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# Indium trichloride catalyzed reductive Friedel-Crafts alkylation of aromatics using carbonyl compounds

Takashi Miyai, Yoshiyuki Onishi, and Akio Baba*

*Department of Applied Chemistry, Faculty of Engineering, Osaka University*
*Yamadaoka, Suita, Osaka 565-0871 Japan*

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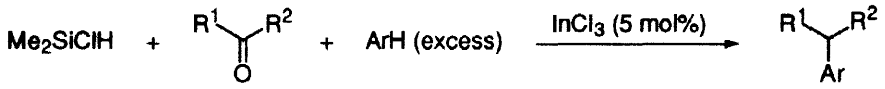
## Abstract

Reductive Friedel-Crafts alkylation of aromatics with aldehydes or ketones using chlorodimethylsilane as a hydride source was effectively promoted by a catalytic amount of indium trichloride, whereas a popular type of Friedel-Crafts catalysts showed less effect. © 1998 Elsevier Science Ltd. All rights reserved.

*Keywords:* indium and compounds; silicon and compounds; Friedel-Crafts reaction; reduction

Friedel-Crafts alkylation of aromatics using alkyl halides, alcohols, alkenes or ethers as alkylating reagents is widely used in organic synthesis. The direct use of carbonyl compounds as alkylating reagents, called as "reductive Friedel-Crafts reaction", is attractive in organic syntheses. Carbonyl compounds, however, have been hardly used because of a shortage of effective hydride sources and requirement of a large amounts of strong acids. In addition, in almost cases appeared, low selectivities of mono alkylated products were noted [1]. Recently, two examples of reductive Friedel-Crafts reactions were successfully reported in which aldehydes were incorporated as alkylating reagents. One is promoted by excess amounts of $Ga_2Cl_4$ in which contaminated moisture is assumed as a hydride source [2]. The other is redox system *via* the acetalisation of aromatic aldehydes with 1,3-diols in the presence of $Sc(OTf)_3$ [3] or trifluoromethanesulfonic acid (TFSA) [4] under refluxing of aromatics. Ketones, unfortunately, are not practically applicable in the latter case. In this paper, we report a novel type of reductive Friedel-Crafts alkylation catalyzed by indium trichloride ($InCl_3$), where chlorodimethylsilane ($Me_2SiClH$) is essential as reductant, and hydrosilylation is followed by alkylation of aromatics (eq.1).



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To the best our knowledge, our system is the first application of silyl hydride for reductive Friedel-Crafts reaction, in which ketones can be utilized as alkylating reagents besides aldehydes. The conditions employed are very mild, and even low reactive aromatics can be effectively alkylated. In addition, only 5 mol% of $InCl_3$ is sufficient.

**Table 1**
$InCl_3$-catalyzed reductive Friedel-Crafts reaction.[a]

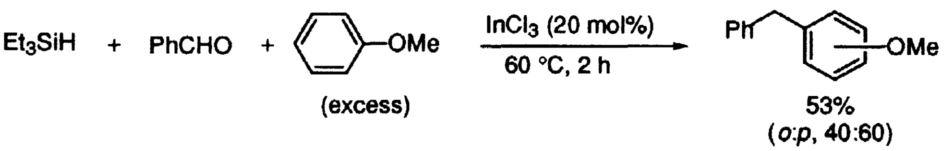
| Entry | $R^1$ | $R^2$ | ArH | Time /h | Temp /°C | Yield /%[b] | *o*:*m*:*p*[b] |
|---|---|---|---|---|---|---|---|
| 1 | Ph | H | PhH | 14 | 25 | 79 | |
| 2[c] | Ph | H | PhH | 36 | 25 | 99 | |
| 3 | Ph | H | PhH | 3 | 60 | 99 | |
| 4[d] | Ph | H | PhH | 0.7 | 60 | 72 | |
| 5[e] | Ph | H | PhH | 3 | 60 | 8 | |
| 6[f] | Ph | H | PhH | 0.7 | 60 | 4 | |
| 7[g] | Ph | H | PhH | 3 | 25 | 8 | |
| 8 | Ph | H | PhMe | 4 | 25 | 85 | 38:8:54 |
| 9 | Ph | H | PhOMe | 2 | 25 | 74 | 34:trace:66 |
| 10 | Ph | H | PhBr | 19 | 25 | 93 | 34:6:60 |
| 11 | *p*-$ClC_6H_4$ | H | PhH | 3 | 60 | 98 | |
| 12 | *n*-$C_5H_{11}$ | H | PhH | 1 | 25 | 0[h] | |
| 13[i] | Ph | Me | PhH | 2 | 80 | 52 | |
| 14 | Ph | Me | PhMe | 1 | 60 | 99 | 15:4:81 |
| 15 | *p*-$ClC_6H_4$ | Me | PhH | 15 | 25 | 62 | |
| 16[d] | *p*-$ClC_6H_4$ | Me | PhH | 1 | 60 | 71 | |
| 17[i] | Me | Me | PhMe | 3 | 100 | 42 | 48:13:39 |
| 18 | -$(CH_2)_5$- | | PhMe | 3 | 110 | 92 | 38:1:61 |

[a] Reaction conditions: catalyst, 0.1 mmol; chlorodimethylsilane, 2 mmol; substrate, 2 mmol; solvent, 10 mL; $N_2$ atmosphere. [b] Yields and selectivities were determined by $^1H$, $^{13}C$ NMR or GLC. [c] $InCl_3$, 1 mol%. [d] $In(OTf)_3$, 20 mol%. [e] $AlCl_3$, 20 mol%. [f] TFSA, 20 mol%. Dibenzyl ether was obtained in 72% yield. [g] $ZnCl_2$, 20 mol%. Dibenzyl ether was obtained in 42% yield. [h] Di-*n*-hexyl ether was obtained quantitatively. [i] $InCl_3$, 20 mol%.

Table 1 exemplifies the results of alkylation using carbonyl compounds. When aromatics were used as solvents, no poly-alkylation was observed in all runs. Treatments are very convenient. To the mixture of $InCl_3$ (0.1 mmol) and aromatic solvent (10 mL) was subsequently added a carbonyl compound (2.0 mmol) and $Me_2SiClH$ (2.0 mmol) at ambient temperature, then the reaction mixture was heated if required.

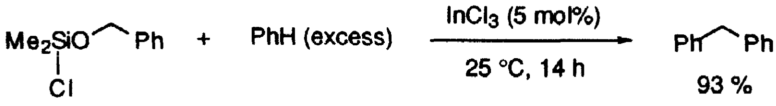
The alkylation of benzene or toluene with benzaldehyde proceeded even at ambient temperature to give high yields of diarylmethanes (entries 1 and 8). It is noteworthy that the amount of $InCl_3$ could be reduced to 1 mol% (entry 2). The benzylation using $AlCl_3$, $ZnCl_2$, or TFSA resulted in low yields less than 10% (entries 5, 6 and 7) in which dibenzyl ether was a main product (entries 6 and 7). These results proved the superiority of $InCl_3$ catalyst on reductive Friedel-Crafts alkylation to the regular type of Friedel-Crafts catalysts. $In(OTf)_3$

was also effective to give over 70% yields (entries 4 and 16). The reaction of benzene with *p*-chlorobenzaldehyde proceeded at 60 °C for 3 h in 98% yield (entry 11). The benzylation of anisole gave a mixture of *ortho-* and *para-*(methoxyphenyl)phenylmethane in 74% yield (entry 9), whereas $Sc(OTf)_3$ catalyst was reported to give low yield [3]. *Ortho-* and *para-*alkylations are predominant in a similar degree to usual Friedel-Crafts reactions. A notable advantage of $InCl_3$-$Me_2SiClH$ is the effective alkylation of deactivated aromatics like halobenzene, and another advantage is the usage of ketones as alkylating reagents. (Bromophenyl)phenylmethane was produced from benzaldehyde and bromobenzene in 93% yield (entry 10). Both aromatic and aliphatic ketones could be utilized to give the corresponding alkylated aromatics in moderate to good yields (entries 13 to 18). No precedents for these advantages have been reported in reductive Friedel-Crafts alkylation. An aliphatic aldehyde like hexanal, however, gave no alkylation products, resulting in the quantitative formation of dialkyl ether (entry 12). All reactions mentioned required the use of $Me_2SiClH$, because neither $Et_3SiH$ nor $MeSiCl_2H$ effected the reaction of benzaldehyde with benzene. However, $Et_3SiH$ could be applicable to only the benzylation of anisole, furnishing a mixture of *ortho-* and *para-*(methoxyphenyl)phenylmethane in 53% yield (eq.2). On the other hand, $MeSiCl_2H$ gave a complicated mixture.



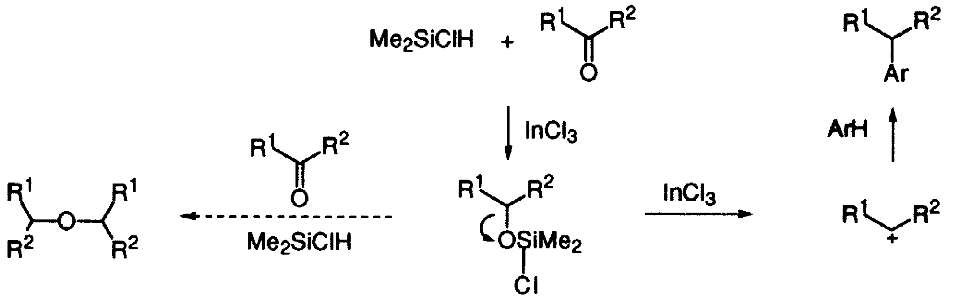
(2)

A plausible mechanism is proposed as shown in Scheme 1, which has a run of three steps; hydrosilylation of carbonyl group, generation of carbocation by desiloxylation, and alkylation of an aromatic. The facile hydrosilylation was demonstrated by the reaction of benzaldehyde and $Me_2SiClH$ in benzene solution at 0 °C. (Benzyloxy)chlorodimethylsilane which independently prepared from benzyl alcohol was treated with benzene at 25 °C for 14 h to give diphenylmethane quantitatively (eq.3). Quite recently, a similar Friedel-Crafts reaction of anisole with isolated trimethylsilyl ether was achieved by trimethylsilyl bis (trifluoromethanesulfonyl) amide as a promoter [5].



(3)

Both of the hydrosilylation and alkylation steps proved to proceed only in the presence of $InCl_3$, and this is the reason why the reductive Friedel-Crafts alkylation was effectively achieved. If the resulting silyl ether reacts with starting carbonyls, the formation of ethers is a serious problem. It is the case of using $ZnCl_2$ or TFSA instead of $InCl_3$ (entries 6 and 7). In fact, although many reductions of carbonyl compounds with silyl hydride in the presence of Lewis- or Brønsted acids such as $BF_3$ [6], $Me_3SiI$ [7], and $CF_3COOH$ [8] have been reported, no application to Friedel-Crafts alkylation has been achieved. In contrast to ketones, alkyl aldehydes are susceptible to react with the resulting silyl ethers even in the $InCl_3$ system (entry 12). Moreover the use of (*n*-hexyloxy)chlorodimethylsilane as alkylating reagent gave no desirable adduct in the presence of $InCl_3$, where the silyl ether was almost recovered. Secondary carbocation from alkyl ketones is more stable to the primary one from alkyl aldehydes, and this is also responsible for the preferable application of the ketones more than the aldehydes. In the formation of carbocation, the strong electronegativity of the chloro-substituent on silicon atom is thought to be responsible for facile cleavage of the O-C bond, and so not trialkylsilane but $Me_2SiClH$ is essential in this system. Of course, the formation of free carbocation is tentatively illustrated.



Scheme 1

In conclusion, we have developed a novel type of reductive Friedel-Crafts alkylation which is promoted by $InCl_3$ and $Me_2SiClH$. This methodology represented the first application of hydrosilane to reductive Friedel-Crafts alkylation. The characteristic function of $InCl_3$ is under investigation.

## Acknowledgement

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