UNPRECEDEDENT SYNTHESIS OF N,N-DIVINYLANIMINES BY TF₂NH-CATALYZED REACTION OF YNAMIDE WITH KETIMINE

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Abstract – TF₂NH-catalyzed synthesis of N,N-divinylamines from ynamides and acetophenone imines 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 (TF₂NH)² catalyzes domino [2 + 2] cycloaddition–cycloreversion reaction of ynamides (1) and aldmines (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 TF₂NH furnished, unexpectedly, not α,β-unsaturated amidines but N,N-divinylamines. In this

![Scheme 1. TF₂NH-catalyzed domino reaction of ynamides and aldmines (R⁴ = H)](image-url)

Dedicated to Professor Dr. Albert Eschenmoser on the occasion of his 85th birthday.
communication, we wish to describe the Tf$_2$NH 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. 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). It was difficult to elucidate its structure owing to considerably simplicity of its $^1$H 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). It indicates that addition reaction of the enamine, derived from 5, to ynamide (1) occurred at $\alpha$-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. 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)](image)

![Figure 1. Crystal structure of 6a (ORTEP drawing)](image)
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

<table>
<thead>
<tr>
<th>entry</th>
<th>1 (R)</th>
<th>time (h)</th>
<th>yield of 6 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>1c (CH2OTBS)</td>
<td>1</td>
<td>69</td>
</tr>
<tr>
<td>2</td>
<td>1d (H)</td>
<td>0.5</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>1e (Ph)</td>
<td>3</td>
<td>trace</td>
</tr>
</tbody>
</table>

* 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


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, ³J(C,F) = 3.6 Hz), 124.4 (q, ¹J(C,F) = 269.5 Hz), 123.9 (q, ²J(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). C₃₅H₄₃F₃N₂O₃Si, 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, Dcalc = 1.247 g/cm³, R = 0.037, Rw = 0.033, GOF = 0.931.