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Lewis acid-mediated [3+2] cycloaddition of allyltriisopropylsilane to *N*-sulfonyl aldimines

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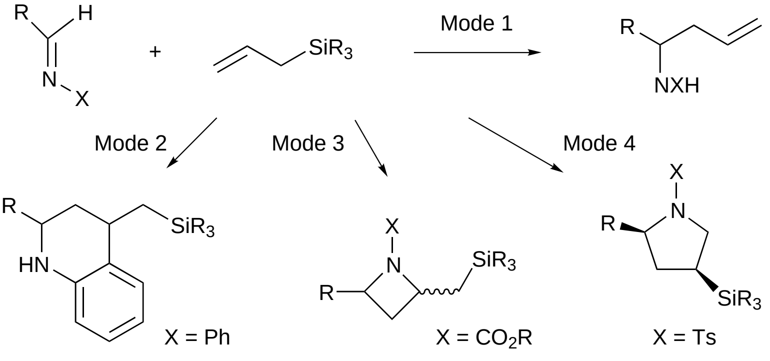
Abstract—$BF_3{\cdot}OEt_2$-mediated [3+2] cycloaddition of allyltriisopropylsilane to *N*-sulfonyl aldimine afforded silyl substituted pyrrolidines in good yields. Excellent *cis* selectivity was observed with aromatic aldimines. © 2001 Elsevier Science Ltd. All rights reserved.

Lewis acid-mediated addition reaction of allylsilane to a carbon–nitrogen double bond constitutes an important reaction for the preparation of homoallylic amines, and a number of Lewis acids have been developed as promoter for the allylation reaction (mode 1).[1] The high nucleophilicity of allylsilane as an allylation reagent originates from the β-silicon effect.[2] Although the synthetic utility of allylsilane as an allyl anion equivalent has been established, Lewis acid-mediated cycloaddition reactions of allylsilane to α,β-unsaturated carbonyl compounds and aldehyde have attracted attention lately as novel method for the preparation of five- and four-membered carbocycles[3–5] as well as heterocycles.[6,7] With respect to the Lewis acid-mediated addition reaction of allylsilane to a carbon–nitrogen bond, we have reported the formation of tetrahydroquinoline derivatives with *N*-aryl aldimines (mode 2).[8] Uyehara reported the formation of [2+2] cycloadducts upon reaction with *N*-acyl aldimines (mode 3).[6f] We wish to report herein that a fourth type of reaction took place smoothly with *N*-sulfonyl aldimines under the influence of $BF_3{\cdot}OEt_2$ to afford pyrrolidine derivatives in good yields (mode 4) (Scheme 1).

First of all, treatment of *N*-tosyl aldimine (**1a**) and allyltriisopropylsilane with $BF_3{\cdot}OEt_2$ (1.1 equiv.) in toluene at 0°C for 8 h gave a cyclization product (**2a**) in 36% yield in addition to an allylation product (**3**). Among the Lewis acids examined, $BF_3{\cdot}OEt_2$ exhibited the best results.[9] Although lowering the reaction temperature decreased the yield of **2a**, the reaction at room temperature improved the yield of **2a** to 44%. On further rise of the reaction temperature to 40°C, the yield slightly dropped to 40%. The stereoselectivity of the present cycloaddition is quite high judging from 400



Scheme 1.

Keywords: allylsilane; cycloaddition; pyrrolidine; imines; $BF_3{\cdot}OEt_2$.

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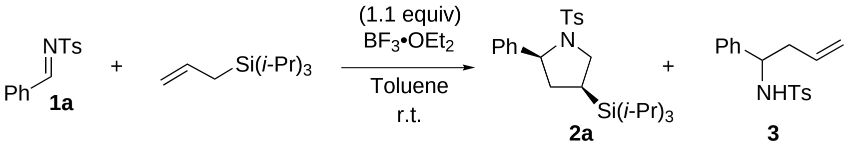
MHz ^{1}H NMR. The relative stereochemistry was unambiguously determined to be *cis* by an X-ray crystallographic analysis. Interestingly, dilution of the reaction conditions facilitated the formation of the cycloadducts by suppressing the formation of the homoallylic amines, and the results are shown in Table 1. Furthermore, increase of the amount of allylsilane improved the yield of **2a**.

Results of the $BF_3 \cdot OEt_2$ mediated cycloaddition of allylsilane (2 equiv.) with various kinds of aromatic imines are shown in Table 2.[10] Pyrrolidines (**2**) were obtained in good yields with excellent *cis* stereoselectivity.

Next, cycloaddition reaction to aliphatic aldimines was examined, and the results are shown in Table 3. Interestingly, the cycloaddition reaction toward aliphatic aldimines completed much quicker to afford the cycloadducts (**2**) in higher yields albeit with little stereoselectivity.

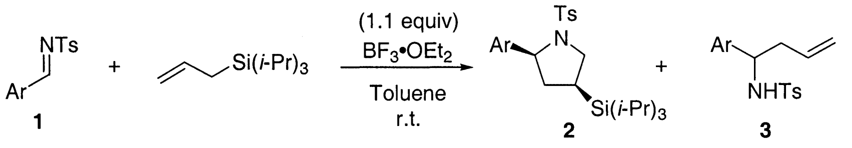
The present results for the formation of [3+2] cycloadduct are in sharp contrast to the Uyehara report,[6e] in which [2+2] cycloadducts were obtained from *N*-acyl or *N*-alkoxycarbonyl substituted aldimines. Actually, treatment of *N*-benzylidenebenzamide and allyltriisopropylsilane with $BF_3 \cdot OEt_2$ in toluene under the identical conditions with Table 2 led to the formation of a [2+2] cycloadduct in 72% yield (*cis*:*trans*=71:29) and none of the [3+2] adduct was obtained. Furthermore, the fact that we could not obtain the [2+2] cycloadduct from aldimine (**1**) bearing a sulfonyl moiety at all under various conditions, including lower reaction temperature, clearly shows that the mode of cyclization depends on the substituents on nitrogen. The present substituent effect can be ascribed to the difference in the nucleophilicity of *N*-COR and *N*-SO_2Ar in the reaction intermediate **4** (Scheme 2). Intramolecular attack of strong nucleophile *N*COR to β-silyl carbocation led to the formation of azetidine by kinetic control, and the less nucleophilic nitrogen bearing a sulfonyl moiety gave pyrrolidine by 1,2-silicon shift under thermody-

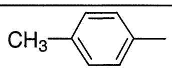
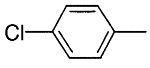
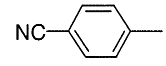
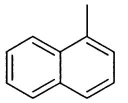
Table 1. Effect of the concentration



Entry	Concentration (mol/L)	Amount of allylsilane	Yield of **2a** (%)	*cis*:*trans*	Yield of **3** (%)
1	0.15	1.2	44	96:6	44
2	0.15	2	44	96:6	44
3	0.075	2	57	96:6	36
4	0.03	2	62	96:6	25
5	0.03	4	73	95:5	25

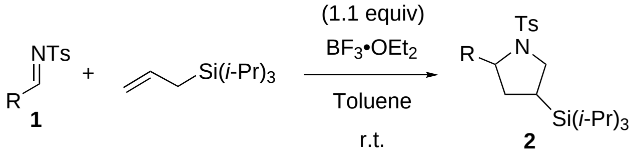
Table 2. Results of the cycloannulation with aromatic imines



Entry	Ar	Reaction time	Yield of **2**/%	cis : trans	Yield of **3**/%
1		7.5 h	60	95:5	34
2		15 h	61	97:7	26
3		1 d	48	97:3	17
4		8 h	58	95 : 5	36

a) 2 equiv of allylsilane was employed. The concentration of **1** is 0.03 mol/L.

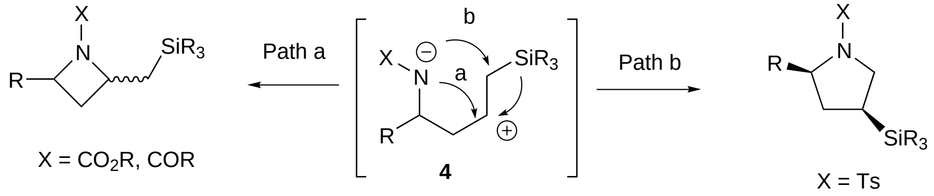
Table 3. Results of the cycloannulation with aliphatic imines[a]



Entry	R	Concentration (mol/L)	Reaction time (h)	Yield of **2** (%)	Ratio[b]
1	Cyclohexyl	0.03	0.5	72	56:46
2	$PhCH_2CH_2$	0.01	0.5	81	59:41
3	$CH_3CH_2CH_2$	0.03	0.5	88	54:46
4	$(CH_3)_2CH$	0.01	0.5	76	55:45
5	CH_3OCO	0.03	4	71	52:48

[a] 2 equiv. of allylsilane was employed.

[b] The relative stereochemistry has not been decided.



Scheme 2.

namic control.[11] Although Panek already reported the formation of pyrrolidine derivatives by the Lewis acid-mediated annulation of functionalized allylsilane with in situ-generated *N*-acyl aldimine,[6d,6l] this is the first example for the formation of pyrrolidine derivatives by the reaction of parent allylsilane with aldimine.[12,13]

In conclusion, we have reported a formation of pyrrolidines by [3+2] cycloaddition reaction of allylsilane with aldimine, in which the *N*-substituent of aldimine is the control factor in the selective formation of five- or four-membered nitrogen heterocycles.

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9. Other Lewis acids examined and yields of **1a** are $SnCl_4$ (11%), $AlCl_3$ (17%), $TiCl_4$ (11%), $ZrCl_4$ (15%).
10. A typical experimental procedure for the preparation of **2a** is described (entry 5, Table 1). To a solution of **1a** (38.8 mg, 0.150 mmol) and allyltriisopropylsilane (145 ml, 0.602 mmol) in toluene (5.0 ml) was added $BF_3 \cdot OEt_2$ (20.5 μL, 0.167 mmol) at room temperature. After being stirred at this temperature for 4.5 h, the reaction mixture was quenched by addition of satd $NaHCO_3$ solution. The aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness. Purification of the crude mixture by thin-layer chromatography (SiO_2, hexane: ethyl acetate = 9:1, v/v) gave **2a** (49.9 mg, 73%) and a homoallylic amine (11.3 mg, 25%). Spectral data of **2a**; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65–7.20 (aromatic, 9H), 4.47 (dd, 1H, $J = 6.9$, 9.7 Hz), 3.95 (dd, 1H, $J = 7.7$, 11.3 Hz), 3.59 (dd, 1H, $J = 11.3$, 12.1 Hz), 2.47–2.42 (m, 1H), 2.41 (s, 3H), 1.86 (ddd, 1H, $J = 9.7$, 13.3, 13.3 Hz), and 1.05–0.99 (m, 22H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.18, 143.04, 135.40, 129.46, 128.37, 127.44, 127.04, 126.24, 65.33, 53.58, 41.66, 24.12, 21.43, 18.88, and 11.06.
11. Example and discussion of the selective formation of four- and five-membered cycloadducts, see: Ref. 5c.
12. In Panek's report,[6d,1] the use of lower temperature (<−78°C) is required to obtain the cycloadducts. Raising the reaction temperature −20°C resulted in the exclusive formation of the homoallylic amines, which is in contrast to our results. Furthermore, the annulation is limited to aromatic imines.
13. Formation of pyrrolidine by [3+2] cycloaddition of allylsilane to *N*-acyliminoester has already been reported though the yields of the cycloadducts are modest. See Ref. 6e.