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Synthesis of Enaminones by Rhodium-Catalyzed Denitrogenative Rearrangement of 1-(*N*-Sulfonyl-1,2,3-triazol-4-yl)alkanols

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Supporting Information

ABSTRACT: Enaminones are synthesized by the rhodium(II)-catalyzed denitrogenative rearrangement reaction of 1-(*N*-sulfonyl-1,2,3-triazol-4-yl)alkanols, which are readily prepared from propargylic alcohols and *N*-sulfonyl azides. Intramolecular 1,2-hydride (or -alkyl) migration occurs with an intermediary α-imino rhodium(II) carbenoid species generated through denitrogenation of the 1,2,3-triazol-4-yl moiety. The resulting enaminones is converted into various heterocycles with replacement of the *N*-sulfonyl group.

Enaminones are important synthetic intermediates for a wide variety of heterocycles contained in natural products and pharmaceutical compounds,[1] and the development of new methods for their synthesis is highly desired.[2−4] We report herein a rhodium(II)-catalyzed denitrogenative rearrangement reaction of 1-(*N*-sulfonyl-1,2,3-triazol-4-yl)alkanols, leading to the formation of enaminones. The starting 1-triazolylalkohols are readily prepared from propargylic alcohols and *N*-sulfonyl azides.[5] Figure 1 depicts how the segments of a propargylic alcohol and *N*-sulfonyl azide construct the product structure through the whole process.

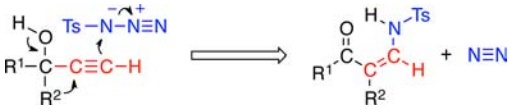
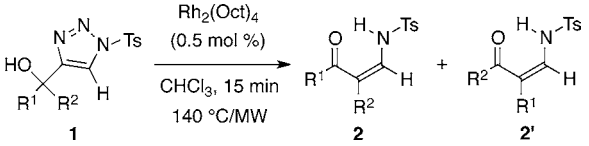


Figure 1. Construction of enaminones from propargylic alcohols and tosyl azide.

Recently, Gevorgyan,[6] Fokin,[6a,7] and our group[8] have reported denitrogenative annulation reactions of *N*-sulfonyl-1,2,3-triazoles with unsaturated organic molecules such as nitriles, alkynes, and alkenes. α-Diazo imine formed by ring−chain tautomerization reacts with a rhodium(II) or nickel(0) complex to generate the corresponding metal carbenoid, which undergoes cyclization with an unsaturated organic molecule. We have recently reported the rhodium(II)-catalyzed denitrogenative hydration reaction of *N*-sulfonyl-1,2,3-triazoles.[9] The intermediate α-imino rhodium(II) carbenoid is electrophilic enough to induce nucleophilic addition of water. This study demonstrated the electron-deficient nature of the carbenoid carbon, and led us to envisage that, with the α-imino rhodium(II) carbenoid generated from 1-(*N*-sulfonyl-1,2,3-triazol-4-yl)alkanol, an electron pushing effect of the hydroxyl group might facilitate intramolecular 1,2-hydride (or -alkyl) migration onto the adjacent electrophilic carbenoid carbon,[10,11] as with the case of the semipinacol rearrangement, leading to the formation of enaminones.

Thus, we initially prepared 1-(*N*-tosyl-1,2,3-triazol-4-yl)-ethanol (**1a**) from but-3-yn-2-ol and tosyl azide according to the method reported by Hu (91% yield).[5c] Then, **1a** was treated with a catalytic amount of $Rh_2(Oct)_4$ (0.5 mol %, Oct = octanoate) in $CHCl_3$ at 140 °C under microwave irradiation (MW) for 15 min.[12] To our delight, (*Z*)-4-(tosylamino)but-3-en-2-one (**2a**) was produced in 94% isolated yield (Table 1, entry 1). The selective production of **2a** suggested the 1,2-hydride migration predominated over 1,2-methyl migration. Substrates **1b−d** possessing a variety of alkyl groups afforded the corresponding products **2b−d** in yields ranging from 79% to 91% (entries 2−4). On the other hand, the reaction of phenyl-substituted substrate **1e** gave a mixture of **2e** (58% yield) and **2e′** (25% yield), suggesting that 1,2-phenyl migration could compete with 1,2-hydride migration (entry 5). In the case of disubstituted substrate **1f**, the phenyl group migrated preferentially over the methyl group (entry 6). With the disubstituted substrate **1g**, the methyl group migrated in preference to the isopropyl group (entry 7). These results

Table 1. Rh(II)-Catalyzed Denitrogenative Rearrangement of 1-(*N*-Tosyl-1,2,3-triazol-4-yl)alkanols 1a−h[a]



1 **2** **2′**

entry	1	R^1	R^2	2 (yield/%)[b]	2′ (yield/%)[b]
1	**1a**	Me	H	**2a** (94)	**2a′** (0)
2	**1b**	*n*-Pr	H	**2b** (91)	**2b′** (0)
3	**1c**	*i*-Pr	H	**2c** (87)	**2c′** (0)
4	**1d**	*t*-Bu	H	**2d** (79)	**2d′** (0)
5	**1e**	Ph	H	**2e** (58)	**2e′** (25)[c]
6	**1f**	Me	Ph	**2f** (86)[c]	**2f′** (5)[c]
7	**1g**	*i*-Pr	Me	**2g** (47)[c]	**2g′** (19)[c]
8	**1h**	Me	Me	**2h** (90)[c]	

[a]Conditions: $Rh_2(Oct)_4$ (1 μmol) and **1** (0.2 mmol) in $CHCl_3$ (4 mL) were heated at 140 °C under microwave irradiation for 15 min. [b]Isolated yield (average of 2 runs). [c]*E*/*Z* isomeric mixtures; **2e′** (30:70), **2f** (12:88), **2f′** (70:30), **2g** (24:76), **2g′** (9:91), **2h** (22:78).

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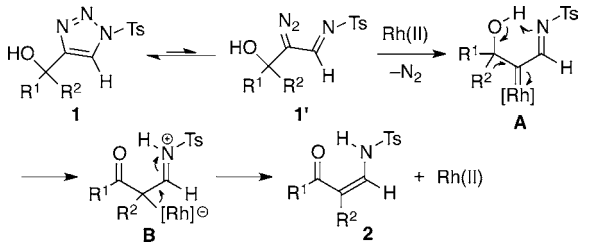
implied the migratory aptitude to be hydride > phenyl > primary alkyl > secondary alkyl. This order was similar to that observed with analogous rhodium(II) carbenoid intermediates.[10a,b,g] With the dimethyl-substituted substrate **1h**, even the less labile methyl group migrated to give the product **2h** in 90% yield (entry 8). The enaminones **2a**–**e** took (*Z*)-configuration, which allowed intramolecular hydrogen bonding between the N–H and carbonyl groups. On the other hand, a mixture of (*E*) and (*Z*)-isomers was observed by ^{1}H NMR for α-substituted enaminones **2e′**–**h**, probably because the planar structure of (*Z*)-configuration with intramolecular hydrogen bonding was disfavored by steric repulsion between R^1 and R^2 substituents.[13]

A plausible mechanism for the production of **2** from **1** is depicted in Scheme 1. Initially, a reversible ring–chain

Scheme 1. Plausible Mechanism for the Formation of 2 from 1



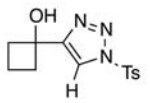
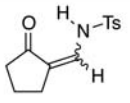
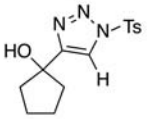
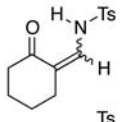
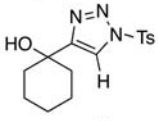
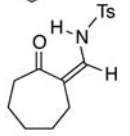
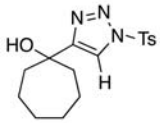
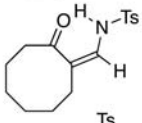
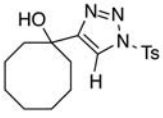
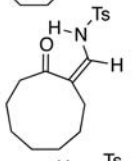
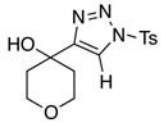
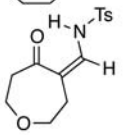
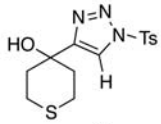
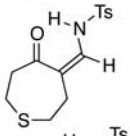
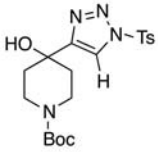
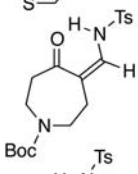
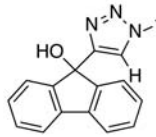
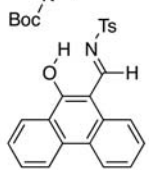
tautomerization of the *N*-sulfonyl-1,2,3-triazol-4-yl moiety of **1** generates α-diazo imine **1′**.[14] The subsequent irreversible reaction of **1′** with rhodium(II) affords α-imino rhodium(II) carbenoid **A** with release of molecular nitrogen. The imine nitrogen acts as a base to deprotonate the hydroxyl group, which exerts an electron-pushing effect to induce 1,2-migration. The resulting anionic rhodium of zwitterionic intermediate **B** releases an electron pair, which flows into the cationic iminium moiety to give the product **2** with regeneration of the rhodium(II) catalyst.

Next, the intramolecular 1,2-alkyl migration reaction was applied to cyclic 1-triazolylalkanols, aiming at ring expansion (Table 2).[15,16] The migration reaction worked well with substrates **3a**–**e** of four- to eight-membered ring structures. The carbocyclic structures were expanded by one carbon, furnishing the products **4a**–**e** in yields ranging from 74% to 95% (entries 1–5). Substrates **3f**–**h** having heteroatoms within their cyclic skeletons were reactive as well to afford the products **4f**–**h**, that were difficult to synthesize via conventional routes starting from symmetrical ketones and formamide acetals (entries 6–8).[3] Interestingly, the ring-expansion reaction of fluorenol-substrate **3i** furnished phenanthrene derivative **4i** in an enol form (entry 9).

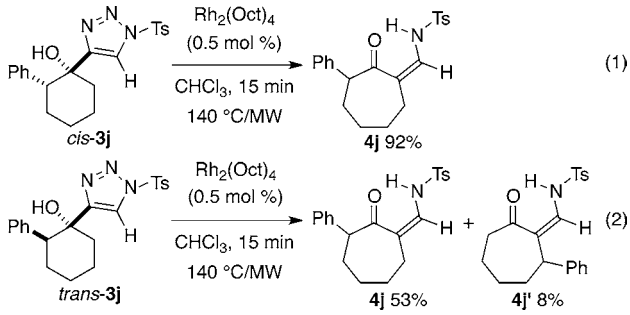
We also investigated the site-selectivity in the migratory step using a diastereomeric pair of unsymmetrical 1-triazolylcycloalkanols. In the case of *cis*-2-phenyl-1-triazolylcyclohexanol **3j**, the methylene carbon selectively migrated to give the product **4j** in 92% yield (eq 1). On the other hand, the *trans*-isomer **3j** afforded a mixture of products **4j** (53% yield) and **4j′** (8% yield) (eq 2). These results indicated that the migratory aptitude with cyclic substrates was not so simple, but also subject to a configurational factor.[17]

The one-pot synthesis of enaminones *starting from propargylic alcohols* was carried out to demonstrate the practical convenience of the present method (eqs 3–5). The enaminones **2a**, **4c**, and **4k** were directly obtained in one-pot

Table 2. Rh(II)-Catalyzed One-carbon Ring-Expansion of 1-(*N*-Tosyl-1,2,3-triazol-4-yl)cycloalkanols 3a–i[a]

entry	substrate **3**	product **4**	yield (%)[b]
1	 **3a**	 **4a**	80[c]
2	 **3b**	 **4b**	90[c]
3	 **3c**	 **4c**	95
4	 **3d**	 **4d**	74
5	 **3e**	 **4e**	78
6	 **3f**	 **4f**	98
7	 **3g**	 **4g**	94[d]
8	 **3h**	 **4h**	95
9	 **3i**	 **4i**	96

[a]Conditions: $Rh_2(Oct)_4$ (1 μmol) and **3** (0.2 mmol) in $CHCl_3$ (4 mL) were heated at 140 °C under microwave irradiation for 15 min. [b]Isolated yield (average of 2 runs). [c]*E*/*Z* isomeric mixtures; **4a** (7:93), **4b** (6:94). [d]Using $Rh_2(Oct)_4$ (2 μmol).



from the corresponding propargylic alcohols **5a**, **5c**, and **5k**, which were all available from commercial sources. Although the

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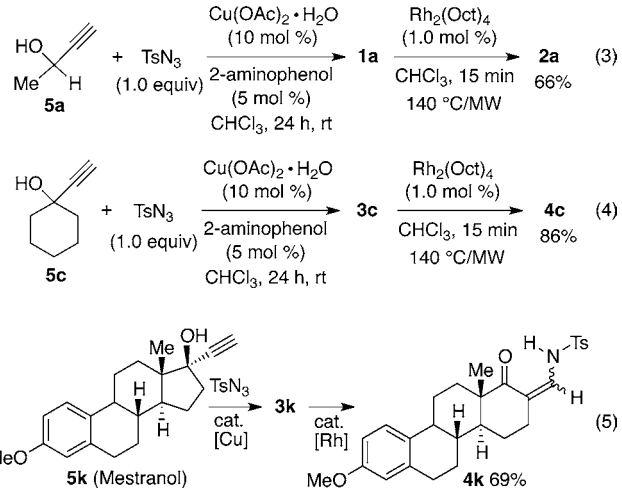
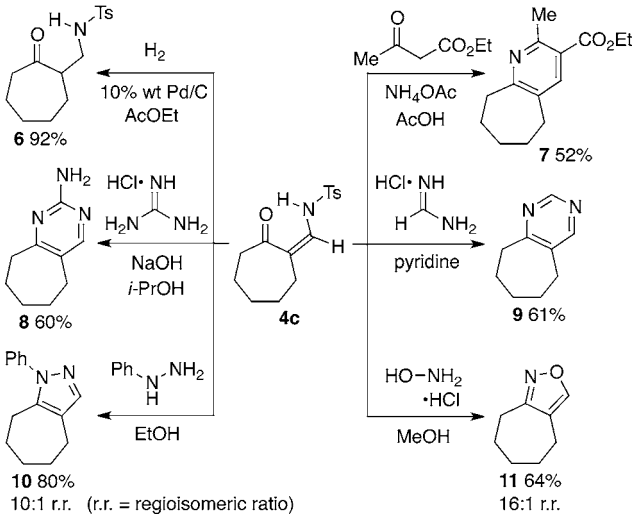


copper catalyst remained in the reaction mixture after the first step, it barely interfered with the second reaction catalyzed by rhodium(II).[6a,9]

The synthetic utility of the products was demonstrated by the further transformations of **4c** shown in Scheme 2. The

Scheme 2. Synthetic Derivatization of Enaminone 4c



carbon−carbon double bond was successfully reduced, giving β-amino ketone **6** in 92% yield when a simple hydrogenation protocol using palladium on charcoal was applied. Various heterocycles **7**−**11** were readily synthesized on treatment with appropriate partners.[18]

In summary, we have developed a significantly step-economical method for the synthesis of enaminones starting from propargylic alcohols and *N*-sulfonyl azides, where molecular nitrogen is the only waste product.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and spectral data for the 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.

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