Annulated Heterocycles

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Rh-Catalyzed Transannulation of Pyridotriazoles with Alkynes and Nitriles**

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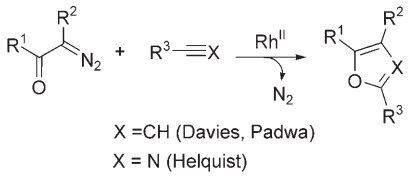
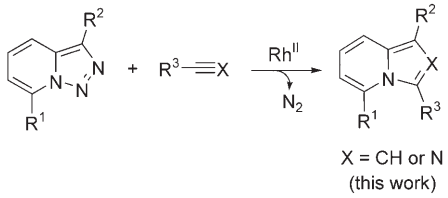
Transition-metal-catalyzed annulations are widely used in the synthesis of heterocyclic compounds.[1] One of the most efficient methods for the construction of five-membered oxygen-containing heterocycles involves the annulation of diazocarbonyl compounds with alkynes and nitriles. Thus, Davies et al.[2] and Padwa et al.[3] have employed this method[4] for the synthesis of furans (X = CH), and Helquist et al.[5] for the preparation of oxazoles (X = N) [Eq. (1)]. In contrast, analogous transformations of α-imino diazo compounds, which may lead to the formation of pyrrole and imidazole rings, are unknown. Herein we report an efficient, direct, Rh-catalyzed transannulation of pyridotriazoles with alkynes and nitriles that leads to indolizines (X = CH) and imidazopyridines (X = N), respectively [Eq. (2)].

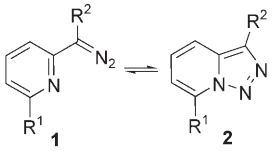


(1)



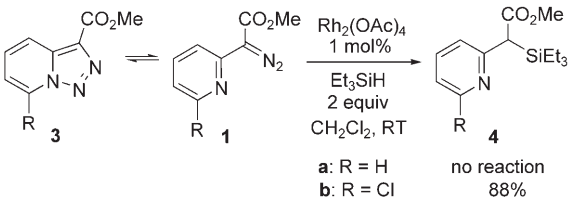
(2)

It has been shown that 2-pyridyl diazo compounds **1**[6] transform into their cyclic triazole form **2**[7] upon storage [Eq. (3)], and it is also known that some of these cyclic triazoles can still undergo transformations that are characteristic of diazo compounds.[8] This phenomenon has been attributed to the closed/open form equilibrium of N-fused triazoles in solution,[9] which can produce trace to significant amounts of **1**. The position of this equilibrium depends on the temperature and the substitution pattern of the triazole.[9b] Thus, introduction of a halogen substituent at C7 (R^1 = Cl) shifts the equilibrium to the left, which has been explained in terms of nonbonding repulsion between the lone pair of the halogen and that of the nitrogen in the *peri* position.[10]



(3)

To evaluate the feasibility of using triazoles as precursors of Rh carbenoids we investigated the reaction of triazoles **3a** and **3b** with triethylsilane in the presence of a catalytic amount of rhodium(II) acetate, which is a method developed by Doyle and coworkers[11] for the efficient trapping of Rh carbenoids [Eq. (4)]. Not surprisingly, pyridotriazoles **3a** and **3b** behave differently under these reaction conditions. Thus, while the 7-H derivative **3a** remains unaffected, the 7-chloro-substituted compound **3b** is smoothly converted into **4**, which is the product of carbenoid insertion into the Si–H bond. These experiments clearly indicate that 7-halo-substituted pyridotriazoles can indeed serve as convenient precursors of Rh carbenoids.



(4)

Next, to test our hypothesis regarding the annulation of α-imino diazo compounds with alkynes to form a pyrrole ring, we treated triazole **3b** with phenylacetylene in the presence of rhodium(II) acetate. This reaction proceeded smoothly to produce a mixture of cyclopropene **5** and indolizine **6a** with yields of 68% and 28% of isolated product, respectively [Eq. (5)]. Surprisingly, cyclopropene **5** does not undergo further isomerization into indolizine **6a** under these reaction conditions.[12] The ratio of these products remained constant throughout the course of the reaction, thereby suggesting an independent path for the formation of **6a**.

We found, however, that the selectivity of the transannulation (**6** over **5**) could be dramatically improved by using

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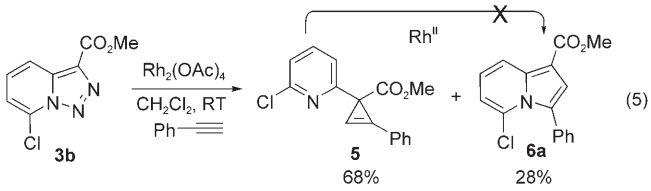
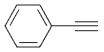
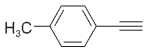
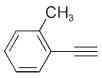
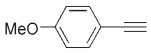
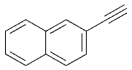
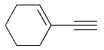
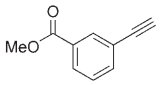


rhodium(II) heptafluorobutyrate as catalyst.[13] Thus, transannulation of **3b** with a series of aryl and alkenyl alkynes[14] proceeded highly chemoselectively (90:10 to 95:5 vs. cyclopropene) to produce indolizines **6**[15] in good yields (Table 1). Electron-rich, electron-deficient, and sterically hindered aryl alkynes were nearly equally effective in this reaction.

Table 1: Rhodium(II)-catalyzed transannulation of triazole **3b** with alkynes.

Entry	Alkyne	Product	Yield [%][a]
1		**6a**	78
2		**6b**	80
3		**6c**	73
4		**6d**	85
5		**6e**	70
6		**6f**	65
7		**6g**	57

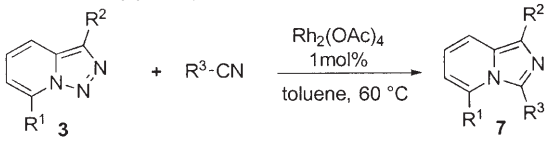
[a] Yield of isolated product. Indolizines **6** were accompanied by 5–10% of the corresponding cyclopropenes **5**; these compounds were readily separable by column chromatography.

Inspired by the successful formation of an N-fused pyrrole ring from the transannulation of triazoles with alkynes, we examined the formation of an N-fused imidazole ring in the reaction of **3** with nitriles and found that pyridotriazoles **3** react smoothly with a variety of aryl, alkyl, and alkenyl nitriles in the presence of $Rh_2(OAc)_4$ (1 mol%) in toluene at 60°C (Table 2) to afford N-fused imidazopyridines **7** in reasonable to high yields.

Both 3-carbomethoxy- (Table 2, entries 1–9) and 3-aryl- (Table 2, entry 10) pyridotriazoles are equally efficient in this reaction. Moreover, 7-bromo- (Table 2, entry 11) and even 7-methoxy-substituted (Table 2, entry 12) triazoles proved to be good substrates for this transannulation reaction.

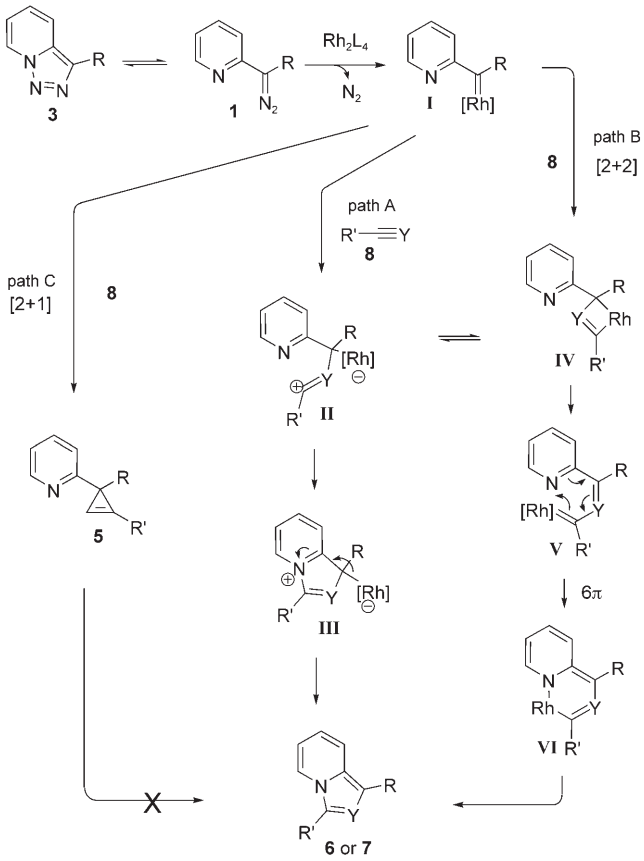
We propose the following mechanism for this novel Rh-catalyzed transformation (Scheme 1). First, pyridotriazole **3** undergoes closed/open form equilibrium[9] to produce small amounts of diazo compound **1** which, upon reaction with rhodium(II) carboxylate, generates the Rh-carbenoid species **I**. A direct nucleophilic attack[18] of alkyne or nitrile **8** on species **I** produces ylide species **II**, according to path A, which

Table 2: Rhodium(II)-catalyzed transannulation of triazoles with nitriles.



Entry	R^1	R^2	Triazole	R^3	Product	Yield [%][a]
1	Cl	CO_2Me	**3b**	*p*-Tol	**7a**	89
2	Cl	CO_2Me	**3b**	Ph	**7b**	83
3	Cl	CO_2Me	**3b**	*p*-Me(O)CC_6H_4	**7c**	54
4	Cl	CO_2Me	**3b**	Bn	**7d**	63
5	Cl	CO_2Me	**3b**	*n*Pr	**7e**	75
6	Cl	CO_2Me	**3b**	*c*Pr	**7f**	74
7	Cl	CO_2Me	**3b**	*t*Bu	**7g**	69
8	Cl	CO_2Me	**3b**		**7h**	66
9	Cl	CO_2Me	**3b**	CH_2SiMe_3	**7i**	70
10	Cl	*p*-$CF_3C_6H_4$	**3c**	Ph	**7j**	82
11	Br	*p*-$CF_3C_6H_4$	**3d**	*p*-Tol	**7k**	73
12	OMe	*p*-$CF_3C_6H_4$	**3e**	*n*Pr	**7l**	51

[a] Yield of isolated product.



Scheme 1. Plausible mechanisms for the Rh-catalyzed transannulation of pyridotriazoles with alkynes and nitriles. Y = N, CR″.

then cyclizes to form **6** or **7** via cyclic zwitterion **III**. Alternatively (path B), [2+2] cycloaddition of **I** and **8** leads to metallacyclobutene **IV**, which can also be formed by cyclization of **II**.[19] Rhodacycle **IV** then undergoes metathesis

to produce Rh carbenoid **V** which, upon 6π-electrocyclization and subsequent reductive elimination, furnishes product **6** or **7**. [2+1] Cycloaddition of **I** with **8** (path C) accounts for the formation of cyclopropene **5** in the presence of rhodium(II) acetate [see Eq. (5)]. As discussed above, **5** does not transform into heterocycle **6** under these reaction conditions.[12]

In summary, we have developed an efficient Rh-catalyzed transannulation of pyridotriazoles for the formation of pyrrolo- and imidazopyridines, which are important fused heterocyclic scaffolds.[20] We have also demonstrated that some of these pyridotriazoles can serve as stable[13] and convenient[21] precursors of Rh carbenoids.

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[13] See the Supporting Information for details.
[14] The use of aliphatic alkynes resulted in sluggish and incomplete reactions.
[15] Halo-substituted N-fused heterocycles can be further functionalized by cross-coupling reactions.[16] We have also found that the chloride in **6a** can be quantitatively removed by treatment with $PdCl_2/HSiEt_3$.[17]
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[21] The use of **3** does not require special slow-addition techniques as the concentration of **1** in the reaction mixture is always low.[9]

