

## Synthesis and Reactivity of Rhodium(II) *N*-Triflyl Azavinyl Carbenes

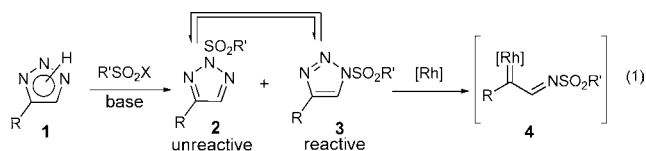
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Diazo carbonyl compounds are versatile reagents which, among other applications, are often used for the generation of transition metal carbenes.<sup>1</sup> The latter are useful synthetic intermediates that readily, and often stereoselectively, add to carbon–carbon and carbon–heteroatom multiple bonds and undergo C–H insertion reactions.<sup>2</sup> Diazo group transfer from a sulfonyl azide to an activated methylene carbon is the most common route to diazo compounds.<sup>3</sup> However, many sulfonyl azides, as well as diazo compounds, are not shelf stable and require precautions in handling. We have recently demonstrated that 1-sulfonyl 4-substituted 1,2,3-triazoles can serve as stable and readily accessible synthetic equivalents of diazo compounds.<sup>4</sup> They undergo facile ring–chain isomerization, and the diazoimine tautomer reacts with transition metal catalysts, resulting in the formation of azavinyl carbenes. These novel intermediates react selectively with nitriles and olefins, resulting in the formation of imidazoles and cyclopropanes, respectively. These reactions require elevated temperatures, and starting sulfonyl triazoles are normally prepared from sulfonyl azides.

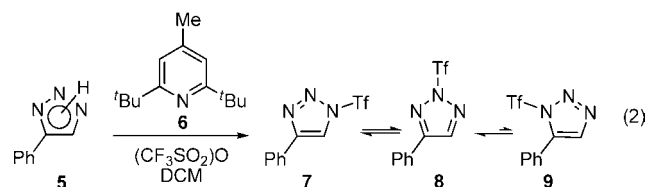
Here we report a new and practical method for the generation of reactive rhodium azavinyl carbenes from stable and readily accessible *NH*-triazoles,<sup>5</sup> which are sulfonylated in situ by triflic anhydride in the presence of a pyridine base (eq 1). The methodology does not involve sulfonyl azides at any stage of the synthesis, and the resulting *N*-triflyl azavinyl carbenes exhibit exceptional reactivity toward olefins, producing cyclopropanes and 1,2-dihydropyrroles with excellent enantio- and diastereoselectivity. The ability to introduce extremely electron withdrawing groups into the triazole nucleus, thereby controlling the electrophilicity of the resulting carbene, is easily the most valuable feature of this new approach. Our attempts to isolate the corresponding *N*-triflyl triazoles were unsuccessful because of their extreme susceptibility to hydrolysis.



We expected that sulfonylation of *NH*-triazoles would lead to a mixture of isomeric *N2*- and *N1*-sulfonylated triazole products **2** and **3**.<sup>6</sup> These two isomers exist in equilibrium, but only the *N1* isomer **3** can undergo ring–chain isomerization forming the diazoimine tautomer which reacts with rhodium complexes, leading to a carbene intermediate **4**.

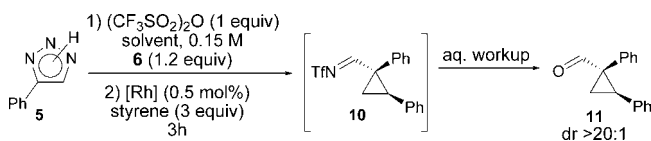
We first examined the sulfonylation reaction of 4-phenyl-*NH*-1,2,3-triazole **5** by triflic anhydride in the presence of pyridine bases (eq 2). 2,6-Di-*tert*-butyl-4-methylpyridine **6** provided optimal results and was used in all subsequent reactions. Monitoring reaction progress by <sup>1</sup>H NMR (from –60 °C to r.t. in 10 °C increments) revealed that the 1,5-disubstituted triazole isomer **9** was indeed

formed in a negligible amount, whereas the expected isomers **7** and **8** were formed in an approximately 1:1 ratio.



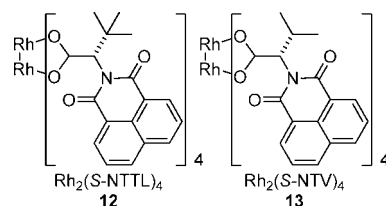
With these conditions in hand, we turned our attention to the rhodium-catalyzed reaction of the in situ generated sulfonyl triazoles with olefins. As illustrated in Table 1, 4-phenyl-*NH*-1,2,3-triazole **5** was reacted with 1 equiv of triflic anhydride in the presence of 1.2 equiv of base **6** at –60 °C. After 10 min, styrene (3 equiv) and 0.5 mol % of Rh<sub>2</sub>(*S*-NTTL)<sub>4</sub>,<sup>7</sup> **12**, were added and the reaction was allowed to warm to RT over 3 h. Cyclopropane **11** was isolated in 35% yield, 98% ee, and dr >20:1 (entry 1). Changing the solvent to 1,2-dichloroethane and increasing the starting temperature of the reaction to –30 °C improved the yield to 65% while maintaining high enantioselectivity (entry 2). Changing the solvent to chloroform further increased the yield to 90% and gave the product with 99% ee (entry 3). The less sterically hindered Rh<sub>2</sub>(*S*-NTV)<sub>4</sub> catalyst **13** resulted in the lower ee (76%, entry 4). The yield of cyclopropane was reduced to 81% when only 2 equiv of styrene were used (entry 5).

**Table 1.** Cyclopropanation of Styrene with 4-Phenyl-*NH*-triazole



entry	solvent	catalyst	equiv of styrene	yield, %	ee, %
1 <sup>a</sup>	DCM	Rh <sub>2</sub> ( <i>S</i> -NTTL) <sub>4</sub>	3	35	98
2	1,2-DCE	Rh <sub>2</sub> ( <i>S</i> -NTTL) <sub>4</sub>	3	65	97
3	CHCl <sub>3</sub>	Rh <sub>2</sub> ( <i>S</i> -NTTL) <sub>4</sub>	3	90	99
4	CHCl <sub>3</sub>	Rh <sub>2</sub> ( <i>S</i> -NTV) <sub>4</sub>	3	88	76
5	CHCl <sub>3</sub>	Rh <sub>2</sub> ( <i>S</i> -NTTL) <sub>4</sub>	2	81	96
6 <sup>b</sup>	CHCl <sub>3</sub>	Rh <sub>2</sub> ( <i>S</i> -NTTL) <sub>4</sub>	3	91	99

<sup>a</sup> Reaction performed at –60 °C. <sup>b</sup> Triazole, the catalyst, and styrene were charged to the reaction vessel at the beginning of the reaction.

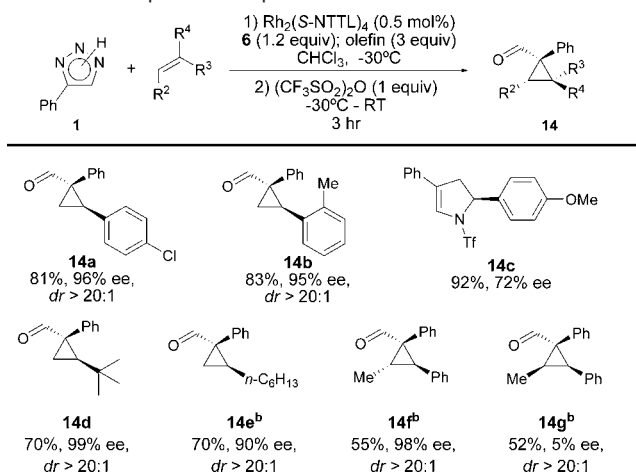


Interestingly, the imine intermediate **10** was never observed, regardless of the method of workup. Basic extraction from saturated

sodium bicarbonate solution allowed for the almost quantitative recovery of base **6**. It was also discovered that all of the components, except for the triflic anhydride, could be charged to the reaction vessel at the beginning of the reaction, without detriment to the yield, diastereo-, or enantioselectivity (entry 6), thus further simplifying the experimental procedure. This approach also allowed a visual readout of the reaction progress: the purple solution of a complex between the *NH*-triazole and rhodium catalyst turned green upon the addition of triflic anhydride, indicating that all *NH*-triazole had been consumed in the reaction.

The scope of the process with respect to the alkene component was next examined (Scheme 1). 2-Methyl- and 4-chlorostyrene gave good yields, as well as excellent ee and dr. However, the electron-rich 4-methoxystyrene gave only 2,3-dihydro-pyrrole **14c** in 92% yield, but with a lower ee of 72%. The reaction of *tert*-butylethene was equally high yielding and selective. Unfortunately, when the less reactive 1-octene was used in the reaction, the product cyclopropane **14e** was isolated in only 35% yield, albeit with excellent ee and dr. Performing the reaction in carbon tetrachloride yielded 70% of **14e**. Finally, trisubstituted alkenes gave acceptable yields of cyclopropanes only when the reactions were performed in carbon tetrachloride. (*E*)-Methyl styrene gave the corresponding cyclopropane **14f** in moderate yield, but with excellent enantioselectivity. In contrast, (*Z*)-methyl styrene gave very low ee, ~5%, although diastereoselectivity was preserved (product **14g**).

#### Scheme 1. Scope with Respect to the Olefin<sup>a</sup>

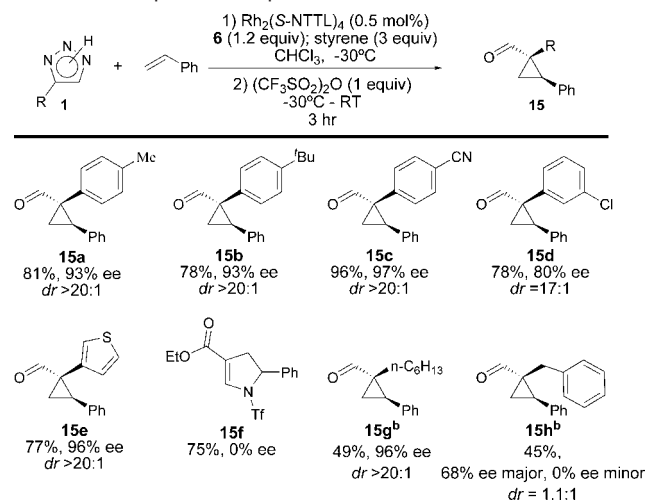


<sup>a</sup> Reactions were performed on 0.35 mmol scale (with respect to the triazole). <sup>b</sup> These reactions were performed in  $\text{CCl}_4$ .

Variation of the substituent on the triazole ring revealed that the reaction proceeded well when *p*-methyl-, **15a**, *p*-*tert*-butyl-, **15b**, and *p*-cyano-, **15c**, 4-phenyl-*NH*-1,2,3-triazoles were used (Scheme 2). Both diastereo- and enantioselectivity were excellent. However, when the *m*-chlorophenyl-*NH*-triazole was used, the dr of the product **15d** eroded to 17:1, and the ee was 80%. We hypothesize that this was due to an unfavorable steric interaction of the *meta*-substituent with the catalyst. When the benzene ring was replaced with a thiophene, the reaction proceeded in a good yield, with excellent ee and dr (**15e**). Introduction of an ester functionality caused the formation of 2,3-dihydropyrrole **15f** in good yield, but unlike 1,2-dihydropyrrole **14c**, racemic **15f** was obtained in 75% yield. This suggests that different mechanisms are responsible for the formation of these products. 4-Alkyl-*NH*-1,2,3-triazole could also be used in the reaction, albeit the yields of cyclopropane were lower due to a competing intramolecular 1,2-hydride shift in the carbene complex.<sup>8</sup> Despite the lower yield, 4-octyl triazole produced

cyclopropane **15g** in excellent enantio- and diastereoselectivity. Unfortunately, benzyl *NH*-triazole yielded a 1.1:1 mixture of diastereomers, with the major diastereomer having an ee of 68%, and the minor found to be racemic (product **15h**).

#### Scheme 2. Scope with Respect to the Triazole<sup>a</sup>



<sup>a</sup> Reactions were performed on 0.35 mmol scale, at 0.15M (with respect to the triazole), and were worked up with sat. aq.  $\text{NaHCO}_3$ . <sup>b</sup> These reactions were performed in  $\text{CCl}_4$ .

In conclusion, the highly reactive rhodium(II) *N*-triflyl azavinyl carbenes can be generated from *NH*-1,2,3-triazoles by their treatment with triflic anhydride in the presence of rhodium(II) carboxylate complexes. These carbene intermediates efficiently engage olefins in highly enantio- and diastereoselective transformations, providing convenient access to homochiral cyclopropane carboxaldehydes and 2,3-dihydropyrroles. Further studies of their reactivity are underway in our laboratories.

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**Supporting Information Available:** Experimental details, characterization data, and NMR spectral charts. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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