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

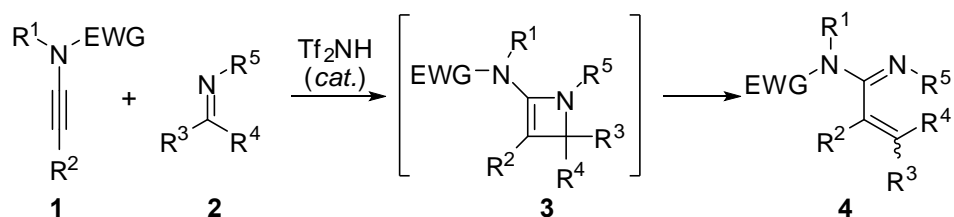
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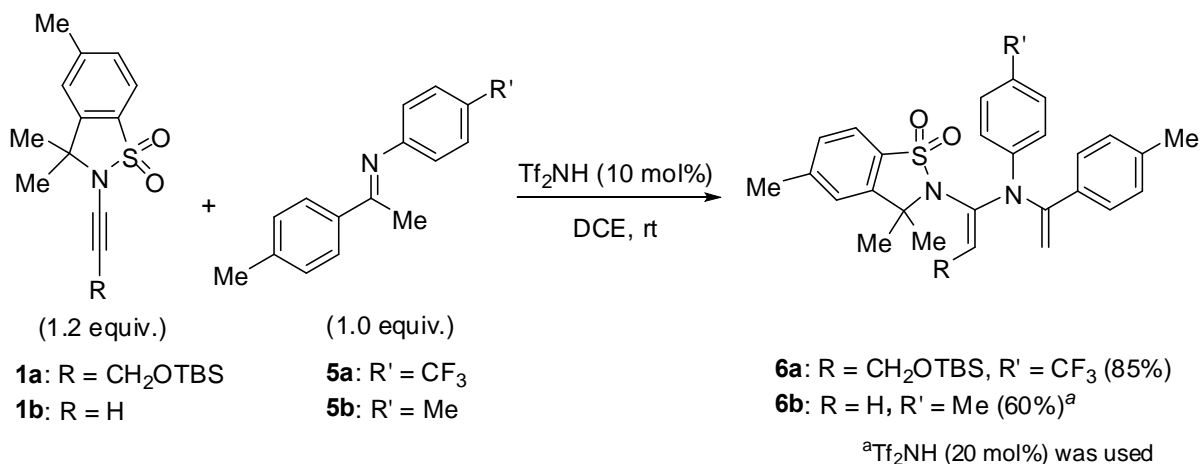
Abstract – Tf_2NH -catalyzed synthesis of *N,N*-divinylamines from ynamides and acetophenoneimines is described. The products would be produced through the formation of the corresponding keteniminiums and enamines by the assistance of the catalyst.

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 alkynes 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



Scheme 1. Tf_2NH -catalyzed domino reaction of ynamides and aldimines ($\text{R}^4 = \text{H}$)

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**)

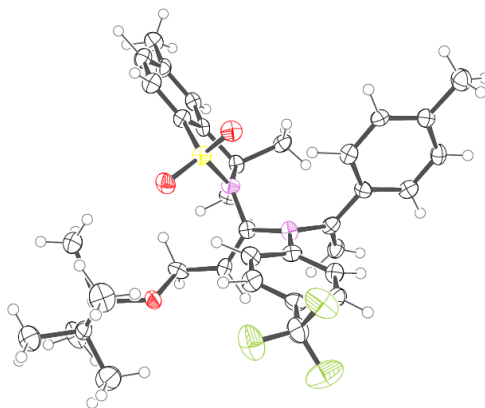
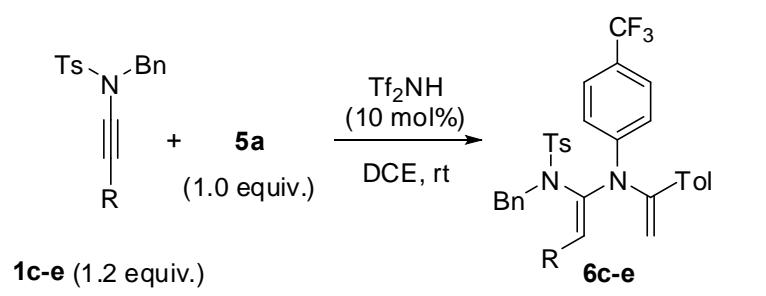


Figure 1. Crystal structure of **6a** (ORTEP drawing)

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 ₂ OTBS)	1	69
2	1d (H)	0.5	82
3	1e (Ph)	3	trace

^a Tf₂NH (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 Tf₂NH would take place. Then, addition of imine (**5**) at the sp² 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 R² 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 Tf₂NH.

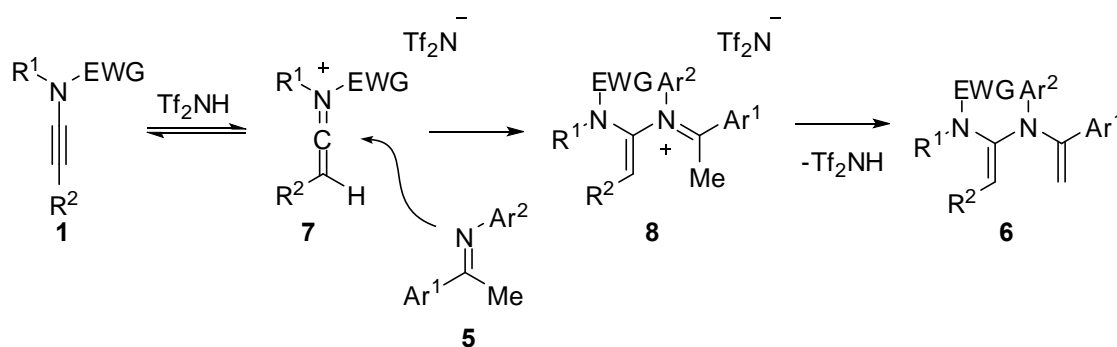


Figure 2. A plausible mechanism

In conclusion, reaction of ynamide with acetophenone imine in the presence of Tf₂NH provides *N,N*-divinylamine through the formation of keteniminium salt.

ACKNOWLEDGEMENTS

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REFERENCES

1. (a) C. A. Zificksak, J. A. Mulder, R. P. Hsung, C. Rameshkumar, and L.-L. Wei, *Tetrahedron*, **2001**, [57, 7575](#). (b) J. A. Mulder, K. C. M. Hsung, and R. P. Hsung, *Synlett*, **2003**, [1379](#). (c) G. Evano, A. Coste, and K. Jouvin, *Angew. Chem. Int. Ed.*, **2010**, [49, 2840](#).
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; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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** (crystallized from MeOH). C₃₅H₄₃F₃N₂O₃SSi, prisms, *monoclinic*, space group *P2₁/n*, *a* = 13.2399(9) Å, *b* = 20.7430(10) Å, *c* = 13.4737(9) Å, β = 108.957(2)°, *V* = 3499.6(4) Å³, *Z* = 4, *D*_{calc} = 1.247 g/cm³, *R* = 0.037, *R*_w = 0.033, GOF = 0.931.
6. (a) T. Sasaki, A. Kojima, and M. Ohta, *J. Chem. Soc. C*, **1971**, [196](#). (b) R. Fandos, M. Lanfranchi, A. Otero, M. A. Pellinghelli, M. J. Ruiz, and J. H. Teuben, *Organometallics*, **1997**, [16, 5283](#).