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Synthesis of *N*-Acylamidines via Rhodium-Catalyzed Reaction of Nitrosobenzene Derivatives with *N*-Sulfonyl-1,2,3-triazoles

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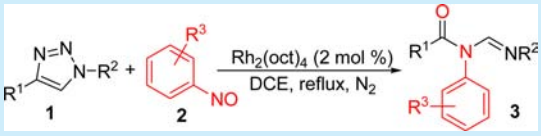
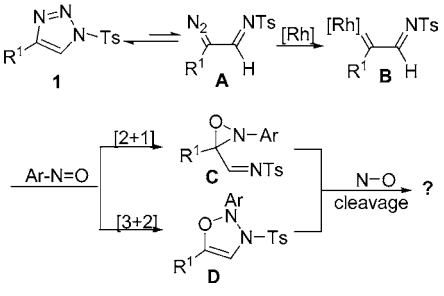
Supporting Information

ABSTRACT: α-Imino rhodium carbene, readily generated from *N*-sulfonyl-1,2,3-triazole, underwent cycloaddition and subsequent rearrangement with a nitrosobenzene derivative to afford *N*-acylamidine. The unprecedented C−C bond cleavage of α-imino carbene was facilitated by the weakness of the N−O bond.



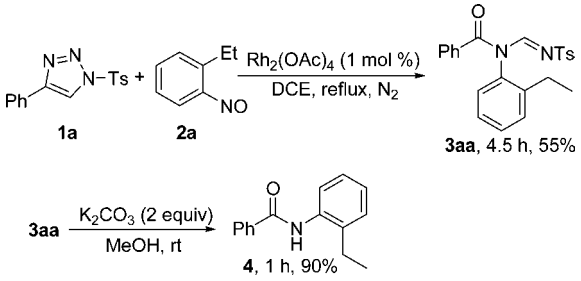
Due to the pioneering works of Gevorgyan and Fokin,[1] α-imino metal carbene, which is inaccessible from the traditional diazo route,[2] can be readily prepared by denitrogenative transformation of *N*-sulfonyl-1,2,3-triazole.[3] Compared with related α-oxo carbene, α-imino carbene offers more synthetic flexibility as a result of increased nucleophilic ability of the nitrogen atom.[4] Hence, the above research opens a new area for developing novel synthetic methods. In the presence of a catalytic amount of rhodium(II) or nickel(0) salts, a variety of weak unsaturated nucleophiles, such as nitriles,[1b] aldehydes,[5] epoxides,[6] formamides,[7] alkynes,[8] allenes,[9] alkenes,[10] furans,[11] pyrroles,[12] indoles,[13] and arenes[14] can easily react with *N*-sulfonyl-1,2,3-triazoles to furnish synthetically useful *N*-heterocycles and acyclic compounds. In a recent publication,[10j] our group used ketene silyl acetal to trap the in situ generated α-imino carbene, and 3-pyrrolin-2-one was obtained in high yield. During our research, we speculated that replacing the electron-rich alkene with nitrosobenzene derivatives may result in the formation of heterocycle **C** or **D** (Scheme 1), and owing to the weakness of the N−O bond,[15]

Scheme 1. Initial Speculation



new transformations based on the cleavage of the N−O bond would be discovered. We attempted the reaction by using triazole **1a**, 1-ethyl-2-nitrosobenzene **2a**, and 1 mol % of $Rh_2(OAc)_4$ (Scheme 2). To our delight, after 4.5 h, a major product **3aa** was isolated and the structure of **3aa** was determined by spectroscopic analyses and X-ray crystallography of its derivative **4** (Figure 1). Notably, the carbon−carbon bond

Scheme 2. Initial Result



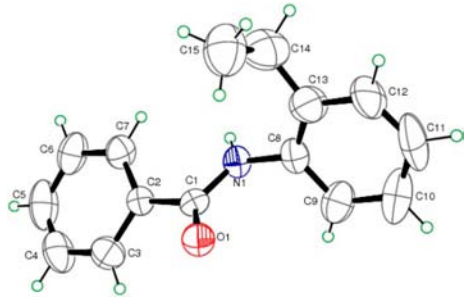


Figure 1. X-ray of compound **4**.

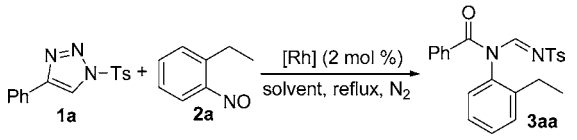
of the α-imino carbene is cleaved in this novel transformation, which has never been observed in previous reports.

With this encouraging result, we then optimized the reaction conditions by changing the rhodium catalyst and the solvent, as is partially summarized in Table 1. Increasing the catalyst loading to 2 mol % led to the formation of **3aa** in 62% yield with enhanced reaction rate (entry 2), whereas a further increase in the amount of catalyst resulted in diminished yield (entry 3). Alteration of the ratio of **1a** and **2a** did not improve the yield of **3aa** (entries 4 and 5). We next attempted the reaction with various rhodium(II) catalysts (entries 6−11), and the yield of **3aa** was further improved to 71% when

Received: November 3, 2014
Published: December 8, 2014

   dx.doi.org/10.1021/ol5031876 | *Org. Lett.* 2014, 16, 6394−6396

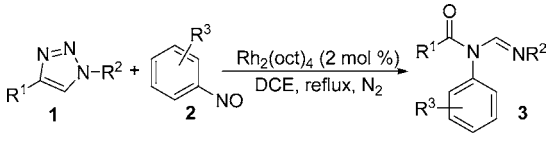
Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	solvent	time (h)	yield[b] (%)
1[c]	$Rh_2(OAc)_4$	DCE	4.5	55
2	$Rh_2(OAc)_4$	DCE	3.0	62
3[d]	$Rh_2(OAc)_4$	DCE	2.5	54
4[e]	$Rh_2(OAc)_4$	DCE	2.5	54
5[f]	$Rh_2(OAc)_4$	DCE	2.5	62
6	$Rh_2(oct)_4$	DCE	4.5	71
7	$Rh_2(Piv)_4$	DCE	5.0	54
8	$Rh_2(esp)_2$	DCE	4.5	63
9	$Rh_2(S\text{-nttl})_4$	DCE	8.0	trace
10	$Rh_2(S\text{-pttl})_4$	DCE	8.5	trace
11	$Rh_2(S\text{-ntv})_4$	DCE	5.5	41
12	$Rh_2(oct)_4$	toluene	4.0	44
13	$Rh_2(oct)_4$	$CHCl_3$	5.0	60
14	$Rh_2(oct)_4$	MeCN	4.0	trace
15	$Rh_2(oct)_4$	$CHCl_2CH_2Cl$	7.0	27

[a]0.2 mmol of **1a**, 0.2 mmol of **2a** and 0.004 mmol of rhodium(II) catalyst dissolved in 2 mL of refluxing solvent under N_2. [b]Isolated yield, average of two runs. [c]0.002 mmol of $Rh_2(OAc)_4$ was used. [d]0.006 mmol of $Rh_2(OAc)_4$ was used. [e]0.3 mmol of **1a** and 0.2 mmol of **2a** were used. [f]0.2 mmol of **1a** and 0.3 mmol of **2a** were used.

Table 2. Reaction Scope[a]



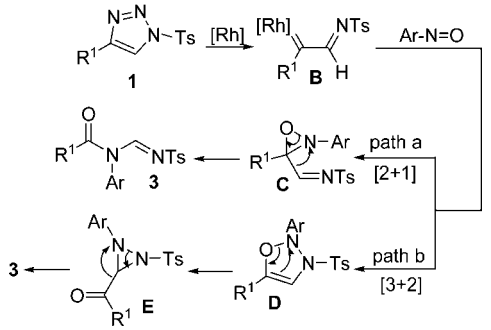
entry	1 (R^1, R^2)	2 (R^3)	time (h)	yield[b] (%)
1	**1b** (Ph, Ms)	**2a** (*o*-Et)	4.5	**3ba** (58)
2	**1c** (Ph, *p*-$BrC_6H_4SO_2$)	**2a** (*o*-Et)	3.0	**3ca** (50)
3	**1d** (Ph, *p*-$MeOC_6H_4SO_2$)	**2a** (*o*-Et)	4.0	**3da** (69)
4	**1e** (Ph, 2-$C_{10}H_7SO_2$)	**2a** (*o*-Et)	4.5	**3ea** (58)
5	**1f** (*p*-$MeOCOC_6H_4$, Ts)	**2a** (*o*-Et)	4.0	**3fa** (67)
6	**1g** (*p*-BrC_6H_4, Ts)	**2a** (*o*-Et)	4.0	**3ga** (85)
7	**1h** (*p*-FC_6H_4, Ts)	**2a** (*o*-Et)	4.0	**3ha** (72)
8	**1i** (*m*-FC_6H_4, Ts)	**2a** (*o*-Et)	5.0	**3ia** (72)
9	**1j** (*m*-$CF_3C_6H_4$, Ts)	**2a** (*o*-Et)	5.0	**3ja** (78)
10	**1k** (*p*-MeC_6H_4, Ts)	**2a** (*o*-Et)	4.0	**3ka** (67)
11	**1l** (3-thienyl, Ts)	**2a** (*o*-Et)	5.0	**3la** (55)
12	**1m** (*p*-BrC_6H_4, Ms)	**2a** (*o*-Et)	4.0	**3ma** (68)
13	**1a** (Ph, Ts)	**2b** (*o*-isopropyl)	4.0	**3ab** (68)
14	**1a** (Ph, Ts)	**2c** (2,5-dimethyl)	1.0	**3ac** (67)
15	**1a** (Ph, Ts)	**2d** (*o*-Br)	4.0	**3ad** (50)
16	**1a** (Ph, Ts)	**2e** (3-chloro-2-methyl)	3.5	**3ae** (52)
17[c]	**1a** (Ph, Ts)	**2f** (H)	4.0	**3af** (48)

[a]In the presence of 0.004 mmol of $Rh_2(oct)_4$, 0.2 mmol of triazole **1**, and 0.2 mmol of **2** were reacted in 2 mL of refluxing DCE under N_2. [b]Yield of isolated products, average of two runs. [c]0.01 mmol of $Rh_2(oct)_4$, 0.2 mmol of triazole **1a**, and 0.3 mmol of **2f** were used.

2 mol % of $Rh_2(oct)_4$ was used (entry 6). The effect of solvent was also examined (entries 12–15), and **3aa** could be detected when the reaction was conducted in toluene, chloroform, or $CHCl_2CH_2Cl$, yet the yield was only between 27% and 60%.

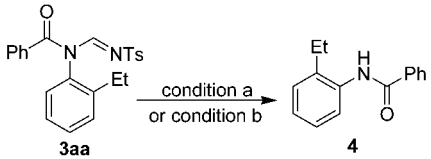
The scope of this transformation is demonstrated by using a wide range of triazoles and nitrosobenzene derivatives (Table 2). Both arylsulfonyl- and alkylsulfonyl-substituted triazoles were suitable substrates in this reaction (entries 1–4). The presence of electron-donating substituents on the aromatic ring (**1a** and **1d**) had a positive effect on the yield of the corresponding products. The reaction could be performed with triazoles possessing various functional groups (entries 5–12), including ester (**1f**), bromo (**1g** and **1m**), fluoro (**1h** and **1i**), trifluoromethyl (**1j**), and thienyl group (**1l**), the corresponding amidine could be obtained in moderate to high yield. Furthermore, the reaction also worked well with other nitrosobenzene derivatives (entries 13–17), furnishing *N*-acylamidine in yields ranging from 48% to 68%.

Scheme 3. Proposed Mechanism



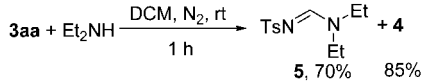
As shown in Scheme 3, two distinct pathways can be envisaged to rationalize the formation of *N*-acylamidine **3**. Treatment of triazole **1** with $Rh_2(oct)_4$ leads to the formation of *α*-imino rhodium carbene **B**, which undergoes 2 + 1 cycloaddition to furnish 1,2-oxaziridine **C** (path a). The cleavage of the N–O bond facilitates the subsequent rearrangement featured with migration of imino group, which gives the final product **3**. In an alternative pathway (path b), 2,3-dihydro-1,2,3-oxadiazole **D** is produced via the O-nucleophilic attack of nitrosobenzene at the carbene carbon of **B** and subsequent cyclization. Compound **D** is unstable, and it could rearrange to diaziridine **E**. After the ring opening and migration of the acyl group, *N*-acylamidine **3** was obtained as the major product.

Benzamide **4** could be easily obtained in high yield when **3aa** was reduced by $NaBH_4$ or hydrolyzed by 10% hydrochloric acid (eq 1). Compound **3aa** could act as a tosylimino transfer reagent when Et_2NH or $BnNH_2$ was used as nucleophile, leading to the formation of formimidamide **5** or **6** in moderate yield (eq 2 and 3).

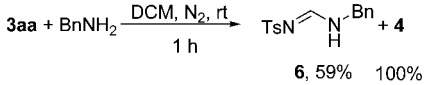


(1)

condition a: $NaBH_4$ (2.2 equiv), THF, 0 °C; 2.0 h, 75%
condition b: 10% HCl (5.0 equiv), THF, rt; 3.5 h, 77%



(2)



(3)

dx.doi.org/10.1021/ol5031876 | Org. Lett. 2014, 16, 6394–6396

In conclusion, we have developed an efficient and novel synthetic approach to *N*-acylamidine involving an N−O bond cleavage triggered rearrangement. This method uses readily available starting materials and proceeds under mild reaction conditions. The C−C bond of α-imino carbene is cleaved for the first time. Two new C−N bonds and a C−O bond are formed in the transformation. Full elucidation of the mechanism is currently underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures, characterization data, and NMR spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was generously supported by the National Natural Science Foundation of China (21002091, 21372204) and the Program for Innovative Research Team of Zhejiang Sci-Tech University (13060052-Y).

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