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Ionic Liquid-accelerated Allylation of Carbonyl Compounds with a Catalytic Amount of Indium Generated from In Situ Reduction of $InCl_3$ with Aluminum

Tsunehisa Hirashita,* Yuki Sato, Dai Yamada, Fusako Takahashi, and Shuki Araki
Omohi College, Graduate School of Engineering, Nagoya Institute of Technology,
Gokiso-cho, Showa-ku, Nagoya, Aichi 466-8555

(Received February 9, 2011; CL-110110; E-mail: hirasita@nitech.ac.jp)

In ionic liquids allylation of carbonyl compounds with a catalytic amount of indium(III) trichloride proceeds smoothly to give the corresponding homoallylic alcohol in the presence of aluminium. The corresponding dimeric ethers are also formed.

Indium-mediated allylations of carbonyl compounds have been extensively studied during the last two decades.[1–4] Allylindium reagents can be prepared from stoichiometric amounts of metallic indium and allylic halides in polar solvents, including water, and can be used for allylation of carbonyl compounds in a Barbier-type manner. We previously reported the allylation of carbonyl compounds with a catalytic amount of indium(III) trichloride and a stoichiometric amount of aluminium(0) in aqueous THF.[5] This method permits us an easy access to reactions of allylic indium reagents with a reduced amount of relatively expensive indium metal. However, this allylation proceeds slowly; a couple of days are needed to complete the reaction. Ionic liquids have emerged in organic synthesis as a recyclable solvent and reactions of organometallic reagents with carbonyl compounds can be performed in ionic liquids.[6–9] Although formation of allylindium reagents in ionic liquids has been reported,[10–12] allylation with a catalytic amount of indium has not appeared.

We initiated a reaction of allyl bromide and benzaldehyde with a catalytic amount of indium(III) trichloride in 1-butyl-3-methylimidazolium hexafluorophosphate ($bmim{\cdot}PF_6$). The reaction, just changing the solvent from aqueous THF as we reported previously, did not proceed (Table 1, Entry 1). Even a stoichiometric amount of metallic indium gave no coupling product (Entry 2). Addition of water was found to show a significant effect on the allylation; the biphase reaction with a proper amount of water afforded the corresponding homoallylic alcohol **3** in high yields in shorter time than those performed in aqueous THF (Entries 3–6). The use of water alone inhibited the allylation (Entry 7). Without $InCl_3$, no reaction proceeded (Entry 8).

Table 1. Allylation of carbonyl compounds in ionic liquid[a]

Entry	Solvent	Time/h	Yield/%
1	$bmim{\cdot}PF_6$	100	0
2[b]	$bmim{\cdot}PF_6$	8	0
3	$bmim{\cdot}PF_6$–H_2O (5:1)	15	95
4	$bmim{\cdot}PF_6$–H_2O (5:1)	7	72
5	$bmim{\cdot}PF_6$–H_2O (5:2)	0.5	100
6	$bmim{\cdot}PF_6$–H_2O (1:1)	4	69
7	H_2O	4	trace
8[c]	$bmim{\cdot}PF_6$–H_2O (5:2)	0.5	0

[a]All reactions were carried out with allyl bromide (1.6 mmol), benzaldehyde (1.0 mmol), $InCl_3$ (0.10 mmol), and Al (1.6 mmol) in $bmim{\cdot}PF_6$ (1 mL) and water. [b]With In(0) powder (100 mol %). [c]Without $InCl_3$.

Table 2. Allylation of benzaldehyde in ionic liquids

$$\mathbf{1} + \underset{160\text{ mol\%}}{\mathbf{2}} \xrightarrow[\text{Ionic liquid-}H_2O\text{ (5:2), rt, 0.5 h}]{InCl_3\text{ (10 mol\%)},\ Al(0)\text{ (160 mol\%)}} \mathbf{3}$$

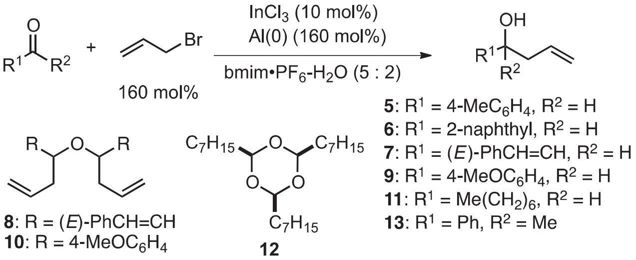
Entry	Ionic liquid	Yield/%
1	$bmim{\cdot}BF_4$	79
2	$emim{\cdot}BF_4$	67
3	$bpy{\cdot}PF_6$	78
4	$bmim{\cdot}Tf_2N$	0
5	$Et_2Me(MeOCH_2CH_2)N{\cdot}Tf_2N$	0

We next screened ionic liquids for this allylation (Table 2). $Bmim{\cdot}BF_4$ and 1-ethyl-3-methylimidazolium tetrafluoroborate ($emim{\cdot}BF_4$) gave **3** in good yields similar to that performed in $bmim{\cdot}PF_6$ (Table 2, Entries 1 and 2). 1-Butyl-4-methylpyridinium hexafluorophosphate ($bpy{\cdot}PF_6$) is also operative (Entry 3). In contrast, the reaction in bis(trifluoromethylsulfonyl)imide (NTf_2) salts did not give **3** (Entries 4 and 5).

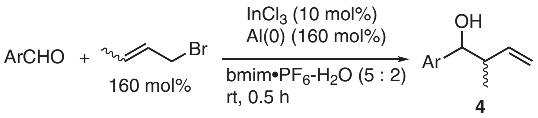
Recycling the ionic liquid and the catalyst was examined. The second use of the ionic liquid resulted in a low yield (40%) and the third recycling gave no coupling product. After repeating the allylation, the viscosity of the ionic liquid became higher. To circumvent this problem, the ionic liquid must be washed with water to remove the resulting aluminium hydroxide and this treatment entailed the addition of a catalytic amount of $InCl_3$ prior to the next reaction. Although it is difficult to selectively remove the aluminium hydroxide while maintaining the indium(III) salt in the ionic liquid at this stage, the ionic liquid can be recycled and reused for this allylation (1st: 86%, 2nd: 99%, 3rd: 81%).

The reaction of crotyl bromide with benzaldehyde in $bmim{\cdot}PF_6$ gave the corresponding homoallylic alcohol **4** with modest diastereoselectivity (eq 1). Allylic indium reagents favor intermolecular chelation with an oxygenated functional group and a pyridyl moiety giving chelation-controlled products even in the presence of water.[13] Salicylaldehyde and 2-pyridinecarbaldehyde often serve as good model compounds for this purpose;[14] however, the former gave modest *syn*-selectivity similar to the reaction of benzaldehyde and with the latter aldehyde the reaction did not proceed, indicating that chelation control may not be operative under the present conditions.

Table 3. Allylation of carbonyl compounds in ionic liquid



Entry	Carbonyl compound	Time/h	Product and Yield/%
1	4-MeC$_6$H$_4$CHO	0.5 [8]	**5**: 61 [96]
2	2-Naphthaldehyde	0.5 [24]	**6**: 41 [66]
3	(*E*)-PhCH=CHCHO	0.5	**7**: 46, **8**: 36
4	4-MeOC$_6$H$_4$CHO	24	**9**: 8, **10**: 60
5	Me(CH$_2$)$_6$CHO	0.5 [24]	**11**: 32 [21], **12**: 43 [56]
6	PhCOMe	24	**13**: 31



(1)

Ar = Ph: 91% (*syn*:*anti* = 64:36)
Ar = *o*-HOC$_6$H$_4$: 89% (*syn*:*anti* = 68:32)
Ar = 2-pyridyl: 0%

A series of carbonyl compounds were then submitted to the optimal conditions (Table 3). *p*-Tolaldehyde and 2-naphthaldehyde gave the corresponding homoallylic alcohols **5** and **6** and the yields were improved by prolonging reaction time (Entries 1 and 2). When cinnamaldehyde and *p*-anisaldehyde were employed, homoallylic alcohols **7** and **9** were obtained in low yields accompanied by unexpected formation of symmetric ethers **8** and **10** (Entries 3 and 4). Aliphatic aldehyde predominantly gave trioxane **12** in modest yield and **12** was accumulated (Entry 5). Acetophenone gave **13** in moderate yield (Entry 6).

It is known that 1,3,5-trioxanes are formed from aldehydes under the influence of ionic liquids[15] and indium salts.[16–18] In the present reaction, aluminium(III) salts and hydrochloric acid may be formed as the reaction proceeds and such Lewis and Brønsted acids, as well as InCl$_3$, are potential catalysts for the cyclization reaction. The symmetric ethers **8** and **10** are thought to be formed via the corresponding cationic intermediates generated by the above acids. In order to clarify the real active catalyst for this etherification, we conducted reactions of homoallylic alcohol **9** while altering the potential catalysts (Table 4). In the presence of InCl$_3$, alcohol **9** was converted into **10** in moderate yield (Entry 1, Table 4). With AlCl$_3$, low conversion was observed (Entry 2). Addition of water increased the yields (Entries 3 and 4). In(OH)$_3$, one possible hydrolysis product of InCl$_3$, did not catalyze the reaction, while combination with hydrochloric acid gave better yield (Entries 5 and 6). The presence of diluted hydrochloric acid alone was found to be enough to promote the reaction in the ionic liquid (Entry 7). It is noted that the use of the ionic liquid is crucial for the formation of symmetric ether **10**. In conventional organic solvents, such as PhMe, CH$_2$Cl$_2$, THF, and DMF, no reaction proceeded.

Table 4. Formation of **10** in ionic liquid[a]

$$\mathbf{9} \xrightarrow[\text{bmim•PF}_6\text{, rt, 0.5 h}]{\text{addtive}} \mathbf{10}$$

Entry	Additive (mol %)	Yield/% (dr)	Recovery of **9**/%
1[b]	InCl$_3$ (10)	20 (83:17)	0
2[b]	AlCl$_3$ (10)	12 (100:0)	0
3	InCl$_3$ (10)	44 (82:18)	0
4	AlCl$_3$ (10)	24 (54:46)	52
5[b]	In(OH)$_3$ (10)	0	91
6	In(OH)$_3$ (10)–1 M HCl (30)	66 (75:25)	0
7	1 M HCl (30)	53 (74:26)	17

[a]Unless otherwise noted, the reaction was performed with **9** (1.0 mmol) in a biphase system consisting of ionic liquid (1 mL) and the aqueous phase (0.4 mL). [b]In the absence of water.

In conclusion, catalytic InCl$_3$ and stoichiometric aluminium mediated allylation of carbonyl compounds proceeds in shorter time by using ionic liquids and water. The use of ionic liquid also brings enhancement of acidity and promotes the formation of the ethers from the homoallylic alcohols. Application of this transformation is currently under survey.

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