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# Indium Trichloride-Promoted Tin-Mediated Carbonyl Allylation in Water: High Simple Diastereo- and Diastereofacial Selectivity

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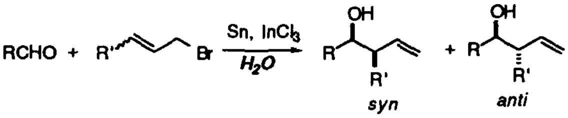
**Abstract:** Tin-mediated additions of allylic bromides to aldehydes and aldoses leads to adduct with high diastereo- and diastereofacial selectivity in the presence of indium trichloride in water. Copyright © 1996 Elsevier Science Ltd

The development of organic reactions in aqueous media for acyclic stereocontrol has recently gained popularity.[1] Among the various organometallic reagents that have been successfully employed, allyltin, allylzinc and allylindium reagents comprise a unique group which undergoes reactions with aldehydes in aqueous media.[2] In connection with our interest in developing new methodology in aqueous media for acyclic stereocontrol, we wish to report that indium trichloride[3a,3b] promoted tin-mediated coupling reactions of carbonyl compounds with various allylic bromides in *water* afforded the allylation products in good yield and high simple diastereo- and diastereofacial selectivities.

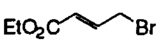
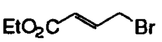
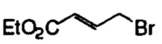
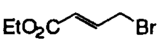
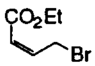
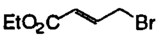
The indium trichloride promoted allylation reaction of aldehyde with allylic bromide is representative (eq 1). The mixture of tin (1 mmol), indium trichloride (0.5 mmol)[3c] and allylic bromide (1 mmol) in water (5 mL) was stirred for 4 hours at room temperature. The aldehyde (0.5 mmol) was then added and stirred until starting aldehyde was not detected by TLC. Commercially available tin powder was used. The yields reported were of isolated materials, following column chromatography over silica gel. All diasteroselectivity ratios were determined by $^1$H NMR analyses after column purification unless otherwise stated.



(eq 1)

In general the reactions were clean and only the γ-products were detected after aqueous workup. The major diastereomer in all cases was found to have the *anti* configuration, as indicated in Table 1. Especially noteworthy is the high *anti* diastereoselectivity (98% de) observed (entry 2 and entry 8). The level of diastereoselectivity of the processes is lower when the reactions are carried out without $InCl_3$ as catalyst (entry 6) or the (Z)-β-alkyl crotonate was used as the allylic bromide (entry 7). Furthermore, we observed no allylation product when the reaction was carried out in DMF. It is also important to note that premixing of indium trichloride, tin and γ-substituted allyl bromide is essential for the success of this reaction to be carried out in water. The stereochemical configuration of the product formed from benzaldehyde with ethyl 4-bromocrotonate was confirmed using the reported method.[4]

Table 1. Indium Trichloride-promoted Tin-mediated Allylation of Aldehydes[a]

| entry | aldehyde | Halide | Conditions | Yield (%)[c] | Isomer ratio[b] (*anti: syn*) |
|---|---|---|---|---|---|
| 1 | C6H5CHO |  | Sn, InCl3, H2O (15 h) | 80 | 50:50 |
| 2 | $C_6H_5CHO$ |  | Sn, $InCl_3$, $H_2O$ (15 h) | 45[d] | $99:1^5$ |
| 3 | $C_6H_5CHO$ |  | Sn, $InCl_3$, $H_2O$ (15 h) | 96 | 85:15 |
| 4 | $CH_2BrCHO$ |  | Sn, $InCl_3$, $H_2O$ (15 h) | 55 | 80:20 |
| 5 | 3-$C_5H_4NCHO$ |  | Sn, $InCl_3$, $H_2O$ (24 h) | 51 | 80:20 |
| 6 | $C_6H_{11}CHO$ |  | Sn, $H_2O$ (18 h) | 60 | 85:15 |
| 7 | $C_6H_{11}CHO$ |  | Sn, $InCl_3$, $H_2O$ (15 h) | 65 | 68:32 |
| 8 | $C_6H_{11}CHO$ |  | Sn, $InCl_3$, $H_2O$ (15 h) | 65 | 99:1 |

a All reaction were carried out on 0.5-1 mmol scale. b The isomer ratio was determined by $^1H$ or $^{13}C$ NMR.
c Isolated yield. d Balance of material is unreacted aldehyde

The strong preference of reactions for the *anti* adduct for the (*E*)- and (Z )-alkyl crotonate suggests that transmetallation is involved. Transmetallation from allyltin with indium trichloride as Lewis acid would proceed *via* an $S_E2'$ process to produce compound **1** which further rearranged to crotylindium reagent to give compound **2a** and some **2b** due to thermodynamic stability. No isomerisation of the starting materials was observed after reactions. The high *anti* selectivity observed in these reactions can be explained by the six-membered transition state as depicted in Figure 1.

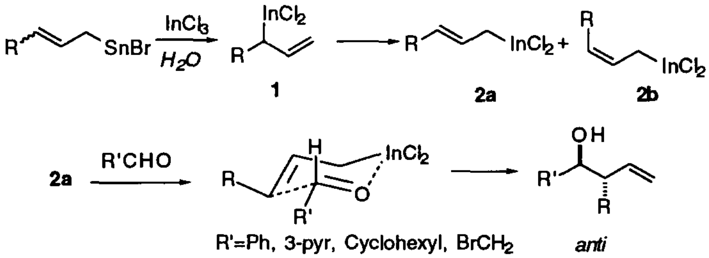
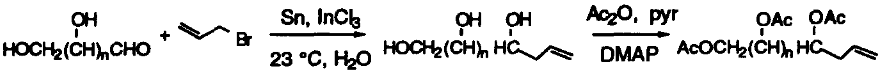


Figure 1

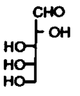
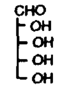
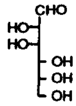
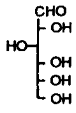
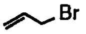
When the same strategy was applied to unprotected carbohydrates with the allyl bromide to investigate the reactivity and diastereofacial selectivity, the reaction was found to proceed smoothly at room temperature in water without heating or ultrasonication (eq 2). After the allylation reaction, the product was peracetylated with acetic anhydride following procedure as described by Whitesides.[2g] Interestingly, in most cases the reactions give the products in moderate to high diastereofacial selectivity. Especially noteworthy is the fact that hexoses reacted with allyl bromide under these conditions to give the corresponding products in high yield and

**high diastereofacial selectivity (Table 2).**



(eq 2)

Table 2. Indium Trichloride-promoted Tin-mediated Allylation of Unprotected Carbohydrate[a]

| entry | starting sugar | halide | conditions | yield(%)[b] | Isomer ratio[c] (*syn:anti*)[2g] |
|---|---|---|---|---|---|
| 1 |  <br>L-arabinose |  | Sn, $InCl_3$, $H_2O$ (24 h) | 90 | 75:25 |
| 2 |  <br>D-Ribose |  | Sn, $InCl_3$, $H_2O$ (24 h) | 92 | 84:16 |
| 3 |  <br>D-Mannose |  | Sn, $InCl_3$, $H_2O$ (24 h) | 85 | 94:6 |
| 4 |  <br>D-Glucose |  | Sn, $InCl_3$, $H_2O$ (24 h) | 60 | 95:5 |

a All reactions were carried out on 0.5-1 mmol scale. b Isolated yield after peracetylation and chromatography.
c As refer to C-2 hydroxyl group relative stereochemistry (determined by $^1H$ or $^{13}C$ NMR)

The formation of high *syn* selective product is most probably due to the 5-membered ring chelation between the C-1 carbonyl group, C-2 hydroxyl of the aldose and the allylindium formed in the transmetalation (Figure 2).

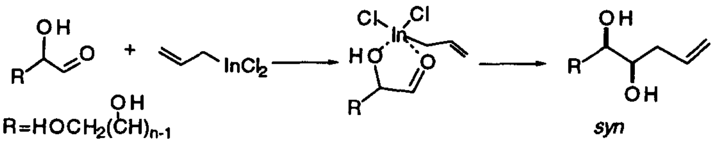


Figure 2

In summary, we reported a new tin-mediated allylation reaction promoted by indium trichloride in water. It is important to note that premixing of tin and indium trichloride is essential for the success of this reaction. It will serve as an attractive approach to the syntheses of homoallylic alcohols stereoselectively which may be readily transformed into various natural products. Further investigations are in progress to increase the applications of tin-mediated allylation reaction promoted by Lewis-acid in water such as the allylation of aldimines and the asymmetric version of the reaction.[6]

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3. (a) Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1995**, *60*, 1920. (b) Yasuda, M.; Miyai, T.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **1995**, *36*, 9497. (c) We have recently found that the reactions proceeded albeit more slowly, with as little as 0.1 equiv. of indium trichloride with respect to tin and allyllic bromide. In contrast to the system reported by Marshall and co-workers (ref. 3a), we have found that premixing of the indium trichloride, allylic bromide and tin increases rate and diastereofacial selectivity of the reaction. We are presently working to determine the fate of the tin species.
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6. This research was assisted financially by the National University of Singapore (Research Grant No. RP 940633, RP 930657 and 950609).

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