$SnCl_2 \cdot 2H_2O$—An Alternative to Lewis Acidic Ionic Liquids

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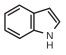
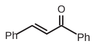
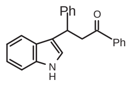
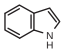
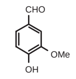
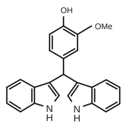
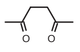
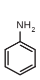
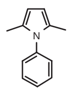
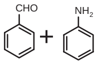
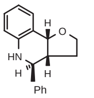
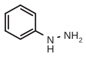
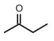
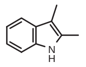
Inexpensive and commercially available $SnCl_2 \cdot 2H_2O$ has been shown to be an alternative to Lewis acidic ionic liquids by carrying out a variety of organic synthesis. The reaction medium is recycleable and the reaction time is comparable with the microwave reactions.

Room temperature ionic liquids (RTILs), which are composed of entire ions, are obtained by the combination of an organic cation and an inorganic anion. As the use of conventional volatile solvents required in various organic synthetic processes are of ecological concern, the RTILs have drawn powerful attention due to their unique properties such as negligible vapour pressure and thermal stability up to 200 °C. The ionic liquids have been found to be excellent solvents and catalysts for a number of reaction. As more and more synthesis can be proceeded in these novel solvent system, the RTILs have shown great promise in commercial applications.[1–6] Despite their successful application as reaction medium in organic synthesis, a practical method for the preparation of RTILs especially in large scale is still not available. A large excess of alkyl halides and organic solvents, such as acetone, toluene, and acetonitrile are always used in the synthesis of RTILs which limits their application. The microwave-assisted synthesis of RTILs reported by Varma and Namboodiri is also difficult to achieve on large-scale preparation.[7]

In our earlier report on $SnCl_2 \cdot 2H_2O$,[8] we have utilized it for the synthesis of variety of quinoline derivatives at room temperature. In continuation of our work on $SnCl_2 \cdot 2H_2O$, we found that $SnCl_2 \cdot 2H_2O$ can be used as an alternative to room temperature Lewis acidic ionic liquids. Thus, the Lewis acid $SnCl_2 \cdot 2H_2O$ is non-toxic, melts near room temperature (melting point 38 °C) and has negligible vapour pressure. All the above properties of $SnCl_2 \cdot 2H_2O$ prompted us to use it as an alternative to eco-benign Lewis acidic ionic liquids. To prove that RTILs can be replaced by molten $SnCl_2 \cdot 2H_2O$, a variety of organic reactions which were already carried out in RTILs were chosen and successfully carried out in molten $SnCl_2 \cdot 2H_2O$. Thus, the conjugate addition of indoles to α, β-unsaturated ketones,[9] the synthesis of bisindolylmethanes,[10] the Paal–Knorr synthesis of pyrroles,[11] the imino Diels–Alder reaction[12] and the Fischer synthesis of indole[13] were successfully carried out in molten $SnCl_2 \cdot 2H_2O$. In all the above reactions $SnCl_2 \cdot 2H_2O$ behaves as medium as well as catalyst. Unlike the reactions in RTILs, the present procedure[14] does not require any additional catalyst like bismuth triflate, dysprosium triflate, copper triflate, and triphenyl phosphonium perchlorate to drive the reaction forward. In the imino Diels–Alder reaction of benzaldehyde, aniline, and dihydrofuran, only *trans*-tetrahydrofuranoquinoline was obtained after column chromatography separation in 97% yield (refer the Support-

Table 1. Reactions carried out on molten $SnCl_2 \cdot 2H_2O$ and comparison with RTILs

Entry	Reactant 1	Reactant 2	Product	Reported condition	Reported yield/%	Our condition	Yield/%
1				$Cu(OTf)_3$ [bmim]BF_4 rt	82–95	$SnCl_2 \cdot 2H_2O$[a] 40 °C	90
2				$Dy(OTf)_3$ [bmim]BF_4 rt	84–99	$SnCl_2 \cdot 2H_2O$ 40 °C	93
3				$Bi(OTf)_3$ [bmim]BF_4 90 °C	85–99	$SnCl_2 \cdot 2H_2O$[a] 40 °C	91
4				[bmim]BF_4 rt	80–92	$SnCl_2 \cdot 2H_2O$[a] 40 °C	97
5				*n*-BPC–$AlCl_3$ N_2/180 °C	41–92	$SnCl_2 \cdot 2H_2O$[a] 100 °C	95

[a] Detailed experimental procedure is given in the Supporting Information.

ing Information for spectral data).

The reaction time is another interesting feature when $SnCl_2 \cdot 2H_2O$ is used as medium. All the reactions shown in Table 1 go to completion in less than 5 min (usual reaction time is 2–3 min, except the Fischer indole synthesis which takes place in 50 min) because in the absence of large volume of organic solvent collisions between the reactants are increased and the total molten $SnCl_2 \cdot 2H_2O$ catalyze the reaction. Thus, the reaction rate is comparable with the microwave reactions. Since $SnCl_2 \cdot 2H_2O$ is a strong reductant, treatment of $SnCl_2 \cdot 2H_2O$ with oxidising agents, nitrates, peroxides, conc. nitric acid should be strictly avoided.

$SnCl_2 \cdot 2H_2O$ is insoluble in dichloromethane. This property was utilized in recycling the reaction medium. Since $SnCl_2 \cdot 2H_2O$ is insoluble in dichloromethane, it was used to bring out the organic part from the reaction mixture. Thus, dichloromethane leaves the $SnCl_2 \cdot 2H_2O$ in reaction vessel, which was recycled for further reactions. The separated dichloromethane was washed twice with water (filtration was carried out if necessary) and then with saturated sodium chloride solution to remove insoluble stannous salts. Thus, in the bis(indolyl)-methane synthesis, the reaction medium was recycled 7 times successfully.[15]

The usual problem associated with $SnCl_2 \cdot 2H_2O$ is that it decomposes and releases excess insoluble inorganic salt when treated with excess water ($SnCl_2 \cdot 2H_2O$ is highly soluble in water). This difficulty during workup after adding water is simplified by doing a filtration. For laboratory scale synthesis, without workup the reaction mixture was directly converted into slurry with suitable adsorbent and loaded on column. Thus, the problem arising in workup was completely eliminated. For example in the conjugate addition of indole to α,β-unsaturated ketones, the reaction mixture was directly converted into slurry with 60–120 mesh silica gel and loaded on column and purified.

In conclusion we have shown that, the behaviour of molten $SnCl_2 \cdot 2H_2O$ which is odourless, inexpensive, and non-toxic is similar to that of room temperature Lewis acidic ionic liquids, in many aspects by carrying out a variety of organic synthesis. Since the reactions proceed completely, more than 90% yields were obtained in all the reactions shown in Table 1. Thus, the commercially available $SnCl_2 \cdot 2H_2O$ is an better alternative to RTILs which are expensive and need to be prepared prior to use in synthesis.

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14 Typical experimental procedure: A two-neck round-bottom flask was fitted with a mechanical stirrer and an oil bath. To this round-bottom flask was added 3 g of $SnCl_2 \cdot 2H_2O$ and stirred at 40 °C. The $SnCl_2 \cdot 2H_2O$ became a viscous liquid. To this viscous liquid was added 1 g (6.5 mmol) of vanillin followed by 1.53 g (13.2 mmol) of indole and stirred at 40 °C. The whole reaction mixture became uniform cherry red colour viscous mass. TLC monitored after 2 min showed that both the starting materials disappeared. To this viscous mass was added small amount of ethanol, stirred, and added 40 mL of ice-cold water and stirred for few min. The solid obtained was filtered under suction and the crude product was dissolved in ethyl acetate, filtered to remove the insoluble stannous salt associated with the reaction mixture. The organic layer thus obtained was dried over anhydrous sodium sulphate, filtered and evaporated the solvent under reduced pressure. The crude product was purified by silica gel (60–120 mesh) column chromatography using petroleum ether (bp 60–80 °C)/EtOAc (9/1) mixture as eluent to obtain 2.25 g (93%) of bis(indolyl)methane.
15 Typical experimental procedure for recycling the reaction medium: A two-neck round-bottom flask was fitted with a mechanical stirrer and an oil bath. To this round-bottom flask was added 6 g of $SnCl_2 \cdot 2H_2O$ and stirred at 40 °C. The $SnCl_2 \cdot 2H_2O$ became a viscous liquid. To this viscous liquid was added 1 g (6.5 mmol) of vanillin followed by 1.53 g (13.2 mmol) of indole and stirred at 40 °C. The whole reaction mixture became uniform cherry red colour viscous mass. TLC monitored after 2 min showed that both the starting materials were disappeared. To this viscous mass was added dichloromethane, stirred and decanted. The organic layer thus obtained was washed twice with water and with saturated sodium chloride solution, dried over anhydrous sodium sulphate and evaporated the solvent. The crude product was purified by silica gel (60–120 mesh) column chromatography using petroleum ether (bp 60–80 °C)/EtOAc (9:1) mixture as eluent to obtain 2.25 g (93%) of bis(indolyl)-methane. The round-bottom flask which contains the $SnCl_2 \cdot 2H_2O$ was again utilized for recycling the reaction medium (successfully recycled 7 times). The yield did not vary much while recycling the reaction medium, thus the yield of seven runs were 93, 93, 91, 90, 88, 88, and 85, respectively.