

# Interruption of Formal Schmidt Rearrangement/Hosomi–Sakurai **Reaction of Vinyl Azides with Allyl/Propargylsilanes**

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**Supporting Information** 

ABSTRACT: An interrupted Schmidt rearrangement/Hosomi-Sakurai reaction of N-tosyl and S-substituted vinyl azides is reported. With BF3. Et<sub>2</sub>O as a Lewis acid promoter, the denitrogenative fragmentation of vinyl azides facilitates the generation of the N/S-stabilized carbocations, which further undergo nucleophilic addition by allyl/propargylsilanes for C-C bond formation. As a result, a variety of homoallylic/allenylic amines can be afforded in good yields under mild reaction conditions with well-defined functional-group tolerance.



🕻 chmidt rearrangement is a well-known and powerful Utransformation of azides to amides via an iminodiazonium (ID) ion with the elimination of N2 and a migration rearrangement of the R group (Scheme 1a).<sup>1</sup> Divergent



transformations for the nitrogen-containing compounds have been developed on the basis of the ID intermediate.<sup>2</sup> Recent theoretical studies have shown that from the common transition state with the ID intermediate the fragmentation product ( $R^+$  and  $R^1CN$ ) might also be involved, depending on the R groups, in a way similar to the Beckmann rearrangement of oximes.<sup>3</sup> The fragmentation was preferred, especially when

the generated carbocations could be stabilized by their adjacent group.<sup>4</sup> Although scarcely explored,<sup>3</sup> the investigation on the novel adjacent group-mediated ID intermediate might lead to fruitful formally interrupted Schmidt rearrangement, which might be further involved in a novel domino and cascade process for the discovery of novel synthetic methodology.

Vinyl azides,<sup>5</sup> possessing both alkene and azide functions, have emerged as a versatile two-/three-atom building block and also an important iminodiazonium (ID) ion precursor<sup>1,2</sup> in Schmidt-type 1,2-migrations (Scheme 1b).<sup>6,7</sup> Recently, the Schmidt-type rearrangement has been creatively extended to a range of carbon-based electrophiles, such as N-tosylaldimines,<sup>8</sup> aldehydes,<sup>8</sup> alcohols,<sup>8,9</sup> propargyl alcohols<sup>9,10</sup> and *p*-quinone methides,<sup>11</sup> affording various amide derivatives. We noticed that the variation in vinyl azides led to fruitful transformations, and the  $\alpha$ -aryl migrating group often works well in these reactions. However, the reactions from  $\alpha$ -functionalized vinyl azides bearing heteroatoms have been seldom explored.<sup>12</sup>

Herein, we focused on the behavior of N- and S-containing vinyl azides, which was easily available using our silvercatalyzed hydroazidation of alkynes,<sup>12,13</sup> under the above Schmidt reaction conditions. We envisioned that the vinyl azides with  $\beta$ -nitrogen or sulfur substitution would interrupt the Schmidt rearrangement by releasing a N2 and an acetonitrile to form a heteroatom-stabilized positive intermediate such as carbimonium ions (Scheme 1c). Similar to the carbocations generated from the interrupted Schmidt rearrangement (Scheme 1a), such an intermediate could potentially further react with nucleophiles to process novel domino and cascade reactions. Thus, we report an interruption

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of formal Schmidt rearrangement/Hosomi–Sakurai reaction<sup>14</sup> of functionalized vinyl azides, leading to a variety of homoallylic/allenylic amines<sup>15</sup> in good yields (Scheme 1c). The heteroatom-stabilized intermediate could be effectively captured by the Hosomi–Sakurai reaction under mild reaction conditions. As far as we can tell, the vinyl azides were first involved in such a formally interrupted Schmidt rearrangement.

Initially, the interrupted Schmidt rearrangement/Hosomi–Sakurai reaction of *N*-tosyl-substituted vinyl azides<sup>12,13</sup> were studied. When the reaction of vinyl azide **1a** and allyltrimethylsilane **2a** was performed in dichloromethane at 30 °C with BF<sub>3</sub>·Et<sub>2</sub>O (1.5 equiv) as a Lewis acid promoter,<sup>8,9</sup> no desired **3a** was observed (entry 1, Table 1). During the

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	Ts N <sub>3</sub>	TMS	Lewis acid (1.5 equiv)	Ts
Ph-N		+	solvent, 30 °C	⊳h <sup>−</sup> <sup>N</sup> ✓∕∕
	1a	2a		3a
en	try	Lewis acid	solvent	3a (%) <sup>b</sup>
1		$BF_3 \cdot Et_2O$	$CH_2Cl_2$	0
2	,	$BF_3 \cdot Et_2O$	MeOH	0
3		$BF_3 \cdot Et_2O$	CH <sub>3</sub> CN	20
4		BF3·Et2O	toluene	80
5		$CuCl_2$	toluene	0
6		$ZnCl_2$	toluene	0
7		$FeCl_3$	toluene	61
8		$TiCl_4$	toluene	53
9	1	BiCl <sub>3</sub>	toluene	30
1	0	TfOH	toluene	70
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<sup>*a*</sup>Reaction conditions: **1a** (0.3 mmol), **2a** (0.6 mmol), Lewis acid (1.5 equiv) in toluene (1 mL) at 30 °C. <sup>*b*</sup>Isolated yields.

solvent screening (entries 2–4), we were glad to find that toluene showed high efficiency, and **3a** could be obtained in 80% yield with toluene as the solvent. Further investigation showed that Lewis acids CuCl<sub>2</sub> and ZnCl<sub>2</sub> were unreactive along with large substrate surplus (entries 5 and 6), while FeCl<sub>3</sub>, TiCl<sub>4</sub>, and BiCl<sub>3</sub> offered decreased yields of **3a** (61%, 53%, and 30%, respectively, entries 6–8). Bronsted acid trifluoromethanesulfonic acid (TfOH) delivered **3a** in 70% yield (entry 10). Thus, use of BF<sub>3</sub>·Et<sub>2</sub>O (1.5 equiv) in toluene at 30 °C (entry 4) were the optimal reaction conditions for this one-pot transformation for the syntheses of homoallylamines. Vinyl azides serve as a carbocation source, and the Hosomi–Sakurai reaction proceeds smoothly under simple Lewis acid conditions without requirement of strong organometallic reagents.

Under the optimal reaction conditions (Table 1, entry 4), the substrate scope of this interrupted Schmidt rearrangement/ Hosomi–Sakurai reaction was investigated first with respect to various *N*-aryl vinyl azides 1 (Scheme 2). Both electrondonating (1b and 1c) and electron-withdrawing group (1d-g) substituted *N*-aryl vinyl azides 1 underwent a smooth reaction to furnish the corresponding homoallylamines 3 in good to excellent yields. Prolonged reaction time was required for the reaction of 1g. *N*-Aryl vinyl azides with multisubstituted aryl rings such as 2,4-dichlorophenyl 1h and 2,6-dimethylphenyl 1i were also compatible, affording 3h and 3i in good yields. It is noteworthy that *N*-naphthyl vinyl azide 1j is also an excellent candidate to afford Hosomi–Sakurai product 3j in 80% yield. Scheme 2. Interrupted Schmidt Rearrangement/Hosomi-Sakurai Reactions for N-Aryl Vinyl Azides<sup>a</sup>



"Reaction conditions: 1 (0.3 mmol), 2a (2 equiv),  $BF_3\cdot Et_2O$  (1.5 equiv) in toluene (1 mL) at 30 °C.

To further broaden the scope of the present protocol, we turned our attention to the use of N-alkyl vinyl azides 4 (Scheme 3). It was observed that the reaction of allylsilane 2a





<sup>a</sup>Reactions were conducted on a 0.5 mmol scale.

with *N*-alkyl vinyl azides (4a-c) bearing different alkyl chain lengths reacted well and afforded the desired products (5a-c)in 81–90% yields. *N*-Alkyl vinyl azides 4d and 4e also gave the corresponding homoallylamines 5d and 5e in good yields. In the case of simple vinyl azide 4f (where  $R^1 = R^2 = H$ ), *N*-tosyl-3-butenylamine 5f was also afforded in 65% yield. Moreover, vinyl azides containing cyclopropyl 4g, cyclohexyl 4h, and tetrahydrofuran motif 4i were well tolerated to produce the desired homoallylamines 5g–i in 77–86% yields. We noticed that vinyl azides bearing acid-sensitive functional groups (4j-p) were also compatible with present conditions. Even the sterically hindered vinyl azide 4q, phenyl-substituted vinyl azide 4s, and naphthalene-substituted vinyl azide 4t worked well in the reaction. Symmetrical divinyl azide 4r could deliver the desired bis-allylated product 5r in 62% yield. To our delight, vinyl azide with  $\beta$ -sulfhydryl substitution could react smoothly, affording the corresponding 5u in moderate yield.

Encouraged by the results obtained above, the interrupted Schmidt rearrangement/Hosomi–Sakurai reaction was applied to the easily accessible propargyltrimethylsilane, instead of allyltrimethylsilane (Scheme 4). Rather than alkynyl deriva-





<sup>*a*</sup>Reaction conditions: 1 or 4 (0.3 mmol), 2b (2 equiv),  $BF_3 \cdot Et_2O$  (1.5 equiv) in toluene (1 mL) at 30 °C.

tives, homoallenylamines were efficiently obtained with good functional group compatibility (Scheme 4). In the selected vinyl azides, both *N*-aryl vinyl azides (1a, 1e, and 1f) and *N*-cyclohexyl vinyl azides 4h reacted well with propargyltrime-thylsilane 2b to furnish the desired allenylamines (6a-d) in 66-72% yields. The reactions for the substrates bearing 2-tetrahydrofuranyl and ester functions also resulted in the desired products 6e and 6f in 61% and 85% yields, respectively.

Homoallylamines and homoallenylamines are important structural subunits of biologically active compounds, especially for the preparation of alkaloids and nitrogen-containing heterocycles.<sup>15–17</sup> We attempted the oxidation of *N*-phenyl-*N*-tosyl-4-butenamine **3a** in the presence of *m*-CPBA, and the desired product 7 was readily achieved in 95% yield (Scheme 5a).<sup>18</sup> In addition, the ring-closing metathesis of *N*,*N*'-bis-allyl-

#### Scheme 5. Applications of Homoallylamine



1,3-propanediamine **5r** with Grubbs II catalyst furnished the 1,5-ditosyl-1,5-diazacycloundec-8-ene **8** in excellent yield (Scheme 5b).<sup>19</sup>

To further investigate the significant effect of N-tosyl moieties on the reactivity of vinyl azides, the mechanism of this novel transformation was demonstrated by density functional theory (DFT) calculations using the M062X/6-

31+G\*\* method (see the Supporting Information for details). Initially, the vinyl azide 1a was activated by  $BF_3$ , 5c,d,8 giving complex 1, which then undergoes denitrogenative fragmentation via concerted elimination of N<sub>2</sub> and C-C bond cleavage of TS1 with an activation barrier ( $\Delta\Delta G$ ) of 22.8 kcal/mol, affording a carbimonium ion 2. The formation of 2 plausibly proceeds via a syn fragmentation mechanism with iminodiazonium ion intermediates.<sup>3b</sup> Sequential nucleophilic addition with organosilicon 2a gives complex 4 (TS2,  $\Delta \Delta G = 7.0$  kcal/ mol). Next, the F atom migration occurs via TS3 ( $\Delta\Delta G = 7.0$ kcal/mol) to form byproducts (TMSF and BF2CH3CN) and release the target product 3a. Finally, BF2CH3CN delivered CH<sub>3</sub>CN and BF<sub>2</sub>OH with the aid of a molecule of water. The case for other reaction site in 1a, which may be activated by BF<sub>3</sub>, was also calculated. We found that the pathway in Figure 1 is more favorable. The calculation results are consistent with our experimental observations.



Figure 1. Mechanistic investigations by DFT study.

In conclusion, we have described the homoallylation/ allenylation of vinyl azides by an interrupted Schmidt rearrangement/Hosomi—Sakurai reaction sequence. Vinyl azides were explored as reactive carbimonium ions and engaged in the one-pot reaction for C–C bond formation. A variety of homoallylic/allenylic amines can be afforded in good yields under mild reaction conditions. The reactions shows excellent functional group tolerance. Further DFT calculations supported that the mechanism plausibly involves a tandem denitrogenative fragmentation/Hosomi—Sakurai reaction.

## ASSOCIATED CONTENT

## **Supporting Information**

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.or-glett.8b03062.

Full experimental procedures, spectroscopic characterizations, computational data and copies of NMR spectra (PDF)

# Accession Codes

CCDC 1859170 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data request/cif, or by emailing

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#### Notes

The authors declare no competing financial interest.

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