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Rhodium-Catalyzed Sommelet Hauser Type Rearrangement of α-Diazoimines: Synthesis of Functionalized Enamides

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**An efficient rhodium catalyzed Sommelet Hauser type rearrangement of sulfur ylides derived from α-thioesters and *N*-sulfonyl-1,2,3-triazoles has been successfully accomplished for the synthesis of various functionalized enamides. The developed reaction involves the unprecendented [2,3]-sigmatrophic rearrangement of sulfur ylides with imine motif. Importantly, the method works well with various substituted α-thioester/-amide/-ketone and substituted *N*-sulfonyl-1,2,3-triazoles and allows the synthesis of diverse enamides derivatives in good to excellent yields. The reaction was also successfully extended to the one-pot synthesis of enamides from terminal alkynes.**

N-Sulfonyl-1,2,3-triazoles have emerged as efficient source for the *in-situ* generation of α-diazoimines through ring-chain isomerism.[1] Trapping of these α-diazoimines with suitable transition metal, particularly rhodium(II) carboxylates, affords α-iminometal carbenoids, which possess dual character where metal attached carbon posses electrophilic character, and imine nitrogen having the nucleophilic character. This unique characteristic of iminocarbene was utilized in number of transformation with diverse coupling partners for the highly efficient and atom/step-economic construction of nitrogen-containing building blocks or *N*-heterocycles. In particular, generation of ylides from α-iminometal carbenoids and various Lewis bases (such as nitrogen,[2] oxygen[3] and sulfur[4] based compounds) followed by rearrangement gained significant interest due to the possible development of new transformations and elegant synthesis of complex structural frameworks. Among them, sulfur-ylide generation and rearrangement employing *N*-sulfonyl-1,2,3-triazoles as a carbene source has been less explored and the development of new transformation for the synthesis of functionalized structural motif are highly warranted.

In the past decades, sulfur ylides were increasingly used in

organic synthesis[5] for the construction of sulfur-containing building blocks and bioactive molecules.[6] The first report on the rhodium catalyzed Doyle-Krimse[7] rearrangement of sulfur-ylide, derived from *N*-sulfonyl-1,2,3-triazoles and allyl thioethers, was independently reported from our lab[8] and Murakami and co-workers[9] for the synthesis of α-sulfenyl imines containing quaternary center (Scheme 1a). Subsequently, 1,2-sulfur migration followed by aza-Diels Alder reaction of thio-tethered *N*-sulfonyl-1,2,3-triazoles was also disclosed for the synthesis of substituted polyhydropyridine derivatives (Scheme 1a).[4d, 4e] Although [2,3]/[1,2]-sigmatropic rearrangements of sulfur ylides derived from α-diazoimines have been extensively studied, Sommelet-Hauser type rearrangement of sulfur ylides derived from α-diazoimines, to the best of our knowledge, is yet to be documented.
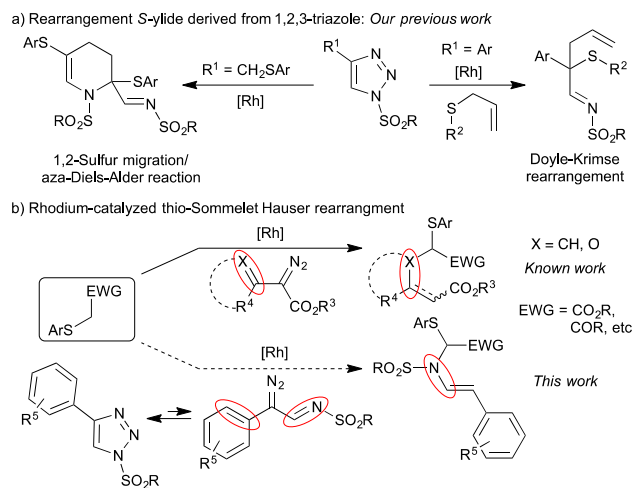
Scheme 1. Rh-catalyzed rearrangement of *S*-ylide derived from triazole.

Sommelet-Hauser rearrangement of sulfur ylide derived from α-diazocarbonyl compounds, known as thio- Sommelet-Hauser rearrangement, has been well documented in the literature.[10] Most of these transformation utilize alkene or arene substituted diazo compound, however, use of carbonyl derivative as part of three-atom unit in the rearrangement has been explored well. Recently, we have demonstrated an

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unprecedented Sommelet-Hauser type rearrangement of sulfur ylide derived from diazo carbonyl compounds and α-thioesters for the synthesis of vinylogous carbonates, which involves the carbonyl group in the rearrangement.[11] Inspired by this unusual observation and to continue our interest in the functionalization of α-diazoimines,[12] we were interested to study the preferential Sommelet-Hauser type rearrangement of sulfur ylides derived from α-thioester and α-diazoimines, which posses both aryl and imine motif for the potential rearrangement (Scheme 1b). The successful development of this reaction would offer synthesis of functionalized arene or enamides, potential building blocks in organic synthesis[13].

To test our hypothesis, 1,2,3-triazole **1a** and α-thioester **2a** were chosen as the model substrates. Reaction of N-sulfonyl 1,2,3-triazole **1a** with α-thioester **2a** in the presence of 2 mol% of $Rh_2(OAc)_4$ in toluene at 120 °C gave enamide N,N-disubstituted enamide **4a** as sole product in 41% yield, which involves rearrangement of imine motif and formation of functionalized arene **3a** was not observed (Table 1, entry 1). The formation of **4a** over the expected **3a** could be explained possibly due to the involvement of destabilising dearomatisation step in rearrangement of aryl moiety, which is absent with imine moiety.

Table 1. Rhodium catalyzed synthesis of enamide **4a**: Optimization[a]
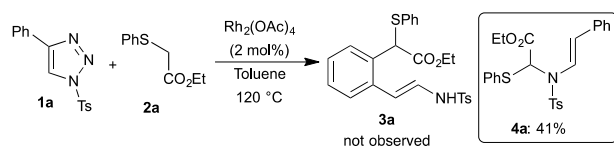

Entry	[Rh] (2 mol%)	Solvent	Temp (°C)	Yield (%)[b]
1	$Rh_2(OAc)_4$	Toluene	120	41
2	$Rh_2(TBSP)_4$	Toluene	120	32
3	$[Cp*Rh(CH_3CN)_3](SbF_6)_2$	Toluene	120	-
4	$[Cp*RhCl_2]_2$	Toluene	120	28
5	$Rh_2(Piv)_4$	Toluene	120	67
6	$Rh_2(Piv)_4$	1,2-DCE	90	43
7	$Rh_2(Piv)_4$	$CHCl_3$	80	52
8	$Rh_2(Piv)_4$	Xylene	140	60[c]
9	$Rh_2(Oct)_4$	Toluene	120	80

[a] Reaction conditions: Triazole **1a** (1 equiv), thioester **2a** (2 equiv), Rh-catalyst (2 mol%), solvent, temp, 5 h. [b] Isolated yields. [c] 3 mol% of $Rh_2(Piv)_4$ was used.

Next, various critical parameters were studied to improve the yield of enamide **4a**. Screening of other rhodium catalysts such as $Rh_2(TBSP)_4$, $[Cp*Rh(CH_3CN)_3](SbF_6)_2$ and $[Cp*RhCl_2]_2$ have proven less reactive than $Rh_2(OAc)_4$ for the present transformation, (Table 1, entries 2-4). Next, use of $Rh_2(Piv)_4$ as catalyst found better than $Rh_2(OAc)_4$ for the present reaction and gave the product **4a** in 67% yield (Table 1, entry 5). The further optimization study was continued with $Rh_2(Piv)_4$ as a catalyst. Decreasing the temperature and changing solvent system from toluene to 1,2-DCE and chloroform led to the formation of **4a** in diminished yield (Table 1, entry 6 and 7). Next, increase in the temperature from 120 °C to 140 °C, and rising catalyst loading from 2 mol% to 3 mol% furnished similar results (Table 1, entry 5 and 8). Interestingly, replacement of

$Rh_2(Piv)_4$ with $Rh_2(oct)_4$ in toluene at 120 °C afforded 80% yield of **4a**, which was chosen as optimized conditions for the further study of substrates scope (Table 1, entry 9).

Having found the suitable conditions for the rearrangement of sulfur ylide, the scope and limitations of various electron deficient thio-derivatives **2** were investigated (Scheme 2). A diverse selection of electron deficient sulfides **2** was subjected under the standard conditions for the synthesis of various thio-substituted enamide derivatives **4** in good yields. Thus, ethyl, methyl and allyl esters of phenylsulfides were successfully converted into corresponding enamides **4a**-**4c** with N-sulfonyl-1,2,3-triazole **1a** under the rhodium catalyzed conditions in 80, 79 and 65% yield, respectively. Next, ester functionality was replaced with acetyl moiety to afford keto-analog of enamide derivative **4d** in 56% yield. Similarly, altering from the carboxylic ester to N,N-diethylamide was also successfully converted to enamide **4e** in 71% yield. The formation and structure of **4e** was unambiguously confirmed by single crystal X-ray analysis (Scheme 2).[14] On the other hand, nitro and cyano tethered phenylsulfides did not afford the corresponding enamides **4f** and **4g**, respectively.
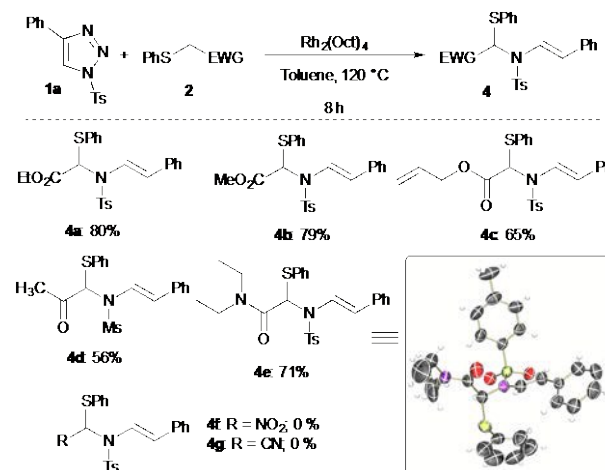

Scheme 2. Rhodium catalyzed synthesis of enamides **4**: Scope of α-thiocarbonyl derivatives.

Following the successful exploration of various electron-withdrawing groups at arylsulfides, related aryl substitutions were also examined to explore the generality of the α-thioesters (Scheme 3). α-Thioesters having electron rich arenes, such as 3-methoxy, 4-methyl, 2,4-dimethyl, 4-methoxyphenyl substituents, underwent smooth reactions to furnish enamide **4h**-**4k** in excellent yields. Similarly, haloarenes substituted α-thioesters also gave enamides **4l**, **4m**, and **4n** in 74, 84, and 80% yield, respectively. Further, reactive functional groups like aroyloxy, OTBDMS substituted arylthio esters were also well tolerated under the optimized conditions to provide **4o**, **4p**, and **4r** in comparable yields. 3,4-Dimethoxyphenyl-sulfide was also successfully converted to enamide **4q** in 68% yield. Subsequently, replacement of phenyl with naphthyl also led to the formation of enamide **4s** in good yield. It is important to note that use of alkyl-derived α-thioesters led to the formation of products **4t** and **4u** in good yield.

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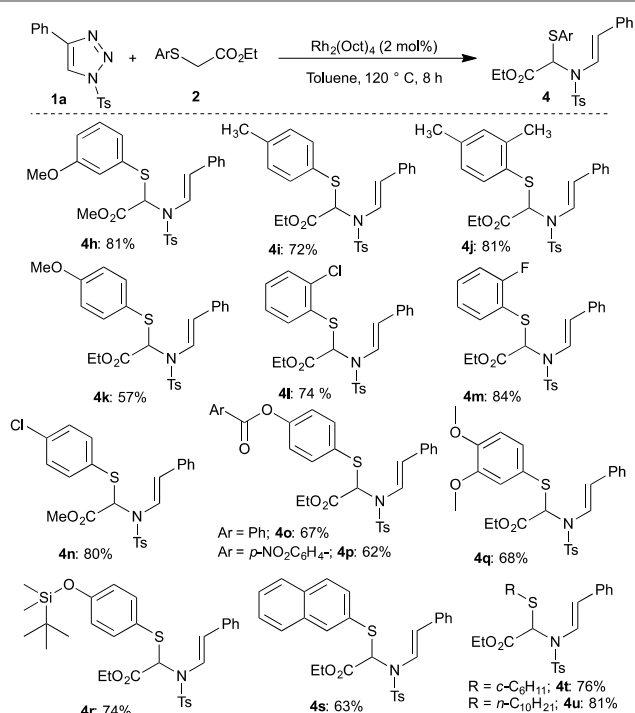
Scheme 3. Scope of aryl group on α-thioesters.

After successfully demonstrating the generality of electron deficient arylsulfides **2** for the synthesis of thio-tethered enamides **3** through rhodium catalyzed rearrangement, the scope of *N*-sulfonyl-1,2,3-triazoles **1** was examined (Scheme 4). Notably, various *N*-substituted 1,2,3-triazoles, such as mesyl, benzenesulfonyl, and *p*-chlorobenzenesulfonyl derivatives furnished corresponding enamides **4v**-**4x** in comparable yields (70-75%).
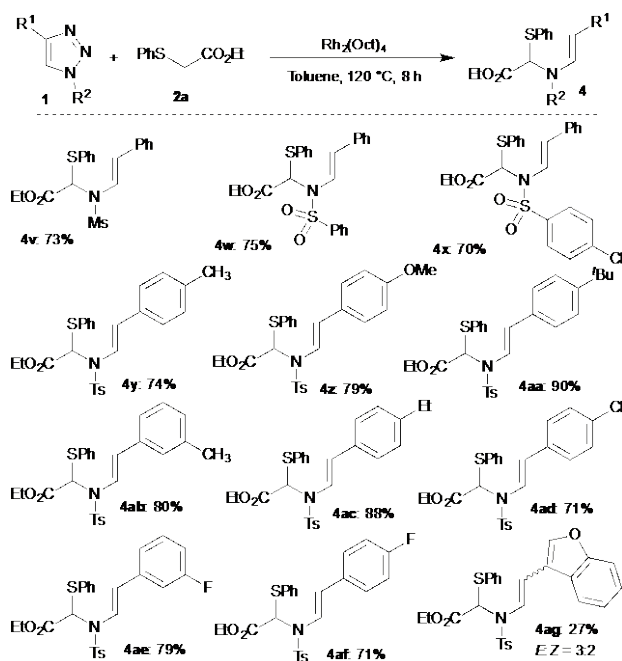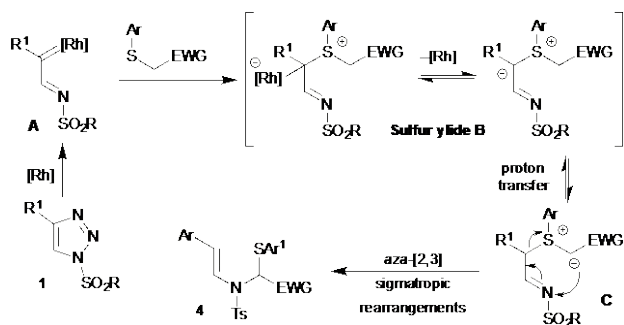

Scheme 4. Scope of *N*- sulfonyl 1,2,3-triazoles.

Similarly, alkyl and electron donating methoxy-substituted aryl containing 1,2,3-triazoles were readily converted to corresponding enamides **4y**-**4ac** in excellent yields. In addition, the optimized conditions was also equally worked well for the halo-substituted aryl containing triazoles, which led to the formation of enamides **4ad**-**4af** in ~70% yields. Unfortunately, present conditions failed to convert the thiophene-derived triazole to corresponding enamide. On the other hand, benzofuran derived triazole afforded the expected **4ag** in low yield as mixture of E/Z isomers.

Next, we focused our attention on the synthesis of enamide **4** from terminal alkyne *via* one-pot transformation. Since the triazoles were obtained from alkyne and azide through copper-catalyzed alkyne-azide cycloaddition,[15] the one-pot transformation of alkyne to direct synthesis of enamide **4a** was examined (Scheme 5a). Delightfully, the reaction of phenylacetylene with tosyl azide in the presence of CuTC in toluene at room temperature for 4 h followed by the addition of α-thioester **2a** and Rh₂(Oct)₄ and subsequent elevation of temperature to 120 °C furnished the expected enamide **4a** in 56% yield. This successful one-pot transformation offers the strategy for the regio and stereoselective functionalization of terminal alkynes. Next, the possible synthetic conversion of enamide **4a** was investigated (Scheme 5b). The sulfur moiety in the synthesized enamide **4a** was readily oxidized to corresponding sulfone **5** in the presence of *m*-CPBA at room temperature in CH₂Cl₂ in 78% yield. Subsequently, hydrogenation of alkene in enamide **4a** over Pd(OH)₂/C in methanol at 65 °C afforded the product **6** in 71% yield, where both alkene and C-S bong got hydrogenated.
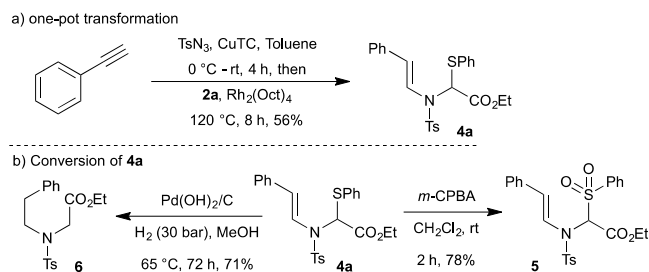
Scheme 5. Synthetic utility. †¹H NMR yield.

Based on our observation and literature precedence,[10e, 10f] the plausible mechanism for the present rhodium catalyzed rearrangement was postulated (Scheme 6). The proposed mechanism begins with the initial formation of rhodium carbenoid **A**, derived from *N*-sulfonyl-1,2,3-triazole **1** and Rh₂(Oct)₄, followed by *in-situ* generation of important sulfur ylide **B** from rhodium carbenoid with α-thioester **2**. The formed ylide **B** cannot undergo any rearrangement, due to the absence suitable bond with conjugated system. Due to the presence of relatively acidic proton α to the ester, next, proton transfer took place from the sulfur-ylide **B** to form new sulfur-ylide intermediate **C**, which on subsequent *aza*-[2,3]-sigmatropic rearrangement would afford the enamide **4**, where imine nitrogen is involved in the rearrangement instead

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of typical Sommelet Hauser rearrangement that involves aryl ring, which might involve destabilizing dearomatisation step.

Scheme 6. Plausible mechanism.

In conclusion, we have successfully demonstrated an efficient rhodium catalyzed Sommelet Hauser type rearrangement of sulfur-ylide derived from α-thioesters and *N*-sulfonyl-1,2,3-triazoles for the synthesis of functionalized enamides. The present methodology is applicable for the wide range of α-thioesters and *N*-sulfonyl-1,2,3-triazoles and offers a method for the synthesis of N,N-disubstituted enamides in good yield. The developed reaction involves an unprecedented Sommelet Hauser type rearrangement involving imine moiety instead of typical aryl group. Furthermore, the one-pot synthesis of enamide from terminal alkyne was also successfully demonstrated to showcase the synthetic potential.

Conflicts of interest

"There are no conflicts to declare".

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