SHORT PAPER

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Organic reactions in ionic liquids: α-tosyloxylation of ketones[†]

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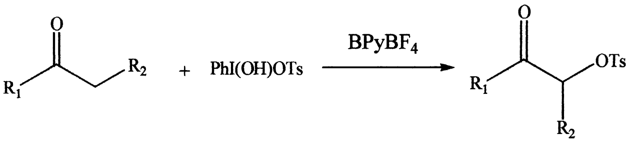
The room temperature ionic liquid, n-butylpyridinium tetrafluoroborate ($BPyBF_4$) is used as a "green" recyclable alternative to classical molecular solvents for the α-tosyloxylation of ketones.

Keywords: ionic liquids, α-tosyloxylation of ketones

Room temperature ionic liquids (RTIL) are liquids that are composed entirely of ions. In fact, ionic liquids can now be produced which remain liquid at room temperature and below (even as low as –90°C) and appear to be undemanding and inexpensive to manufacture.[1–5] Ionic liquids offer an attractive alterative to conventional organic liquids for clean synthesis, as they are easy to recycle, lack flammability, and possess effectively no vapour pressure. Compared with classical molecular solvents, the ionic liquids are environmentally benign reaction media.[6–9] To date some of the more important reactions have been carried out and investigated in ionic liquids, for example, polymerisation,[10] hydrogenation,[11] hydroformylation,[11] Diels–Alder reaction,[12] Wittig reaction,[13] Heck reaction,[14] Michael addition,[15] Suzuki cross-coupling reaction,[16] epoxidation,[17] 1,3-dipolar cycloaddition,[18] oxidation of aromatic aldehydes,[19] the Knoevenagel and Robinson annulation[20] *etc.*

The α-sulfonoxylations of ketones are very important reactions, because α-sulfonoxy ketones contain the same general features as α-halo ketones and they are important intermediates. They have been used as precursors to α-keto cations,[21] as Favorski rearrangement substrates,[22] and they react with appropriate nucleophilies to offer a variety of valuable synthetic materials. On the other hand, the sulfonoxy group is a strong electron-withdrowing group[23] that can acidify the α-hydrogen significantly.

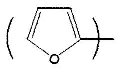
Here, we have examined the α-tosyloxylation of enolisable ketones by the reaction of ketones with [hydroxy(tosyloxy)iodo]benzene (HTIB, **2**) in anionic liquid at 90°C (Scheme 1). For this study, the accessible and cheaper ionic liquid, *n*-butylpyridinium tetrafluoroborate ($BPyBF_4$) was a strong candidate and was synthesised according to the procedures reported in the literature.[24] We found that α-tosyloxylation of ketones occurred easily by the treatment of ketones with HTIB(**2**) in $BPyBF_4$. In fact, simple stirring of a mixture of ketone and HTIB in $BPyBF_4$ at 90°C for 1 hour gave, after extraction with ether, the desired α-tosyloxyketone with good yield. The results are summarised in Table 1 (Entries 1–8). The products were characterised by ^1H NMR, IR, m.p. and elemental analysis which were consistent with literature data.



1 2 3

Scheme 1

Table 1 Synthesis of α-tosyloxy ketones (**3**)

Entry	R$_1$	R$_2$ /%	Yield[a] /°C	M.p.[b] /°C	Lit.m.p. /°C
1 **3a**[c]	Ph	H	83	90–92	92–93[25]
2 **3b**	p-FC_6H_4	H	91	105–106	
3 **3c**	p-Br C_6H_4	H	84	126–128	132–133[26]
4 **3d**		H	75	64–66	65–67[27]
5 **3e**	CH_3	H	83	32–33	35[25]
6 **3f**	CH_2CH_3	CH_3	51	Oil	Oil[25]
7 **3g**	CH_3	CH_2COCH_3	74	80–82	82–83[25]
8 **3h**[g]	$-(CH_2)_4-$		47	71–73	74–76[25]
9 **3a**[d]	Ph	H	83	90–92	92–93[25]
10 **3a**[e]	Ph	H	81	90–92	92–93[25]
11 **3a**[f]	Ph	H	81	90–92	92–93[25]

[a] Isolated yield based on ketone. [b] Melting points are uncorrected. [c] First run using RTIL. [d] Second run using recycled RTIL. [e] Third run using recycled RTIL. [f] Fourth run using recycled RTIL. [g] Reaction of cyclohexanone and HTIB at room temperature for 24 hours.

Our experiments showed that after the isolation of the product, the ionic liquid can be reused several times with no appreciable decrease in yield (Table 1, Entries 9–11). The ionic liquid $BPyBF_4$ can truly be compared with classical molecular solvents, with the added advantage of an increase in the yield in some cases. For example, using the classical molecular solvent method,[26] the yield of α-tosyloxy acetone is 71% and the preparation of α-tosyloxy cyclohexanone(**3h**) takes 3 days and the yield is only 40%.

In conclusion, the room temperature ionic liquid $BPyBF_4$ is an attractive clean synthetic alternative to classical molecular solvents for α-tosylation of ketones, There are many obvious advantages including simplicity of the methodology, the ease of product isolation, the potential for recycling.

Experimental

IR spectra were recorded using KBr pellets on a VECTOR-22 Infrared Spectrophotometer. ^1H NMR spectra were recorded on a

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

BRUKER-400Hz Spectrometer using $CDCl_3$ as the solvent with TMS as an internal standard. Elemental analysis was performed on a Carlo Erba EA 1106 instrument.

Typical procedure for synthesis of α–tosyloxy ketones: Acetophenone (0.12 g, 1 mmol) and HTIB (0.392 g, 1 mmol) were added successively with efficient stirring to $BPyBF_4$ (2 ml). The resulting mixture was stirred for 1 hour at 90°C. Subsequently, the reaction mixture was extracted with diethyl ether (5×10 ml). The combined ethereal solution was evaporated under reduced pressure. The crude product was purified by preparative TLC (ethyl acetate/cyclohexane=1:3) to obtain **3a** (0.24g , 83% yield) as a white solid.

Spectroscopic data : **3a:** IR (cm^{-1}) 1713 (C=O), 1358, 1175 (O=S=O). ^1H NMR, ppm: δ 2.45 (s, 3H), 5.26 (s, 2H), 7.34–7.87 (m, 9H).

3b: IR (cm^{-1}) 1701 (C=O), 1363, 1176 (O=S=O). ^1H NMR, ppm: δ 2.45 (s, 3H), 5.21 (s, 2H), 7.12–7.16 (t, 2H), 7.34–7.36 (d, 2H), 7.83–7.90 (m, 4H). MS *m/z* 308 (M^+ 0.50), 123 (100.00). Anal. Calcd. SorC_8H_7OF, C, 58.43 H, 4.25; Found C, 58.39 H, 4.30%.

3c: IR (cm^{-1}) 1702 (C=O), 1361, 1176 (O=S=O). ^1H NMR, ppm: δ 2.45 (s, 3H), 5.20 (s, 2H), 7.34–7.36 (d, 2H), 7.61–7.63 (d, 2H), 7.70–7.72 (d, 2H), 7.83–7.85 (d, 2H).

3d: IR (cm^{-1}) 1694 (C=O), 1351, 1169 (O=S=O). ^1H NMR, ppm: δ 2.45 (s, 3H), 5.09 (s, 2H), 6.58–6.59 (m, 1H), 7.33–7.37 (m, 3H), 7.61 (m, 1H), 7.85–7.87 (d, 2H).

3e: IR (cm^{-1}) 1744 (C=O), 1364, 1176 (O=S=O). ^1H NMR, ppm: δ 2.21 (s, 3H), 2.46 (s, 3H), 4.49 (s, 2H), 7.37–7.39 (d, 2H), 7.80–7.82 (d, 2H).

3f: IR (cm^{-1}) 1724 (C=O), 1366, 1178 (O=S=O). ^1H NMR, ppm: δ 1.00–1.04(t, 3H), 1.34–1.35(t, 3H), 2.46 (s, 3H), 2.56–2.63(m, 2H), 4.78–4.83(q, 1H), 7.36–7.38 (d, 2H), 7.80–7.82 (d, 2H).

3g: IR (cm^{-1}) 1595 (C=O), 3440 (OH), 1379, 1176 (O=S=O). ^1H NMR, ppm: δ 1.96 (s, 6H), 2.48 (s, 3H), 7.39–7.40 (d, 2H), 7.82–7.84 (d, 2H), 14.76 (s, 1H).

3h: IR (cm^{-1}) 1732 (C=O), 1358, 1177 (O=S=O). ^1H NMR, ppm: δ 1.64–1.73 (m, 2H), 1.89–1.99 (m, 3H), 2.27–2.33 (m, 2H), 2.44 (s, 3H), 2.53–2.56 (m, 1H), 4.88–4.92 (m, 1H), 7.33–7.36 (d, 2H), 7.83–7.85 (d, 2H).

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