Indium Triiodide (InI_3)-Catalyzed Allylation of Carbonyl Compounds by Allylic Tins

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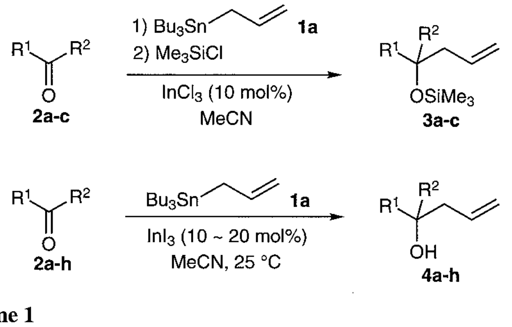
Abstract: Indium triiodide is an effective catalyst for the allylation of aldehydes *via* the transmetallation with allylic tin compounds. Moreover, the chelation-controlled allylation of α-alkoxyketones proceeded with a catalytic amount of indium triiodide.

Organotin compounds are versatile reagents for organic synthesis because of their manifold availability. An appropriate activation, however, is often required for their synthetic use.[1] A generation of other metallic species by transmetallation is one of promising activation methods.[2] The transmetallation between indium trichloride ($InCl_3$) and organotin compounds has recently attracted much attention[3] because of the unique reactivities of organoindium reagents.[4] The reaction using the transmetallation, however, needs an equimolar amount of $InCl_3$.[3] In a previous paper we have reported that $InCl_3$-catalyzed alkynylation of aldehydes with alkynyltins took place *via* the solvent-controlled transmetallation in the presence of chlorotrimethylsilane (Me_3SiCl).[5] In the course of extending this method to allylation of carbonyl compounds, we found that a catalytic amount of indium triiodide (InI_3) was sufficient to promote the allylation even in the absence of Me_3SiCl (Scheme 1). In addition, this InI_3-catalyzed system promoted the stereoselective allylations; predominant formation of *anti*-adducts from *E*-form of allylic tins and a chelation-controlled allylation of α-alkoxyketones.



Scheme 1

Table 1 shows the results of $InCl_3$-catalyzed allylation of aldehydes assisted by Me_3SiCl. Allyltributyltin (**1a**) and Me_3SiCl were subsequently added to a solution of aldehydes and $InCl_3$ (10 mol%) in acetonitrile, furnishing homoallyl trimethylsilyl ethers **3** in excellent yields (entries 1, 4 and 6). An equimolar amount of Me_3SiCl appeared to be essential for the catalytic use of $InCl_3$, because in the absence of Me_3SiCl, the formation of homoallyl alcohols **4** was strikingly depressed (entries 2 and 7) except for the allylation of benzaldehyde (entry 5). This method has a synthetic advantage for the facile isolation of silyl ethers produced after usual aqueous workup perhaps because of the weak acidic conditions and sluggishness of $InCl_3$ for water. In many cases, the isolation has required the addition of a base under carefully controlled conditions.[6] When an equimolar amount of $InCl_3$ was used without Me_3SiCl, 92% yield of homoallyl alcohol **4a** was obtained (entry 3).

Table 1. Indium Trichloride Catalyzed Allylation of Aldehydes.

Entry	Aldehyde	Temp /°C	Time /min	Yield /%[a]
1	**2a**: trimethylacetaldehyde	25	15	99[b]
2[c]	**2a**: trimethylacetaldehyde	25	15	35[d]
3[e]	**2a**: trimethylacetaldehyde	25	15	92[d]
4	**2b**: benzaldehyde	0	10	99[b]
5[c]	**2b**: benzaldehyde	25	10	94[d]
6[f]	**2c**: 3-phenylpropionaldehyde	25	15	92[b]
7[c]	**2c**: 3-phenylpropionaldehyde	25	15	23[d]

[a] GLC yield. [b] Homoallyl trimethylsilyl ether was obtained. [c] Without Me_3SiCl. [d] Homoallyl alcohol was obtained. [e] An equimolar amount of $InCl_3$ was used without Me_3SiCl. [f] Me_3SiCl was added *via* an addition funnel over 15 min.

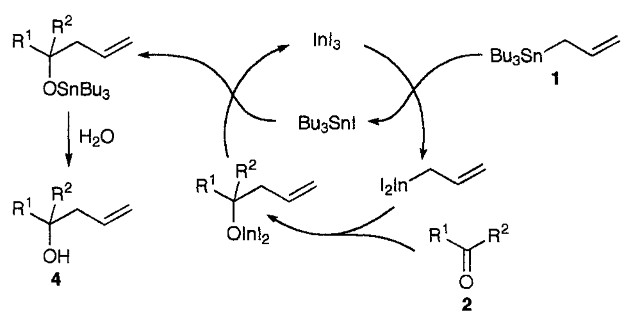
Next, InI_3 was employed as a catalyst instead of $InCl_3$, which was found to effectively promote the allylation even in the absence of Me_3SiCl as shown in Table 2.

To a mixture of InI_3 (10 mol%) and allylic tin **1a** in acetonitrile was added aldehyde **2a** at 25 °C. After 60 min, homoallyl alcohol **4a** was obtained in 92% yield (entry 1). Premixing of aldehydes and InI_3 resulted in decline of yield (entry 3). In this catalyst system, either aromatic (entry 6) or alkyl aldehyde (entry 7) gave the corresponding adducts **4** in high yields. When Me_3SiCl was added, the corresponding silyl ether **3a** was obtained in 85% yield (entry 2). The generation of allylic indium species is plausibly involved because fast transmetallation between InI_3 and allyltributyltin **1a** was confirmed by ^{119}Sn NMR in which quantitative formation of tributyltin iodide (Bu_3SnI) was observed in acetonitrile at 25 °C. Although the activation of carbonyl moieties by InI_3 as a Lewis acid can not be completely excluded at this stage, the acidity of InI_3 being weaker than $InCl_3$ supposed the participation of the transmetallation. A plausible catalytic cycle by InI_3 requiring no trap reagents like Me_3SiCl is shown in Scheme 2.

Table 2. Indium Triiodide Catalyzed Allylation.

Entry	Carbonyl Compound	Time	Yield /%[a]
1	**2a**: trimethylacetaldehyde	1 h	92
2[b]	**2a**: trimethylacetaldehyde	15 min	85[c]
3[d]	**2a**: trimethylacetaldehyde	1 h	71
4[e]	**2a**: trimethylacetaldehyde	1 h	39
5[f]	**2a**: trimethylacetaldehyde	1 h	38
6	**2b**: benzaldehyde	5 min	98
7[g]	**2c**: 3-phenylpropionaldehyde	30 min	88
8	**2d**: 2-methoxyacetophenone	10 min	89
9	**2e**: acetophenone	17 h	48
10	**2f**: benzoin methyl ether	2 h	88 (94% de)[h]
11	**2g**: benzoin	16 h	80 (80% de)[h]
12	**2h**: benzoin *i*-propyl ether	3 h	81 (24% de)[h]
13[i]	**2f**: benzoin methyl ether	30 min	76 (99% de)[c,h]
14[j]	**2g**: benzoin	30 min	81 (99% de)[c,h]

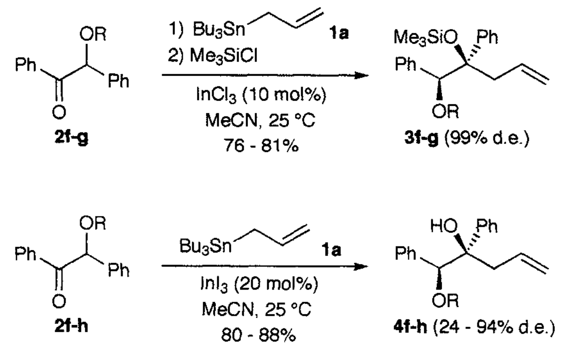
[a] GLC yield. [b] An equimolar amount of Me_3SiCl was added. [c] Homoallyl trimethylsilyl ether was obtained. [d] Aldehyde and InI_3 were premixed. [e] An equimolar amount of $InCl_3$ was used. [f] An equimolar amount of Bu_3SnI was added. [g] 0.2 equiv of InI_3 was added. [h] NMR yield. [i] Instead of InI_3, 0.1 equiv of $InCl_3$ was added with an equimolar amount of Me_3SiCl. [j] Me_3SiCl was added *via* an addition funnel over 30 min.



Scheme 2

In this cycle, effective trap by Bu_3SnI formed in the first transmetallation between InI_3 and allyltributyltin is postulated. It was a little surprising that the addition of an equimolar amount of InI_3 (entry 4) or that of Bu_3SnI (entry 5) suppressed the allylation in contrast to the case of $InCl_3$ where a quantitative allylation was observed as aforementioned (Table 1, entry 3). A large amount of Bu_3SnI might depress the transmetallation or decompose an intermediate. In any way, the use of a catalytic amount of InI_3, not stoichiometric, is essential for the effective allylation.

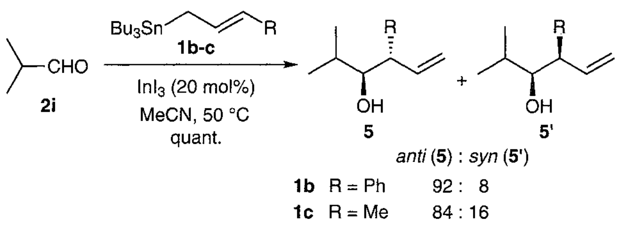
The more effective allylation of 2-methoxyacetophenone (89% yield in 10 min, entry 8) compared to that of acetophenone (48% yield in 17 h, entry 9) indicated the presence of strong chelation between indium center and methoxy oxygen (Scheme 3).



Scheme 3

As expected, the chelation-controlled allylation of benzoin methyl ether **2f** took place, giving *syn* adduct **4f** in 94% d.e. (entry 10). In general, stoichiometric Lewis acids have been indispensable in chelation-controlled addition.[7] Moreover, benzoin bearing free hydroxy group which is incompatible with Lewis acids like $AlCl_3$ and BF_3 could be successfully applicable although a long reaction time was needed (entry 11). A sterically hindered benzoin isopropyl ether **2h**, however, decreased the diastereoselectivity to 24% d.e. (entry 12). The catalytic system, $InCl_3$-Me_3SiCl, promoted the chelation-controlled allylation more effectively perhaps due to the stronger acidity of indium chloride compounds than the iodide (99% d.e., entries 13 and 14), completing even the allylation of benzoin within 30 min by dropwise addition of Me_3SiCl (entry 14).

Next the stereochemistry in the reaction of γ-substituted *E*-allylic tins like **1b** and **1c** with isobutyraldehyde **2i** was investigated, in which *anti* adducts were predominantly produced (Scheme 4). This stereochemical outcome strongly suggests the idea that allylindium species generated by the transmetallation react with aldehydes through a cyclic transition state.[8] A similar example of the $InCl_3$-Me_3SiCl system has been briefly reported in our previous paper.[5]



Scheme 4

In conclusion, InI_3 proved unique catalysts in the allylation using allylic tin compounds, demonstrating some synthetic advantages; convenient synthesis of homoallyl alcohol and highly chelation-controlled allylation even by a catalytic amount of indium triiodide.

Acknowledgements

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