LEWIS ACID PROMOTED [4+2] ANNULATION OF ALLYLSILANE AND ALLYLGERMANE WITH ALDIMINE; PREPARATION OF TETRAHYDROQUINOLINES†

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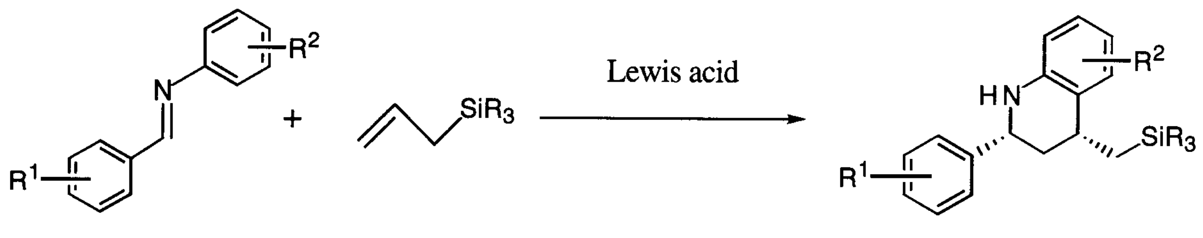
Abstract– On treatment of aldimines derived from aromatic aldehydes and aniline with allylsilane in the presence of Lewis acid, [4+2] cycloannulation took place smoothly to afford tetrahydroquinoline derivatives in moderate to good yields.

The development of efficient methods for the construction of carbocycles as well as heterocycles is desired and thus numerous kinds of novel synthetic methods have been developed. Lewis acid-promoted [3+2] as well as [2+2] cycloaddition of allylsilane with α,β-unsaturated ketone or carbonyl compounds has recently been established as efficient strategy[1] for the stereoselective synthesis of both 5-membered[2,3] and 4-membered silyl-substituted ring compounds.[4,5] Allylsilane bearing a sterically demanding silyl group suppressed the Hosomi-Sakurai reaction,[6] thereby promoting the formation of the cycloadducts in high yields.

On the other hand, acid-promoted [4+2] hetero Diels-Alder reaction of electron-rich olefin with aldimine, derived from aldehyde and aniline, has been developed for the construction of 1,2,3,4-tetrahydroquinoline derivatives.[7,8] Enantioselective aza Diels-Alder reactions have been achieved recently.[9] Although electron-rich alkenes such as vinyl ether, vinyl sulfide, and cyclopentadiene have been employed frequently as olefin counterpart, annulation reactions of aldimines with allylic metals have not been studied. As part of our continuing effort to explore cycloannulation reactions using allylsilane,[10,11] we wish to report herein Lewis acid-promoted cycloannulation of allylsilane and allylgermane with the aldimines derived from aromatic aldehyde and anilines.[12]



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† This paper is dedicated to Professor Teruaki Mukaiyama in pre-celebration of his 73rd birthday.

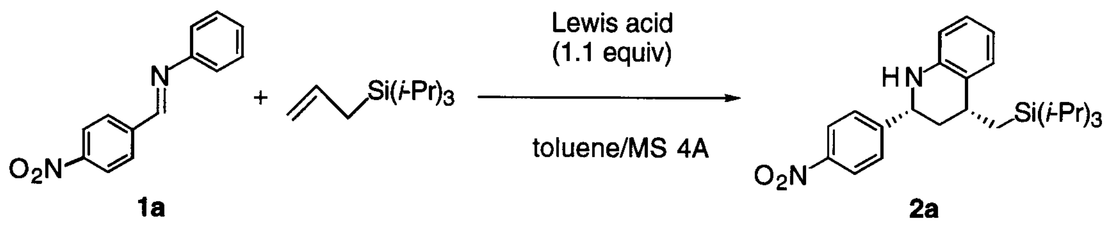


Table 1. Effect of Lewis acid

Entry	Lewis acid	Conditions	Yield /% (*cis*:*trans*)
1	$SnCl_4$	0 °C/ 3 h	91 (84:16)
2	$BF_3 \bullet OEt_2$	0 °C–rt / 4.6 h+23 h	15 (78:22)
3	$TiCl_4$	0 °C–rt / 7.0 h+15 h	13 (81:19)
4	$ZrCl_4$	0 °C–rt / 5.0 h+19 h	4 (-)
5	$Sc(OTf)_3$	rt / 22 h	55 (74:26)

At the outset, an aldimine (**1a**) and allyltriisopropylsilane were treated with several kinds of Lewis acid in toluene in the presence of MS 4A and the results are shown in Table 1. $SnCl_4$ turned out to be most effective as a promoter and furnished a cyclization product (**2a**) in an excellent yield in favor of the *cis*-isomer. The relative stereochemisty of **2a** was unambiguously determined by ^1H NMR multiple NOE study.

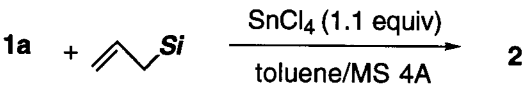


Table 2. Effect of silyl substituents

Entry	*Si*	Conditions	Yield/% (*cis*:*trans*)
1	$Si(i\text{-}Pr)_3$	0 °C/3.0 h	91 (84:16)
2	$Si(i\text{-}Pr)_2(C_6H_4)\text{-}p\text{-}OMe$	0 °C/3.5 h	84 (83:17)
3	$Si(i\text{-}Pr)_2Ph$	0°C/2.0 h	75 (83:17)
4	$SiPh_2(t\text{-}Bu)$	0 °C/4.1 h	74 (89:11)
5	$SiMe_2Ph$	rt/2.0 h	62 (74:26)
6	$SiMe_3$	0 °C/2.0 h	61 (77:23)

Next, the effect of the silyl group was studied and the results are shown in Table 2. Allylsilane bearing bulkier silyl group gave cycloadducts in higher yields. Allyltriisopropylsilane furnished the adduct (**2**) in the highest yield.

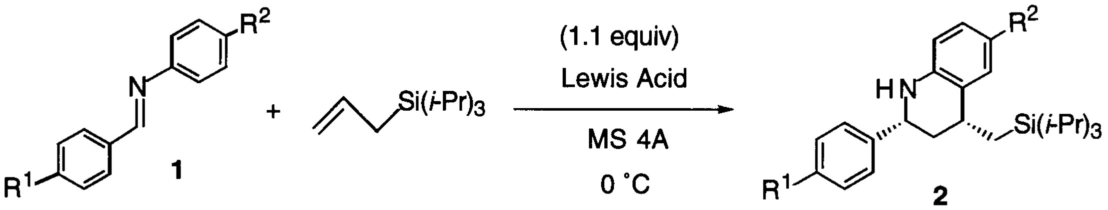
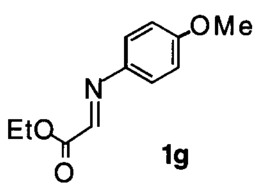


Table 3. Results of the cycloaddition with various aldimines

Entry	R^1	R^2	Starting material	Lewis Acid	Solvent	Product	Yield/% (*cis*:*trans*)
1	NO_2	H	**1a**	$SnCl_4$	Toluene	**2a**	91 (84:16)
2	CF_3	H	**1b**	$SnCl_4$	Toluene	**2b**	73 (84:16)
3	CN	H	**1c**	$SnCl_4$	Toluene	**2c**	46 (78:22)
4	H	COOEt	**1d**	$SnCl_4$	Toluene	**2d**	30 (85:15)
5	H	COOEt	**1d**	$SnCl_4$	CH_2Cl_2	**2d**	85 (50:50)
6	H	H	**1e**	$SnCl_4$	Toluene	**2e**	4 (89:11)
7	H	H	**1f**	$BF_3•OEt_2$	CH_3CN	**2f**	45 (55:45)
8	X[a]	OMe	**1g**	$SnCl_4$	Toluene	**2g**	47 (55:45)

a) An aldimine derived from glyoxylate (**1g**) was employed.

The potential and scope of the cyclization reaction with various aldimines in the presence of $SnCl_4$ as a Lewis acid are presented in Table 3. Aromatic aldimine bearing electron withdrawing group gave cycloadducts in good yields. An aldimine derived from benzaldehyde and aniline gave poor result with $SnCl_4$ and use of $BF_3•OEt_2$ as a Lewis acid afforded the adduct in moderate yield. An aldimine derived from glyoxylate (**1g**) also furnished the adduct.



1g

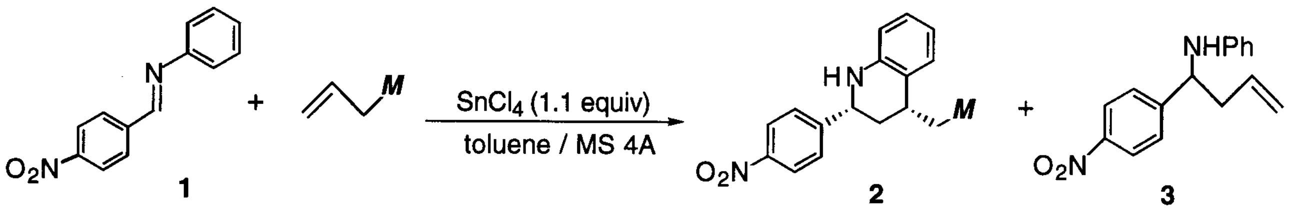


Table 4. Effect of the allylmetal

Entry	*M*	Conditions	Yield of **1**/% (*cis*:*trans*)	Yield of **3**/%
1	Si(*i*-Pr)$_3$	0 °C/3.0 h	91(84:16)	0
2	Ge(*i*-Pr)$_3$	0 °C/ 12 min	47(66:34)	4
3	$SnBu_3$	rt/overnight	0	17

Cycloaddition reaction with allylgermane and allylstannane was studied and the results are shown in Table 4. Allylgermane also worked as olefin counterpart for the present cycloannulation reaction though the yields was lower than that of allylsilane. We have already observed the reduction of the yield of the cycloadducts by using allylgermane in place of allylsilane.[13] Allylstannane, however, did not afford the cycloadduct at all. Because nucleophilicity of the allylic metals is in the order allylstannane > allylgermane > allylsilane [14] and the bond strength is in the order C-Si > C-Ge > C-Sn, we can conclude that the yields of the adducts depend not on the nucleophilicity but on the bond strength of the carbon-metal bonds. This results clearly imply that present cycloaddition reaction takes place stepwise not by concerted manner.

In summary, Lewis acid promoted cycloannulation of allylmetals and aldimines was studied.

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