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Enhancement of Cyclopropanation Chemistry in the Silver-Catalyzed Reactions of Aryldiazoacetates

Janelle L. Thompson and Huw M. L. Davies*

Department of Chemistry, University at Buffalo, The State University of New York, Buffalo, New York 14260

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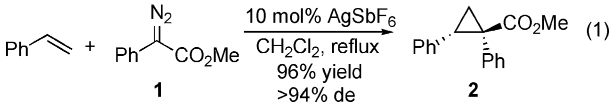
The transition-metal catalyst has a crucial effect on modulating the decomposition chemistry of diazo compounds.[1] Dirhodium catalysts have supplanted the traditional copper catalysts because in general they give much cleaner transformations for many reactions, such as cyclopropanation, C−H insertion, and ylide formation.[1] The silver-catalyzed decomposition of diazo ketones is a component of the venerable Arndt-Eistert homologation.[1,2] The resulting highly reactive silver carbenoids undergo a Wolff rearrangement instead of the typical reaction seen with dirhodium catalysis. Effective intermolecular reactions in silver carbenoid chemistry with ethyl diazoacetate have been limited to reactions catalyzed by silver scorpionate catalysts.[3−5]

The profound effect of the carbenoid structure on carbenoid reactivity has become widely recognized.[1,6] The traditional carbenoids functionalized with one or two electron acceptor groups (ester, ketone, phosphonate, etc.) are highly electrophilic.[1] We have found that carbenoids with a donor (aryl, vinyl, or alkynyl) and an acceptor group are much more chemoselective than the traditional carbenoids.[6] This has led to a number of highly stereoselective synthetic methods such as cyclopropanation,[7] [4 + 3] cycloaddition,[8] [3 + 2] cycloaddition,[9] and intermolecular C−H insertion.[3a,10] In this paper, we demonstrate that the silver hexafluoroantimonate ($AgSbF_6$)-catalyzed reactions of donor/acceptor-substituted carbenoids offer new synthetic opportunities, which cannot be achieved with dirhodium catalysis.

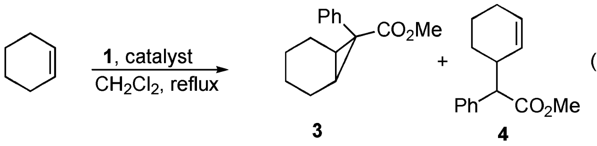
The first stage of this project was to screen the commonly available silver salts in the cyclopropanation of styrene with methyl phenyldiazoacetate **1** (eq 1). $AgSbF_6$ gave the highest yield (96%) in this reaction, generating the cyclopropane **2** with very high diastereoselectivity (>94% de). The catalytic activity of the silver salt seems to be dependent upon the counterion, as more tightly bound counterions (e.g., AgO_2CCF_3, AgOAc, Ag_2SO_4) gave poor yields or no reaction at all.[11]



(1)

Having demonstrated that the silver carbenoid is capable of intermolecular cyclopropanation, a comparative study of the reactivity profile of silver- versus dirhodium-catalyzed reactions was performed. In rhodium-catalyzed reactions of donor/acceptor carbenoids, monosubstituted alkenes and 1,2-disubstituted alkenes efficiently undergo cyclopropanation.[7] Cis-1,2-disubstituted alkenes are less favorable substrates for cyclopropanation and intermolecular C−H insertion becomes a competing process. Trans-1,2-disubstituted or more highly substituted alkenes are sterically protected and very few examples of their cyclopropanation by donor/acceptor carbenoids are known.[7d] Controlling the selectivity between cyclopropanation and C−H insertion would be highly beneficial, and silver catalysis was found to have a profound influence on this selectivity.

A comparison between $AgSbF_6$- and rhodium(II) acetate-catalyzed reactions was conducted with a range of substrates. Silver catalysis strongly favors cyclopropanation as can be seen in the reaction between cyclohexene and methyl phenyldiazoacetate (**1**) (eq 2). The cyclopropane **3** was produced in high yield (88%) and diastereoselectivity (>94% de), while the rhodium acetate-catalyzed reaction gave a mixture of **3** and the C−H insertion product **4** in a 1:2.2 ratio.

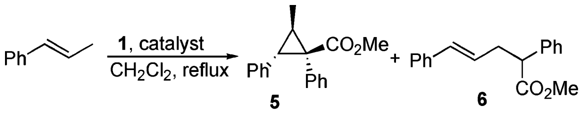


(2)

catalyst	yield^a, %	ratio **3:4**
$AgSbF_6$	88	>15:1
$Rh_2(OAc)_4$	44	1:2.2

^{a} = combined yield

Further investigation into a more highly substituted system, *trans*-*β*-methylstyrene, gave even more contrasting results. The $AgSbF_6$-catalyzed reaction yielded the cyclopropane **5** in excellent yield (80%) and diastereoselectivity (>94% de), retaining the trans orientation between the phenyl and methyl groups in the final product (eq 3). The same reaction catalyzed by rhodium acetate gave only a 4% yield of the C−H insertion product **6**; carbene dimerization was the dominant product despite the presence of the substrate in large excess. This result confirms that the rhodium-catalyzed reactions of donor/acceptor-substituted carbenoids are especially inefficient at mediating the cyclopropanation reaction of trans-1,2-disubstituted alkenes, but the silver-catalyzed reactions have a very different reactivity profile.



(3)

catalyst	yield, %	ratio **5:6**	de, %
$AgSbF_6$	80	>20:1	>94
$Rh_2(OAc)_4$	4	1:>20	

The results of the $AgSbF_6$-catalyzed cyclopropanation of a range of alkenes are summarized in Table 1. Only the reaction with 1,1-diphenylethylene (entry 5) can be effectively achieved under rhodium catalysis. In entries 1−3 the cyclopropanation of cyclic cis alkenes is very effective with $AgSbF_6$, but allylic C−H insertion

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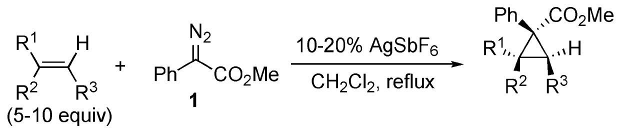
Table 1. Silver-Catalyzed Cyclopropanation with **1**



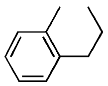
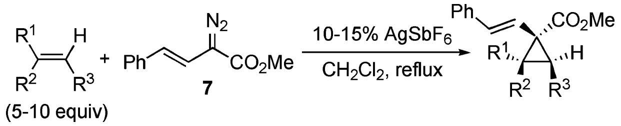
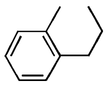
entry	R^1	R^2	R^3	yield, %
1	H	$-(CH_2)_4-$		88
2	H	$-(CH{=}CHCH_2CH_2)-$		79
3	H			80
4	H	H	Ph	96
5	Ph	Ph	H	82
6	Me	H	Ph	80
7	H	Me	Ph	86
8	Ph	H	Ph	84
9	H	Ph	Ph	54

Table 2. Silver-Catalyzed Cyclopropanation with **7**

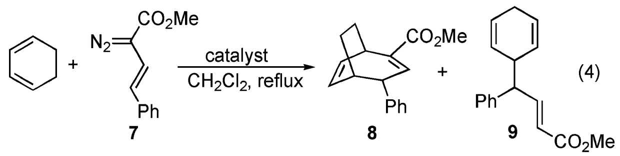


entry	R^1	R^2	R^3	yield, %
1	H	$-(CH_2)_4-$		43
2	H	$-(CH{=}CHCH_2CH_2)-$		67[a]
3	H			57
4	H	H	Ph	82
5	Ph	Ph	H	56[b]
6	Me	H	Ph	65
7	Ph	H	Ph	34

[a] Includes 15% of insertion product. [b] Reaction conducted at room temperature.

is a major competing reaction in rhodium-catalyzed reactions.[12] $AgSbF_6$-catalyzed cyclopropanation of more hindered substrates can also be achieved (entries 6−10), despite the fact that these substrates give virtually no cyclopropanation when the reaction is catalyzed by rhodium(II) acetate. In every case the cyclopropanation is highly diastereoselective, and no second diastereomer was evident by NMR.

Silver catalysis also has a major effect on the chemistry of vinyldiazoacetates as illustrated in eq 4. $AgSbF_6$-catalyzed reaction of the vinyldiazoacetate **7** with 1,3-cyclohexadiene resulted in primarily a tandem cyclopropanation/Cope rearrangement[6] to form the formal [4 + 3] cycloadduct **8** in 52% yield (eq 4). In contrast, the rhodium acetate-catalyzed reaction gave a 1.4:1 ratio of the cycloadduct **8** and the C−H functionalization product **9** derived from a combined C−H activation/Cope rearrangement.[13] Table 2 summarizes the $AgSbF_6$-catalyzed cyclopropanation of a range of alkenes by vinyldiazoacetate **7**. Only the reactions with styrene (entry 4) and 1,1-diphenylethylene (entry 5) can be effectively achieved under rhodium catalysis.[12] For the other substrates, the rhodium(II) acetate-catalyzed reactions gave either a mixture or no cyclopropanation products. The cyclopropanations are all highly diastereoselective, as is characteristic for the donor/acceptor carbenoids.[7]



(4)

catalyst	yield[a], %	ratio **8:9**
$AgSbF_6$	67	5.4:1
$Rh_2(OAc)_4$	36	1.4:1

[a] = combined yield

In conclusion, these studies show that $AgSbF_6$ is an effective catalyst for the reactions of donor/acceptor substituted carbenoids and shows a different reactivity profile from the traditional rhodium-catalyzed reactions. Most notably, sterically hindered alkenes, which are unreactive under rhodium(II) acetate-catalyzed conditions, can be effectively cyclopropanated under silver-catalyzed conditions.

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Supporting Information Available: Full experimental procedures for the rhodium acetate-catalyzed reactions and the characterization of new compounds are detailed. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) See Table 3 in the Supporting Information for a description of the effect of other silver salts on this reaction.
(12) See the Supporting Information for a detailed description of the corresponding rhodium-catalyzed reactions.
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