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PHOSPHONIUM IONIC LIQUID–CATALYZED MICHAEL ADDITION OF MERCAPTANS TO α,β-UNSATURATED KETONES

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A clean and efficient Michael addition reaction on chalcones using phosphonium ionic liquid catalyst (PhosIL-Cl) is described. The method provides several advantages, such as simple workup, environmental friendliness, mild conditions, and excellent yields. In addition, the ionic liquid was chosen as a green solvent, recovered, and reused several times in subsequent reactions.

Keywords: Chalcones; Michael addition; phosphonium ionic liquids; thiol

INTRODUCTION

Environmental pressure to reduce waste and reuse materials has driven studies in green chemistry. Ionic liquids (ILs) have recently emerged as an alternative to organic solvents in traditional chemical reactions, mainly because of their stability, insolubility in organic solvents, low volatility, and easy recyclability.[1] These advantages render the use of ILs more ecofriendly than the organic solvents. Phosphonium ILs have attracted growing interest in the past few years because of their negligible vapor pressure, high thermal capacity, and wide liquid range.

Michael addition is one of the most important carbon–carbon and carbon–heteroatom bond-forming reaction in organic synthesis.[2] The addition of thiols to electron-deficient alkenes is a very useful process for making carbon–sulfur bonds. 1,4-Addition of thiols to α,β-unsaturated carbonyl compounds to form carbon–sulfur bonds constitutes a key reaction in various biosynthetic processes as well as in organic synthesis.

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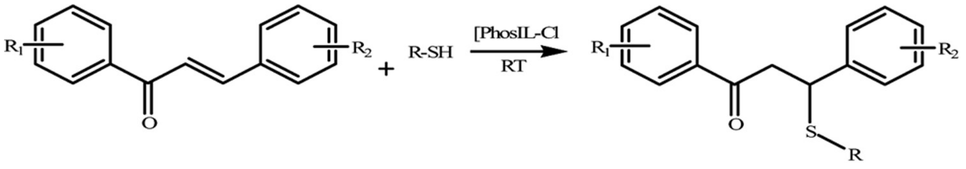


1 **2** **3(a-l)**

Scheme 1. Synthesis of 3-substituted thio-1,3-diphenyl propan-1-one.

Numerous methods have been reported in the literature regarding the 1,4-addition of thiols to electron-deficient olefins activated by different bases.[3] These reactions were also investigated using Lewis bases[4] and different Lewis acids[5] such as $FeCl_3$, $InCl_3$, $InBr_3$, $Bi(NO_3)_3$, $Hf(OTf)_3$, $Bi(OTf)_3$, $Yb(Otf)_3$, and $Cu(BF_4)_2$. Alternatively, modified methods had been used for these reactions, using materials and techniques such as ILs,[6] L-proline,[7] iodine,[8] transition metals, *p*-TsOH–KSF, microwaves,[9] ultrasound, heteropoly acids, NH_4Cl,[10] fluorapatite,[11] water,[12] KF/Al_2O_3,[13] natural phosphate, organocatalysis,[14] MgO, thiourea,[15] and $NaHSO_4 \cdot SiO_2$.[16] However, many of these methods suffer from harsh reaction conditions, toxic reagents, prolonged reaction times, poor yields, and low selectivity. In many cases, the catalyst and excess reagents are not recoverable. With the goal of avoiding the typical disadvantages resulting from the presence of such catalysts, a large number of alternative procedures have been developed in the past few years. Although several modifications have been made to counter these problems, there is a need to develop better strategies for the Michael addition reaction, which is achieved using phosphonium ILs as catalysts.

In continuation of our work in IL-catalyzed reaction,[17] herein we describe a simple and convenient method for the Michael addition of mercaptans to α,β-unsaturated ketones using tetradecyl (trihexyl) phosphonium chloride ionic liquid (PhosIL-Cl) in excellent yields and short reaction time at room temperature (Scheme 1).

RESULTS AND DISCUSSION

Phosphonium-based ILs are highly basic[18] and have the generic formula $[PR_3R'] X$, where both R and R′ are alkyl groups and X is a halide.[19] A large radius and polarizable lone pair make them more nucleophilic. The structural formula of PhosIL-Cl is shown in Fig. 1.

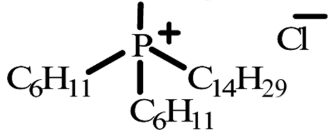
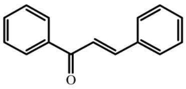
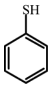
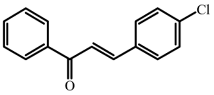
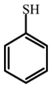
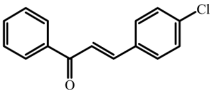
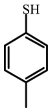
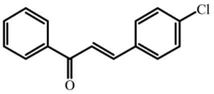
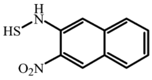
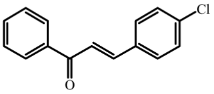
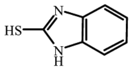
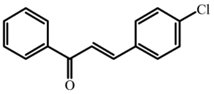
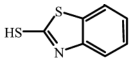
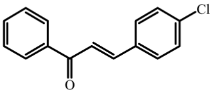
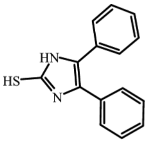
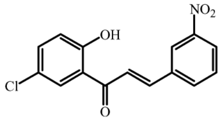
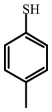
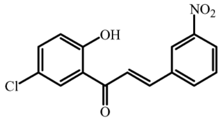
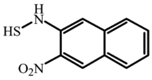
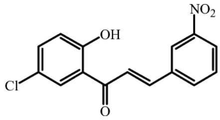
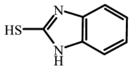
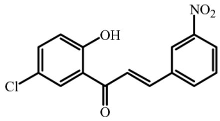
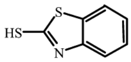
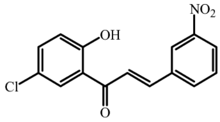
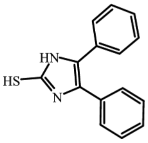


Figure 1. Structure of tetradecyl-(trihexyl)-phosphonium chloride ionic liquid [PhosIL-Cl].

Table 1. Michael addition of thiol on chalcones using phosphonium ionic liquids

Products	Chalcones	Thiol	Time (h)	Mp (°C)	Yield (%)[a]
3a			2.5	111–112	90
3b			2.5	64–67	85
3c			3	Oil	88
3d			2.5	105–106	90
3e			3	123–124	85
3f			3	107–108	88
3g			3.5	121–122	80
3h			2.5	Oil	90
3i			2.5	98–100	88
3j			3	160–162	85
3k			3	116–117	88
3l			3.5	128–130	82

[a]Isolated and unoptimized yield.

Table 2. Performance of recycled phosphonium ionic liquids

		Yield (%) of PhosIL-Cl		
Entry	Products	Recycle 1	Recycle 2	Recycle 3
1	**3a**	97	96	96
2	**3b**	95	95	94

Phosphonium salts are more thermally stable than ammonium salts. Phosphonium-based ILs have greater viscosities than the ammonium counterparts, at room temperature. However, on heating at 70–100 °C, their viscosities generally decrease, and the addition of reactants or catalysts can also further reduce the viscosity. An important difference between imidazolium and phosphonium ILs is the acidic protons present in the former. Compared to phosphonium cations, imidazolium cations are not entirely inert and interact with solutes either through hydrogen bonding or through the aromatic nature of ring system. Tetralkylphosphonium salts do not have such acidic protons or aromatic rings; consequently, they have less potential for interaction with solutes. Recently, phosphonium ILs were used[20] in the degradation of phenol, esterification, Wittig reaction, Heck reactions, and Suzuki cross-coupling reactions.

In a model condensation reaction, thiol and chalcone in tetradecyl (trihexyl) phosphonium chloride IL were stirred at room temperature. After completion of reaction as monitored by thin-layer chromatography (TLC), the usual workup afforded pure products (Table 1). The reaction proceeded cleanly at room temperatures. After completion of the reaction, addition of water and hexane to the reaction mixture resulted in the formation of a three-phase system, with the organic layer at the top, IL in the middle, and aqueous layer at the bottom. The products were isolated from the organic layer by extraction/decantation. Isolation of product was easy because phosphonium ILs have remarkable solvent properties. Phosphonium IL was recovered and reused several times in subsequent reactions with negligible change in its efficiency (Table 2).

EXPERIMENTAL

Materials and Methods

Melting points were measured in open glass capillaries on a Perfit Electrothermal melting-point apparatus and are uncorrected. ^{1}H NMR spectra were recorded at room temperature on a 200-MHz Varian Inova Spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as internal standard. Infrared (IR) spectra (using KBr pellets) were obtained from a Varian 640 Fourier transform (FT)–IR instrument. The reactions were monitored on TLC using precoated plates (silica gel on aluminum, Merck). Column chromatography was performed using Acme silica gel (100–200 mesh). All reagents were obtained from commercial sources and used without further purification. Solvents for chromatography were distilled before use. The products were also characterized by comparison of their melting points with literature values.

General Experimental Procedure

A mixture of chalcone (1 mmol) and thiol (1 mmol) in 2 ml PhosIL-Cl was stirred at room temperature for an appropriate time. After completion of the reaction as monitored by TLC, water and hexane (5 + 5 ml) were added to the reaction mixture, which resulted in the formation of a three-phase system: organic layer on the top, IL in the middle, and aqueous layer at the bottom. The obtain product (**3a–l**) was isolated from the organic layer by successive extractions (3 × 10 ml) using hexane/ethyl acetate (9.5:0.5). The IL was washed with water and hexane, dried, and reused several times to carry out the same experiment. The crude product was purified by column chromatography using hexane/ethyl acetate (8:2) as an eluent and characterized by comparison of IR, ^{1}H NMR, and melting point with literature values (Table 1).

Spectral Data of Selected Compounds

1,3-Diphenyl-3-phenylsulfenylpropan-1-one (3a). IR (KBr) ν: 1680 cm^{-1}; ^{1}H NMR (300 MHz CDCl$_3$) δ: 3.85 (H, dd, CH$_2$), 4.05 (H, dd, CH$_2$), 5.20 (H, t, CH), 7.20–7.80 (13H, m, ArH), 7.9 (2H, d, ArH); MS (*m*/*z*): 318 (M+): 205, 109.

3-(4-Chlorophenyl)-1-phenyl-3-phenylsulfenylpropan-1-one (3b). IR (KBr) ν: 1730 cm^{-1}; ^{1}H NMR (300 MHz CDCl$_3$) δ: 3.65 (2H, m CH$_2$, m), 4.97 (H, t, CH), 7.15–7.55 (12H, m, ArH), 7.9 (2H, d, ArH); MS (*m*/*z*): 353 (M+): 241.81, 109.

CONCLUSION

In summary, a simple and efficient process has been reported using recyclable phosphonium IL. The selectivity of reaction makes this method more attractive and useful than the present methodologies.

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