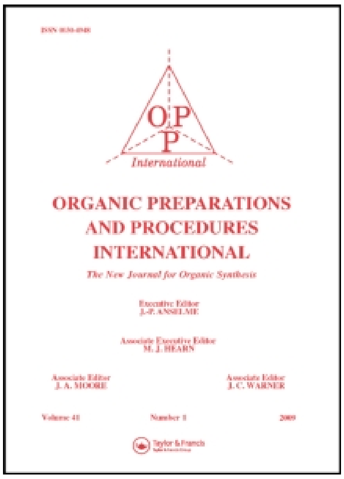

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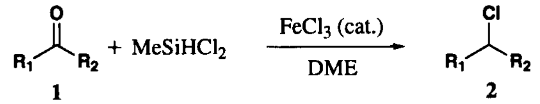
Deoxygenative chlorination is an important method for the conversion of organic molecules with oxygen functionalities to their chlorides.[1] The reaction of carbonyl compounds with PCl_5, or WCl_6 is a well-known route to vinyl chlorides, *gem*-dichlorides or 1,1,2-trichlorides.[2] However, the direct conversion of carbonyl compounds into organic halides has been largely unexplored. Recently, Baba and coworkers[3] reported that $In(OH)_3$ was an effective catalyst for the deoxygenative halogenation of aromatic aldehydes or ketones in good yields by using chlorodimethylsilane in chloroform, but that this method failed with aliphatic aldehydes. Furthermore, the use of chlorinated solvent does not meet the increasing requirement of a friendly environment. Thus more economical catalysts and new eco-friendly solvents are desirable. Herein we report the $FeCl_3$ catalyzed deoxygenative chlorination of aldehydes and ketones with dichloromethylsilane.



a) $R_1 = C_6H_5$, $R_2 = H$; b) $R_1 = 4\text{-}ClC_6H_4$, $R_2 = H$; c) $R_1 = 2\text{-}ClC_6H_4$, $R_2 = H$; d) $R_1 = 4\text{-}CH_3C_6H_4$, $R_2 = H$; e) $R_1 = 4\text{-}CH_3OC_6H_4$, $R_2 = H$; f) $R_1 = 4\text{-}HO(O)CC_6H_4$, $R_2 = H$; g) $R_1 = 4\text{-}CH_3O(O)CC_6H_4$, $R_2 = H$; h) $R_1 = 4\text{-}NO_2C_6H_4$, $R_2 = H$; i) $R_1 = PhCH_2$, $R_2 = H$; j) $R_1 = C_6H_5$, $R_2 = CH_3$; k) $R_1 = 4\text{-}ClC_6H_4$, $R_2 = CH_3$; l) $R_1 = 4\text{-}CH_3C_6H_4$, $R_2 = CH_3$; m) $R_1 = R_2 = (CH_2)_4$; n) $R_1 = R_2 = (CH_2)_5$; o) $R_1 = C_4H_9$, $R_2 = H$; p) $R_1 = C_5H_{11}$, $R_2 = H$

A series of experiments were carried out to search for an appropriate Lewis acid and the results are shown in *Table 1*. All runs were carried out for 3-6 hours. Among the seven Lewis acids tested, $FeCl_3$ gave the best results. Benzaldehyde (**1**) afforded benzyl chloride (**2a**) exclusively with dichloromethylsilane catalyzed by $FeCl_3$ in 1,2-dimethoxyethane at reflux (*Table 1, entry 2*). When the reaction was performed at room temperature, no benzyl chloride was detected even upon a prolonged reaction time (11 h) *(Entry 3)*. With chlorodiphenylsilane, trichlorosilane and triethoxysilane/chlorotrimethylsilane (as the hydride and chloride sources) instead of

Table 1. Screening of Catalysts and Reaction Conditions for the Deoxygenative Chlorination of Benzaldehyde with Chlorosilanes[a]

Entry	catalyst	Chlorosilane	Solvent	Time (h)	Yield[b] (%)
1	none	$MeHSiCl_2$	DME	4	0
2	$FeCl_3$	$MeHSiCl_2$	DME	3	98
3[c]	$FeCl_3$	$MeHSiCl_2$	DME	11	0
4	$FeCl_3$	Ph_2HSiCl_2	DME	4	68
5	$FeCl_3$	$HSiCl_2$	DME	4	56
6	$FeCl_3$	$HSi(EtO)_3$+Me_3SiCl_2	DME	6	45
7	$AlCl_3$	$MeHSiCl_2$	DME	4	34
8	$Sc(OTf)_3$	$MeHSiCl_2$	DME	4	46
9	$Yb(OTf)_3$	$MeHSiCl_2$	DME	4	traces
10	$InCl_3$	$MeHSiCl_2$	DME	3	43
11	$TiCl_3$	$MeHSiCl_2$	DME	4	0
12	$ZnCl_2$	$MeHSiCl_2$	DME	6	40
13	$FeCl_3$	$MeHSiCl_2$	THF	3	3
14	$FeCl_3$	$MeHSiCl_2$	CH_3CN	6	0
15	$FeCl_3$	$MeHSiCl_2$	$HCCl_3$	6	0
16	$FeCl_3$	$MeHSiCl_2$	Toluene	6	0

a) Unless otherwise noted, benzaldehyde (1 mmol) and catalyst (0.05 mmol) were allowed to react with chlorosilanes (1.1 mmol) under reflux (DME: 84°C, THF: 65°C, CH_3CN: 82°C, $HCCl_3$: 61°C Toluene: 110°C) for 4-6 h; b) NMR yield; c) At room temperature, only benzoic acid (56%), and the starting material benzaldehyde (44%) were detected.

dichloromethylsilane, benzyl chloride (**2a**) was formed in moderate yield (*Entries 4-6*). Product **2a** was also obtained by using $AlCl_3$, $Sc(OTf)_3$, $InCl_3$, or $ZnCl_2$ as the catalyst, but the yields were low (*Entries 7, 8, 10 and 12*). $Yb(OTf)_3$ or $TiCl_4$ showed no catalytic effect and the starting benzaldehyde was recovered quantitatively (*Entries 9 and 11*). When the reaction catalyzed by $FeCl_3$ was carried out in solvents other than DME, such as dry THF, CH_3CN, $CHCl_3$ and toluene, benzyl chloride (**2a**) was obtained in a very low yield (*Entry 13*), or the reaction failed entirely (*Entries 14-16*). Thus the deoxygenative chlorination at reflux in dry 1,2-dimethoxyethane with dichloromethylsilane catalyzed by $FeCl_3$ was developed for the standard reaction conditions.

On the basis of the results obtained with benzaldehyde, we investigated the scope of this methodology. As shown in *Table 2*, substituted aromatic aldehydes and ketones underwent deoxygenative chlorination under the optimized reaction conditions (*Table1, entry 2*) to give the corresponding chlorides in good yields; ester, nitro, carboxy groups were not affected. It should

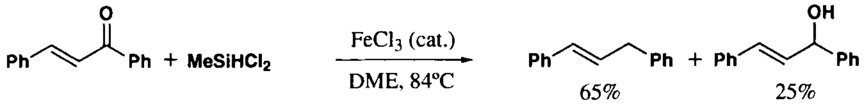


Table 2. $FeCl_3$-catalyzed Deoxygenative Chlorination of Carbonyl Compounds by Dichloromethylsilane in DME[a]

Entry	Cmpd	Yield[b] (%)	Time (h)	bp. (°C)	*lit.* bp. (°C)
1	**2a**	88	4	176-181	177-181
2	**2b**	92	3	218-220	216-222
3	**2c**	93	4	212-214	213-214
4	**2d**	90	4	198-200	200
5	**2e**	55	4	117 (14 mm)	117-118 (14 mm)
6	**2f**	82	4	201-203	201-202[c]
7	**2g**	84	4	240-242	240
8	**2h**	95	4	71-72	70-73[c]
9	**2i**	85	4	80-83 (16 mm)	82-84 (16 mm)
10	**2j**	87	4	89-91 (16 mm)	90 (16 mm)
11	**2k**	90	3	57-58 (0.11 mm)	58 (0.11 mm)
12	**2l**	83	4	35 (0.3 mm)	35 (0.3 mm)
13	**2m**	75	6	113-115	114
14	**2n**	66	6	141-143	142
15	**2o**	65	12	106-108	107-108
16	**2p**	76	12	159-162	159-161

a) All reactions were carried out with carbonyls **1** (1 mmol), $FeCl_3$ (0.05 mmol) and dichloromethylsilanes (1.1 mmol) in reflux DME; b) Isolated yields based on **1** used; c) mp.

be noted that the deoxygenative chlorination of aliphatic aldehydes catalyzed by $FeCl_3$, such as phenylacetaldehyde, valeraldehyde and heptaldehyde (***1i*, *1o*, *1p***) also proceeded well giving 2-chloroethylbenzene, 1-chloropentane and 1-chloroheptane, respectively. The corresponding chlorides were also obtained from aliphatic ketones such as cyclopentanone and cyclohexanone (***1m*, *1n***). Under the similar reaction conditions, chalcone did not afford the (*E*)-chloride, but gave the reduced products (*E*)-1,3-diphenylpropene (65%) and (*E*)-1,3-diphenylprop-2-en-ol (25%).

In summary, we present the first $FeCl_3$ catalyzed deoxygenative chlorination of carbonyl compounds with dichloromethylsilane. The inexpensive catalyst and chlorinated solvent-free conditions may make this method useful for the preparation of organic halides from simple carbonyl compounds.

EXPERIMENTAL SECTION

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. Infrared spectra were recorded on a Perkin-Elmer 683 spectrometer in KBr with absorption in cm^{-1}. ^1H-NMR spectra were determined on a Bruker AC 400 MHz instrument with CCl_4 used as the solvent. Chemical shifts are expressed in δ downfield from internal standard tetramethylsilane. Mass spectra were recorded on HP5989B mass spectrometer. Elemental analyses were carried out on an EA 1110 instrument.

General Experimental Procedure. Anhydrous $FeCl_3$ (8.1 mg, 0.05 mmol) in DME (5 mL) was added to a three-necked flask with stirring at room temperature. When the color of the mixture turned to deep blue, the carbonyl compound (1 mmol) and chlorosilane (1.1 mmol) were added to the solution. The resulting mixture was refluxed for indicated time (*Table 2*) until the disappearance of carbonyl compounds (monitored by TLC). Then the mixture was cooled to room temperature, quenched with dilute hydrochloric acid (0.3 M) and extracted with diethyl ether (3 x 20 mL). The combined organic layer was washed with aqueous $NaHCO_3$ (10 mL) and saturated brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by preparative TLC on silica gel with ethyl acetate and cyclohexane (1:8) as eluent to afford pure products.

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