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Tetrahedron Letters 44 (2003) 3629–3630

TETRAHEDRON
LETTERS

The first Corey–Chaykovsky epoxidation and cyclopropanation in ionic liquids☆

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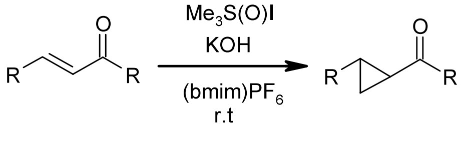
Received 12 February 2003; revised 7 March 2003; accepted 14 March 2003

Abstract—The first Corey–Chaykovsky epoxidation and cyclopropanation using trimethyl sulfonium iodide/trimethyl sulfoxonium iodide and KOH as base in the recyclable ionic liquid, (bmim)PF_6 are described. © 2003 Elsevier Science Ltd. All rights reserved.

Cyclopropanes and epoxides are small, highly strained skeletons and are present in several natural products.[1] Besides this, epoxides also play a major role as building blocks for ‘C–C’ and ‘C–X’ bond (X = N, O and S) formation.[2] Hence the synthesis of these classes of compounds has attracted the interest of a wide range of synthetic chemists. Generally cyclopropane rings are constructed by the addition of a carbene to an olefin.[3] Epoxides can be prepared by peracid oxidation of the corresponding olefin. Alternatively cyclopropanes can be prepared by addition of trimethyl sulfoxonium iodides to enones whereas epoxides can be prepared by addition of trimethyl sulfonium iodides to aldehydes/ketones in the presence of a base such as sodium hydride or *n*-BuLi[4] (popularly called Corey–Chaykovsky salts). These reactions are conventionally carried out in THF or DMSO as solvents. Toda et al.[5] have also proved that these reactions can be performed in the absence of solvent albeit on small scale.

In recent years ionic liquids[6] have proved themselves as attractive solvents for organic synthesis because of their ease of recyclability, rapid reaction times and high yields. Several conventional organic transformations have been reported in ionic solvents as alternative solvent media. Surprisingly however, there is no report on epoxidation or cyclopropanation using a trimethyl sulfoxonium salt in ionic liquids. Herein, we report for the first time cyclopropanation and epoxidation in the ionic solvent (bmim)PF_6 (Scheme 1).



Scheme 1.

In the initial studies, cyclohex-2-enone (entry 1, Table 1) was subjected to cyclopropanation using trimethyl sulfoxonium iodide and KOH as base in (bmim)PF_6. Within two hours at room temperature we observed clean formation of product **1a** in 95% yield.[7] To generalize this protocol, the readily available terpene (*R*)-carvone (entry 2, Table 1) was subjected to the above reaction conditions to give cyclopropyl carvone **2a** in 92% yield. Chalcone substrates (entries 3 and 4, Table 1) also behaved well and produced the expected targets in high yields. 1-Phenylbut-2-en-1-one (entry 5, Table 1) and 1,4-diphenylpent-2-en-1-one were also no exceptions.

To check the efficiency of recycling (bmim)PF_6, cyclohex-2-enone (Table 2) was subjected to cyclopropanation[8] using KOH as base and, after four runs, the yield of the corresponding cyclopropane was very high.

To check the efficiency of epoxidations, several aldehydes and ketones were subjected to trimethyl sulfonium iodide and KOH in (bmim)PF_6 (Scheme 2 and Table 3). To our satisfaction the aldehydes (entries 1–4) and the ketone (entry 5) produced epoxides in 77–91%

Keywords: epoxidation; cyclopropanation; ionic liquids; trimethyl sulfoxonium iodide; Corey–Chaykovsky reaction.

☆ IICT Communication No. 030129.

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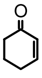
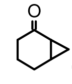
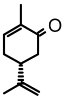
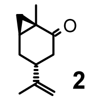
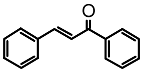
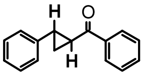
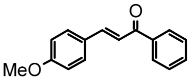
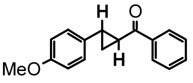
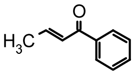
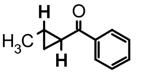
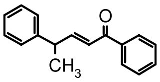
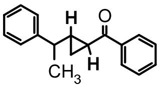
0040-4039/03/$ - see front matter © 2003 Elsevier Science Ltd. All rights reserved.
doi:10.1016/S0040-4039(03)00732-9

Table 1. Cyclopropanation of olefins using $Me_3S(O)I$ and KOH in $(bmim)PF_6$

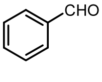
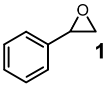
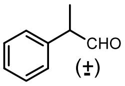
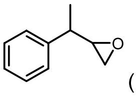
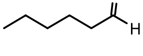
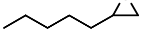
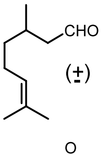
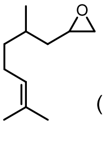
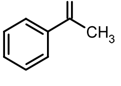
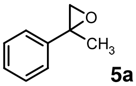
Entry	Substrate	Product[a]	Yield (%)[b]
1		 **1a**	95
2		 **2a**	92
3		 **3a**	94
4		 **4a**	92
5		 **5a**	91
6		 **6a**	90

a Products were characterized by ^1H NMR and mass spectroscopy.
b Isolated yields of products.

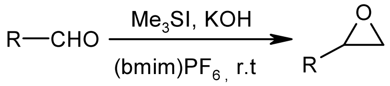
Table 2. Cyclopropanation of cyclohex-2-enone showing the recyclability of $(bmim)PF_6$

Run	1	2	3	4	5
Isolated yield (%)	95	95	93	91	90

Table 3. Epoxidation of carbonyl compounds using Me_3SI and KOH in $(bmim)PF_6$

Entry	Substrate	Product[a]	Yield (%)[b]
1		 **1a**	87
2	 (±)	 **2a** (1:1)	91
3		 **3a**	77
4	 (±)	 **4a** (1:1)	93
5		 **5a**	90[c]

a Products were characterized by ^1H NMR and mass spectroscopy.
b Isolated yields of products.
c 2-phenylpropanaldehyde was formed as a by-product (20%) on standing in the ionic liquid.



Scheme 2.

yields in 2 h. In the case of acetophenone, we observed rearrangement of **5a** to 2-phenylpropanaldehyde on standing which may be attributed to the Lewis acidity of the ionic liquid.

In conclusion, we have demonstrated for the first time, epoxidation and cyclopropanation using sulfonium and sulfoxonium salts can be achieved in the ionic liquid $(bmim)PF_6$ with recycling.

Acknowledgements

C.N. and V.J. thank the CSIR, New Delhi, for financial assistance.

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7. *General procedure for cyclopropanation and epoxidation*: A 25 mL flask was charged with $(bmim)PF_6$ (2 mL), substrate (2 mmol), trimethyl sulfonium iodide/trimethyl sulfoxonium iodide (2.2 mmol) and KOH (2.4 mmol) and stirred for 2 h at room temperature. After completion of the reaction, the mixture was extracted with Et_2O (3×10 mL). The combined ether extracts were concentrated on a rotary evaporator and the crude product was purified by column chromatography on silica gel to give the desired product.
8. After every run, the product was isolated by extraction with ether and additional KOH, olefin and salt were added in one portion and reaction sequence repeated.