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$GaCl_3$-catalyzed [4+2] annulations of allyltrimethylsilane and trimethyl(propargyl)silane with aldimines

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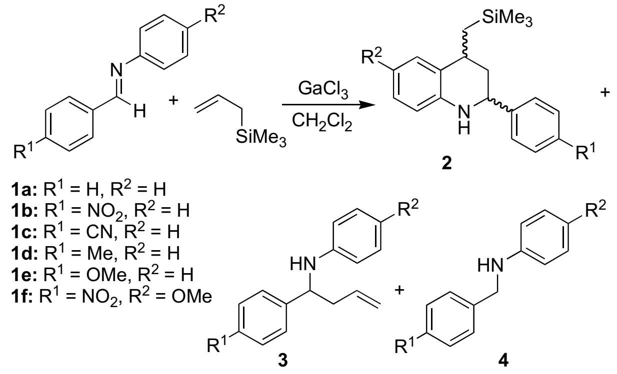
Abstract—The $GaCl_3$-catalyzed reaction of allyltrimethylsilane and aldimines gave tetrahydroquinolines in good yields. Similarly, 4-methylquinoline was obtained by using trimethyl(propargyl)silane via a dehydrogenation process.

1. Introduction

A tetrahydroquinoline unit can be found in various natural products and its biological activities are of interest for potential drugs.[1] Tetrahydroquinolines are generally prepared by the aza-Diels–Alder reaction of arylimines with dienophiles.[2] Alternatively, the reaction of Schiff bases with allyl Grignard reagents, followed by a ring closure under acidic conditions, gave 2-substituted tetrahydroquinolines.[3] The reaction of aldimines with allylsilanes catalyzed by a stoichiometric amount of $SnCl_4$ directly afforded tetrahydroquinolines.[4] Lewis acid-mediated reactions of allylsilanes with electrophiles are known as one of the most fundamental C–C bond forming processes[5] and a wide range of Lewis acids have been utilized for this purpose. Among them, gallium salts have been recently introduced into organic synthesis as versatile catalysts for C–C bond formation[6] including allylations of carbonyl compounds[7] and alkynes[8] using allyltrimethylsilane. However, a catalytic allylation of imines has not appeared. Here we disclose a $GaCl_3$-catalyzed reaction of allyltrimethylsilane with aldimines giving tetrahydroquinolines in high yields, and also mention a reaction of propargylsilane with imine yielding a 4-substituted quinoline.

2. Results and discussion

The $GaCl_3$-catalyzed reaction of allyltrimethylsilane and benzylideneaniline (**1a**) was performed by changing solvent (Scheme 1 and Table 1). In CH_2Cl_2, tetrahydroquinoline **2a** was obtained in 20% yield along with homoallylamine **3a** and benzylamine (**4a**) (entry 1). THF gave poor results (entry 2). The yield of **2a** in benzene was similar to that found in CH_2Cl_2 (entry 3). The reaction did not proceed in *n*-hexane (entry 4). $Ga(OTf)_3$ was ineffective in promoting the reaction (entry 5). As CH_2Cl_2 was found to be a proper solvent for the consecutive reaction, a series of imines were submitted to the allylation in CH_2Cl_2 and the results are summarized in Table 2. The use of less amount of $GaCl_3$ resulted in the erosion of the yields (Table 2, entry 1). When increased amounts of $GaCl_3$ were used, the yields of **2a** were increased (entries 2–4). The use of aldimine **1b** having a nitro group improved the yield considerably; the reactions with catalytic amounts of $GaCl_3$ afforded tetrahydroquinoline **2b** in high yields (entries 5–7).



Scheme 1.

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Table 1. Allylation of benzylidenaniline (**1a**) with allyltrimethylsilane[a]

Entry	Solvent	t (h)	Yield (%)		
			2a	**3a**	**4a**
1	CH_2Cl_2	3	20 (50:50)	3	23
2	THF	19	7 (66:34)	8	5
3	Benzene	20	15 (71:29)	1	17
4	*n*-Hexane	20	Trace	0	0
5[b,c]	CH_2Cl_2	22	0	0	0

[a] All reactions were performed with **1a** (1.0 mmol), allyltrimethylsilane (1.5 mmol), and $GaCl_3$ (10 mol %) at room temperature.

[b] $Ga(OTf)_3$ was used.

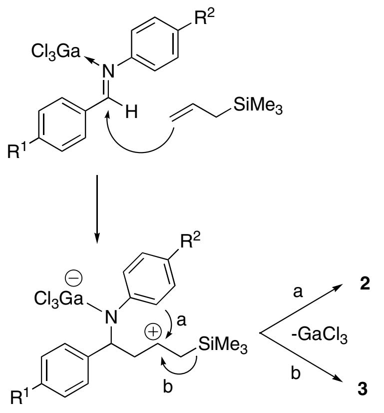
[c] Imine **1a** was recovered in 92%.

Table 2. $GaCl_3$-catalyzed reactions of benzylideneanilines with allyltrimethylsilane[a]

Entry	**1**	$GaCl_3$ (mol %)	t (h)	Yield (%)[b]		
				2 (cis:trans)	**3**	**4**
1	**1a**	2	5	**2a**: 13 (51:49)	**3a**: 2	**4a**: 18
2	**1a**	10	3	**2a**: 28 (50:50)	**3a**: 3	**4a**: 23
3	**1a**	50	1	**2a**: 39 (24:76)	**3a**: 4	**4a**: 23
4	**1a**	100	3	**2a**: 83 (58:42)	**3a**: 4	0
5	**1b**	2	2	**2b**: 46 (56:44)	**3b**: 12	0
6	**1b**	10	1	**2b**: 83 (55:45)	**3b**: 15	0
7	**1b**	50	3	**2b**: 72 (54:46)	**3b**: 10	0
8	**1b**	100	3	**2b**: 15 (52:48)	**3b**: 31	0
9	**1c**	2	3	**2c**: 47 (64:36)	**3c**: 15	0
10	**1c**	10	3	**2c**: 70 (57:43)	**3c**: 15	0
11	**1d**	10	3	**2d**: 25 (50:50)	0	**4d**: 11
12	**1d**	100	3	**2d**: 21 (58:42)	12	0
13	**1d**	100	21	**2d**: 63 (68:32)	0	0
14	**1e**	10	3	**2e**: 5 (65:35)	0	0
15	**1e**	100	3	**2e**: 3 (80:20)	**3e**: 9	0
16	**1e**	100	19	**2e**: 1 (75:25)	**3e**: 7	0
17	**1f**	5	1	**2f**: 63 (62:38)	**3f**: 4	**4f**: 5
18	**1f**	10	3	**2f**: 84 (55:45)	**3f**: 5	**4f**: 11
19	**1f**	20	3	**2f**: 86 (57:43)	**3f**: 4	**4f**: 5

[a] All reactions were carried out with **1a** (0.50 mmol), allyltrimethylsilane (0.75 mmol), and $GaCl_3$ in CH_2Cl_2 at room temperature.

[b] Isolated yield.



Scheme 2.

Table 3. Effect of other Lewis acids[a]

Entry	Lewis acid	Yield (%)	
		2b (dr)	**3b**
1	$BF_3{\cdot}OEt_2$	32 (62:38)	5
2	$Sc(OTf)_3$	13 (69:31)	2
3	$Yb(OTf)_3$	2 (50:50)	Trace

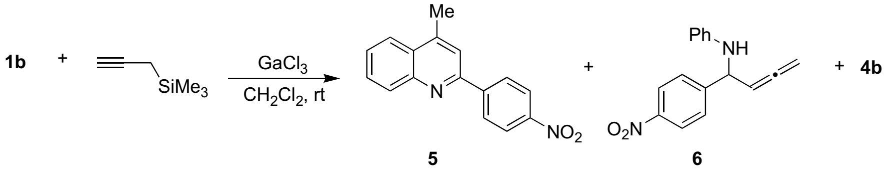
[a] All reactions were performed with **1b** (0.50 mmol), allyltrimethylsilane (0.75 mmol), and Lewis acid (10 mol %) in CH_2Cl_2 at room temperature for 19 h.

However, an equimolar amount of $GaCl_3$ gave poor results (entry 8). Aldimine **1c** possessing a cyano group showed similar results (entries 9 and 10). In contrast, the reactions of aldimine **1d** substituted by a methyl group were sluggish and a longer time was required to complete the reaction (entries 11–13). Aldimine **1e** derived from anisaldehyde remained intact even after prolonged reaction with a stoichiometric amount of $GaCl_3$ (entries 14–16). To improve the yield of **2**, an electron-donating group was introduced into the benzene ring on the imine nitrogen, which is expected to promote the intramolecular Friedel–Crafts attack (path a) before the elimination of the trimethylsilyl group (path b) (Scheme 2). Thus, **1f** was prepared from *p*-anisidine and was submitted to the reaction. As expected, the yield of **3f** was decreased and tetrahydroquinoline **2f** was obtained selectively (entries 17–19 vs entries 5–8).

Other Lewis acids were investigated for this transformation (Table 3). Compared with the case involving $GaCl_3$ (Table 2, entry 6), the reactions gave poor yields: $BF_3{\cdot}OEt_2$ afforded **2b** in 32% yield after 19 h (Table 3, entry 1). Rare earth triflates, $Sc(OTf)_3$ and $Yb(OTf)_3$, proved less useful for this reaction (entries 2 and 3). The allylation of imines promoted by a combinational use of $InCl_3$ and Me_3SiCl has been reported, where **3** and **4** were obtained in modest yields and the formation of tetrahydroquinoline **2** was not observed.[9]

Next, trimethyl(propargyl)silane was employed in place of allyltrimethylsilane (Table 4). The Lewis acid catalyzed reactions of propargylsilane with aldehydes,[10] acetals[11] and alcohols[12] have hitherto been reported; however, the reaction with imines has not been explored. When the reaction of **1b** was performed in the presence of 10 mol % $GaCl_3$, a mixture of quinoline **5** (20%), the reduction product **4b** (21%), and a trace amount of allene **6** were obtained (entry 1). An increasing amount of $GaCl_3$ gave a higher yield of **5** in a shorter reaction time (entry 2). In entries 1 and 2, products **5** and **4b** were obtained in almost coincident yields, suggesting that imine **1b** works as a hydrogen acceptor from a precursor to **5**. A plausible mechanism for the generation of **5**, **6**, and **4b** is shown in Scheme 3. The propargylation of **1b** generates intermediate **A**, which undergoes an intermolecular cyclization (path a) or an elimination of the trimethylsilyl group leading to **6** (path b). The former gives a transient allylsilane **B**, which undergoes further protonolysis and oxidative aromatization with **1b**. To avoid the consumption of imine **1b** during the aromatizing process, the reactions in the presence of another hydrogen acceptor were examined. Chloranil (tetrachloro-*p*-benzoquinone) was found to be a choice of dehydrogenation agent.[13] No formation of **4b** was observed in the presence of chloranil (entries 3–5). The best

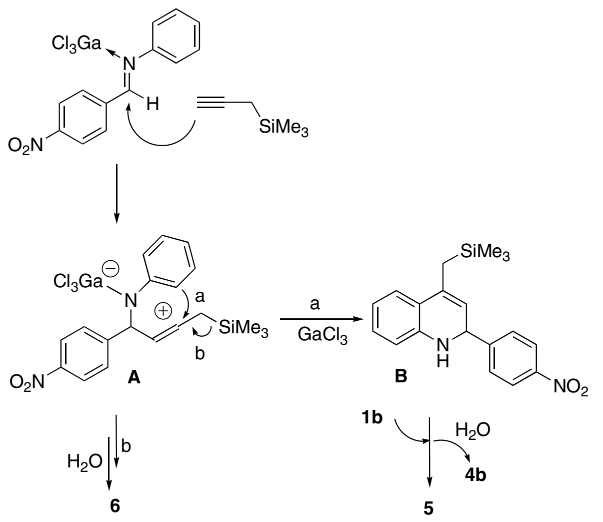
Table 4. $GaCl_3$-catalyzed reactions of benzylideneaniline with trimethyl(propargyl)silane[a]



Entry	$GaCl_3$ (mol %)	Chloranil (mol %)	t (h)	Yield (%)			
				5	**6**	**4b**	**1b**
1	10	0	68	20	2	21	35
2	20	0	20	36	4	32	11
3	20	100	19	42	2	0	59
4	50	100	1 (21)[b]	64 (64)[b]	0 (5)[b]	0	11
5	100	100	1	56	0	0	4

[a] All reactions were performed with **1b** (0.50 mmol), trimethyl(propargyl)silane (0.75 mmol), and $GaCl_3$ in CH_2Cl_2 (2 mL) at room temperature.

[b] **1a** was used in place of **1b**.



Scheme 3.

yield of **5** was obtained using 50 mol % $GaCl_3$ and 100 mol % chloranil (entry 4). The reaction of **1a** in place of **1b** was tested under the best conditions for **1b**. The corresponding quinoline was obtained in good yield, although longer time was required (entry 4).

In conclusion, we have demonstrated that a catalytic amount of $GaCl_3$ effectively promotes the coupling of allyl- and propargylsilanes with imines to give tetrahydroquinolines and quinolines, respectively. Further application of this process is currently underway.

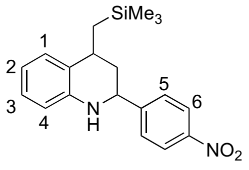
3. Typical procedure

All reactions were performed under argon atmosphere.

3.1. $GaCl_3$-mediated reaction of allyltrimethylsilane with imine 1b

(Table 2, entry 6) To a solution of imine **1b** (113 mg, 0.50 mmol) in CH_2Cl_2 (2 mL), $GaCl_3$ (0.1 M in CH_2Cl_2, 0.50 mL, 0.05 mmol) was added at 0 °C and the mixture was stirred for 5 min. Allyltrimethylsilane (120 μL, 0.75 mmol) was added and the reaction mixture was stirred at room temperature for 1 h. After quenching by water (2 mL), the products were extracted with diethyl ether. The extracts were washed with brine and dried over Na_2SO_4. After the solvent was removed under reduced pressure, the residue was separated by chromatography on silica gel (hexane–EtOAc = 50:1 then EtOAc) to give **2b** (114 mg, 83%, dr 55:45) and **3b** (20 mg, 15%). The diastereomeric ratio was determined by ^1H NMR.

3.2. 1,2,3,4-Tetrahydro-2-(4-nitrophenyl)-4-[(trimethylsilyl)methyl]quinoline (2b)



Mp 121–122 °C (Et_2O); ^1H NMR (200 MHz, $CDCl_3$, δ ppm) 0.07 (s, 9H, TMS_{cis}), 0.11 (s, 9H, TMS_{trans}), 0.76–2.24 (m, 4H, $CH_2 \times 2$), 2.93–3.02 (m, 1H, benzyl H_{trans}), 3.18–3.30 (m, 1H, benzyl H_{cis}), 4.00 (br s, 1H, NH_{cis}), 4.14 (br s, 1H, NH_{trans}), 4.56 (dd, 1H, $J = 2.6$, 11.2 Hz, $NHCH_{cis}$), 4.69 (dd, 1H, $J = 4.3$, 9.5 Hz, $NHCH_{trans}$), 6.57–6.62 (m, 1H, H4), 6.72–6.82 (m, 1H, H2), 7.05 (t, 1H, $J = 7.4$ Hz, H3), 7.25 (d, 1H, $J = 7.6$ Hz, H1), 7.58–7.64 (m, 2H, H5), 8.20–8.27 (m, 2H, H6); Calcd for $C_{19}H_{24}N_2O_2Si$ C, 67.02; H, 7.10; N, 8.23. Found C, 66.74; H, 7.13; N, 8.12.

3.3. *N*-[1-(4-Nitrophenyl)but-3-enyl] aniline (3b)[14]

^1H NMR (300 MHz, $CDCl_3$, δ ppm) 2.40–2.62 (m, 2H), 4.12 (br s, 1H), 4.42 (dd, $J = 5.7$, 7.5 Hz, 1H), 5.10–5.22 (m, 2H), 5.62–5.80 (m, 1H), 6.42 (d, $J = 8.7$ Hz, 2H), 6.64 (t, $J = 7.5$ Hz, 1H), 7.04 (dt, $J = 7.5$, 8.7 Hz, 2H), 7.50 (d, $J = 8.7$ Hz, 2H), 8.12 (d, $J = 8.7$ Hz, 2H).

3.4. $GaCl_3$-mediated reaction of trimethyl(propargyl)silane with imine **1b**

(Table 3, entry 4) To a solution of imine **1b** (113 mg, 0.50 mmol) and chloranil (124 mg, 0.50 mmol) in CH_2Cl_2 (2 mL), $GaCl_3$ (1.0 M in CH_2Cl_2, 0.25 mL, 0.25 mmol) was added at 0 °C and the mixture was stirred for 5 min. Trimethyl(propargyl)silane (120 μL, 0.75 mmol) was added and the reaction mixture was stirred at room temperature for 1 h. After quenching by water (2 mL), the products were extracted with diethyl ether. The extracts were washed with brine and dried on Na_2SO_4. After the solvent was removed under reduced pressure, the residue was separated by chromatography on silica gel (hexane–EtOAc = 30:1 then EtOAc) to give **5** (85 mg, 64%) and recovered **1b** (12 mg, 11%).

3.5. 4-Methyl-2-(4-nitrophenyl)quinoline (5)[15]

^1H NMR (200 MHz, $CDCl_3$, δ ppm): 2.82 (s, 3H), 7.61 (t, 1H, $J = 7.0$ Hz), 7.73–7.82 (m, 2H), 8.04 (d, 1H, $J = 7.0$ Hz), 8.19 (d, 1H, $J = 8.0$ Hz), 8.30–8.41 (m, 4H).

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