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Synthetic and Mechanistic Studies of Indium-Mediated Allylation of Imines in Ionic Liquids

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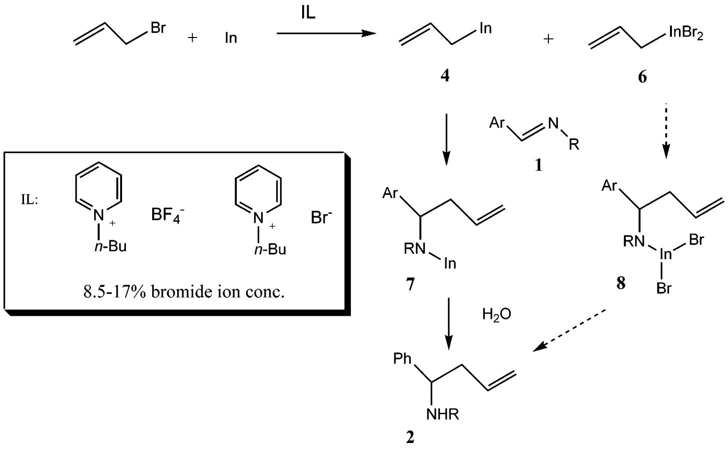

Aldimines derived from aryl and non-enolizable aliphatic aldehydes were allylated with allyl bromide mediated by indium powder in [bpy][BF$_4$] (bpy = *N*-butylpyridine) to give good yields of the corresponding homoallylic amines. Selective formation of monoallylated amines can be achieved by varying the amount of bromide ion additive in the form of [bpy][Br]. The transient organoindium intermediates, allylindium(I) and allylindium(III) dibromide formed in the reaction, were studied by NMR spectroscopy to explain the selectivity.

Introduction

Because of concern for the environment, there has been extensive recent research into the use of environmentally benign reaction media to replace volatile organic solvents.[1] Indium-mediated allylation of carbonyl compounds to give the corresponding homoallylic alcohols has been extensively studied in the past 2 decades,[2] especially with the discovery that the reaction can be carried out in aqueous media.[3] Indium-mediated allylation of imines to give homoallylic amines in water, on the other hand, has been less explored.[4] This is because of the known hydrolytic instability of imines in water[5] and the fact that indium can cause the reductive dimerization of imines.[6] So far, only hydrolytically robust and activated imine analogues

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(1) (a) Anastas P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, U.K., New York, NY, 1998. (b) Abraham, M.; Moens, L. *Clean Solvents: Alternative Media for Chemical Reactions and Processing*; ACS Symposium Series No. 819; American Chemical Society: Washington, DC, 2001.

(2) (a) Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1831. For review, see: (b) Cintas, P. *Synlett* **1995**, 1087. (c) Podlich, J.; Maier, T. C. *Synthesis* **2003**, 633.

(3) (a) Li, C. J.; Chan, T. H. *Tetrahedron Lett.* **1991**, *32*, 7017. (b) Chan, T. H.; Yang, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3228. (c) For, review, see: Li, C. J.; Chan, T. H. *Tetrahedron* **1999**, *55*, 11149.

(4) For reviews of metal-mediated allylation of imines in organic solvents, see: (a) Bloch, R. *Chem. Rev.* **1998**, *98*, 1407. (b) Kobayashi, S.; Ishitani, H. *Chem. Rev.* **1999**, *99*, 1069. (c) Keck, G. E.; Enholm, E. J. *J. Org. Chem.* **1984**, *50*, 146. (d) Yamamoto, Y.; Komatsu, T.; Maruyama, K. *J. Org. Chem.* **1985**, *50*, 3115. (e) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *49*, 7395. (f) Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395. (g) Wang, D. K.; Dai, L. X.; Hou, X. L. *Tetrahedron Lett.* **1995**, *36*, 8649. (g) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (i) Andrade, C. K. Z.; Oliveira, G. R. *Tetrahedron Lett.* **2002**, *43*, 1935. (j) Choucair, B.; Leon, H.; Mire, M. A.; Lebreton, C.; Mosset, P. *Org. Lett.* **2000**, *2*, 1851.

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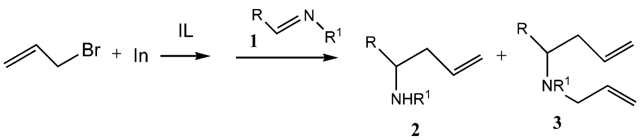
SCHEME 1



such as sulfonimines,[7] hydrazones,[8] and oxime ethers[9] have been employed in aqueous indium-mediated allylation. In addition to water,[10] supercritical carbon dioxide,[11] room-temperature ionic liquids (ILs),[12] and, of course, solvent-free conditions[13] have also been explored as reaction media to replace organic solvents. Recently, it has been reported that imines **1** (Scheme 1) can undergo allylation mediated by indium under solvent-free conditions to give a mixture of the monoallylated species **2** and the bis-allylated species **3**.[14] Indium-mediated allylation of imines in ionic liquids has not been reported, but a similar reaction in a nonvolatile solvent, poly(propylene glycol), has been reported with a limited range of substrates.[15] As part of our program on the study of organometallic reactions in ionic liquids,[16] we report here our results on the indium-mediated allylation of imines.

Results and Discussion

(1) Preliminary Studies. In the initial stage, we examined the allylation reaction of benzaldehyde imines **1** in the ionic liquid [bmim][BF$_4$] (bmim = *N*-butyl-*N'*-methylimidazolium). As we can see in Table 1, when the imine was derived from aniline (**1a**, R = Ph, entry 1), the homoallylic amine **2a** was obtained in moderate yield. However, the equivalent reaction with imine derived from benzylamine (**1b**, R = PhCH$_2$, entry 2) gave a mixture of products **2** and **3**, the mono- and bis-allylated species. Similar mixtures of **2b** and **3b** were obtained irrespective of the change in the reaction temperature, the relative ratios of In to allyl bromide and imine, or the kind of IL used (entries 2−7). In addition to [bmim][BF$_4$], we have used [emim][BF$_4$] (emim = *N*-ethyl-*N'*-methylimidazolium), [moemim][BF$_4$] (moemim = *N*-(methoxyethyl)-*N'*-methylimidazolium), and [bpy][BF$_4$] (bpy = *N*-butylpyridinium) as the reaction media. While there were variations in the yield, the product was invariably a mixture of **2b** and **3b**. In the case of [bpy][BF$_4$], we have also carried out the reaction with the addition of ZnF$_2$ or trimethylsilyl chloride ((TMS)Cl).[17] The reactions gave more or less the same mixture with similar yields (entries 8 and 9).

In the allylation reaction in [bpy][BF$_4$], we noticed that the reaction was highly irreproducible, giving at times little or no formation of the allylated amine **2** when different batches of ionic liquids were used. We finally realized that the reaction depended critically on the batch and purity of [bpy][BF$_4$] as we had previously observed for alkylzinc reactions in [bpy]-[BF$_4$].[16c] These observations prompted us to examine the ionic liquid precursor [bpy][Br] as the additive for the reaction. The results are summarized in Table 2. Indeed, the allylation reaction of **1a** gave no or low yield of homoallylic amine **2a** in pure [bpy][BF$_4$] (entry 1) or with only about 4% of [bpy][Br] added (entry 2). The yield of **2a** was substantially increased when about 8% of [bpy][Br] was added and the reaction temperature was increased (entries 4 and 5). With a lesser amount of imine **1a** relative to that of In and allyl bromide, the yield of **2a** was essentially quantitative with >8.5% bromide ion in the reaction media (entries 5−7). An observable effect of the addition of bromide ion (in the form of [bpy][Br]) was that the indium metal powder did not form a cake together during the reaction when about 8.5% of bromide ion was added.

Addition of [bpy][Br] was also found to have an equally remarkable effect on the allylation of **1b**. No allylation occurred in its absence (entry 8). When about 4.3% of bromide ion was added, a mixture of products **2b** and **3b** resulted (entries 9 and 10). To our delight, in the presence of 8.5% bromide ion, the allylation of **1b** gave **2b** only in excellent yield without the formation of **3b** (entries 11 and 12). The use of larger excess of [bpy][Br] gave a similar result (entries 13 and 14). Finally, if excess allyl bromide (2.5 equiv to In) was added to the reaction mixture after the overnight stirring, the eventual product was exclusively **3b** (entry 16), suggesting that **3b** was derived from the allylation of **2b** or more likely its precursor before hydrolytic workup.

(2) Mechanistic Investigations. (a) The Nature of the Allylindium Intermediates in Ionic Liquids. We have also studied the reaction mechanism of the indium-mediated allylation reaction in ionic liquids. Our first task was to identify the reactive allylindium intermediates formed. It is known from our previous study of the reaction of indium metal with allyl bromide in water that a transient reactive species, allylindium(I) (**4**), is formed.[3b] Compound **4** has a characteristic methylene proton NMR signal at δ 1.7 ppm (d, $J = 8$ Hz) in D$_2$O (Scheme 2). In contrast, when indium metal reacts with allyl bromide in an organic solvent such as dimethylformamide (DMF), the ^{1}H NMR has two sets of allylic methylene signals at δ 1.75 (d, $J = 8$ Hz) and δ 2.02 (d, $J = 8$ Hz) in DMF-d_7.[2a,3a] Previously, the allylindium species in DMF was assigned to have the indium sesquihalide structure **5** to account for the two sets of methylene

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(5) (a) Paquette, L. A. In *Green Chemistry, Frontiers in Chemically Benign Synthesis and Processes*; Anastas, P. J., Williamson, T. C., Eds.; Oxford University Press: Oxford, U.K., New York, NY, 1998; p 261 and footnote 49. (b) Vilaivan, T.; Winotapan, C.; Shinada, T.; Ohfune, Y. *Tetrahedron Lett.* **2001**, *42*, 9073.

(6) Lalyanam, N.; Rao, G. V. *Tetrahedron Lett.* **1993**, *34*, 1647.

(7) (a) Chan, T. H.; Lu, W. *Tetrahedron Lett.* **1998**, *39*, 8605. (b) Lu, W.; Chan, T. H. *J. Org. Chem.* **2000**, *65*, 8589. (c) Lu, W.; Chan, T. H. *J. Org. Chem.* **2001**, *66*, 3467.

(8) (a) Kumar, H. M. S.; Anjaneyulu, S.; Reddy, E. J.; Yadav, J. S. *Tetrahedron Lett.* **2000**, *41*, 9311. (b) Miyabe, H.; Ueda, M.; Nishimura, A.; Naito, T. *Org. Lett.* **2002**, *4*, 131. (c) Miyabe, H.; Yamaoka, Y.; Naito, T.; Takemoto, Y. *J. Org. Chem.* **2004**, *69*, 1415. (d) Cook, G. R.; Maity, B. C.; Kargbo, R. *Org. Lett.* **2004**, *6*, 1741. (e) Cook, G. R.; Kargbo, R.; Maity, B. *Org. Lett.* **2005**, *7*, 2767.

(9) (a) Miyabe, H.; Nishimura, A.; Ueda, M.; Naito, T. *Chem. Commun. (Cambridge)* **2002**, 1454. (b) Bernardi, L.; Cere, V.; Femoni, C.; Pollicino, S.; Ricci, A. *J. Org. Chem.* **2003**, *68*, 3348.

(10) Li, C. J.; Chan, T. H. *Organic Reactions in Aqueous Media*; John Wiley & Sons: New York, 1997.

(11) Jessop, P. *Chemical Synthesis Using Supercritical Fluids*; Wiley-VCH: Weinheim, Germany, 1999.

(12) Rogers, R. D.; Seddon, K. R. *Ionic Liquids: Industrial Applications to Green Chemistry*; Oxford University Press: Washington, DC, 2002.

(13) (a) Tanaka, K.; Toda, F. *Chem. Rev.* **2000**, *100*, 1025. (b) Varma, R. S. *Green Chem.* **1999**, 43.

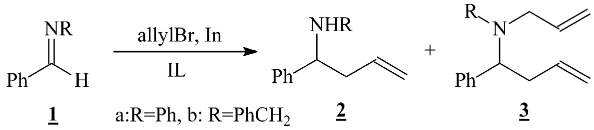
(14) Andrews, P. C.; Peatt, A. C.; Raston, C. L. *Tetrahedron Lett.* **2004**, *45*, 243. A likely drawback associated with solvent-free reaction is that many solid aldehydes did not give a satisfactory result as the mixture tended to solidify readily and gave incomplete reaction.

(15) Andrews, P. C.; Peatt, A. C.; Raston, C. L. *Green Chem.* **2004**, *6*, 119. At present, this method is applicable only to sulfonimines and aldimines derived from aromatic anilines and aldehydes.

(16) (a) Law, M. C.; Wong, K. Y.; Chan, T. H. *Green Chem.* **2002**, *4*, 328. (b) Law, M. C.; Wong, K. Y.; Chan, T. H. *Green Chem.* **2004**, *6*, 241. (c) Law, M. C.; Wong, K. Y.; Chan, T. H. *J. Org. Chem.* **2005**, *70*, 10434. (d) Law, M. C.; Wong, K. Y.; Chan, T. H. *Chem. Commun. (Cambridge)* **2006**, 2457.

(17) Wang, D.; Dai, L.-N.; Hou, X.-L. *Tetrahedron Lett.* **1995**, *36*, 8649.

TABLE 1. Indium-Mediated Allylation Reaction in Ionic Liquids (IL)[a]



entry	IL	additive	**1**	**1**/In/allylBr (mmol)	temp (°C)	yield[b] (%) 2	yield[b] (%) 3
1	[bmim][BF$_4$]	/	**1a**, R = Ph	1/1/1	Rt	48	0
2	[bmim][BF$_4$]	/	**1b**, R = CH$_2$Ph	1/1/1	Rt	27	14
3	[bmim][BF$_4$]	/	1b	1/1/1	50	18	21
4	[bmim][BF$_4$]	/	1b	1/2/2	rt	43	15
5	[emim][BF$_4$]	/	1b	1/1/1	rt	17	12
6	[moemim][BF$_4$]	/	1b	1/1/1	rt	35	33
7	[bpy][BF$_4$]	/	1b	1/1/1	rt	25	21
8	[bpy][BF$_4$]	ZnF$_2$ (0.5 eqiv)	1b	1/1/1	rt	32	12
9	[bpy][BF$_4$]	(TMS)Cl (0.5 eqiv)	1b	1/1/1	rt	28	12

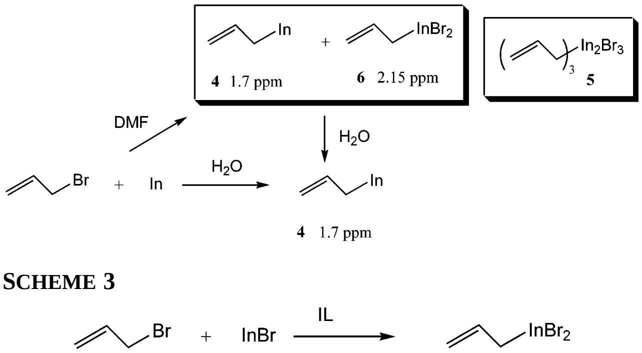
[a] Reaction conditions: In and allyl bromide in the indicated millimoles ratios were stirred in IL (1 mL) for 1 h at room temperature. Imine **1** was then added, and the stirred mixture was brought to the indicated temperature for 12 h. [b] Yields of **2** and **3** were determined by ^{1}H NMR.

TABLE 2. Effect of Bromide Ion on Product Distribution in the Allylation of Imines 1[a]

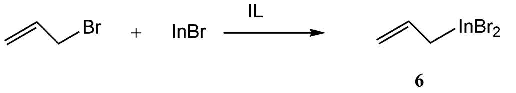
entry	[bpy][Br] added (% Br$^-$)	imine **1**	In/allylBr/**1** (mmol)	temp (°C)	isolated yield[d] (%) 2	isolated yield[d] (%) 3
1	− (0)	**1a**	1/1/1	rt	0	0
2	0.05 g (4.3)	**1a**	1/1/1	rt	21	0
3	0.1 g (8.5)	**1a**	1/1/1	rt	43	0
4	0.1 g (8.5)	**1a**	1/1/1	50	93	0
5	0.1 g (8.5)	**1a**	1/1/0.5	rt	100	0
6[b]	0.1 g (8.5)	**1a**	1/1/0.5	rt	82	0
7	0.15 g (12.8)	**1a**	1/1/0.5	rt	100	0
8	0.2 g (17.1)	**1a**	1/1/0.5	rt	100	0
9	− (0)	**1b**	1.5/1.5/1	rt	0	0
10	0.05 g (4.3)	**1b**	1.5/1.5/1	rt	41	39
11	0.05 g (4.3)	**1b**	1/1/1	rt	29	34
12	0.1 g (8.5)	**1b**	1.5/1.5/1	rt	90	0
13	0.1 g (8.5)	**1b**	1/1/0.5	rt	100	0
14	0.1 g (17.1)	**1b**	1/1/0.5	rt	100	0
15	0.2 g (17.1)	**1b**	1/1/1	rt	93	
16[c]	0.2 g (8.5)	**1b**	1/1/0.5	rt	0	100

[a] Reaction conditions: In and allyl bromide in the indicated mmol ratios were stirred in pure [bpy][BF$_4$] (1 mL with the indicated amount of [bpy][Br] added) for 1 h at room temperature. Imine **1** prepared in ionic liquid via condensation reaction of benzaldehyde with aniline was added to the presynthesized allylic indium compounds prepared as described above at the indicated temperature for 12 h. [b] Entry 6: All the starting materials including pure imine **1** were added at the beginning of the reaction in the same reaction vessel. [c] Entry 16: excess amount of allyl bromide (2.5 equiv to In) was added to the reaction mixture after overnight stirring. [d] Yields were determined by ^{1}H NMR.

SCHEME 2



SCHEME 3



6

signals.[18] The structural assignment was clearly incorrect as the δ 1.75 species could be extracted into D$_2$O and found to be identical to allylindium(I). It was concluded by us that the two sets of signals at δ 1.75 and δ 2.15 in DMF were due to the formation of two allylindium compounds, one of which at δ 1.7 was **4** and the other tentatively assigned to have allylindium(III) dibromide (**6**) or its dimer as the structure.[19,20] What then are the structures of the reactive allylindium species formed in ionic liquids?

We had previously reported that in the ionic liquid, [emim][BF$_4$], indium reacted with allyl bromide to give, in the ^{1}H NMR, two sets of allylic methylene signals at δ 1.75 (d, J = 8 Hz) and δ 2.02 (d, J = 8 Hz).[16a] We have now repeated the same reaction of allyl bromide and indium (at 1:1 ratio of 1.5 mmol) at room temperature in pure [bpy][BF$_4$] (1 mL). In 10 min, two sets of allylic signals were revealed at δ 1.75 and δ

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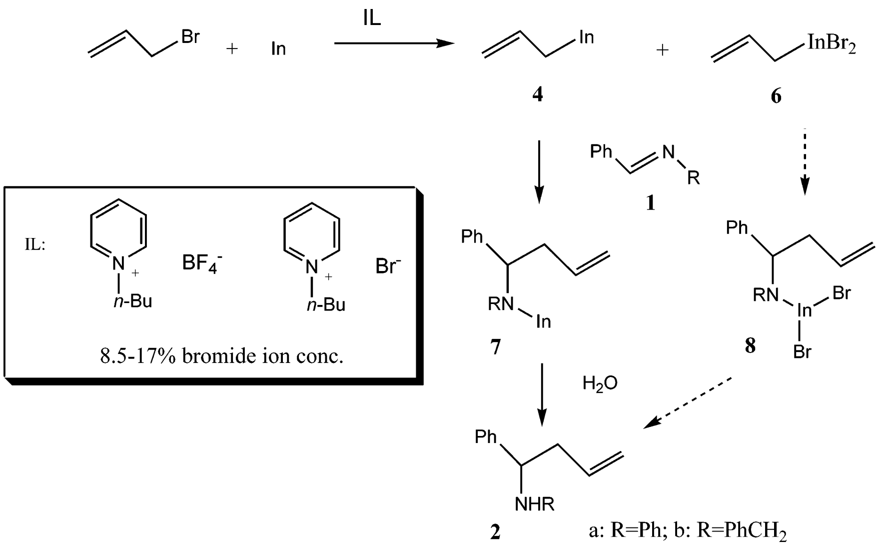
(18) (a) Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1831. (b) Araki, S.; Shimizu, T.; Johar, P. S.; Jin, S. J.; Butsugan, Y. *J. Org. Chem.*, **1991**, *56*, 2538.

(19) Formation of allylindium(III) diiodide was reported by the reaction of indium(I) iodide with allyl iodide in THF with the allylic methylene signal at 2.1 ppm in THF-d_8. Araki, S.; Ito, H.; Katsumura, N.; Butsugan, Y. *J. Organomet. Chem.* **1989**, *369*, 291.

(20) The formation of allenylindium(I) and allenlylindium(III) dibromide in the reaction of indium with propargyl bromide has been reported. Miao, W.; Chung, L. W.; Wu, Y.-D.; Chan, T. H. *J. Am. Chem. Soc.* **2004**, *126*, 13326.

SCHEME 4

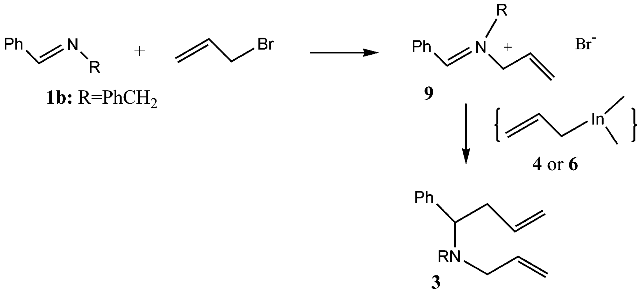


2.04 at a ratio of about 1:2. However, the signal at δ 1.75 gradually reduced and finally disappeared completely when the mixture was left for another 10−30 min. At the same period, the signal at δ 2.04 was enhanced. Since we have already found that **4** has the methylene signal at δ 1.7 ppm in D_2O and at δ 1.75 ppm in DMF, we conclude therefore that the set of methylene signals at δ 1.75 ppm in either [emim][BF_4] or [bpy]-[BF_4] have the **4** structure as well. To elucidate the structure of the second allylindium species at δ 2.04, we examined the reaction of indium(I) bromide with allyl bromide in [bpy][BF_4]/[bpy][Br] to give allylindium dibromide (**6**) (Scheme 3).[19] The reaction was found to be quite slow and there was still over 50% of the starting allyl bromide left after 3 h. Informatively, there were indeed methylene signals at δ 2.04 together with new olefinic peaks at δ 4.71 and 4.88 identical to the second species formed from indium and allyl bromide, indicating that the allylindium species formed is **6**.

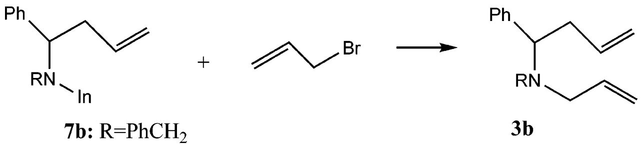
We have also investigated the relationship of the two allylindium species in [bpy][BF_4] by ^{1}H NMR with toluene as the internal standard. The intensity ratio of these two signals varied with time. The one at δ 1.75 declined gradually in intensity, whereas the signal at 2.04 increased, suggesting that **4** can be converted to **6** in the reaction mixture. The rate of conversion of **4** to **6** can be slowed down, however, if the ionic liquid [bpy][BF_4] contained some [bpy][Br] (between 8.5 and 17.5%).

(b) Formation of Homoallylic Amines 2. We then tried to examine the relative reactivity of **4** and **6** toward imine electrophiles. The reaction of allyl bromide with indium at room temperature in the system [bpy][BF_4]/[bpy][Br] (8.5% of bromide) was monitored by ^{1}H NMR. At the stage when both **4** and **6** were present in almost equal amounts, a small quantity of imine **1a** (0.5 equiv) was added to the mixture. The peaks corresponding to **4** were found to be reduced in intensity, and a new set of signals corresponding to the amido indium adduct **7a** could be observed. Eventually, compound **4** completely disappeared and only compound **6** together with the product **7a** were observed. The structure of adduct **7a** was confirmed by quenching the reaction mixture at this stage to give the monoallylic amine **2a**. This experiment therefore demonstrates that **4** reacts with imine **1a** to give the homoallylic amine **2a** via the adduct **7a** (Scheme 4). The alternative possibility of the reaction of **6** with imine **1a** to give the putative intermediate **8a** and then **2a** was either not operative or too slow to compete with the formation of **7a** with the limited amount of **1a** available.

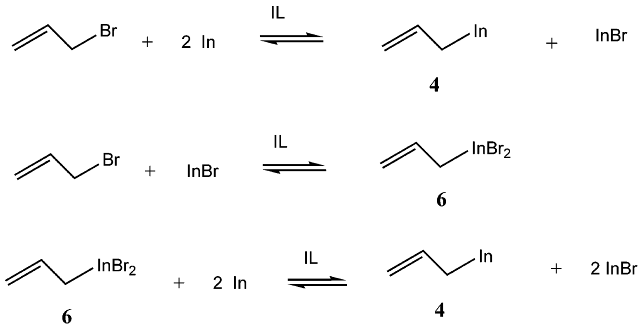
SCHEME 5



SCHEME 6

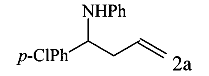
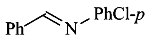
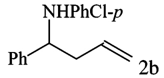
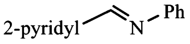
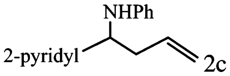
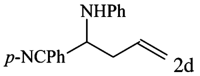
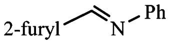
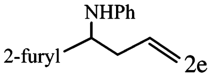
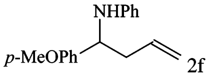
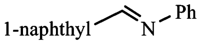
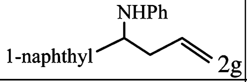
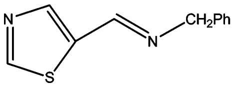
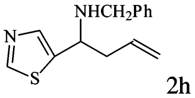
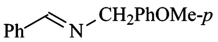
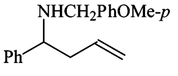
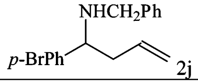
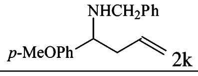
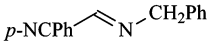
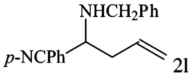
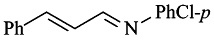
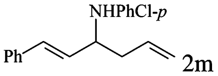


SCHEME 7



(c) Formation of Bis-allylated Amines 3. It has been proposed, under the solvent-free reaction conditions, that the bis-allylation product **3** was formed through an iminium salt **9** followed by nucleophilic addition of allylindium species (Scheme 5).[14] This was supported by the reaction of MeI and *N*-benzylideneaniline, which generated the presumed iminium salt.[21] To elucidate whether this may account for the formation

TABLE 3. Indium-Mediated Allylation Reaction of Aldimines[a]

Entry	Imine	In/allylBr/imine (mmol)	[Bpy][Br] /g	Homoallylamine	Yield (%)[b]
1	p-ClPhCH=NPh	1 / 1 / 0.5	0.1	 2a	70
		1.5 / 1.5 / 0.5			95
2		1.5 / 1.5 / 0.5	0.1	 2b	82
3		1.5 / 1.5 / 0.5	0.1	 2c	87
4	p-NCPhCH=NPh	1.5 / 1.5 / 0.5	0.1	 2d	70
			0.2		95
5		1.5 / 1.5 / 0.5	0.2	 2e	93
6	p-MeOPhCH=NPh	1.5 / 1.5 / 0.5	0.2	 2f	62
7		1.5 / 1.5 / 0.5	0.2	 2g	80
8		1.5 / 1.5 / 0.5	0.2	 2h	65
9		1.5 / 1.5 / 0.5	0.1	 2i	66
			0.2		91
10	p-BrPhCH=NCH$_2$Ph	1.5 / 1.5 / 0.5	0.2	 2j	99
11	p-MeOPhCH=NCH$_2$Ph	1.5 / 1.5 / 0.5	0.2	 2k	83
12		1.5 / 1.5 / 0.5	0.2	 2l	76
13		1.5 / 1.5 / 0.5	0.2	 2m	93

[a] Reaction conditions: Aldimines (0.5 mmol generated in situ in [bpy][BF$_4$]) was added to allylindium compounds (prepared in situ from the indicated amount of allyl bromide and indium) in [bpy][BF$_4$] (1 mL) with the indicated amount of [bpy][Br] added. The mixture was stirred overnight at room temperature. [b] Isolated yield.

of the bis-allylated amine **3** in ionic liquids, we investigated the possibility of generating the iminium ion in situ in ionic liquid by reacting allyl bromide and imine **1b**. However, the iminium salt **9** was not observed by ^{1}H NMR; the signals of allyl bromide and the imine **1b** remained unchanged regardless of reaction time and temperature (up to 50 °C). Since no iminium salt was involved in the allylation reaction, the bis-allylated product cannot be coming from the competitive nucleophilic attack of iminium salt by allylindium species.

We then tried to see whether the bis-allylated amine **3b** could be formed from the mono-allylated species. When 0.5 equiv of imine **1b** was added to 1.5 equiv of allylindium species (a 1:1 mixture of **4** and **6**, in situ generated by reacting indium and allyl bromide) in [bpy][BF$_4$]/[bpy][Br] (8.5% bromide), **4** was completely reacted. The mixture was left with unreacted **6** and the amido−indium adduct **7b**, Addition of a second aliquot of allyl bromide (0.5 equiv) to the reaction mixture at this stage was found to give bis-allylated product **3b** with **6** more or less unchanged in intensity. This proves that the bis-allyated amine **3b** can be derived from the reaction of **7b** with allyl bromide (Scheme 6).

There remains the question of whether allylindium(III) dibromide (**6**) could react with imine **1b** to give the bis-allylated amine **3b** as well. Instead of treating the above reaction mixture containing **6** and amido−indium adduct **7b** with a second aliquot of allyl bromide, it was quenched with a second aliquot of imine **1b** (0.5 equiv). Examination by ^{1}H NMR showed that the signal of adduct **7b** was enhanced slowly. To account for the enhanced amount of **7b**, we postulate that compound **6** can undergo reversible reaction to generate **4** which reacts rapidly with imine **1b** to give adduct **7b**.

(d) An Overview. From these observations, an overview of the mechanism of indium-mediated allyation of imine in IL

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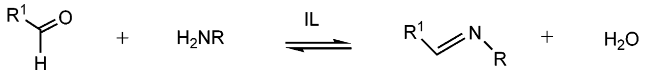
(21) Bohme, H.; Viehe, H. G. *Iminium Salts in Organic Chemistry.* Advances in Organic Chemistry; John Wiley & Sons: New York, 1976; Vol. 9.

TABLE 4. Yields of Imines from Aldehydes with Amines in Ionic Liquid Conditions[a]



entry	R^1	R	solvent	time	temp/^{0}C	yield^b (%)
1	Ph	Ph	[bpy][BF$_4$]	12 h	rt	80
2^c	Ph	Ph	[bpy][BF$_4$]	12 h	rt	90
3^d	Ph	Ph	[bpy][BF$_4$]	12 h	rt	94
4	Ph	Ph	[bpy][BF$_4$]	1 h + 2 h	rt/50	(94)
5	Ph	Ph	[bmim][BF$_4$]	1 h + 2 h	rt/50	(96)
6	*p*-ClPh	Ph	[bpy][BF$_4$]	1 h + 2 h	rt/50	(97)
7	*p*-BrPh	Ph	[bpy][BF$_4$]	1 h + 2 h	rt/50	(97)
8	2,6-dichloroPh	Ph	[bpy][BF$_4$]	1 h + 2 h	rt/50	(91)
9	NCPh	Ph	[bpy][BF$_4$]	1 h + 2 h	rt/50	(95)
10	*p*-MeOPh	Ph	[bpy][BF$_4$]	1 h + 2 h	rt/50	91.7
11	*p*-HOPh	Ph	[bpy][BF$_4$]	1 h + 2 h	rt/50	100
12	*trans*-PhCH═CH	Ph	[bpy][BF$_4$]	1 h + 2 h	rt/50	(99)
13	2-furyl	Ph	[bpy][BF$_4$]	1 h + 2 h	rt/50	100
14	2-pyridyl	Ph	[bpy][BF$_4$]	1 h + 2 h	rt/50	100
15	Ph	*p*-ClPh	[bpy][BF$_4$]	1 h + 2 h	rt/50	98
16	Ph	*p*-MeOPh	[bpy][BF$_4$]	1 h + 2 h	rt/50	100
17	Ph	CH$_2$Ph	[bpy][BF$_4$]	3 h	rt	(99)
18	Ph	*p*-MeOPhC H$_2$	[bpy][BF$_4$]	1 h + 2 h	rt	100

[a] Reaction conditions: Aldehyde (1 mmol) and amine (1 mmol) was added to the IL (2 mL) and stirred at room temperature for a specified time period followed by heating under vacuum at 50 °C for specified time. [b] Measured by ^{1}H NMR (isolated yields in parentheses). [c] Entry 2: 5 Å molecular sieves (small spheres) were added to the reaction mixture. [d] Entry 3.: 4 Å molecular sieves (fine powder) were added to the reaction mixture.

begins to emerge. First, indium reacts with allyl bromide in IL to give **4** together with indium(I) bromide. Subsequent reaction of InBr with allyl bromide gives **6**. There is a dynamic equilibrium between **4** and **6**, eventually with **6** predominant. The conversion between **4** and **6** may be mediated by indium metal and indium bromide according to Scheme 7. When bromide ion is present in greater than 8.5%, it retards the conversion of **4** to **6**, thus facilitating the formation of the mono-allylated amine **2** according Scheme 4.

(3) Allylation of Aldimines Mediated by Indium. With these mechanistic insights, we were able to devise reaction conditions that allow monoallylation of the imines. The standard reaction condition we have adopted involved the reaction of aldimine, indium powder, and allyl bromide in predried ionic liquid in a 0.5:1.5:1.5 ratio stirred overnight at room temperature. The homoallylic amine was extracted with ethyl acetate. There was no decomposition of starting materials or the production of homoallylic alcohols. The reaction proceeded smoothly with a variety of aldimines (Table 3). Both electron-rich and electron-deficient substituents bearing imines were found to be allylated smoothly. Heterocycles such as pyridine, furan, and thiazole did not present any difficulty (entries 3, 5, and 8). Imine derived from 1-naphthaldehyde worked well even though the 1-position may be relatively sterically hindered (entry 9). In cases where R is an α,*β*-unsaturated group, 1,2-addition was obtained without 1,4-addition (entry 13).[22] It is noteworthy that reactions could be performed on *N*-benzylidenebenzylamine and its analogues with good yields and excellent control of mono-allylated species formation.[23]

(4) Synthesis of Imines from Carbonyl Compounds and Amines in Ionic Liquids. We can also carry out the allylation with imines generated in situ from the aldehydes and amines in the ionic liquids. The aldehydes used can be aryl, heteroaryl, and α,*β*-unsaturated aldehydes. The amines can be substituted anilines and benzylamines. The aldehydes and amines were simply mixed in [bpy][BF$_4$] (or [bmim][BF$_4$]) and warmed to 50 °C under vacuum for a specified time. The water byproduct was presumably removed under these conditions, and the formation of imines was essentially quantitative. The results are summarized in Table 4. The imines thus formed were then allylated directly as described previously.

Conclusions

In conclusion, aldimines undergo nucleophilic addition with allylindium reagents generated from indium and allyl bromide to give the corresponding homoallylic amines in good to excellent yields in the presence of bromide ions. [bpy][BF$_4$]/[bpy][Br] was found to be a suitable reaction medium for the reaction. The nature of the allylindium species formed depends on the solvents used. In aqueous media, only allylindium(I) species was formed, whereas in the organic solvents and IL system, both allylindium(I) and allylindium(III) dibromide were observed. Allylindium(I) was found to be more reactive toward imines and responsible for the formation of the monoallyated amine **2**. There appears to be an equilibrium between allylindium(I) and diallylindium(III) dibromide, which accounts for the formation of the bis-allylated amine **3**. The presence of bromide ion appears to affect the equilibrium and help ensure the sufficient presence of allylindium(I) in the IL and, therefore, on reactions with imines, a good yield of **2**.

Experimental Section

(1) Preparation of Ionic Liquids. The crude *N*-butylpyridinium tetrafluoroborate ([bpy][BF$_4$]) was prepared by metathesis reaction in acetonitrile (300 mL) from sodium tetrafluoroborate (121 g, 1.1 mol,) (purchased commercially with 98% purity in fine powder form) and its bromide precursor [bpy][Br] (216 g, 1.0 mol) which was in turn prepared from the microwave-assisted method.[11] The

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[22] This is in contrast to the reaction of organolithiums, where both 1,2- and 1,4-addition were observed. See, for examples: Tamioka, K.; Inoue, I.; Shindo, M.; Kago, K. *Tetrahedron Lett.* **1990**, *31*, 6681.

[23] When R has an sp^3 carbon linked to nitrogen, the corresponding aldimines are generally less reactive, leading to poor yields and incomplete reactions or even no reaction at all. For examples, see: (a) Beuchet, P.; Marrec, N. L.; Mosset, P. *Tetrahedron Lett.* **1992**, *33*, 5959. (b) Nakamura, K.; Nakamura, H.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 2614.

mixture was stirred for 3 days at room temperature and then filtered. The filtrate was evaporated and the residue crude [bpy][BF_4] was vacuum-dried overnight at 70 °C (0.1 mmHg) and stored under nitrogen. Pure [bpy][BF_4] could be obtained by column chromatography of the crude [bpy][BF_4] on silica gel with dichloromethane as eluent.[12] The recovery of [bpy][BF_4] after chromatography was about 60%.

(2) Typical Procedure for the Preparation of Benzylideneanilines in Ionic Liquid. A 50 mL reaction tube was charged with the ionic liquid (2 mL). A mixture of benzaldehyde (1 mmol) and aniline (1 mmol) was added to ionic liquid (2 mL) at room temperature under nitrogen. The reaction mixture was stirred vigorously for the specified time and temperature as indicated in Table 4.

(3) Allyation of Imines in Ionic Liquids. Pure [Bpy][BF_4] (1 mL) with the indicated amount of [bpy][Br] added was used as reaction media. Indium and allylBr (in millimoles specified) were added and stirred at room temperature (rt) for 1 h. Imine (0.5 mmol generated in situ in IL) was then added to the reaction mixture and stirred at rt overnight. The resulting mixture was quenched with a few drops of saturated ammonium chloride solution followed by extraction with ethyl acetate (3 × 10 mL). After removal of the solvent in vacuum, the residue was purified by flash chromatography on silica gel to yield the pure adduct amine **2**.

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Supporting Information Available: ^1H and ^{13}C NMR spectra of compounds of **2a**−**2m** and **3b** and other physical data. This material is available free of charge via the Internet at http://pubs.acs.org.

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