



SelectfluorTM-mediated allylstannation of aldehydes and imines

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Abstract—Reactions of aldehydes and imines with allyltributyltin catalyzed by SelectfluorTM in acetonitrile result in the formation of homoallylic alcohols and amines in good yields with excellent moisture and air tolerance. © 2002 Elsevier Science Ltd. All rights reserved.

Allylstannanes have been widely used for the efficient conversion of aldehydes and ketones to useful homoallylic alcohols.¹ Although a number of Lewis acids have been found to promote this reaction,^{1,2} some Lewis acids (e.g. AlCl₃ and TiCl₄) are very sensitive to moisture and difficult to handle in large-scale processes. Recently, some rare earth metal triflates were used to catalyze the allylstannation of aldehydes.^{2–5} However, these catalysts still need activation before use. New promoters with low toxicity, moisture and air tolerance, and low cost continue to merit exploration.

SelectfluorTM (1-chloromethyl-4-fluoro-1,4-diazoniabicyclo [2,2,2]octane bis(tetrafluoro-borate)) (Fig. 1) has recently been introduced commercially as a user-friendly electrophilic fluorinating reagent. It fluorinates a wide variety of electron-rich carbon centers with high yields.⁶ In addition, SelectfluorTM can be used easily to make 2-deoxy-2-fluoroglycosides from glycals under mild conditions.^{7,8} It also activates thioglycosides to form a reactive sulfonium intermediate suitable for glycosidation or further breakdown to form glycosyl fluorides. In the presence of dimethyl sulfide, it converts the anomeric hydroxyl to glycosyl fluoride.^{7,8} Mecha-

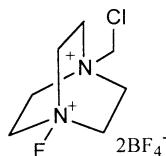


Figure 1. Structure of SelectfluorTM.

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nistic studies indicate that SelectfluorTM acts as an electrophilic fluorinating reagent in a two-electron process.⁸ The enantioselective fluorination can also be achieved when SelectfluorTM is used in combination with quinine derivatives.⁹ Most recently, we have reported that SelectfluorTM can act as an excellent deprotection reagent for the *p*-methoxybenzylidene (PMP), tetrahydropyranyl (THP) and dithiane groups due to its Lewis acidity.¹⁰ Considering SelectfluorTM's easy to use and stability, we further examined its utility in the allylstannation reactions.

The experimental results are shown in Table 1.¹¹ Both aromatic and aliphatic aldehydes gave satisfying results. The reaction usually proceeded to completion in hours when a stoichiometric amount of SelectfluorTM was used with acetonitrile as solvent. We found that the reaction was quite slow and usually gave approximately 60% conversion after 24 h if a catalytic amount (0.05 equiv.) of SelectfluorTM was used. No product was formed under these conditions in the absence of SelectfluorTM.

Succinic dialdehyde (40% aqueous solution) (entry 7, Table 1) afforded only the monoallylation product even with excess tributylallyl tin. We found that ketones, such as benzophenone and acetophenone, could not be allylated under our experimental conditions. There was no obvious reaction based on TLC even after the reaction mixture was heated at reflux for several hours, perhaps due to the low reactivity and steric hindrance of ketones.

Encouraged by this result, we examined if SelectfluorTM can promote the allylation of imines to form homoallylic amines,¹² especially, directly from aldehydes, amines, and allyltributyltin in a one-pot fashion (Table

Table 1. Allylation of aldehydes with tributylallyltin facilitated by Selectfluor™

$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{H} + \text{CH}_2=\text{CH}-\text{CH}_2-\text{SnBu}_3 \xrightarrow[\text{CH}_3\text{CN}]{\text{Selectfluor}^\text{TM}}$		$\text{R}-\text{CH}(\text{OH})-\text{CH}_2-\text{CH}=\text{CH}_2$		
entry	aldehyde	reaction time (h)	product	yield (%)
1		1.0		93
2		2.0		86
3		1.0		87
4		3.0		90
5		1.5		76
6		2.0		83
7		3.0		82

Table 2. One-pot allylation of imines with tributylallyltin using Selectfluor™ as a promoter

$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{H} + \text{H}_2\text{N}-\text{R}' + \text{CH}_2=\text{CH}-\text{CH}_2-\text{SnBu}_3 \xrightarrow[\text{CH}_3\text{CN}]{\text{Selectfluor}^\text{TM}}$		$\text{R}-\text{CH}(\text{NHR}')-\text{CH}_2-\text{CH}=\text{CH}_2$			
entry	aldehyde	amine	reaction time (h)	product	yield (%)
1			1.5		73
2			1.5		73
3			1.0		87
4			2.0		67
5			3.0		46
6			1.5		64

2).⁵ Although it has been reported that Selectfluor™ can electrophilically fluorinate amines,¹³ the reaction of Selectfluor™ with aromatic amines was found to be slow relative to the allylstannation reactions in our study. After optimizing the reaction conditions, we found that 1.5 equiv. of amines and 1.5 equiv. of Selectfluor™ could give acceptable yields (Table 2).¹⁴ In our experiments, 1.0 equiv. of Selectfluor™ was added to the mixture of aldehyde and amine at first. After 5 min, 1.5 equiv. of allyltributyltin were added. The second portions of Selectfluor™ (0.5 equiv.) and allyltributyltin (1.5 equiv.) were added after 30 min. The yields of the one-pot allylstannations ranged from moderate (46% for 1-naphthaldehyde and *p*-anisidine) to good (87% for *trans*-cinnamaldehyde and aniline). The undesirable coupling of aldehyde and allyltributyltin was usually less than 10%, except 1-naphthaldehyde (entry 5, Table 2) where 22% alcohol was isolated, presumably caused by steric hindrance.

In summary, we have demonstrated that Selectfluor™ can be used as an excellent promoter for the allylation reaction of aldehydes and imines with allyltributyltin in a very straightforward one-step route to afford homoallylic alcohols or amines. The reaction is not air or moisture sensitive. In our experiment, all reactions were carried out directly from commercial reagents in air. Because Selectfluor™ is not so toxic and relatively cheap, we believe that it is a good promoter for the extensively used allylstannation reaction. Further investigation of the mechanism and the scope of the utility of Selectfluor™ is ongoing in our laboratory.

References

1. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293.
2. (a) Kobayashi, S. *Synlett* **1994**, 689–701; (b) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31–46.
3. Aspinall, H. C.; Greeves, N.; McIver, E. G. *Tetrahedron Lett.* **1998**, *39*, 9283–9285.
4. Aspinall, H. C.; Bissett, J. S.; Greeves, N.; Levin, D. *Tetrahedron Lett.* **2002**, *43*, 319–321.
5. Aspinall, H. C.; Bissett, J. S.; Greeves, N.; Levin, D. *Tetrahedron Lett.* **2002**, *43*, 323–325.
6. Banks, R. E.; Besheesh, M. K.; Mohialdin, S. N.; Sharif, I. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2069–2076.
7. Burkart, M. D.; Zhang, Z.; Hung, S.-C.; Wong, C.-H. *J. Am. Chem. Soc.* **1997**, *119*, 11743–11746.
8. Vincent, S. P.; Burkart, M. D.; Tsai, C.-Y.; Zhang, Z.; Wong, C.-H. *J. Org. Chem.* **1999**, *64*, 5264–5279.
9. Shibata, N.; Suzuki, E.; Asahi, T.; Shiro, M. *J. Am. Chem. Soc.* **2001**, *123*, 7001–7009.
10. Liu, J.; Wong, C.-H. *Tetrahedron Lett.*, in press.
11. **General procedure for preparation of homoallylic alcohols:** Allyltributyltin (375 μ L, 1.2 mmol) was added to a mixture of *trans*-cinnamaldehyde (100 μ L, 0.80 mmol) and Selectfluor™ (354 mg, 1.0 mmol) in CH₃CN (5 mL) at room temperature. A second portion of allyltributyltin (375 μ L, 1.2 mmol) was added after 30 min. After the reaction proceeded to completion in 1 h, H₂O (10 mL) was added and the mixture was extracted with CH₂Cl₂ (10 mL \times 2). The organic layers were combined, dried (Na₂SO₄) and concentrated in vacuo. The residue was purified by flash chromatography (silica, 12:1 hexanes:EtOAc) to afford the product as an oil (130 mg, 93%). ¹H NMR (500 MHz, CDCl₃) δ 7.36 (br. d, *J*=8.5 Hz, 2H), 7.30 (br. t, *J*=8.5 Hz, 2H), 7.23 (tt, *J*=1.1, 7.0 Hz, 1H), 6.58 (d, *J*=16.1 Hz, 1H), 6.22 (dd, *J*=6.3, 16.1 Hz, 1H), 5.83 (m, 1H), 5.15 (m, 2H), 4.33 (m, 1H), 2.40 (m, 2H), 2.03 (d, *J*=2.2 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃): 136.57, 133.99, 131.49, 130.24, 128.49, 127.58, 126.40, 118.38, 71.64, 41.91; ESI *m/e* calcd for (M⁺) C₁₂H₁₄O: 174; found: 174 (M⁺).
12. Keck, G.; Enholm, E. J. *J. Org. Chem.* **1985**, *50*, 146–147.
13. Singh, R. P.; Shreeve, J. M. *Chem. Commun.* **2001**, *13*, 1196–1197.
14. **General procedure for preparation of homoallylic amines:** Selectfluor™ (283 mg, 0.8 mmol) was added to a mixture of *trans*-cinnamaldehyde (100 μ L, 0.80 mmol) and aniline (110 μ L, 1.2 mmol) in CH₃CN (5 mL) at room temperature. After the reaction mixture was stirred for 5 min, allyltributyltin (373 μ L, 1.2 mmol) was added. After 30 min, the second portions of Selectfluor™ (142 mg, 0.4 mmol) and allyltributyltin (373 μ L, 1.2 mmol) were added to the mixture. After the reaction proceeded to completion, H₂O (10 mL) was added and the mixture was extracted with CH₂Cl₂ (10 mL \times 2). The organic layers were combined, dried (Na₂SO₄) and concentrated in vacuo. The residue was purified by flash chromatography (silica, 25:1 hexanes:EtOAc) to afford the product as yellow oil (173 mg, 87%). ¹H NMR (600 MHz, CDCl₃) δ 7.33 (d, *J*=8.3 Hz, 2H), 7.21 (t, *J*=7.4 Hz, 2H), 7.16 (t, *J*=7.4 Hz, 1H), 7.14 (t, *J*=7.0 Hz, 2H), 6.68 (t, *J*=7.6 Hz, 1H), 6.63 (d, *J*=8.3 Hz, 2H), 6.58 (d, *J*=15.8, 1H), 6.17 (dd, *J*=6.1, 15.8 Hz, 1H), 5.83 (m, 1H), 5.15 (m, 2H), 4.03 (m, 1H), 3.82 (s, 1H), 2.45 (m, 2H); ¹³C NMR (150 MHz, CDCl₃): 147.42, 136.85, 134.34, 131.43, 130.18, 129.12, 128.46, 127.33, 126.31, 118.28, 117.39, 113.46, 54.65, 40.45; HRMS *m/e* calcd for (M⁺) C₁₈H₁₉N: 249.1517; found: 272.1412 (M+Na).