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Rhodium-catalyzed denitrogenative thioacetalization of N-sulfonyl-1,2,3-triazoles with disulfides: an entry to diverse transformation of terminal alkynes†

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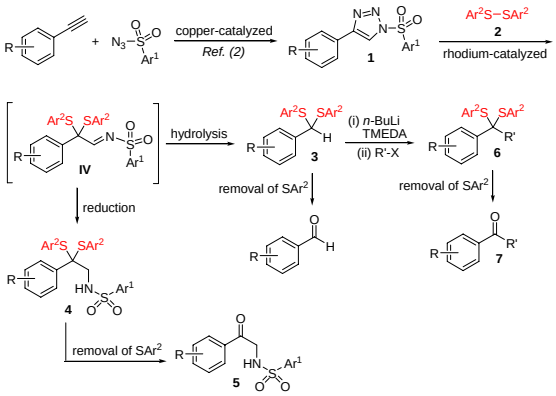
An efficient and useful rhodium-catalyzed denitrogenative thioacetalization of *N*-sulfonyl-1,2,3-triazoles has been developed for the first time. The protocol uses readily available *N*-sulfonyl-1,2,3-triazoles and diaryl disulfides as the starting materials, the corresponding hydrolytic and reductive products with thioacetals were obtained in good to excellent yields, and the reactions were carried out well under the mild conditions with tolerance of some functional groups. Further, the generated thioacetals could be transferred into some useful compounds. Therefore, the present method provides a novel and valuable strategy for diverse transformation of alkynes.

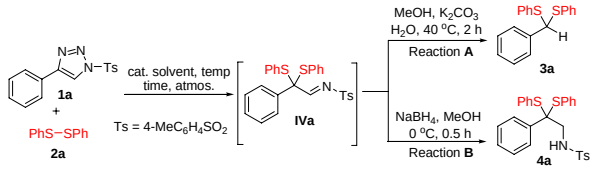
Alkynes are an important class of organic compounds, and they provide various opportunities for transformations of diverse organic molecules.[1] For example, copper-catalyzed cycloaddition of terminal alkynes with *N*-sulfonyl azides can easily get *N*-sulfonyl-1,2,3-triazoles.[2] Recently, *N*-sulfonyl-1,2,3-triazoles have attracted some attention because they can transfer into useful *α*-imino metal carbenes in the presence of transition metals,[3] the generated *α*-imino and metal carbene parts exhibit high nucleophilic and electrophilic reactivity, and some interesting reactions have been developed by using various partners.[4] On the other hand, thioacetalization of carbonyl groups is a popular protocol in organic synthesis,[5] and it is often used in synthesis of various molecules because of inherent stability of the thioacetals under both acidic and basic conditions.[6] The traditional methods for synthesis of thioacetals are from the reaction of carbonyl compounds with thiols or dithiols in the presence of protic and Lewis acids.[7] In addition, thioacetalization of diazo compounds has also been investigated.[8] To the best of our knowledge, thioacetalization of *N*-sulfonyl-1,2,3-triazoles has not been reported thus far. As shown in Scheme 1, our strategy in this paper is as follows: copper-catalyzed cycloaddition of terminal alkynes with *N*-sulfonyl azides provides *N*-sulfonyl-1,2,3-triazoles according to the previous literatures,[2] and rhodium-catalyzed denitrogenative thioacetalization *N*-sulfonyl-1,2,3-triazoles with disulfides gives intermediates **IV**. Hydrolysis of **IV** affords 1-(aryl(arylthio)methylthio)benzene (**3**), alkylation of **3** leads to **6**, and removal of Ar^2S in **3** and **6** yields aldehydes and ketones (**7**). Reduction of **IV** generates 2-aryl-2,2-bis(arylthio)-*N*-sulfonylethanamine (**4**), and deprotection of **4** affords 1-aryl-2-(sulfonylamino)ethanone (**5**).



Scheme 1 Our strategy for diverse transformation of terminal alkynes in which a key rhodium-catalyzed denitrogenative thioacetalization of *N*-sulfonyl-1,2,3-triazoles with disulfides is performed.

As shown in Scheme 2, reaction of 4-phenyl-1-tosyl-1*H*-1,2,3-triazole (**1a**) with diphenyl disulfide (**2a**) was used as the model to screen optimized conditions including Rh catalysts, solvents, temperature, time and atmosphere. The results showed that **1a** almost quantitatively transformed into 2-phenyl-2,2-bis(phenylthio)-*N*-tosylethanimine (**IVa**) (determination by TCL) by using 2.5 mol% $Rh_2(Oct)_4$ as the catalyst, toluene as the solvent at 60 °C under nitrogen atmosphere for 6 h (*see Supporting Information for the details*). After a work-up, **IVa** was isolated in only 44% yield because of instability of **IVa** during the work-up, so we decided to continue the following two procedures (Reactions **A** and **B**). When **IVa** was hydrolyzed in the presence of aqueous K_2CO_3 at 40 °C for 2 h (Reaction **A**), 1-(phenyl(phenylthio)methylthio)benzene (**3a**) was obtained in 75% yield (entry 1). Reduction of **IVa** with $NaBH_4$ provided 2-

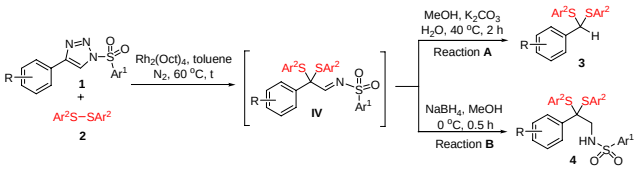
phenyl-2,2-bis(phenylthio)-*N*-tosylethanamine (**4a**) in 81% yield (Reaction **B**) (entry 1).

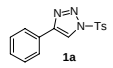
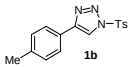
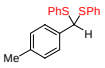
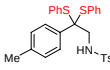
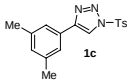
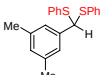
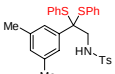
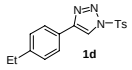
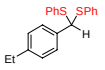
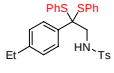
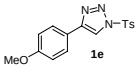
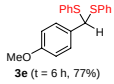
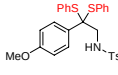
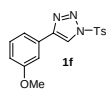
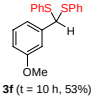
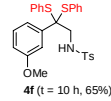
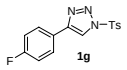
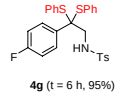
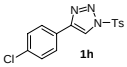
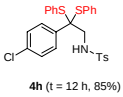
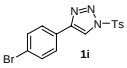
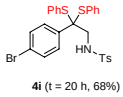
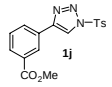
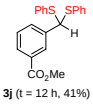
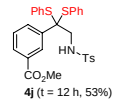
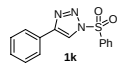
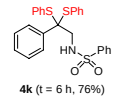
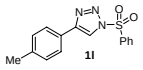
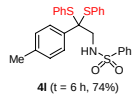
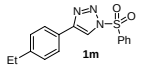
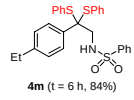
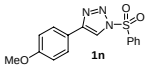
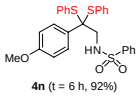


Scheme 2 Optimization of conditions on rhodium-catalyzed thioacetalization of 4-phenyl-1-tosyl-1*H*-1,2,3-triazole (**1a**) with diphenyl disulfide (**2a**) leading to 2-phenyl-2,2-bis(phenylthio)-*N*-tosylethanimine (**IVa**), and synthesis of 1-(phenyl(phenylthio)methylthio)benzene (**3a**) and 2-phenyl-2,2-bis(phenylthio)-*N*-tosylethanamine (**4a**).

After getting the optimized conditions, we investigated the scope for the rhodium-catalyzed denitrogenative thioacetalization of *N*-sulfonyl-1,2,3-triazoles (**1**) with disulfides (**2**) and synthesis of **3** and **4** (Table 1). For substituent R in **1**, the substrates containing electron-donating groups provided higher yields than those containing electron-withdrawing groups. For Ar^1, the substrates with electron-withdrawing groups exhibited slightly better reactive activity than those with neutral and electron-donating groups. Diaryl disulfides (**2**) with electron-donating groups afforded higher yields than those with electron-withdrawing groups. Unfortunately, aliphatic *N*-sulfonyl-1,2,3-triazoles and dialkyl disulfides were poor substrates. The rhodium-catalyzed denitrogenative thioacetalization of *N*-sulfonyl-1,2,3-triazoles (**1**) with disulfides (**2**) showed tolerance of some functional groups including ether (entries 5, 6, 14 and 16), C-F bond (entry 7), C-Cl bond (entries 8, 15 and 20), C-Br bond (entries 9 and 17), ester (entry 10), and CF_3 (entry 18).

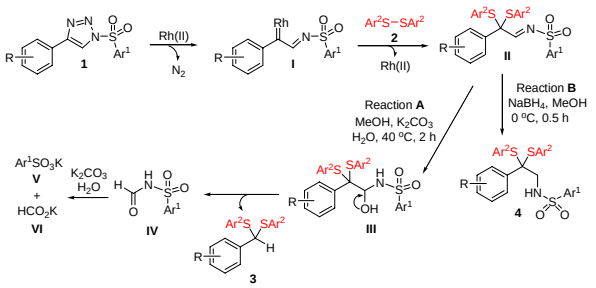
Table 1 Rhodium-catalyzed denitrogenative thioacetalization of *N*-sulfonyl-1,2,3-triazoles (**1**) with disulfides (**2**) and synthesis of **3** and **4**.[a]



Entry	1	3 (Time, Yield[b])	4 (Time, Yield[b])
1	 **1a**	 **3a** (t = 6 h, 75%)	 **4a** (t = 6 h, 81%)
2	 **1b**	 **3b** (t = 6 h, 82%)	 **4b** (t = 6 h, 82%)
3	 **1c**	 **3c** (t = 6 h, 66%)	 **4c** (t = 6 h, 78%)
4	 **1d**	 **3d** (t = 6 h, 84%)	 **4d** (t = 6 h, 84%)
5	 **1e**	 **3e** (t = 6 h, 77%)	 **4e** (t = 6 h, 92%)
6	 **1f**	 **3f** (t = 10 h, 53%)	 **4f** (t = 10 h, 65%)
7	 **1g**	 **3g** (t = 6 h, 83%)	 **4g** (t = 6 h, 95%)
8	 **1h**	 **3h** (t = 12 h, 70%)	 **4h** (t = 12 h, 85%)
9	 **1i**	 **3i** (t = 20 h, 53%)	 **4i** (t = 20 h, 68%)
10	 **1j**	 **3j** (t = 12 h, 41%)	 **4j** (t = 12 h, 53%)
11	 **1k**	**3a** (t = 6 h, 75%)	 **4k** (t = 6 h, 76%)
12	 **1l**	**3b** (t = 6 h, 70%)	 **4l** (t = 6 h, 74%)
13	 **1m**	**3d** (t = 6 h, 67%)	 **4m** (t = 6 h, 84%)
14	 **1n**	**3e** (t = 6 h, 90%)	 **4n** (t = 6 h, 92%)
15	**1o**	**3h** (t = 12 h, 74%)	**4o** (t = 12 h, 85%)
16	**1p**	**3a** (t = 6 h, 81%)	**4p** (t = 12 h, 82%)
17	**1q**	**3a** (t = 6 h, 82%)	**4q** (t = 6 h, 85%)
18	**1r**	**3a** (t = 6 h, 88%)	**4r** (t = 6 h, 89%)
19	**1a**	**3k** (t = 12 h, 81%)	**4s** (t = 12 h, 82%)
20	**1a**	**3l** (t = 16 h, 71%)	**4t** (t = 16 h, 78%)
21	**1k**	**3k** (t = 12 h, 89%)	**4u** (t = 12 h, 96%)

[a] Reaction conditions: under nitrogen atmosphere, *N*-sulfonyl-1,2,3-triazole (**1**) (0.2 mmol), disulfide (**2**) (0.22 mmol), $Rh_2(Oct)_4$ (0.005 mmol), PhMe (2.0 mL), temperature (60 °C), time (6-20 h) in a sealed Schlenk tube for reaction of **1** with **2**. For Reaction **A**, MeOH (2.0 mL),

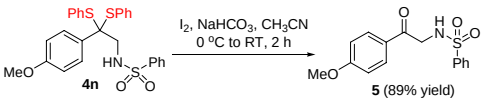
K_2CO_3 (0.4 mmol), H_2O (0.2 mL) at 40 °C for 2 h; For Reaction **B**, $NaBH_4$ (0.2 mmol), MeOH (0.5 mL) at 0 °C for 0.5 h. [b] Isolated yield.



Scheme 3 Possible mechanism for the rhodium-catalyzed denitrogenative thioacetalization and synthesis of **3** and **4**.

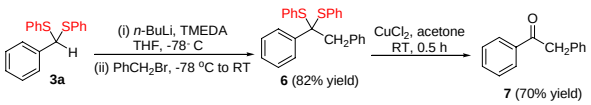
A possible mechanism on the rhodium-catalyzed denitrogenative thioacetalization of *N*-sulfonyl-1,2,3-triazoles (**1**) with disulfides (**2**) and synthesis of **3** and **4** is suggested in Scheme 3 according to the results above and the previous references.[3,4] Treatment of **1** with Rh(II) catalyst affords **I** freeing nitrogen, reaction of **I** with **2** gives thioacetalizating product **II** regenerating Rh(II) catalyst. Addition of water to imine in **II** under basic aqueous condition provides **III**, and desorption of amide (**IV**) from **III** yields **3**. Hydrolysis of **IV** in the presence of K_2CO_3 leads to **V** and **VI** (*note: Ar^1SO_3H was obtained after the resulting solution was acidified with 1 M HCl in our experiments*). Reduction of imine in **II** with $NaBH_4$ in methanol affords **4**.

Deprotection of thioacetals was attempted. As shown in Scheme 4, **4n** transformed into **5** in 89% yield in the presence of I_2 and $NaHCO_3$ in acetonitrile.[4o,9] Therefore, the present method is useful approach to *α*-amino ketone derivatives from *N*-sulfonyl-1,2,3-triazoles.



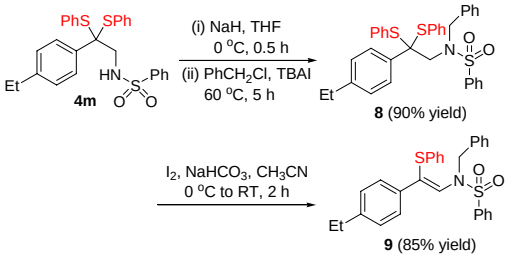
Scheme 4 Deprotection of thioacetal **4n**.

As shown in Scheme 5, treatment of **3a** with *n*-BuLi in the presence of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) and the subsequent reaction with 1-(bromomethyl)benzene[10] provided **6** in 82% yield. Removal of PhS in **6** gave ketone **7** in the presence of $CuCl_2$ in acetone.



Scheme 5 Preparation of ketone **7** from **3a**.

We explored further application of **4**. After treatment of **4m** with NaH in THF, 1-(chloromethyl)benzene was added, and **8** was prepared in 90% yield. Reaction of **8** in the presence of I_2 and $NaHCO_3$ in acetonitrile afforded **9** in 85% yield (Scheme 6).[11] Therefore, the results above indicates that the rhodium-catalyzed denitrogenative thioacetalization of *N*-sulfonyl-1,2,3-triazoles is a very useful strategy for synthesis of various molecules.



Scheme 6 Synthesis of **9** from **4m** (TBAI = Tetrabutylammonium iodide).

In summary, we have developed an efficient and useful rhodium-catalyzed denitrogenative thioacetalization of *N*-sulfonyl-1,2,3-triazoles, and the corresponding hydrolytic and reductive products with thioacetals were obtained in good to excellent yields. The protocol uses readily available *N*-sulfonyl-1,2,3-triazoles and diaryl disulfides as the starting materials, and the reactions were carried out well under the mild conditions with tolerance of some functional groups. Further, the generated thioacetals could be transferred into some useful compounds. Therefore, the present method provides a novel and valuable strategy for diverse transformation of alkynes.

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† Electronic Supplementary Information (ESI) available: Full experimental details, characterization and NMR spectra of the target products are provided. See DOI: 10.1039/b000000x/

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