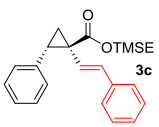
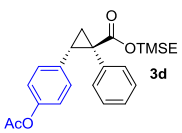
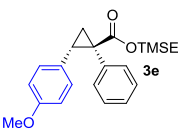
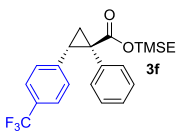
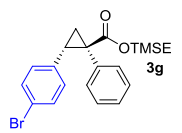


Entry	Catalyst	Yield (%)	ee (%)
1	**Rh_2(*S*-DOSP)$_4$**	**87**	**87**
2	Rh_2(*S*-BTPCP)$_4$	67	43
3	Rh_2(*S*-PTAD)$_4$	46	−35
4	Rh_2(*S*-NTTL)$_4$	35	−51

On the basis of the initial evaluation, Rh_2(*S*-DOSP)$_4$ was used to study the scope of the cyclopropanation with a series of TMSE aryldiazoacetates and styrene derivatives. The results are summarized in Table 2. The enantioselectivity of **3a** was slightly higher in pentane, therefore it was used in the scope study (see Table 1, entry 1 and Table 2, entry 1). The Rh_2(*S*-DOSP)$_4$-catalyzed cyclopropanation of TMSE aryldiazoacetates was fairly general with respect to the donor group on the diazoacetates, as cyclopropanes **3a**–**3c** were formed in high yields and high levels of enantioselectivity when the reactions were conducted at room temperature. Both 4-bromophenyl and styryl substituted TMSE diazoacetates yielded the cyclopropanes **3b** and **3c** with fairly high levels of enantioinduction (88% and 85% ee, respectively, entries 2 and 3). Both electron-withdrawing and electron-donating substituents were well tolerated on the styrene derivative as well (entries 4–7). Both the 4-methoxy and 4-trifluoromethyl substituted styrenes afforded the cyclopropanes in 72% yield. The 4-acetoxy and 4-

Table 2
Substrate scope of the cyclopropanation of TMSE aryldiazoacetates and styrenes



Entry	Product	rt (% yield, % ee)	−40 °C(% yield, % ee)
1		86% yield 88% ee	69% yield 96% ee
2		73% yield 89% ee	63% yield 96% ee
3		64% yield 85% ee	71% yield 87% ee
4		61% yield 88% ee	65% yield 96% ee
5		72% yield 81% ee	76% yield 91% ee
6		72% yield 84% ee	50% yield 96% ee
7		74% yield 86% ee	67% yield 96% ee

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