Fe(OTf)$_3$-Catalyzed Reaction of Benzylic Acetates with Organosilicon Compounds

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Abstract: Fe(OTf)$_3$-catalyzed reaction of benzylic acetates with allyltrimethylsilane, azidotrimethylsilane, and cyanotrimethylsilane afforded the corresponding allylated, azido, and cyano products in high yields. 2-Trimethylsilyl-substituted benzofuran and indole worked well to furnish the benzyl-substituted benzofuran and indoles.

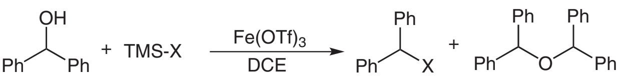
Key words: iron-catalyzed reaction, allylation, azidation, cyanation, benzylic acetates, organosilanes

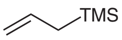
Lewis acids play a very important role in promoting carbon–carbon bond formation in organic synthesis.[1] In recent years, much attention was focused in such bond formation with the aid of catalysts such as BF_3,[2] Tf_2NH,[3] InX_3,[4] BiX_3,[5] and ZrX_4.[6] In some cases, high reaction temperature and even microwave conditions[7] are necessary to make the reaction possible. Although these transition metals are efficient, they are generally costly. As such, it is essential to come out with more effective methods in carrying out the bond formation.

Iron exists in abundant and can be easily obtained from nature, thus it is regarded as one of the lowest cost and environmentally friendly metals that can efficiently catalyze many organic reactions as compared to the other conventional Lewis acids.[8] Iron-mediated organic reactions have attracted a great deal of recent attention which include the Friedel–Crafts type reactions,[9] cross-coupling reactions,[10] allylations,[11] and other transformations.[12] We have been interested in the catalytic activity of iron salts as the Lewis acid in organic reactions and report a new efficient iron(III)-catalyzed reaction of benzylic acetates with various organosilanes.

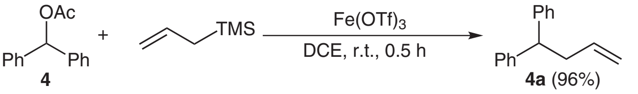
We initially explore the efficiency of iron salts in allylation of benzylic alcohols as shown in Table 1. When diphenylmethanol (**1**) was treated with allyltrimethylsilane in the presence of 5 mol% iron triflate in 1,2-dichloroethane at room temperature for two hours, a 31:59 mixture of allylated product **2** and ether **3** was obtained, whereby similar observations were previously noted.[13] The formation of **3** depended very much on the nature of organosilanes and this was exemplified in the results. When vinyltrimethylsilane (entry 2) and ethynyltrimethylsilane (entry 3) were used under the same conditions, ether **3** was isolated exclusively, whereas the desired azidation product **2** was obtained when employing azidotrimethylsilane (entry 4).

Table 1 Reaction of Diphenylmethanol with Organosilanes[a]



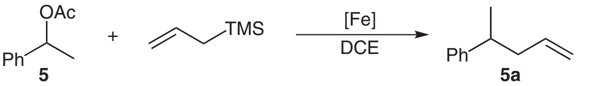
Entry	TMSX	Time (h)	Isolated yield of **2** (%)	Isolated yield of **3** (%)
1		2	31	59
2		2	–	95
3	≡—TMS	2	–	93
4	$TMSN_3$	2	96	–

[a] Conditions: **1** (0.30 mmol), TMSX (0.36 mmol), $FeCl_3$ (5 mol%), and AgOTf (15 mol%) in 1,2-dichloroethane (DCE) at r.t.



Scheme 1 Allylation of **4** with allyltrimethylsilane

Table 2 Optimizing Reaction Conditions with Various Catalysts



Entry	Catalyst (mol%)	Temp (°C)	Time (h)	Yield (%)[a]
1	Fe(acac)$_3$ (5)	80	15	0
2	FeF_3 (5)	80	15	0
3	$FeCl_2$ (5)	r.t.	15	48 (40)[b]
4	$FeBr_3$ (5)	r.t.	3	89
5	$FeCl_3$ (5)	r.t.	9	89
6	$FeCl_3$ (5), AgOTf (15)	r.t.	0.5	96

[a] Isolated yields.
[b] Recovery yield of starting material.

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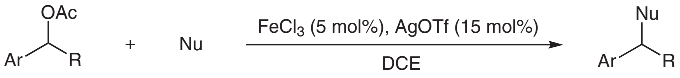
Table 3 Reactions of Benzylic Acetates with Various Organosilanes



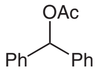
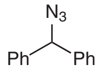
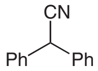
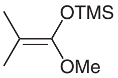
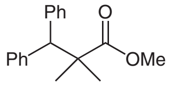
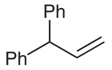
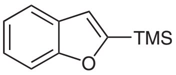
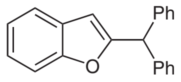
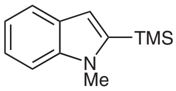
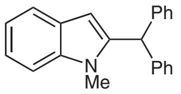
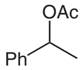
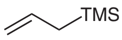
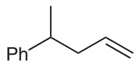
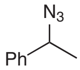
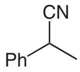
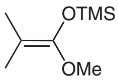
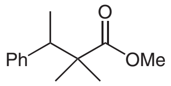
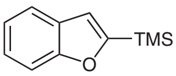
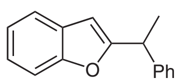
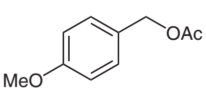
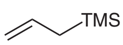
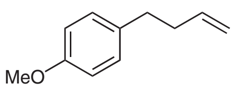
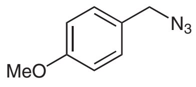
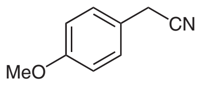
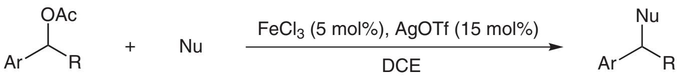
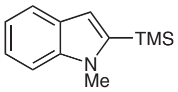
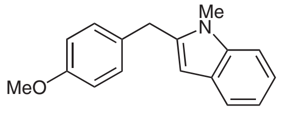
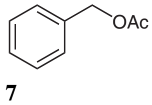
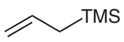
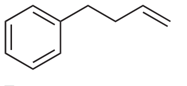
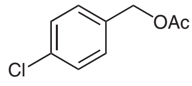
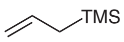
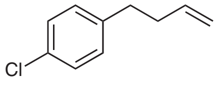
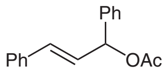
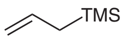
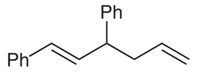
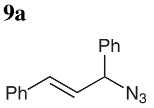
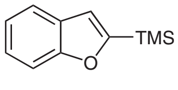
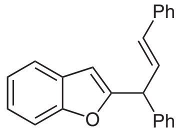
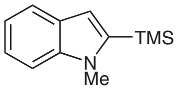
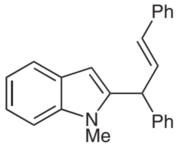
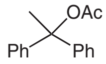
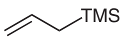
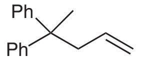
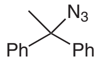
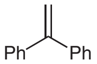
Entry	Acetate	Nu	Temp (°C)	Time (h)	Product	Yield (%)[a]
1	 **4**	TMSN$_3$	r.t.	1	 **4b**	97
2	**4**	TMSCN	50	1	 **4c**	88
3	**4**		r.t.	6	 **4d**	92
4	**4**		80	12	 **4e**	0
5	**4**		r.t.	1	 **4f**	88
6	**4**		r.t.	1	 **4g**	90
7	 **5**		r.t.	0.5	 **5a**	96
8	**5**	TMSN$_3$	r.t.	1	 **5b**	86
9	**5**	TMSCN	80	14	 **5c**	0
10	**5**		80	3	 **5d**	0
11	**5**		80	16	 **5e**	69
12	 **6**		r.t.	1	 **6a**	67
13	**6**	TMSN$_3$	r.t.	2	 **6b**	85
14	**6**	TMSCN	80	2	 **6c**	78

Table 3 Reactions of Benzylic Acetates with Various Organosilanes (continued)

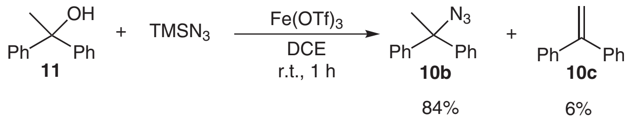


Entry	Acetate	Nu	Temp (°C)	Time (h)	Product	Yield (%)[a]
15	**6**		r.t.	2	 **6d**	66
16	 **7**		80	18	 **7a**	0
17	 **8**		80	18	 **8a**	0
18	 **9**		80	24	 **9a**	71
19	**9**	TMSN$_3$	r.t.	2	 **9b**	82
20	**9**		80	24	 **9c**	59
21	**9**		80	24	 **9d**	56
22	 **10**		r.t.	2	 **10a**	87
23	**10**	TMSN$_3$	r.t.	0.5	 **10b**  **10c**	60:37

Conditions: 0.30 mmol of benzylic acetate, 0.36 mmol of Nu, 5 mol% FeCl$_3$ and 15 mol% AgOTf in DCE.
[a] Isolated yields.

To obviate the problem of the unwanted ether formation, benzhydryl acetate **4** was employed in the allylation reaction. When **4** was subjected under the same conditions, the desired product was isolated in 96% yield without any formation of ether **3** as shown in Scheme 1. Thus, the remaining reactions were carried out with the benzylic acetates.[14] To determine the optimum conditions, the catalytic efficiency of various iron salts was also examined using 1-phenylethyl acetate (**5**). As shown in Table 2, Fe(acac)$_3$ and FeF$_3$ proved no catalytic activity in allylations (Table 2, entries 1 and 2), whereas FeCl$_2$ was effective to some extent in the catalysis (entry 3). The use of FeBr$_3$ and FeCl$_3$ dramatically increased the reactivity, thus were discovered to be very effective catalysts under mild reaction conditions (entries 4 and 5). The addition of AgOTf further improved the efficiency of iron catalyst (entry 6), which reduced the reaction time significantly and gave high yield (96%). Although FeCl$_3$ still produced excellent and comparable yields, it still proceeded at a much slower rate without AgOTf. Thus, remaining reactions were carried out using 5 mol% Fe(OTf)$_3$ (generated in situ),[15] whereas FeCl$_3$ and FeBr$_3$ are expected to be used in the present study. With the optimized conditions on hand, we studied reactions of benzylic acetates with various organosilanes such as vinyl-, cyano-, and azidotrimethylsilane.

The experimental results with primary and secondary benzylic acetates (**4**–**6**, **9**) using 5 mol% Fe(OTf)$_3$ in 1,2-dichloroethane were summarized in Table 3. The reaction of **4** with azidotrimethylsilane and TMS enol ether proceeded smoothly at room temperature to give **4b** and **4c** in 97% and 92% yield (entries 1 and 3), respectively. Similarly, **4** worked well with cyanotrimethylsilane (entry 2) but the reaction was somewhat slow and required gentle heating at 50 °C for one hour. In the case of vinyltrimethylsilane, the reaction did not occur, even under prolonged heating at 80 °C (entry 4), although the similar conversion was achieved with InCl$_3$ and BiBr$_3$.[1,6] We next examined the possibility of using electron-rich alkenylsilanes such as 2-trimethylsilyl-substituted benzofuran and indole. When **4** was reacted with 2-trimethylsilyl benzofuran and indole under the standard conditions, the reaction proceeded cleanly at room temperature, yielding the desired product in 88% and 90% yield, respectively (entries 5 and 6). In the case of **5**, allyltrimethylsilane and azidotrimethylsilane worked well, yielding the desired products in high yields (entries 7 and 8). However, **5** did not react with cyanotrimethylsilane (entry 9) and TMS enol ether (entry 10) in refluxing 1,2-dichloroethane, although it reacted slowly with 2-trimethylsilylbenzofuran at reflux (entry 11). In the case of primary benzylic acetates, the reactivity depended very much on the nature of the substituent of the phenyl ring. For example, benzyl acetate (**7**) did not react readily with allyltrimethylsilane even at prolonged heating conditions (entry 16), and the starting material was recovered unchanged. A similar result was observed with 4-chlorobenzyl acetate (**8**, entry 17). However, 4-methoxybenzyl acetate (**6**) was much more reactive than benzyl acetate and reacted with allyltrimethylsilane (entry 12) at ambient temperature within one hour. In addition, **6** worked well with azidotrimethylsilane, cyanotrimethylsilane, and 2-trimethylsilylindole (entries 13–15). This is because **6** contained the electron-donating methoxy group attached at the aromatic ring that gave stabilizing effects to the carbocation intermediate via resonance. This accelerated the rate of reaction, hence **6** proceeded faster under mild conditions as compared to **5** and **7**. Secondary (*E*)-1,3-diphenylallyl acetate (**9**) was also reacted with several organosilanes. However, **9** was not very reactive, and thus required prolonged heating for allylation (entry 18) and alkenylation (entries 20 and 21) to occur. Finally, allylation of tertiary 1,1-diphenylethyl acetate (**10**) proceeded smoothly at room temperature (entry 22) but the azidation afforded a 60:37 mixture of the desired azide **10b** and olefin **10c** (entry 23). When alcohol **11** was used, **10b** was increased to 84% together with a small amount of **10c** (6%, Scheme 2).



Scheme 2 Azidation of **11**

In conclusion, we have developed efficient Fe(OTf)$_3$-catalyzed reactions of benzylic acetates with various organosilanes. The present method proved a wide scope of interest, making it a useful and attractive process.[1,7,18]

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References and Notes

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(14) Reaction of(methoxymethylene)dibenzene (Ph_2CHOMe) with allyltrimethylsilane in the presence of 5 mol% $Fe(OTf)_3$ in DCE at r.t. for 5 h afforded **4a** (73%) but the allylation of **3** did not occur, even under prolonged heating at 80 °C.

(15) $Fe(OTf)_3$ was prepared from 5 mol% $FeCl_3$ and 15 mol% AgOTf in DCE. Filtration was done to remove the AgCl precipitate, and the catalyst was used to repeat the allylation. The reaction time and yield observed were comparable to the $Fe(OTf)_3$ generated in situ without filtration. For instance, the allylation of **4** under the similar conditions afforded **4a** in 89% yield.

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(17) **General Procedure for the Reaction of Benzylic Acetates with Organosilanes: But-3-ene-1,1-diyldibenzene (4a)**
Anhydrous $FeCl_3$ (2.4 mg, 0.015 mmol) and AgOTf (11.5 mg, 0.045 mmol) was carefully weighed inside a glove box and stirred in DCE (2 mL) for 5 min. Allyl trimethylsilane (41.1 mg, 0.36 mmol) and benzhydryl acetate **4** (67.9 mg, 0.3 mmol) were then added to the prepared catalyst solution and stirred for 0.5 h at r.t. The residual crude product was concentrated in vacuo and purified by silica gel column chromatography using *n*-hexane as eluent to afford the desired product **4a** (60.0 mg, 96% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.23 (m, 8 H), 7.19–7.15 (m, 2 H), 5.75–5.68 (m, 1 H), 5.05–4.93 (m, 2 H), 4.01 (t, *J* = 7.8 Hz, 1 H), 2.84–2.80 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.5, 136.8, 128.4, 127.9, 126.2, 116.3, 51.2, 39.9.

(18) **^{1}H NMR and ^{13}C NMR Data of Previously Unknown Compounds**

2-Benzhydryl-1-methyl-1*H*-indole (4g)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.17 (m, 13 H), 6.97 (t, *J* = 7.6 Hz, 1 H), 6.40 (s, 1 H), 5.66 (s, 1 H), 3.68 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.1, 137.4, 129.0, 128.7, 128.2, 127.3, 126.1, 121.6, 120.0, 118.8, 118.2, 109.1, 48.8, 32.6. HRMS (EI$^+$): *m/z* calcd for $C_{22}H_{20}N$ [M + 1]: 298.1596; found: 298.1603.

2-(4-Methoxybenzyl)-1-methyl-1*H*-indole (6d)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 7.6 Hz, 1 H), 7.29–7.18 (m, 4 H), 7.06 (t, *J* = 7.4 Hz, 1 H), 6.82 (d, *J* = 8.4 Hz, 2 H), 6.72 (s, 1 H), 4.04 (s, 2 H), 3.77 (s, 3 H), 3.71 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.7, 137.1, 133.5, 129.5, 127.8, 127.0, 121.5, 119.2, 118.7, 114.7, 113.7, 109.1, 55.2, 32.6, 30.6, 29.2. HRMS (EI$^+$): *m/z* calcd for $C_{22}H_{20}N$ [M + 1]: 252.1388; found: 252.1393.

(*E*)-2-(1,3-Diphenylallyl)-1-methyl-1*H*-indole (9d)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 8.0 Hz, 1 H), 7.37–7.18 (m, 13 H), 7.01 (t, *J* = 7.4 Hz, 1 H), 6.74–6.69 (m, 2 H), 6.43 (d, *J* = 16.0 Hz, 1 H), 5.11 (d, *J* = 7.6 Hz, 1 H), 3.72 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.5, 137.5, 137.4, 132.7, 130.4, 128.4, 127.3, 127.2, 127.1, 126.3, 121.6, 120.0, 118.8, 117.0, 109.2, 46.1, 32.7. HRMS (EI$^+$): *m/z* calcd for $C_{24}H_{22}N$ [M + 1]: 324.1752; found: 324.1746.