Silylstannations of α,β-unsaturated carbonyl compounds *via* the generation of Bu_3Sn^- in ionic liquids

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The tributylstannyl anion, Bu_3Sn^-, can be generated in imidazolium based ionic liquids from $Me_3SiSnBu_3$ and reacted with α,β-unsaturated carbonyl compounds to afford 3-tributylstannylated products in good yields.

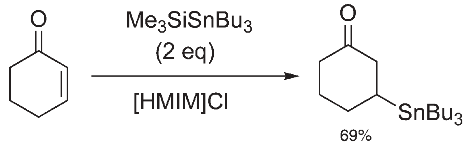
Ionic liquids have been established as viable alternative solvents for a growing variety of applications.[1] They have now seen wide use as solvents in many chemical reactions,[2] have been used in separations[3] and as lubricants,[4] and have shown promise in catalytic applications[1,2,5] to mention but a few applications. Ionic liquids are now quite well known for their rather unique set of properties which make them attractive replacements for conventional solvents. Among these properties are their inherent lack of volatility, non-flammability, and polar, non-coordinating nature. They are also excellent solvents for organic, inorganic, and polymeric materials yet are insoluble in selected organic solvents and in some cases water. These solubility characteristics enable them to be easily recycled and used in biphasic applications and typical extractions. Despite their growing popularity, ionic liquids have been used in comparatively few reactions involving organometallic reagents to form new covalent bonds (*i.e.* carbon–carbon bonds). This undoubtedly stems from the acidity of the proton on C-2 of the *N,N′*-dialkylimidazolium ring on which the most commonly utilized ionic liquids are based. The basicity of the metal–carbon bond in organometallic reagents most frequently results in the abstraction of this proton affording a highly reactive carbene species.[6] Notable examples of organometallic reagents used in ionic liquids to form new covalent bonds include the reaction of phenyl magnesium bromide with benzaldehyde in THF–tetradecyl(trihexyl)phosphonium chloride mixtures[7] and the reaction of organozinc reagents in 8-ethyl-1,8-diazabicyclo[5,4,0]-7-undecenium trifluoromethanesulfonate, [EtDBU]OTf.[8] Further examples showing the potential of organometallic reactions in ionic liquids are the Freidel–Crafts acylation of ferrocene[9] and the silylstannation of terminal alkynes.[10]

Silylstannane reagents, $R_3SiSnR'_3$, are versatile organometallic reagents in organic synthesis.[11] These compounds contain a silicon–tin bond and are easily synthesized by generating a trialkyltin anion followed by a quench with a trialkylsilyl chloride. The resulting silylstannanes can be added across unsaturated organic compounds such as alkynes and enones. These reagents are particularly interesting since one or both metals may be incorporated into the product generated through their reaction with unsaturated substrates. The new C–Sn or C–Si bonds in these adducts can then act as "handles" for further manipulation.

Useful tributylstannyl anions have been generated from silylstannanes through nucleophilic displacement of the trialkylsilyl moiety. This can be achieved through reaction of the silylstannane with "naked" cyanide (*i.e.* NaCN, 18-Crown-6) or less successfully with potassium *tert*-butoxide.[12] The trialkyltin anion generated in these systems reacts in a conjugate sense with enones to afford 3-triaklylstannylated silyl enol ethers. Benzyltriethylammonium chloride can be used in place of the "naked" cyanide ion providing a safer route to these useful adducts; however, this methodology still utilizes hepatotoxic dimethylformamide, DMF, as a solvent.[13]

Owing to their well documented properties mentioned above, ionic liquids have been deemed "green" solvents. We report herein the use of ionic liquids as a means to reduce or eliminate the use of DMF, an otherwise very toxic solvent, in the silylstannation of α,β-unsaturated carbonyl compounds while at the same time improving yields of isolated products. The amount of DMF used in the silylstannation of enones has been reduced in one case through the use of 1-butyl-3-methylimidazolium tetrafluoroborate, $[BMIM]BF_4$, while at the same time enhancing the isolated yield of the stannylated product. When 1-hexyl-3-methylimidazolium chloride, [HMIM]Cl, is used alone as the solvent not only has the complete elimination of DMF in this reaction been accomplished but also the benzyltriethylammoinium chloride has been replaced by the solvent [HMIM]Cl (Scheme 1).

Our first attempt to improve this reaction through replacement of DMF with the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate, $[BMIM]BF_4$, resulted in a severe decrease in the isolated yield of 3-tributylstannylcyclohexanone (Table 1, Entry 2) even after extended reaction times and elevated temperatures. We then surmised that if we used 1-butyl-3-methylimidazolium chloride, [BMIM]Cl, in place of $[BMIM]BF_4$ in a binary solvent system with DMF then we not only should be able to reduce the amount of the noxious DMF used but should also be able to eliminate the need to add benzyltriethylammonium chloride to the reaction mixture since [BMIM]Cl is itself a quaternary organic chloride. Hence, when a 1 : 1 ratio (v/v) of DMF : [BMIM]Cl was used as the solvent system the isolated yield



Scheme 1 Silylstannation of cyclohex-2-en-1-one in 1-hexyl-3-methylimidazolium chloride, [HMIM]Cl.

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Table 1 Silylstannation of cyclohex-2-en-1-one

Entry	Conditions	Yield (%)[a]
1	DMF, $BnEt_3NCl$, room temp., 26 h	60
2	$[BMIM]BF_4$, $BnEt_3NCl$, 60–70 °C, 8 d	13
3	1 : 1 DMF, [BMIM]Cl, room temp., 3d	75
4	1 : 3 DMF, [BMIM]Cl, room temp., 4d	80
5	[BMIM]Cl, 60–70 °C, 2 d	39
6	$[BMIM]BF_4$, [BMIM]Cl, 60–70 °C, 2d	50
7	$[BMIM]PF_6$, [BMIM]Cl, 60–70 °C, 4d	33
8	[HMIM]Cl, room temp., 2d	69

[a] Isolated yield.

of the 3-stannylated product increased to 75% isolated yield (Table 1, Entry 3) compared to a 60% isolated yield when using DMF alone (Table 1, Entry 1).[13] When the proportion of DMF was reduced further to a 1 : 3 ratio of DMF : [BMIM]Cl the yield increased to an 80% isolated yield of the 3-stannylated product, albeit after extended reaction times (Table 1, Entry 4).

When DMF was totally removed from the reaction mixture and only [BMIM]Cl was present the reaction had to be heated to between 60 and 70 °C since the melting point of [BMIM]Cl falls in this range. The yield dropped to a disappointing 39% isolated yield under these conditions (Table 1, Entry 5). Our attempts to improve the solution characteristics of the system by adding equal volumes of either $[BMIM]BF_4$ or $[BMIM]PF_6$ to [BMIM]Cl also did not result in improved yields when compared to the reaction run in DMF alone (Table 1, Entries 6 & 7). However, these systems did allow the elimination of both DMF and the benzyltriethylammonium chloride additive.

The optimum results for the silylstannation of cyclohex-2-en-1-one were obtained when a room temperature ionic liquid was used. We chose 1-hexyl-3-methylimidazolium chloride, [HMIM]Cl, since it is a liquid well below room temperature (*i.e.* −85 °C) allowing us to easily conduct the reaction at room temperature.† We could therefore avoid using DMF in this reaction. Furthermore, since the solvent is also a chloride salt we would not require the addition of any additives such as benzyltriethylammonium chloride. Thus, when tributyl(trimethylsilyl)stannane was reacted with cyclohex-2-en-1-one at room temperature in [HMIM]Cl we obtained a 69% isolated yield of 3-tributylstannylcyclohexanone (Table 1, Entry 8).

A selected series of α,β-unsaturated carbonyl compounds was then reacted under the same conditions at room temperature using only [HMIM]Cl as the solvent to perform a cursory survey of the scope of the reaction conducted in an ionic liquid alone. Only a few examples have been reported under conventional conditions (*i.e.* without ionic liquids) for the conjugate addition of tributylstannyl anions generated from silylstannanes with the best reported yield being *ca.* 60%.[13,14] As can be seen in Table 2 superior yields compared to conventional systems can be obtained when using [HMIM]Cl as the solvent.

Table 2 Silylstannation of selected α,β-unsaturated carbonyl compounds in [HMIM]Cl

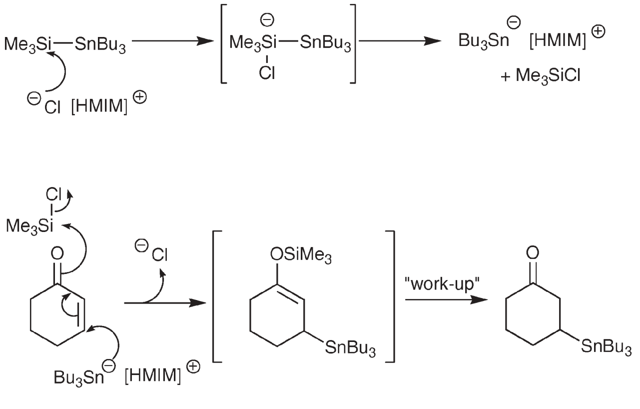
Starting material	Yield (%)[a]
Cyclohex-2-en-1-one	69
Cyclopent-2-en-1-one	69
trans-4-Phenyl-3-buten-2-one	72

[a] Isolated yields.

We believe that the reaction proceeds by initial attack of the silicon atom in $Me_3SiSnBu_3$ by the chloride ion of [HMIM]Cl affording a hypervalent silicon species which then gives rise to TMSCl and the tributylstannyl anion. The tributylstannyl anion then reacts in a 1,4-conjugate sense with the α,β-unsaturated carbonyl compound that further reacts with the TMSCl formed *in situ* to form the silyl enol ether. In forming the silyl enol ether the chloride ion is regenerated and hence can be regarded as a catalytic species. The silyl enol ether is destroyed during aqueous work-up to afford the observed 3-stannylated product (Scheme 2).

Evidence supporting this mechanism was obtained through observation of a [HMIM]Cl–$Me_3SiSnBu_3$ mixture using electrospray mass spectrometry run in the negative mode (Fig. 1). A series of peaks are observed centred around *m/z* 291 which corresponds to the Bu_3Sn^- anion containing the most abundant isotope of tin (*i.e.* ^{120}Sn). The isotopic pattern observed in the ESI-MS is consistent with the isotopic distribution for tin hence confirming its presence. Confirmation of the presence of the anion comes from the fact that the ESI-MS was run under negative mode.

Hence, we have demonstrated that features of the silylstannation of α,β-unsaturated carbonyl compounds can be improved through use of ionic liquids. The overall isolated yield of 3-stannylated product can be improved either by reducing the amount of DMF used through replacement with an ionic liquid, $[BMIM]BF_4$, or through the use of an ionic liquid alone, [HMIM]Cl. From a green



Scheme 2 Suggested mechanism for the silylstannation of cyclohex-2-en-1-one in 1-hexyl-3-methl-imidazolium chloride, [HMIM]Cl.

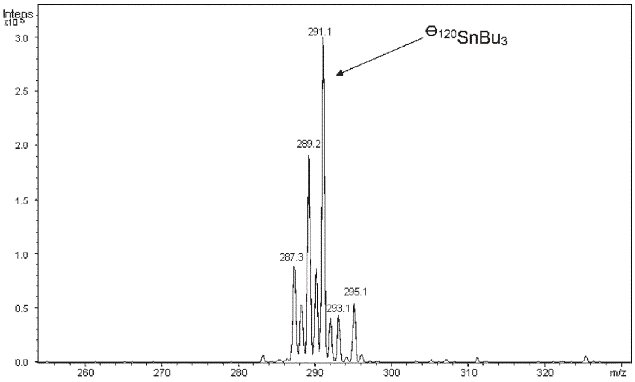


Fig. 1 Electrospray mass spectrum (negative mode) of [HMIM]Cl + $Me_3SiSnBu_3$.

chemistry[15] point of view we have dramatically improved this process by eliminating a harmful solvent and also by eliminating the need to add benzyltriethylammonium chloride to the reaction. In essence we have demonstrated that [HMIM]Cl is in fact a task specific ionic liquid, TSIL, in that it acts not only as a solvent but also as a catalyst for this reaction. Noteworthy is the fact that the intermediate species, [HMIM]$SnBu_3$, represents a new ionic liquid in and of itself. Such an ionic liquid will be useful as both a solvent and a reagent. Such a dual role for [HMIM]$SnBu_3$ is possible since this compound is not only a liquid but also contains the reactive anion Bu_3Sn^-; a very useful synthon in organic chemistry. [HMIM]$SnBu_3$ is one of the first, if not the first, 1,3-dialkylimidazolium ionic liquids that contains an anion basic enough to extract a proton from water and other protic sources such as alcohols but which is not basic enough to remove the C-2 proton from the imidazolium cation.

Efforts are underway in our laboratory to more comprehensively study the scope and limitations of this ionic liquid system and others used for the silylstannation of α,β-unsaturated carbonyl compounds. We are currently characterizing [HMIM]$SnBu_3$ formed from the reaction between $Me_3SiSnBu_3$ and [HMIM]Cl. These results will be the topic of a forthcoming publication describing the full details of the study.

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Notes and references

† *Representative Procedure:* [HMIM]Cl (2.00 g) was added to an oven-dried, vacuum-cooled 25 mL round bottom flask equipped with a magnetic stirbar. The flask was placed under vacuum at 70 °C for 4 h to ensure dryness of the ionic liquid. After cooling the flask to room temperature the vacuum was released under an argon atmosphere. Cyclohex-2-en-1-one (0.10 mL, 1.0 mmol) and $Bu_3SnSiMe_3$ (0.70 mL, 2.0 mmol) were injected through a septum *via* a syringe. The mixture was stirred at room temperature for 2 d. 10 mL of distilled water was added to the reaction and the reaction mixture was extracted with diethyl ether (4 × 15 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo* to afford a clear oil. The oil was purified by flash column chromatography (hexane–ethyl acetate) to afford a clear, colourless oil (265 mg, 69% yield). IR (neat): ν_{CO} 1709 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.79–0.95 (m, 15H, –$Sn(CH_2CH_2CH_2CH_3)_3$); 1.25–1.35 (sextet, 6H, $Sn(CH_2CH_2CH_2CH_3)_3$ J = 7.3 Hz); 1.44–1.58 (m, 6H, $Sn(CH_2CH_2CH_2CH_3)_3$); 1.60–2.50 (m, 9H, H2, H3, H4, H5, H6). ^{13}C NMR ($CDCl_3$): δ 8.0, 13.6, 25.2, 24.4, 29.2, 30.1, 31.2, 42.3, 46.5, 212.4. MS: *m*/*z* 331 ($M^+ - Bu$), 275 ($M^+ - Bu_2$), 217 ($M^+ - Bu_3$), 177 ($SnBu^+$).

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