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TRIFLIC IMIDE CATALYZED [3+2] CYCLOADDITION OF ALDIMINES WITH α,α -DIMETHYLALLYLSILANE

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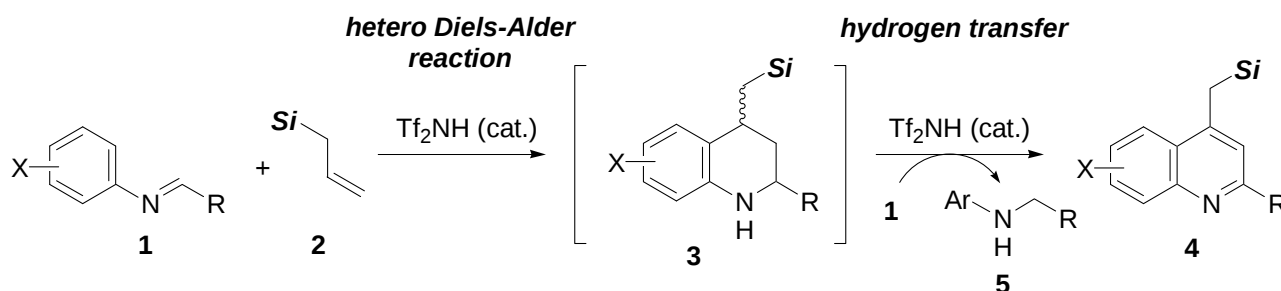
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Abstract – Tf₂NH-catalyzed [3+2] cycloaddition of *N*-aryl imines with α,α -dimethylallylsilane to give substituted pyrrolidines is described. We have found the mode of cycloaddition depends upon α -substituents of allylsilanes.

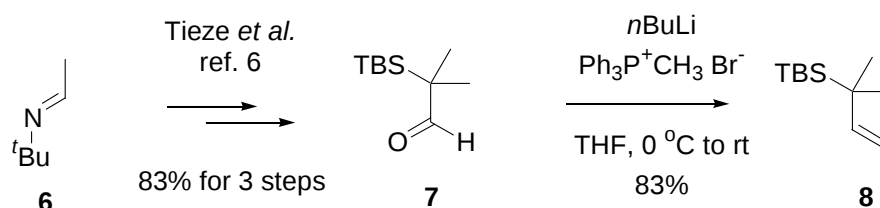
Triflic imide (Tf₂NH), which is recognized as a super Brønsted acid,¹ catalyzes several classes of C-C bond formation reactions.² We have shown Tf₂NH efficiently activates imines in hetero Diels-Alder reaction of imines with 2-siloxydienes.^{3,4} Moreover, we have recently reported Tf₂NH-catalyzed cascade hetero Diels-Alder and hydrogen transfer reaction.⁵ Namely, treatment of *N*-aryl imine (**1**) with allylsilane (**2**) in the presence of a catalytic amount of Tf₂NH afforded substituted quinoline (**4**) in a single operation along with amine (**5**). Notably, in the cascade reaction Tf₂NH activates two mechanistically distinct reactions, such as hetero Diels-Alder reaction of **1** with **2** and hydrogen transfer between produced tetrahydroquinoline (**3**) and imine (**1**) (Scheme 1). During the course of our study, we observed that reaction of **1** with α,α -dimethylallylsilane in the presence of Tf₂NH furnished, unexpectedly, not



Scheme 1. Cascade hetero Diels-Alder and hydrogen transfer reaction catalyzed by Tf₂NH

quinolines but substituted pyrrolidines. In this communication, we wish to describe the Tf_2NH catalyzed [3+2] cycloaddition of imines with α,α -dimethylallylsilane.

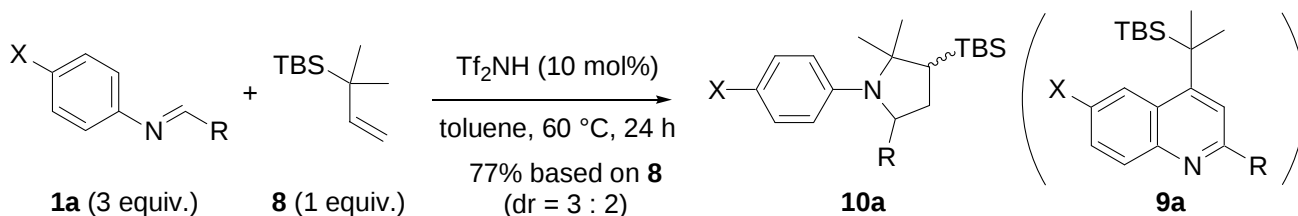
α,α -Dimethylallylsilane (**8**) bearing *tert*-butyldimethylsilyl (TBS) moiety was prepared by Wittig reaction of α -silylisobutyraldehyde (**7**), which was synthesized from acetaldehyde *tert*-butylimine (**6**) in 3 steps,⁶ in 83% yield (Scheme 2). Imines (**1a-1h**) were prepared from the corresponding aldehydes and anilines according to a reported procedure.⁷



Scheme 2. Preparation of α,α -dimethylallylsilane

First of all, reaction of **1a** (3 equiv) with **8** (1 equiv) was attempted for the purpose of preparation of quinoline (**9**) under the reported conditions.⁵ As the result, neither **9** nor tetrahydroquinoline was observed, but formation of substituted pyrrolidine (**10a**), which corresponds to a [3+2] cycloadduct, was obtained in 77% yield (Scheme 3). When a mixture of **1a** and **8** (molar ratio = 1 : 1.2) was treated with a catalytic amount of Tf_2NH (10 mol%) in toluene at 60 °C for 24 h, **10a** was obtained in 84% yield as a 3 : 2 mixture of diastereomers (Table 1, entry 1). In 1,2-dichloroethane, which has been reported to be an appropriate solvent for the Tf_2NH -catalyzed hetero Diels-Alder reaction,⁵ [3+2] cycloaddition also promoted to furnish **10a** in 76% yield (entry 2). ^1H NMR spectra of each diastereomer of **10a**,⁸ in which two sets of doublet peaks derived from *p*-trifluoromethylaniline moiety were observed, ruled out production of [4+2] cycloadducts, such as tetrahydroquinoline or quinoline (**9**). Careful recrystallization of a diastereomeric mixture of **10a** from MeOH gave single crystals of *cis*-**10a**, which corresponds to the major diastereomer. The structure of *cis*-**10a** was confirmed unambiguously by an X-ray analysis (Figure 1).⁹ As shown in Table 1, benzylidene and heteroarylidenes except for 2-pyridylidene imine (**1e**) underwent [3+2] cycloaddition to give substituted pyrrolidines (**10**) in 44—94% yield. All products were obtained as a diastereomeric mixture (*cis* : *trans* = 1 : 1 — 3 : 2). In the reaction of **1b**, homoallylamine (**11b**) was obtained in 27% yield along with **10b** (entry 3). Since almost no formation of **11b** was observed at the early stage of the reaction, not Hosomi-Sakurai type allylation to **1b**¹⁰ but decomposition of **10b** via β -silyl carbocation intermediate would cause formation of **11b**. Actually, treatment of isolated **10b** with Tf_2NH (10 mol%) in refluxing toluene afforded **11b** exclusively. Reaction of α,β -unsaturated imine (**1h**) was unsuccessful only to give a mixture of unidentified compounds (entry 10). We have assessed the multicomponent variant starting from three materials: an allylsilane, an aldehyde and an aniline (Scheme

4). Treatment of a mixture of **8**, *p*-tolylaldehyde (**12**) and *p*-trifluoromethylaniline (**13**) (molar ratio = 1.2 : 1 : 1) with 10 mol% of Tf₂NH in toluene furnished the desired pyrrolidine (**10a**) in 78% yield as a 3 : 2 mixture of diastereomers.



Scheme 3. [3+2] Cycloaddition of **1a** (X = CF₃, R = *p*-tolyl) with **8** in the presence of Tf₂NH

Table 1. Tf₂NH-catalyzed [3+2] cycloaddition of **1** with **8**^a

entry	imine (R, X)	%yield of 10 ^b	dr (<i>cis</i> : <i>trans</i>) ^c
1	1a (<i>p</i> -MeC ₆ H ₄ , CF ₃)	84	3 : 2
2 ^d	1a	76	1 : 1
3 ^e	1b (<i>o</i> -NO ₂ C ₆ H ₄ , CF ₃)	61	3 : 2
4	1c (2-furyl, CF ₃)	44	3 : 2
5	1d (2-thienyl, CF ₃)	60	3 : 2
6 ^f	1d	70	3 : 2
7	1e (2-pyridyl, CF ₃)	0	—
8	1f (<i>p</i> -MeC ₆ H ₄ , NO ₂)	94	1 : 1
9	1g (<i>p</i> -MeC ₆ H ₄ , Br)	47	3 : 2
10	1h ((<i>E</i>)-CH=CH-Ph, CF ₃)	complex mixture	—

^aStandard conditions: **1** (1.0 equiv.), **8** (1.2equiv.), Tf₂NH (10 mol%), in toluene, at 60 °C, for 24 h. ^bYields were calculated based on **1**. ^cDiastereomeric ratio was determined by ¹H NMR.

^dReaction was carried out in 1,2-dichloroethane.

^eHomoallylamine (**11b**) was obtained in 27% yield. ^f20 Mol% of Tf₂NH was used.

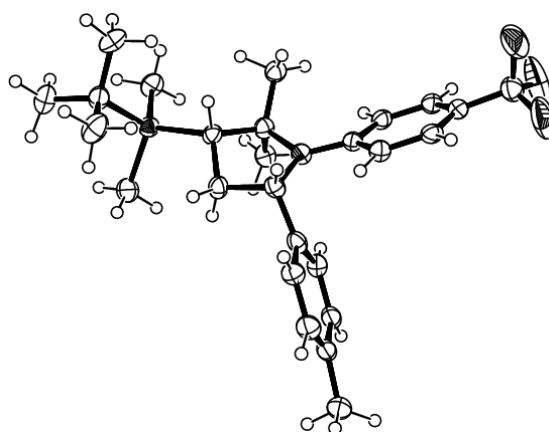
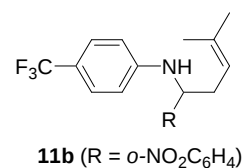
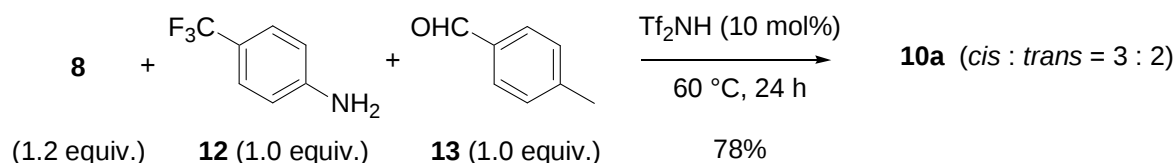


Figure 1. Crystal structure of *cis*-**10a** (ORTEP drawing)



Scheme 4. Multicomponent reaction catalyzed by Tf_2NH

In sharp contrast to our previous results,⁵ the mode of cycloaddition depends upon α -substitution of the allylsilane. A plausible mechanism for reactions of imines with allylsilanes is outlined in Figure 2. With α -nonsubstituted allylsilane (**2**), [4+2] cycloaddition took place to give tetrahydroquinolines **3** through a stepwise manner. Namely, $\text{S}_{\text{E}}2'$ reaction of **2** to imine (**1**) in the presence of Tf_2NH would afford β -silyl cation intermediate (**14**), and then intramolecular addition of the aromatic carbon of **14** would promote to furnish [4+2] cycloadduct (**3**) (mode a). If intramolecular addition of the nitrogen atom of **14** takes place, azetidine (**15**) would be produced (mode b). In contrast, in the reaction with α,α -disubstituted allylsilane (**8**), intermediate (**14**) would transform into more stable β -silyl cation (**16**) or siliranium cation (**17**) by 1,2-silyl shift or silacyclopropanation, respectively.¹¹ Then, intramolecular addition of the nitrogen atom of **16** or **17** would afford [3+2] cycloadduct (**10**) (mode c).

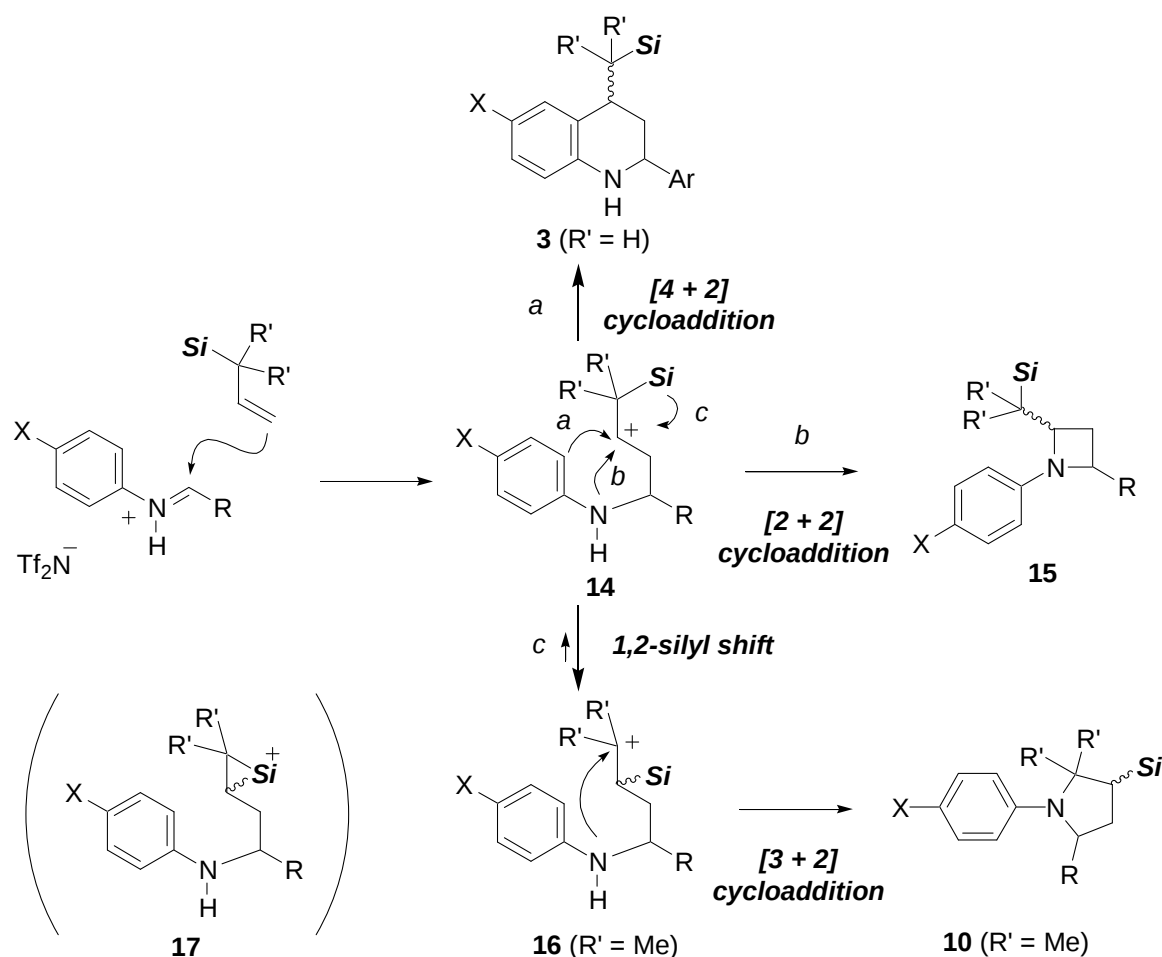


Figure 2. A plausible mechanism for [3 + 2] cycloaddition and substituent effects

Although several studies on cycloaddition reactions of imines with allylsilanes have been reported,^{12–15} studies to control modes of the cycloadditions are quite limited. Akiyama and his co-workers described [3+2] cycloaddition of *N*-sulfonyl imines with triisopropylsilylpropene in the presence of a stoichiometric amount of BF₃·OEt₂,^{13d} whereas *N*-acyl and *N*-aryl imines took place [2+2]¹⁴ and [4+2] cycloadditions,¹⁵ respectively. They concluded *N*-substituent of imines would be a control factor in the selective formation of [2+2], [3+2], or [4+2] cycloadducts. Our abovementioned study indicates α -substitution of allylsilane is one of factors to control the mode of cycloaddition of *N*-aryl imines with allylsilanes.

In conclusion, reaction of imines with α,α -dimethylallylsilane in the presence of Tf₂NH provides substituted pyrrolidines by [3+2] cycloaddition. We found the mode of cycloaddition depends upon α -substituents of allylsilanes. It is noteworthy that, to the best of our knowledge, it is the first example to achieve the catalytic [3+2] cycloaddition of imines with allylsilanes.

ACKNOWLEDGEMENTS

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- 2H), 7.05 (d, $J = 8.0$ Hz, 2H), 6.67 (d, $J = 8.0$ Hz, 2H), 4.74 (dd, $J = 10.3, 6.3$ Hz, 1H), 2.41 (ddd, $J = 12.3, 6.3, 5.5$ Hz, 1H), 2.40 (s, 3H), 1.78 (ddd, $J = 14.9, 12.3, 10.3$ Hz, 1H), 1.64 (s, 3H), 1.54 (dd, $J = 14.9, 5.5$ Hz, 1H), 0.92 (s, 9H), 0.19 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 147.8, 140.9, 136.4, 129.4, 125.9, 125.2 (q, $^3J_{\text{C,F}} = 3.6$ Hz), 124.0, 123.0 (q, $^1J_{\text{C,F}} = 269.9$ Hz), 117.7 (q, $^2J_{\text{C,F}} = 32.4$ Hz), 116.3, 66.7, 65.6, 39.7, 38.5, 27.5, 27.1, 26.8, 21.1, 17.2, $-4.7, -6.0$; LRMS (FAB) m/z 447 (M^+), for *trans*-**10b**; ^1H NMR (400 MHz, CDCl_3) δ 7.29 (d, $J = 8.8$ Hz, 2H), 7.09 (m, 4H), 6.63 (d, $J = 8.8$ Hz, 2H), 4.74 (m, 1H), 2.42 (m, 1H), 2.31 (s, 3H), 1.88 (dd, $J = 12.4, 5.1$ Hz, 1H), 1.81 (s, 3H), 1.66 (m, 1H), 1.49 (s, 3H), 0.75 (s, 9H), 0.18 (s, 3H), 0.03 (s, 3H).
9. Crystal data for *cis*-**10a**. $\text{C}_{26}\text{H}_{36}\text{F}_3\text{NSi}$, *monoclinic*, space group $P2_1/n$, $a = 13.8584(3)$ Å, $b = 9.9621(2)$ Å, $c = 17.7342$ Å, $\beta = 91.7284(9)^\circ$, $V = 2447.25(8)$ Å³, $Z = 4$, $D_{\text{calc}} = 1.215$ g/cm³, $R = 0.050$, $R_w = 0.064$, GOF = 1.416.
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