HETEROCYCLES, Vol. 77, No. 1, 2009, pp. 187 - 192. © The Japan Institute of Heterocyclic Chemistry
Received, 13th May, 2008, Accepted, 27th June, 2008, Published online, 30th June, 2008.
DOI: 10.3987/COM-08-S(F)17

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

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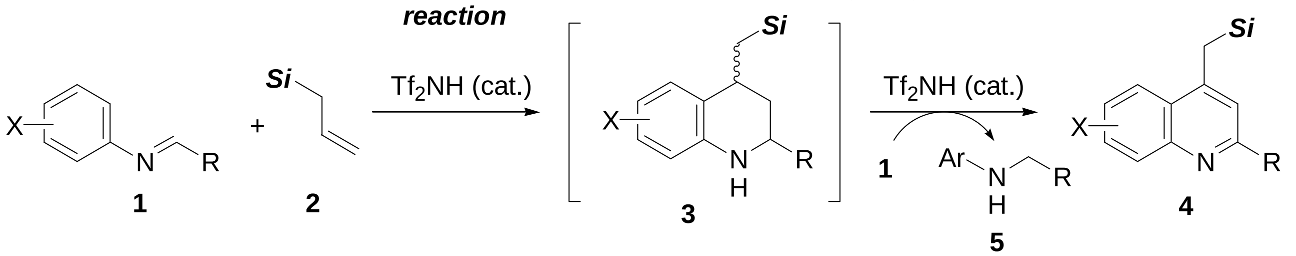
Abstract – Tf_2NH-catalyzed [3+2] cycloaddition of *N*-aryl imines with α,α-dimethylallylsilane to give substituted pyrrolidines is described. We have found the mode of cycloaddition depends upon α-substituents of allylsilanes.

Triflic imide (Tf_2NH), which is recognized as a super Brønsted acid,[1] catalyzes several classes of C-C bond formation reactions.[2] We have shown Tf_2NH efficiently activates imines in hetero Diels-Alder reaction of imines with 2-siloxydienes.[3,4] Moreover, we have recently reported Tf_2NH-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 Tf_2NH afforded substituted quinoline (**4**) in a single operation along with amine (**5**). Notably, in the cascade reaction Tf_2NH 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 Tf_2NH furnished, unexpectedly, not

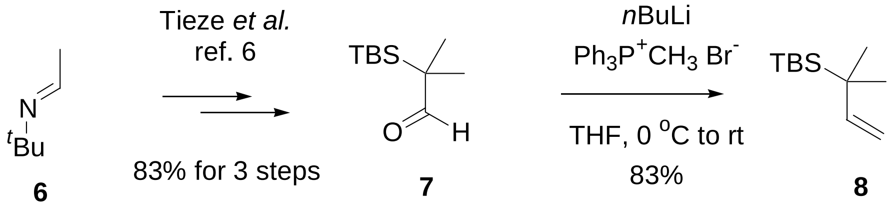


Scheme 1. Cascade hetero Diels-Alder and hydrogen transfer reaction catalyzed by Tf_2NH

This paper is dedicated to Professor Emeritus Keiichiro Fukumoto on the occasion of his 75th birthday.

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

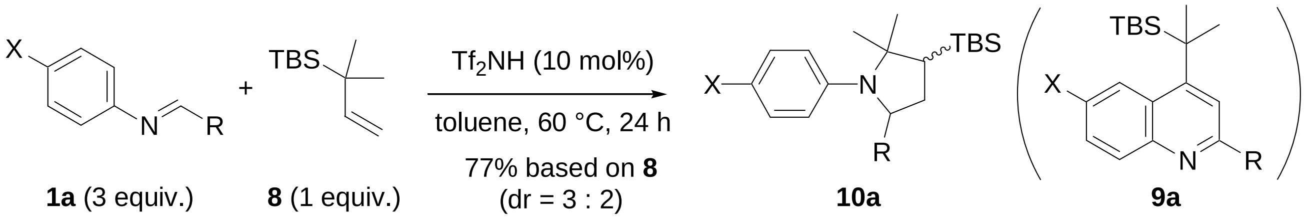
α,α-Dimethylallylsilane (**8**) bearing *tert*-butyldimethylsilyl (TBS) moiety was prepared by Wittig reaction of α-silylisobutyraldehyde (**7**), which was synthesized from acetaldehyde *tert*-butylimine (**6**) in 3 steps,[6] in 83% yield (Scheme 2). Imines (**1a**-**1h**) were prepared from the corresponding 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). ^{1}H 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 recrystalization 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 heteroarylidene imines 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 Tf_2NH in toluene furnished the desired pyrrolidine (**10a**) in 78% yield as a 3 : 2 mixture of diastereomers.

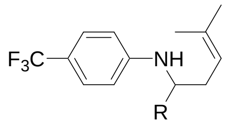


Scheme 3. [3+2] Cycloaddition of **1a** (X = CF_3, R = *p*-tolyl) with **8** in the presence of Tf_2NH

Table 1. Tf_2NH-catalyzed [3+2] cycloaddition of **1** with **8**[a]

entry	imine (R, X)	%yield of **10**[b]	dr (*cis* : *trans*)[c]
1	**1a** (*p*-MeC_6H_4, CF_3)	84	3 : 2
2[d]	**1a**	76	1 : 1
3[e]	**1b** (*o*-$NO_2C_6H_4$, 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** (*p*-MeC_6H_4, NO_2)	94	1 : 1
9	**1g** (*p*-MeC_6H_4, Br)	47	3 : 2
10	**1h** ((*E*)-CH=CH-Ph, CF_3)	complex mixture	—

[a] Standard conditions: **1** (1.0 equiv.), **8** (1.2equiv.), Tf_2NH (10 mol%), in toluene, at 60 °C, for 24 h. [b] Yields were calculated based on **1**. [c] Diastereomeric ratio was determined by ^1H NMR. [d] Reaction was carried out in 1,2-dichloroethane. [e] Homoallylamine (**11b**) was obtained in 27% yield. [f] 20 Mol% of Tf_2NH was used.



11b (R = *o*-$NO_2C_6H_4$)

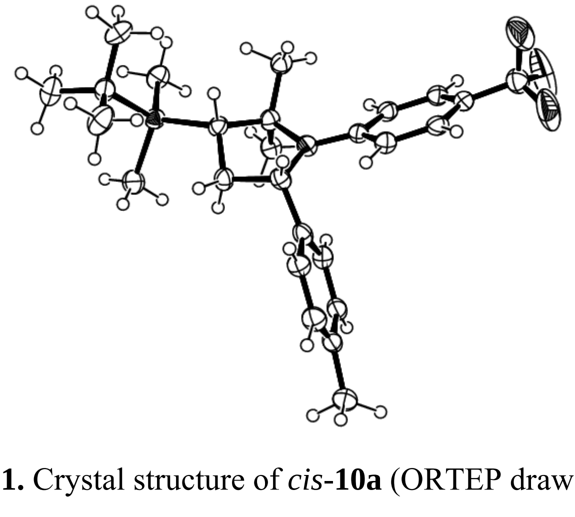
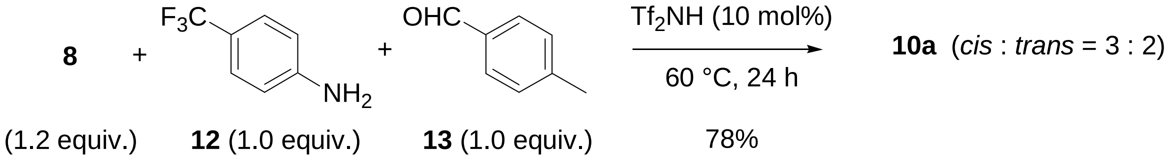


Figure 1. Crystal structure of *cis*-**10a** (ORTEP drawing)



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, S_E2' 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 silacyclopronation, respectively.[11] Then, intramolecular addition of the nitrogen atom of **16** or **17** would afford [3+2] cycloadduct (**10**) (mode c).

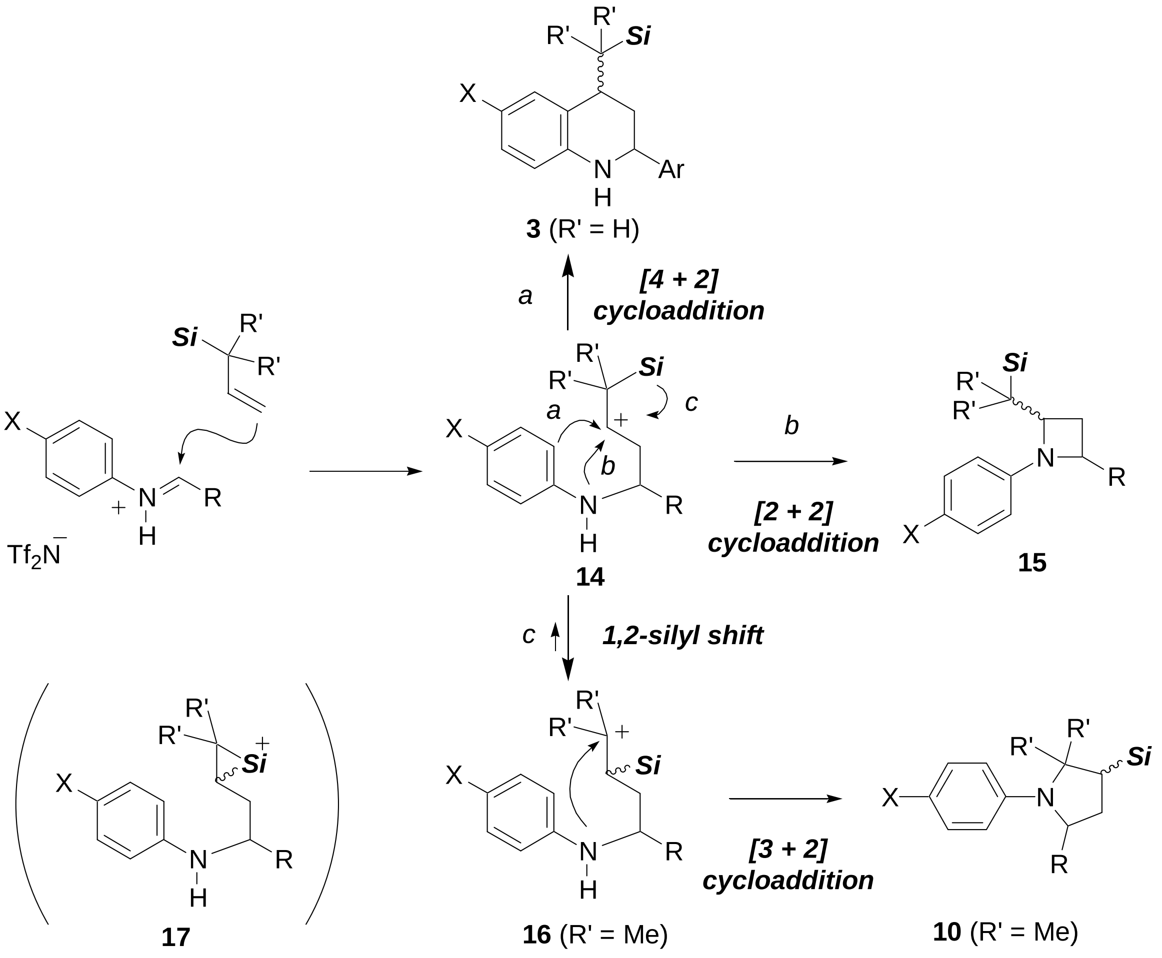


Figure 2. A plausible mechanism for [3 + 2] cycloaddition and substituent effects

Although several studies on cycloaddition reactions of imines with allylsilanes have been reported,[12—15] studies to control modes of the cyloadditions are quite limited. Akiyama and his co-workers described [3+2] cycloaddition of *N*-sulfonyl imines with triisipropylsilylpropene in the presence of a stoichiometric amount of BF_3-OEt_2,[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 Tf_2NH 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

This work was financially supported by a Grant-in-Aid for Scientific Research and Targeted Proteins Research Program from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

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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, $^3J_{(C,F)}$ = 3.6 Hz), 124.0, 123.0 (q, $^1J_{(C,F)}$ = 269.9 Hz), 117.7 (q, $^2J_{(C,F)}$ = 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**; ^{1}H 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**. $C_{26}H_{36}F_3NSi$, *monoclinic*, space group $P2_1$/n, a = 13.8584(3) Å, b = 9.9621(2) Å, c = 17.7342 Å, β = 91.7284(9)°, V= 2447.25(8) Å^3, Z = 4, D_{calc} = 1.215 g/cm^3, R = 0.050, R_w = 0.064, GOF = 1.416.
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