Imine Allylations by Allylic Trichlorotins Derived from α,α-Diisopropylhomoallylic Alcohols with Tin(II) Chloride and *N*-Chlorosuccinimide

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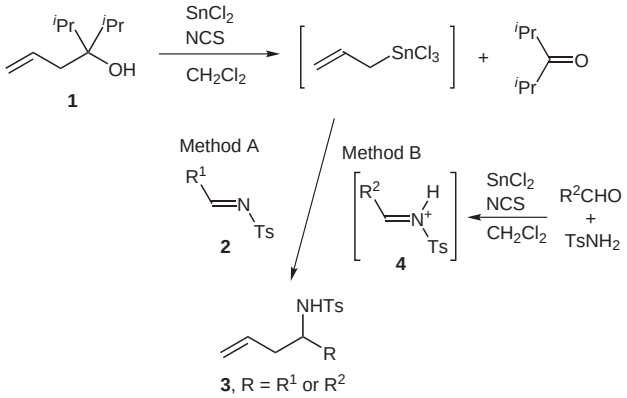
Abstract: Allylic trichlorotins, prepared in situ from α,α-diisopropylhomoallylic alcohols with tin(II) chloride and *N*-chlorosuccinimide in dichloromethane at –40 ºC, cause nucleophilic addition to *N*-tosylimines or *N*-tosyliminiums to afford the corresponding α-substituted homoallylic amines.

Key words: nucleophilic additions, allylations, organometallic reagents, allylic tins, homoallylic amines

Grignard-type (non-Barbier-type) allylation of imines and their analogues (imine allylation) with allylic metal reagents has been well established,[1,2] while Barbier-type imine allylation with allylic halides and reducing agents has made little progress.[3] The imine allylation by allylic halides, esters and alcohols with tin(II) halides cannot be achieved under the same Barbier conditions as those for the carbonyl allylation by allylic halides, esters and alcohols with tin(II) halides, which is one of the most convenient methods for introduction of allylic functions.[4] The failure of the imine allylation that needs polar solvents such as THF, DMF and 1,3-dimethylimidazolidin-2-one to dissolve tin(II) halides can probably be ascribed to instability of imines and iminiums to slight moisture.[5] Barbier-type imine allylation may need water-immiscible nonpolar solvents such as dichloromethane, chloroform and toluene, which cannot be usually used because of the insolubility of tin(II) halides. Thus, a new methodology will be required for in situ preparation of allylic tin species in the nonpolar solvents. We have found that trichlorotin homoallyloxides, derived from sterically hindered α,α-diisopropylhomoallylic alcohols with tin(II) chloride and NCS in dichloromethane,[6] cause retro-allylation[7] to produce allylic trichlorotin species, which can be applied to carbonyl allylation.[8] We here report that allylic trichlorotins, prepared from α,α-diisopropylhomoallylic alcohols with tin(II) chloride and NCS in dichloromethane, cause nucleophilic addition to *N*-tosylimines or *N*-tosyliminiums (imine allylation) to produce the corresponding homoallylic amines.

A typical procedure in Barbier-type allylation of *N*-tosylaldimines **2** with α,α-diisopropylhomoallyl alcohol (**1**)[8] is as follows using the optimum conditions of the carbonyl allylation by **1** with tin(II) chloride and NCS (Method A in Scheme 1, entry 1 in Table 1): To the solution of **1** (2.0 mmol), *N*-benzylidenetosylamide (**2**, R^1 = Ph, 1.0 mmol) and tin(II) chloride (4.0 mmol) in dichloromethane (3 mL) was added NCS (4.0 mmol) at –40 ºC. After 1 hour, the cooling bath was removed, and the reaction mixture was stirred for 24 h at ambient temperature. After the usual work-up, purification by column chromatography (silica gel, hexane–ethyl acetate = 10:1) and then HPLC (Japan Analytical Industry Co. Ltd., LC-908; JAIGEL-2H; chloroform) afforded 0.23 g (76%) of *N*-tosyl-1-phenyl-3-butenylamine (**3**, R = Ph). This imine allylation needs more than two equimolar amounts of tin(II) chloride and NCS each to **1**; the allylation of **2** (R^1 = Ph) does not proceed with one equimolar amount of tin(II) chloride and NCS each to **1**. The results are summarized in Table 1 (entries 1–9). Readily prepared and relatively moisture-stable *N*-tosylaldimines can be employed for this imine allylation, except for the aldimines bearing strongly coordinating or chelating ligands (entries 6 and 7). This imine allylation could not be applied to straight-chain aldimines, because of the difficulty in preparing them and their instability. Thus, we hoped that *N*-tosyliminiums **4**, prepared in situ (without isolation) from aldehydes and tosylamide with $SnCl_2$–NCS,[9] could be employed for the imine allylation by **1** with $SnCl_2$–NCS (Method B in Scheme 1). The in situ preparation of **4** with some different types of aldehydes was applied to the imine allylation by **1**, as summarized in Table 1 (entries 10–19). The instability of iminium ions seems to be relative to yields of homoallylic amines **3**; relatively high yields in cases of iminiums bearing electron-withdrawing groups (entries 10–13), while low yields in cases of iminiums derived from α,β-unsatur-



Scheme 1

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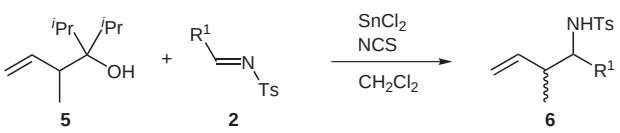
ated cinnamaldehyde and 4-methoxybenzaldehyde bearing an electron-donating group (entries 15 and 16). Unstable aliphatic iminiums can be used for this imine allylation, though the yields are not high (entries 17–19). A typical procedure is as follows (entry 10): To the solution of **4**, prepared from benzaldehyde (1.0 mmol) and tosylamide (1.0 mmol) with tin(II) chloride (1.2 mmol) and NCS (1.2 mmol) at 0 °C in dichloromethane (2 mL), was added the solution of 2-propenyltrichlorotin, prepared from **1** (2.0 mmol) with tin(II) chloride (4.0 mmol) and NCS (4.0 mmol) at –40 °C in dichloromethane (2 mL), at 0 °C. The reaction mixture was stirred for 41 h. After the mixture had been worked up and purified, 0.22 g (73%) of *N*-tosyl-1-phenyl-3-butenylamine (**3**, R = Ph) was obtained.

Table 1 Allylation of **2** or **4** by **1** with Tin(II) Chloride and NCS

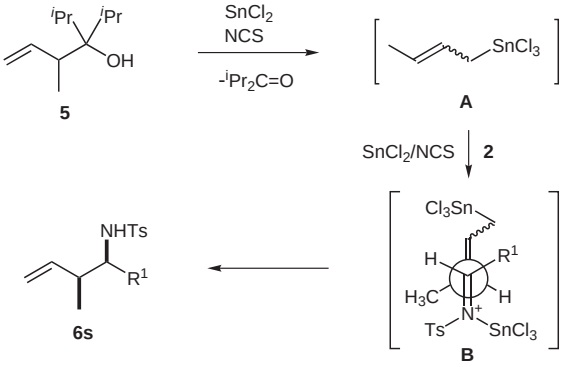
Entry	R	Method	Time (h)	**3**, Yield (%)[a]
1	Ph	A	24	76
2	4-ClC_6H_4	A	24	71
3	4-$MeOOCC_6H_4$	A	24	68
4	4-MeC_6H_4	A	24	79
5	4-$MeOC_6H_4$	A	24	63
6	4-$O_2NC_6H_4$	A	50	27
7	2-Furyl	A	27	9
8	PhCH=CH	A	24	83
9	Me_3C	A	24	62
10	Ph	B	41	73
11	4-ClC_6H_4	B	23	58
12	4-NCC_6H_4	B	17	77
13	4-$MeOOCC_6H_4$	B	15	73
14	4-MeC_6H_4	B	21	35
15	4-$MeOC_6H_4$	B	21	14
16	PhCH=CH	B	48	11
17	$PhCH_2CH_2$	B	23	39
18	C_6H_{13}	B	45	30
19	*c*-C_6H_{11}	B	24	36

[a] Isolated yields.



Scheme 2

Regioselectivity and diastereoselectivity using α,α-diisopropyl-β-methylhomoallyl alcohol (**5**)[8] were investigated under the same conditions as those for the allylations of **2** or **4** respectively by **1**. The allylations of **2** by **5** proceeded regioselectively and diastereoselectively to produce 1-substituted *N*-tosyl-2-methyl-3-butenylamines **6** (R^1 = Ph, 19 h, 43%, *syn*/*anti* = 83:17; R^1 = 4-ClC_6H_4, 20 h, 43%, *syn*/*anti* = 84:16; R^1 = 4-$MeOOCC_6H_4$, 27 h, 53%, *syn*/*anti* = 82:18; R^1 = 4-$MeOC_6H_4$, 30 h, 35%, *syn*/*anti* = 83:17) (Scheme 2).[10] No allylation of **4** by **5** occurred in cases of the same substituents R^1 as those of **2**. A plausible mechanism, which explains the *syn*-diastereoselection in the allylation of **2** by **5**, is shown in Scheme 3. An *E*,*Z* mixture of 2-butenyltrichlorotin (**A**), derived from **5** with tin(II) chloride and NCS, probably forms an acyclic antiperiplanar transition state (**B**) with *N*-tosylimines **2**, which coordinate to excess tin(IV) species, to produce *syn* adduct **6s** preferentially.[11]



Scheme 3

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(5) The use of imines such as *N*-benzylideneaniline and *N*-benzylidenetosylamide in the allylation with tin(II) halides did not afford homoallylic amines but homoallylic alcohols in low yields.

(6) Tin(II) chloride is insoluble in dichloromethane, and dissolves in dichloromethane containing an equimolar amount of alcohol to the tin(II) by adding an equimolar amount of NCS to the tin(II).

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(10) The *syn*-diastereoselectivity in the allylations by **5** was confirmed by the comparison of ^{1}H NMR spectra with authentic samples prepared by the imine allylation by 1-bromo-2-butene with indium.[3] In addition the diastereoselectivity in ref.[9] has been mistaken; *syn* adducts are major, similarly to the imine allylation by **5**.

(11) The *E*:*Z* ratio of **A** could not be determined by the ^{1}H NMR observation of the reaction of **5** with $SnCl_2$ and NCS in CD_2Cl_2 either at –40 ºC or at room temperature. Since the *E*:*Z* ratios of α-adducts in the carbonyl allylation by **5** are ca. 1:1 to 1:4,[8] the 2-butenyltrichlorotin intermediate is presumed to be an *E*,*Z* mixture.