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Olefin cyclopropanation with aryl diazocompounds upon catalysis by a dirhodium(II) complex

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ABSTRACT

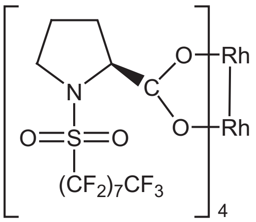
A dirhodium(II) complex with *N*-perfluorooctylsulfonylprolinate ligands is found to catalyze the cyclopropanation of olefins with simple aryl diazomethanes. In contrast to previously reported dirhodium(II) catalysts, the present complex works well not only with very electron-rich olefins such as enol ethers, but also with styrenes. Consequently, the present catalyst allows to prepare functionalized diarylcyclopropanes in moderate yields with good diastereoselectivity for the *cis* product, whereas the enantioselectivity of the reaction appears negligible.

Transition metal-catalyzed olefin cyclopropanation with diazocompounds is one of the best known reactions involving organometallic catalysis[1] and has been extensively employed for the preparation of structurally diverse cyclopropanes, which are widely used building blocks or intermediates for organic synthesis. In fact, the cyclopropane unit is present in various agrochemicals and pharmaceuticals; furthermore, it can be cleaved in a variety of ways to yield molecules with increased complexity.[2,3] However, cyclopropanation with diazocompounds also presents some limitations: for example, only diazocompounds bearing at least one electron-withdrawing group can be efficiently employed as reagents. In most other cases (with the only notable exception of simple diazomethane) the diazo reagent is either not sufficiently stable and/or inefficiently transferred to the olefin by the metal catalyst, which instead promotes the formation of coupling products of the diazocompound itself.

Direct cyclopropanations with simple aryl diazocompounds not substituted by an electron-withdrawing group at the carbon atom, like the parent compound phenyl diazomethane, have been occasionally reported in the past, mainly using group 8 metal centers as reaction promoters or catalysts.[4,5] In particular, certain iron[4c] and ruthenium[5a] porphyrin catalysts display a synthetically useful reactivity, yielding with model olefin acceptors such as styrene mainly the *trans* cyclopropane product. In contrast, the catalytic efficiency exhibited by dirhodium(II) complexes, which rank among the best cyclopropanation catalysts known to date, proved scarce, with the parent dirhodium(II) acetate being active mainly with very electron rich olefin acceptors such as enol ethers.[4c,6]

A few years ago, we reported that the perfluoroalkylated complex **I** (Scheme 1), closely related to the highly successful *N*-arylsulfonylprolinate complexes originally proposed by McKervey[7] and extensively developed by Davies,[1b,8] is an efficient and easily recoverable and recyclable catalyst for asymmetric carbene transfer reactions (cyclopropanations, insertions into C–H bonds).[9] In this contribution, we show that the same compound can be employed as catalyst for the cyclopropanation of styrenes and other olefins with simple aryl diazocompounds, yielding the cyclopropanation product in moderate yields with good *cis* stereoselectivity.

tetrakis-Dirhodium(II)-*N*-(4-*t*-butylphenyl)sulfonylprolinate was already tested several years ago by Davies as the catalyst for the cyclopropanation of styrene with phenyl diazomethane (Scheme 2) and found to produce only trace yields of cyclopropanation products.[10] Consequently, we were quite surprised to record



I

Scheme 1.

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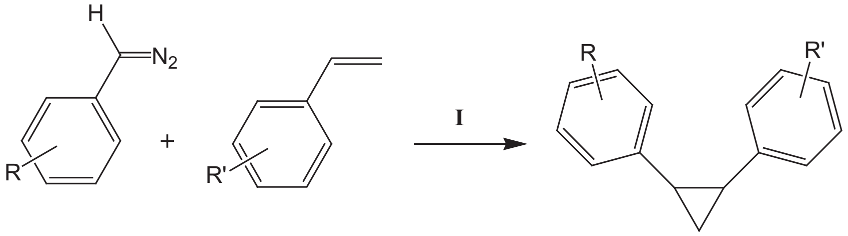

Scheme 2.

Table 1
Synthesis of cyclopropanes from olefins and diazocompounds

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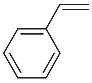
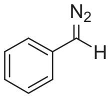
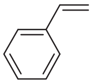
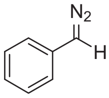
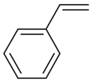
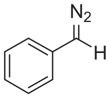
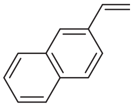
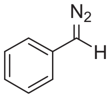
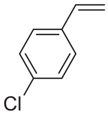
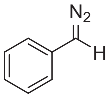
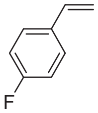
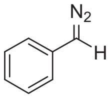
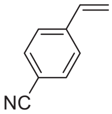
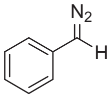
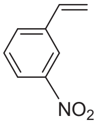
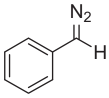
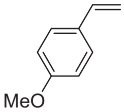
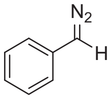
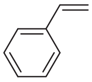
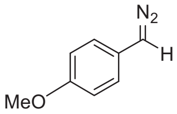
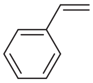
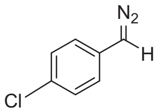
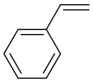
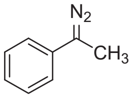
1			10	1	56	88:12
2			10	2	56	75:25
3			20	1	76	71:29
4			10	1	20	80:20
5			10	1	54	87:13
6			10	1	57	84:16
7			10	1	17	88:12
8			10	1	14[d]	84:16[d]
9			10	1	50	80:20
10			10	1	6	83:17
11			10	1	48	85:15
12			10	1	0	–

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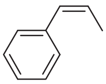
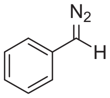
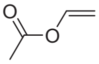
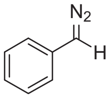
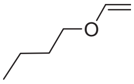
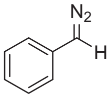
Table 1 (*continued*)

Entry	Olefin	Diazocompound	Olefin/diazo	$\mathbf{I}^a$ (mol %)	Yield^b (%)	dr^c
13			10	1	0	–
14			10	1	6	80:20
15			10	1	96	83:17

Reaction conditions: see Ref. 11.

[a] **I** (mol %) with respect to the limiting reagent (the aryl diazomethane).

[b] Isolated yields.

[c] Diastereomeric ratio (cis:trans).

[d] Yields after 48 h reaction time.

in the same reaction with our closely related catalyst **I** an isolated cyclopropanation yield of 56%, under conventional reaction conditions (1 equiv diazocompound, 10 equiv styrene, 1 mol % catalyst, controlled diazocompound addition over 5 h, toluene, 14 h),[11] other products being coupling or decomposition products of the diazocompound. In accordance with previous findings, the observed stereoselectivity was found to be opposite to that exhibited by iron and ruthenium porphyrins, which are known to yield preferentially the *trans* cyclopropanation product.[4c,5a]

We have briefly examined the effect of changing the reaction conditions on the yield of the reaction (Table 1, entries 1–3). Increasing the amount of catalyst from 1 to 2 mol % had no significant effect on the overall yield in cyclopropanation products whereas the selectivity for the *cis* product was lowered. On the contrary, working with a greater excess of olefin acceptor (20 equiv instead of 10) significantly improved the cyclopropanation yields but also decreased the diastereoselectivity. Consequently, in our further investigations we decided to keep on working with 10 equiv olefin and 1 mol % catalyst.

The scope and limitations of the reaction have been examined, particularly with reference to the effect of the nature of the substituents on the aromatic ring of the olefin and/or of the diazocompound.[12] As expected, cyclopropanation is favored by electron-donating substituents at the olefin and by electron-withdrawing substituents at the aryldiazocompound. The former raises the HOMO energy of the olefin and consequently its tendency to add the intermediate carbene (Table 1, entries 4–9), the latter stabilizes the diazocompound as well as the intermediate metal carbene against decomposition, thereby favoring its effective transfer (Table 1, entries 10 and 11). It is important to remark that this opposite effect of the nature of the substituents on the olefin and on the diazocompound potentially allows the preparation of diarylcyclopropanes bearing a wide range of substituents at the aryl groups, since electron-donating substituents can be conveniently incorporated in the alkene whereas electron-withdrawing substituents can be placed on the aryldiazomethane. On the other hand, the presence of additional electron-donating substituents on the carbene carbon of the aryldiazocompound is not tolerated: in fact, no cyclopropanation product is observed with methyl phenyl diazomethane (Table 1, entry 12).

In this way, an isolated yield of 50–60% in diarylcyclopropane products can be reached, with a diastereomeric ratio which is apparently almost independent of the nature of the substituents on the reagents, ranging from 80:20 to 88:12 and always favoring the *cis* isomer. It needs to be remarked that the employed synthetic procedure involves the preliminary preparation of the diazocompound reagent,[12] which is, however, not isolated: instead, the as-synthesized diazocompound solution can be directly employed as the reagent for the cyclopropanation reaction.[11]

We have also performed a preliminary evaluation of the scope of the reaction with respect to the olefin substrate. For example, a 1,2-disubstituted olefin such as *cis*-propenylbenzene did not add the carbene (Table 1, entry 13), in contrast to a less sterically encumbered 1,1-disubstituted olefin such as α-methylstyrene, which is known to be much more prone to give cyclopropanation products.[4,5] Incidentally, the group of Che also reported much lower yields for a 1,2 disubstituted olefin (*trans*-propenylbenzene) compared to an analogous 1,1-disubstituted one (α-methylstyrene) using a ruthenium porphyrin catalyst.[5a] Vinyl acetate also gave poor yields (Table 1, entry 14), as previously reported using simple dirhodium(II) acetate as the catalyst.[4c,6] On the contrary, a more electron-rich olefin substrate such as butyl vinyl ether gave as expected a high yield (96%) in cyclopropanation products (Table 1, entry 15), again similarly to what has been previously reported with simple dirhodium(II) acetate.[6] The diastereoselectivity for the cis product remained good in all cases. Finally, we investigated on the enantioselectivity of the reaction by subjecting the isolated products to chiral HPLC analysis following an analytical protocol previously described by Berkessel et al. for diphenylcyclopropanes.[5b] Unfortunately, the enantioselectivity of the reaction proved in all cases negligible for both diastereomeric cyclopropane products.

In conclusion, we have demonstrated that in contrast to previous reports a *tetrakis*-dirhodium(II) prolinate complex such as **I** is an efficient catalyst for cyclopropanations of olefins with aryl diazomethanes. This catalyst promotes the reaction not only with very electron-rich olefins such as enol ethers, but also with styrenes, which opens the way to the synthesis of substituted diarylcyclopropanes. The reaction is featured by negligible enantioselectivity but by good diastereoselectivity for the *cis* diarylcyclopropane product.

Acknowledgments

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11. *General procedure for the catalytic tests*. Complex **I** (15 μmol or 30 μmol) and olefin (15 mmol or 30 mmol) were dissolved in 20 mL 1:1 toluene/tetrahydrofuran under an inert argon atmosphere. To this solution, the diazocompound solution (1.5 mmol), freshly prepared as described in Ref. 12, was added over a 5 h period using a syringe pump. The reaction mixture was left under stirring overnight at room temperature, after which it was evaporated to dryness under reduced pressure. The resulting oil was then purified by column chromatography over silica gel (petroleum ether/ethyl acetate, 98:2 v:v) to afford the cyclopropanation products. The configuration of the various diastereoisomers was attributed by comparing their NMR spectra with those of the pure diastereoisomers previously reported in the literature.
12. *General procedure for the synthesis of the aryl diazocompounds*. Commercial benzaldehyde tosylhydrazone, or *p*-substituted benzaldehyde tosylhydrazone prepared according to Ref. 13, (1.5 mmol) was dissolved in 10 mL toluene and slowly added to a solution of 0.041 g benzyltriethylammonim chloride in 4.1 mL aqueous NaOH (14% w/w) under an inert argon atmosphere. The reaction mixture was heated to 70 °C and maintained at that temperature with stirring for 2 h. A progressive red coloration of the solution was observed. After cooling to room temperature, the organic phase was quickly separated from the aqueous phase, washed twice with 5 mL water, dried with Na_2SO_4 for 30 min, filtered, and immediately employed as the reagent for the cyclopropanation reaction.
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