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Synthesis of Penta-2,4-dien-1-imines and 1,2-Dihydropyridines by Rhodium-Catalyzed Reaction of *N*-Sulfonyl-1,2,3-triazoles with 2-(Siloxy)furans

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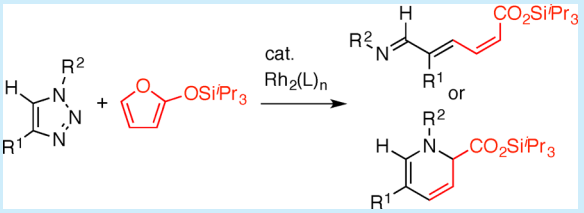
Supporting Information

ABSTRACT: A rhodium(II)-catalyzed reaction of *N*-sulfonyl-1,2,3-triazoles with 2-(siloxy)furans is reported. Either open-chain penta-2,4-dien-1-imines or cyclic 1,2-dihydropyridines are selectively obtained depending on the ligand on rhodium(II).



N-Sulfonyl-1,2,3-triazoles have emerged as the latent precursors of α-imino carbenoid species.[1] The electron-withdrawing sulfonyl group on the ring nitrogen induces the ring−chain tautomerization to generate transient α-imino diazo compounds.[2] They promptly react with present transition metal complexes, rhodium(II) carboxylate dimers in most cases, to form metal carbene complexes with extrusion of molecular nitrogen. A number of synthetically useful transformations involving these metal carbene complexes as the key intermediate have been developed during the past decade.[3] In 2013, Davies and co-workers disclosed a fascinating transannulation reaction of *N*-sulfonyl-1,2,3-triazoles with electron-rich 2,5-dialkylfurans to afford substituted pyrroles (Figure 1a).[4] During the subsequent year, three groups reported the

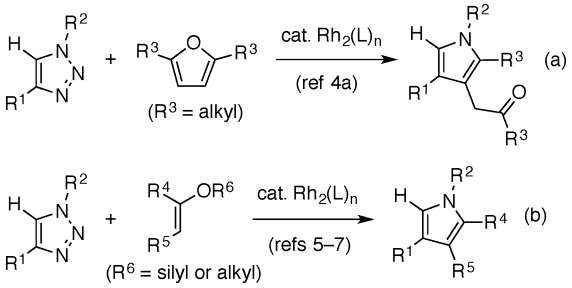


Figure 1. Rh(II)-catalyzed reaction of triazoles with (a) 2,5-dialkylfurans and (b) silyl or alkyl enol ethers.

synthesis of substituted pyrroles by a rhodium(II)-catalyzed [3 + 2] annulation reaction of triazoles with silyl or alkyl enol ethers, which were significantly more nucleophilic than 2,5-dialkylfurans (Figure 1b).[5−7] Those results led us to examine the use of 2-(siloxy)furans as the analogous electron-rich and nucleophilic partner for the carbenoid species.[8] We now report that either open-chain penta-2,4-dien-1-imines or cyclic 1,2-dihydropyridines, not pyrrole derivatives, are selectively obtained by a rhodium(II)-catalyzed reaction of *N*-sulfonyl-1,2,3-triazoles with 2-(siloxy)furans. The products would be valuable intermediates for the synthesis of polysubstituted piperidines,[9] such as aza sugars.[10]

Initially, 4-phenyl-1-tosyl-1,2,3-triazole (**1a**) was prepared from phenylacetylene and tosyl azide according to Fokin's procedure[11] using copper(I) thiophene-2-carboxylate (CuTC). Then the isolated triazole **1a** (0.2 mmol) was treated with 2-(triisopropylsiloxy)furan (**2a**) (1.5 equiv) in chloroform at 70 °C in the presence of 1.0 mol % $Rh_2(esp)_2$ (esp = $\alpha,\alpha,\alpha',\alpha'$-tetramethyl-1,3-benzenedipropionate)[12] and 4 Å molecular sieves (MS) (Table 1, entry 1). After 2 h, the formation of a 34:66 mixture of penta-2,4-dien-1-imine **3aa** and 1,2-dihydropyridine **4aa** was observed by ^{1}H NMR analysis of the crude reaction mixture. The product selectivity notably varied depending on the ligand on rhodium(II). In the case of the pivalate ligand, the product ratio slightly shifted to **3aa** (**3aa**:**4aa** = 57:43) (entry 2). On the other hand, **3aa** became predominant (**3aa**:**4aa** = 78:22) when the sterically bulkier *N*-naphthoyl-*tert*-leucinate (NTTL) ligand[13] was employed (entry 3). The reaction with *N*-mesyl-1,2,3-triazole **1b** in place of **1a** proceeded even at room temperature with the exclusive formation of **3ba** (**3ba**:**4ba** ≥ 95:5), which was isolated in 76% yield after modified silica gel chromatography (entry 4).[14] None of the 1,2-dihydropyridine **4ba** was detected in the ^{1}H NMR spectrum of the reaction mixture in this case.

The formation of products **3** and **4** is reasonably explained by assuming the dichotomous pathways depicted in Scheme 1. Ring−chain tautomerization of **1** generates α-diazo imine **1′**, which promptly reacts with the rhodium(II) complex to afford α-iminorhodium(II) carbene complex **A** with extrusion of molecular nitrogen. The electrophilic character of **A** is suitably combined with the highly electron-rich and nucleophilic character of 2-(triisopropylsiloxy)furan (**2a**) to allow cyclo-

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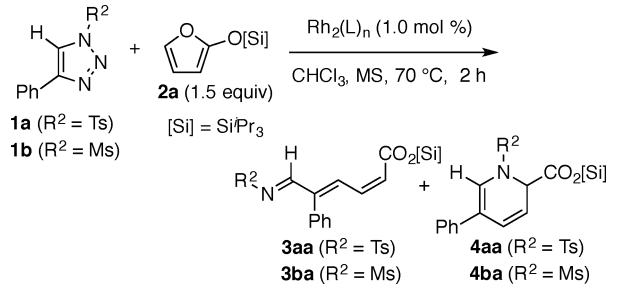
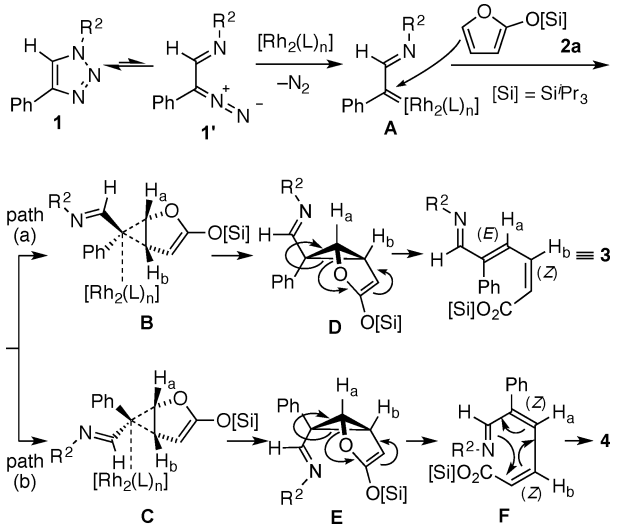
Table 1. Rh(II)-Catalyzed Reaction of *N*-Sulfonyl-1,2,3-triazoles 1 with 2-(Siloxy)furan 2a[a]



				yields (%)[b]	
entry	1	R^2	$Rh_2(L)_n$	3	4
1	**1a**	**Ts**	**Rh_2(esp)$_2$**	**32**	**61 (47)**
2	**1a**	Ts	$Rh_2(OCO^tBu)_4$	50	37
3	**1a**	Ts	Rh_2[(*S*)-NTTL]$_4$	69	19
4[c]	**1b**	**Ms**	**Rh_2[(*S*)-NTTL]$_4$**	**89 (76)**	**<3**

[a]On a 0.20 mmol scale. Ts = *p*-toluenesulfonyl. Ms = methanesulfonyl. [b]^{1}H NMR yields using $CHCl_2CHCl_2$ as an internal standard; isolated yields are shown in parentheses. [c]At room temperature for 4 h.

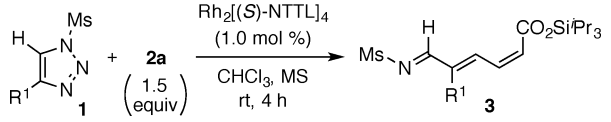
Scheme 1. Proposed Mechanism for the Formation of 3 and 4



propanation of **2a** at its remote double bond. There are two diastereomeric faces for carbenoid **A** to approach **2a**, and the two transition state models **B** and **C** become conceivable depending on which face the carbenoid **A** prefers for approaching **2a**.[15] The *N*-sulfonylimino group is more stereodemanding than the phenyl group, and transition state **B** with the bulkier imino group on the convex side is more stable than the other diastereomeric transition state **C**. The sterically bulkier NTTL ligand augments the differentiation between **B** and **C** to favor transition state **B**: the sterically more demanding NTTL ligands destabilize the crowded and hence disfavored transition state **C** even more, improving the selectivity. The use of *N*-mesyl triazole **1b** in place of **1a** as the substrate mitigates the steric congestion to promote the cyclopropanation even at room temperature. Then the major bicyclic intermediate **D** undergoes ring opening in a stereospecific manner to afford (2*E*,4*Z*)-penta-2,4-dien-1-imine **3**, which is readily isolated by chromatography [path (a)]. On the other hand, an analogous stereospecific ring opening of minor bicyclic intermediate **E** gives (2*Z*,4*Z*)-penta-2,4-dien-1-imine **F**. Because of the 2*Z* configuration, spontaneous 6π-electrocyclization follows, leading to the production of **4** [path (b)].

Variation of the *N*-mesyl triazole was examined for the selective production of open-chain imines **3** by the reaction with 2-(siloxy)furan **2a** at room temperature using Rh_2[(*S*)-NTTL]$_4$ as the catalyst (Table 2). Triazoles **1c**–**g**, possessing

Table 2. Synthesis of (2*E*,4*Z*)-Penta-2,4-dien-1-imines 3 from Various Triazoles and 2-(Siloxy)furan 2a[a]

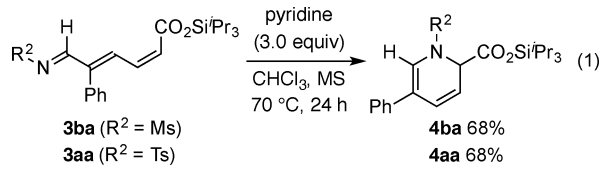


entry	1	R^1	3	yield (%)[b]
1	**1c**	*p*-$MeOC_6H_4$	**3ca**	98
2	**1d**	*p*-MeC_6H_4	**3da**	85
3	**1e**	*p*-BrC_6H_4	**3ea**	83
4	**1f**	*p*-$CF_3C_6H_4$	**3fa**	87
5	**1g**	3-thienyl	**3ga**	92
6	**1h**	1-cyclohexenyl	**3ha**	69[c]

[a]On a 0.20 mmol scale. [b]Isolated yields. [c]24 h.

an electronically diverse array of aryl and heteroaryl groups at the 4-position, selectively afforded the corresponding penta-2,4-dien-1-imines **3ca**–**ga** in yields ranging from 83% to 98% (entries 1–5). 1-Cyclohexenyl-substituted triazole **1h** was also a suitable substrate (entry 6). None or little (<5% yield) of the corresponding 1,2-dihydropyridines **4** were detected in the ^{1}H NMR spectra of the crude reaction mixtures.

Interestingly, the isolated **3ba** gradually isomerized to the cyclic dihydropyridine **4ba** when it was heated at 70 °C in chloroform in the presence of pyridine (3.0 equiv). After 24 h, **4ba** was obtained in 68% yield by chromatography (eq 1). The



isolated **3aa** also underwent the pyridine-mediated isomerization to **4aa** in an analogous manner. We assume that pyridine mediates the isomerization of **3** from its 2*E* isomer to its 2*Z* isomer, which then undergoes 6π-electrocyclization to give **4**.

The pyridine-mediated isomerization of **3** into **4** was successfully integrated into a one-pot sequential procedure for the selective production of 1,2-dihydropyridines **4** from *N*-tosyl triazole **1a** using Rh_2(esp)$_2$ as the catalyst (Table 3). Thus, the Rh_2(esp)$_2$-catalyzed reaction of **1a** with **2a** was immediately followed by the pyridine-mediated isomerization, and a single isolation procedure afforded cyclized **4aa** in 80% yield (entry 1). Moreover, the reaction was amenable to a larger-scale experiment using 1.2 g of **1a** (4.0 mmol), and **4aa** was isolated in 71% yield. Various 1,2-dihydropyridines **4ia**–**qa** were produced from *N*-tosyl triazoles **1i**–**q** and **2a** (entries 2–10). None of the corresponding penta-2,4-dien-1-imines **3** were detected in the ^{1}H NMR spectra of the crude reaction mixtures.

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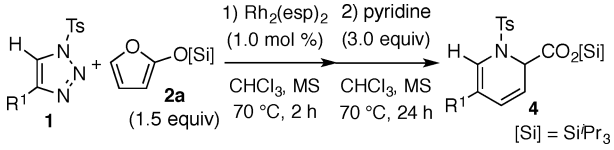
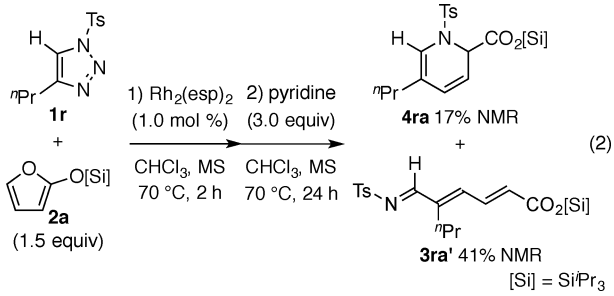
Table 3. One-Pot Synthesis of 1,2-Dihydropyridines 4 from Various Triazoles and 2-(Siloxy)furan 2a[a]



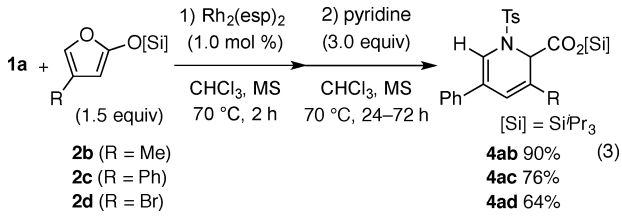
entry	1	R^1	4	yield (%)[b]
1	**1a**	Ph	**4aa**	80
2	**1i**	*p*-$MeOC_6H_4$	**4ia**	78
3	**1j**	*p*-MeC_6H_4	**4ja**	70
4	**1k**	*p*-BrC_6H_4	**4ka**	79
5	**1l**	*p*-$EtO_2CC_6H_4$	**4la**	75
6	**1m**	*p*-$CF_3C_6H_4$	**4ma**	63
7	**1n**	*m*-MeC_6H_4	**4na**	76
8	**1o**	*o*-BrC_6H_4	**4oa**	46
9	**1p**	3-thienyl	**4pa**	84
10	**1q**	1-cyclohexenyl	**4qa**	85

[a]On a 0.20 mmol scale. [b]Isolated yields.

In the case of *n*-propyl-substituted triazole **1r**, the product **4ra** was produced in 17% NMR yield together with uncyclized and isomerized **3ra′** (41% NMR yield) (eq 2).

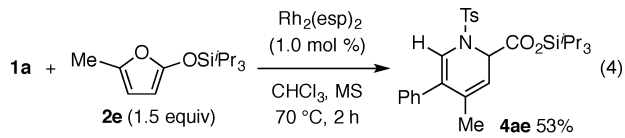


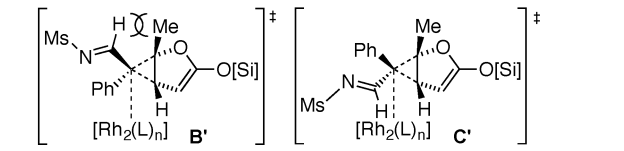
2-(Siloxy)furans **2b−d** possessing a substituent at the 4-position were applied to the sequential reaction with **1a**. The corresponding dihydropyridines **4ab−ad** were obtained in good to high yields (eq 3).

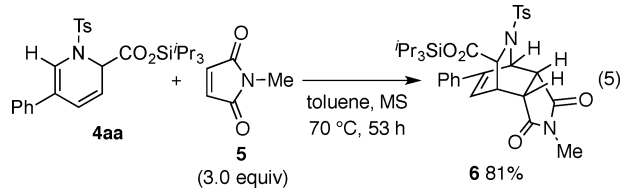


When 5-methyl-2-(siloxy)furan **2e** was subjected to the $Rh_2(esp)_2$-catalyzed reaction with **1a**, the dihydropyridine **4ae** was selectively produced in 53% yield without any formation of the corresponding penta-2,4-dien-1-imine **3ae** (eq 4).[16] The transition state **C′** would be dominant because, with the other transition state **B′**, the repulsive interaction between the imino group and the methyl group would be significant. On the other hand, the $Rh_2(esp)_2$-catalyzed reaction of 3-methyl-2-(triisopropylsiloxy)furan with **1a** was sluggish, affording the corresponding product in 17% yield.

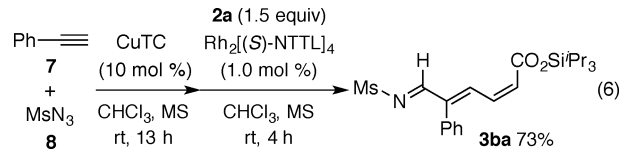
The resulting dihydropyridine **4aa** acted as the diene in a [4 + 2] cycloaddition reaction with *N*-methylmaleimide (**5**). Only the *endo* adduct **6** was obtained in 81% yield (eq 5). The structure of **6** was determined by NMR studies.







A sequential one-pot procedure starting from phenylacetylene (**7**) and mesyl azide (**8**) was performed to save the time and solvent required for a workup/purification after the triazole synthesis (eq 6). A mixture of **7**, **8**, CuTC, and MS was



stirred for 13 h to form triazole **1b**. Subsequently, **2a** and $Rh_2[(S)\text{-NTTL}]_4$ were added to the same reaction vessel, which was further stirred at room temperature for 4 h. Penta-2,4-dien-1-imine **3ba** was thus obtained in 73% overall yield.

In summary, an efficient synthetic route to penta-2,4-dien-1-imines and 1,2-dihydropyridines from *N*-sulfonyl-1,2,3-triazoles and 2-(siloxy)furans has been developed.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b03143.

Experimental procedures and spectral data for the new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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(16) Unlike the cases with 2,5-dialkylfurans, no substituted pyrrole was formed. See ref 4a.

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