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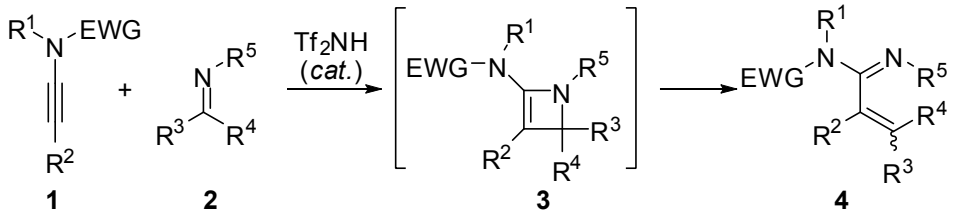
UNPRECEDENTED SYNTHESIS OF *N,N*-DIVINYLAMINES BY Tf_2NH-CATALYZED REACTION OF YNAMIDE WITH KETIMINE

Naoya Shindoh, Yoshiji Takemoto,* and Kiyosei Takasu*

[1]Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan
E-mail: kay-t@pharm.kyoto-u.ac.jp

Abstract – Tf_2NH-catalyzed synthesis of *N,N*-divinylamines from ynamides and acetophenoneimines is described. The products would be produced through the formation of the corresponding keteniminiums and enamines by the assistance of the catalyst.

Ynamides, which are a class of nitrogen-substituted alkynes, have been paid a great attention as a versatile reactant in organic synthesis over the past decade.[1] Ynamides are more stable and easy-handling chemicals compared to their related ynamines, and they display an interesting reactivity. For example, the alkynens easily react with electrophiles at β-position. On the other hand, they can interact with nucleophiles at α-position through the formation of the keteniminium species. Ynamides can be also employed as substrates for a variety of cycloaddition reactions. We have recently reported that triflic imide (Tf_2NH)[2] catalyzes domino [2 + 2] cycloaddition−cycloreversion reaction of ynamides (**1**) and aldimines (**2**) (Scheme 1).[3] The domino reaction affords α,β-unsaturated amidines bearing di- or tri-substituted alkene moiety (**4**) in good yields through the formation of 2-amino-2-azetines (**3**). During the course of our continuous study, we observed that reaction of **1** with acetophenone imine (**5**) in the presence of Tf_2NH furnished, unexpectedly, not α,β-unsaturated amidines but *N,N*-divinylamines. In this

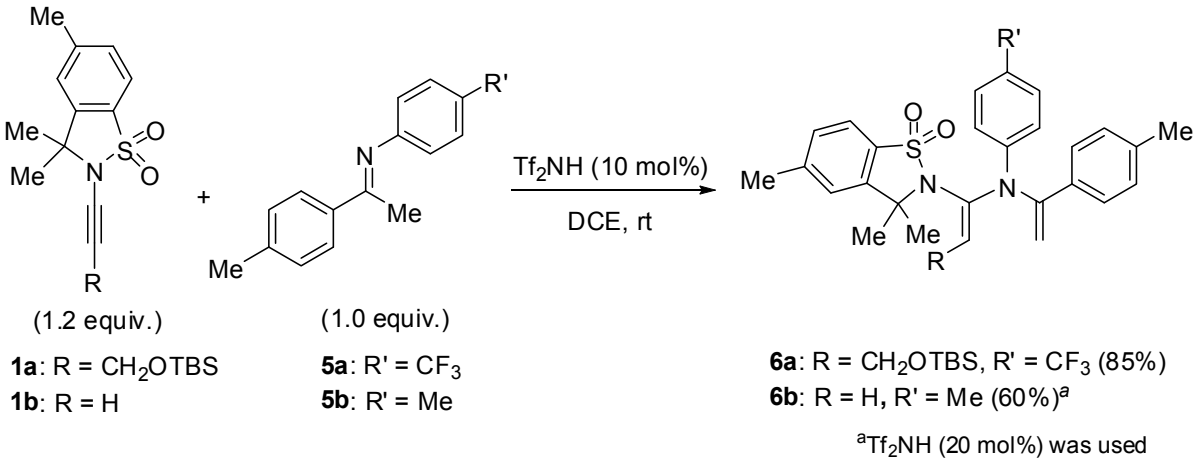


1 **2** **3** **4**

Scheme 1. Tf_2NH-catalyzed domino reaction of ynamides and aldimines (R^4 = H)

Dedicated to Professor Dr. Albert Eschenmoser on the occasion of his 85th birthday.

communication, we wish to describe the Tf_2NH catalyzed addition reaction of ynamides with ketimines. Reaction of yne-sultam (**1a**) (1.2 equiv.) with acetophenoneimine (**5**) (1.0 equiv.) was attempted for the purpose of preparation of amidines bearing tetra-substituted olefin (**4**) under the reported conditions.[3] As the result, formation of neither **4** nor azetine (**3**) was observed, but 2-amino-3-azapenta-1,4-diene (**6a**) was obtained in 85% yield as a single geometrical isomer (Scheme 2).[4] It was difficult to elucidate its structure owing to considerably simplicity of its ^1H NMR spectrum; only 7 singlet peaks were observed between 5.5 to 0 ppm. Finally, the structure of **6a** was assigned by X-ray crystallography (Figure 1).[5] It indicates that addition reaction of the enamine, derived from **5**, to ynamide (**1**) occurred at α-position under the conditions, exclusively. It is noteworthy that the acyclic 2-amino-3-azapentadiene is a rare skeleton among the class of *N,N*-divinylamines.[6] Although its diaminoalkene and divinylamine moieties seem to be reactive, **6a** is stable to be isolated and handled under both the solution and solid states. When the reaction was carried out with terminal alkyne (**1b**) and imine (**5b**), 3-azapentadiene (**6b**) was obtained in 60% yield. The product (**6b**) was found to be slightly unstable under acidic conditions.



Scheme 2. Unexpected catalytic reaction of ynamides (**1**) and ketimines (**5**)

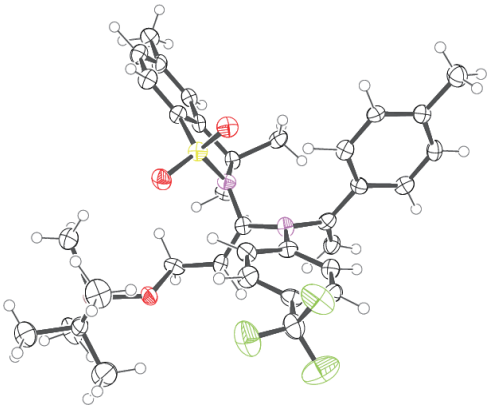
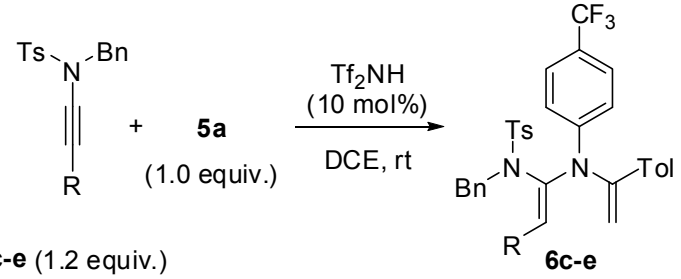


Figure 1. Crystal structure of **6a** (ORTEP drawing)

Ynamide (**1c**) bearing toluenesulfonyl (tosyl) and benzyl groups on the nitrogen atom also reacted with **5a** to furnish **6c** in 69% yield, but it was observed that the reaction rate slightly decreased (Table 1, entry 1). Whereas terminal alkyne (**1d**) afforded the desired 3-azapentadiene (**6d**) in 82% yield (entry 2), formation of a trace amount of **6e** was observed in the reaction of phenylalkyne (**1e**) (entry 3). We supposed that steric bulkiness of the alkynyl substituent would affect on the reactivity.

Table 1. Reaction of yne-tosylamides



entry	**1** (R)	time (h)	yield of **6** (%)
1[a]	**1c** (CH_2OTBS)	1	69
2	**1d** (H)	0.5	82
3	**1e** (Ph)	3	trace

[a] Tf_2NH (15 mol%) was used.

In contrast to the reaction of ynamides with aldimines (*see* Scheme 1), [2 + 2] cycloaddition with ketimine (**5**) would be prevented owing to its weak electrophilicity and steric bulkiness. A plausible mechanism for reactions of **1** with **5** is outlined in Figure 2. Formation of keteniminium salt (**7**) from **1** by the assistance of Tf_2NH would take place. Then, addition of imine (**5**) at the sp^2 nitrogen atom to **7** at the *sp* carbon would take place to give the iminium intermediate (**8**). The imine nucleophile would attack from the opposite side of R^2 substituent of **7** to avoid the steric hindrance. Finally, deprotonation of **8** results in the formation of *N,N*-divinylamine (**6**) along with a regeneration of Tf_2NH.

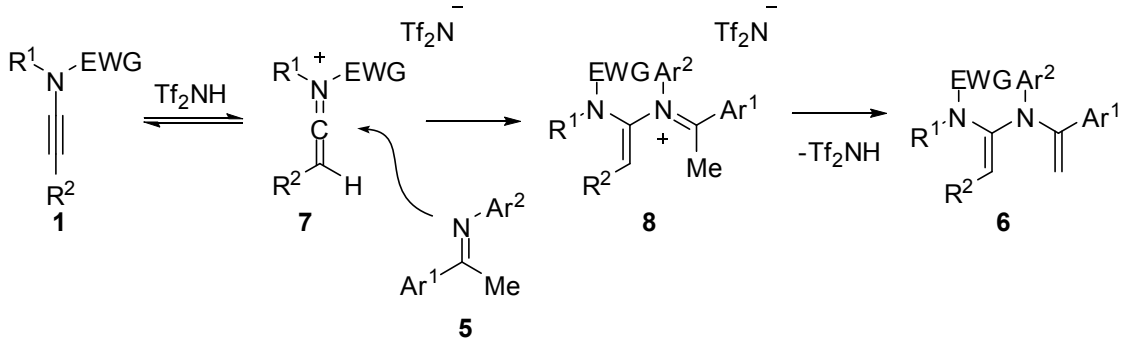


Figure 2. A plausible mechanism

In conclusion, reaction of ynamide with acetophenone imine in the presence of Tf_2NH provides *N,N*-divinylamine through the formation of keteniminium salt.

ACKNOWLEDGEMENTS

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2. K. Takasu, *Synlett*, 2009, 1905.
3. N. Shindoh, Y. Takemoto, and K. Takasu, *Chem. Eur. J.*, 2009, **15**, 7026.
4. Spectral data for **6a**; Mp 187−188 °C; IR (KBr) 2947, 2855, 1610, 1325, 1287 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.0 Hz, 1H), 7.15 (s, 1H), 7.06 (d, J = 8.0 Hz, 2H), 5.69-5.66 (m, 2H), 5.22 (s, 1H), 4.03 (bs, 2H), 2.45 (s, 3H), 2.28 (s, 3H), 1.65 (bs, 6H), 0.77 (s, 9H), −0.12 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.6, 147.9, 144.8, 143.8, 138.3, 134.2, 134.0, 131.3, 129.9, 129.8, 129.0, 127.3, 126.0 (q, $^{3}J_{(C,F)}$ = 3.6 Hz), 124.4 (q, $^{1}J_{(C,F)}$ = 269.5 Hz), 123.9 (q, $^{2}J_{(C,F)}$ = 32.2 Hz), 122.5, 122.3, 120.6, 111.3, 64.7, 60.4, 25.7, 21.8, 21.1, 18.0, −5.4 (one of the peaks of methyl groups is missing, maybe due to the overlap.); LRMS (FAB) *m/z* 525 (M^{+}−136).
5. Crystal data for **6a** (crystalyzed from MeOH). $C_{35}H_{43}F_3N_2O_3SSi$, prisms, *monoclinic*, space group $P2_1/n$, a = 13.2399(9) Å, b = 20.7430(10) Å, c = 13.4737(9) Å, β = 108.957(2)°, V = 3499.6(4) $Å^3$, Z = 4, D_{calc} = 1.247 g/cm^3, R = 0.037, R_w = 0.033, GOF = 0.931.
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