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Green approach for the conversion of olefins into *vic*-halohydrins using *N*-halosuccinimides in ionic liquids☆

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Abstract—Alkenes undergo smooth bromo- and iodohydroxylation with *N*-bromo- and *N*-iodosuccinimides/water, respectively, using the air and moisture stable ionic liquid [bmim]BF_4 as a novel recyclable reaction medium in high to quantitative yields. *N*-Halosuccinimides show enhanced reactivity in ionic liquids thereby reducing the reaction times and improving the yields considerably.

vic-Halohydrins have found widespread application in organic synthesis. They are key intermediates in the synthesis of several halogenated marine natural products[1] and also in various useful synthetic transformations.[2] These halo derivatives are widely applicable in industrial processes for the synthesis of drugs, pharmaceuticals, agrochemicals, pigments and photographic materials.[3] The most common method for the preparation of halohydrins involves ring-opening of epoxides by hydrogen halides. These procedures are generally associated with by-products such as *vic*-dihalides and 1,2-diols.[4] Substantial efforts have been made in the last few years to develop new procedures for converting epoxides into halohydrins under mild conditions.[5] Only a few methods have been developed for the preparation of *vic*-halohydrins directly from olefins[6] many of which often involve the use of expensive reagents and the formation of mixtures of products resulting in low yields of the halohydrins. Among various brominating agents,[7] NBS is one of the most popular and inexpensive for allylic, benzylic and aromatic nuclear brominations under mild conditions.[8] A major advantage of the use of NBS as a brominating agent is that the by-product, succinimide, can be easily recovered and reconverted to NBS.

Ionic liquids are used as 'green solvents' and possess unique properties such as good solvating ability, wide temperature liquid range, tunable polarity, high thermal stability, immiscibility with a number of organic solvents, negligible vapour pressure and ease of recyclability.[9] Due to the stabilization of charged intermediates by ionic liquids, they can promote unprecedented selectivities and reaction rates compared with conventional solvents. Due to their distinct advantages, ionic liquids can make a great contribution to green chemistry.[10]

We herein report the use of an ionic liquid/water system as a novel and recyclable polar reaction media for the halogenation of olefinic systems using *N*-halosuccinimides (Scheme 1).[11]

Treatment of styrene with NBS or NIS in 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4) ionic medium afforded 2-bromo- or 2-iodo-1-phenylethanol in 92% and 96% yields, respectively. In a similar manner, various substituted alkenes were converted into the corresponding bromo- and iodohydrins in high to quantitative yields. In all cases, the reactions proceeded rapidly at 27 °C with high selectivity. Alkenes with methyl-substituted aromatic substituents also reacted smoothly with *N*-halosuccinimides in ionic liquids to produce the corresponding halohydrins, significantly without halogenation of the alkyl side-chain (Table 1, entries b and i and Table 2, entry d). Since the products were partially soluble in [bmim]BF_4 ionic liquid, they could be easily isolated by simple extraction with ether. The remaining

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Keywords: Ionic liquids (ILs); Alkenes; Halohydroxylation; Halohydrins.

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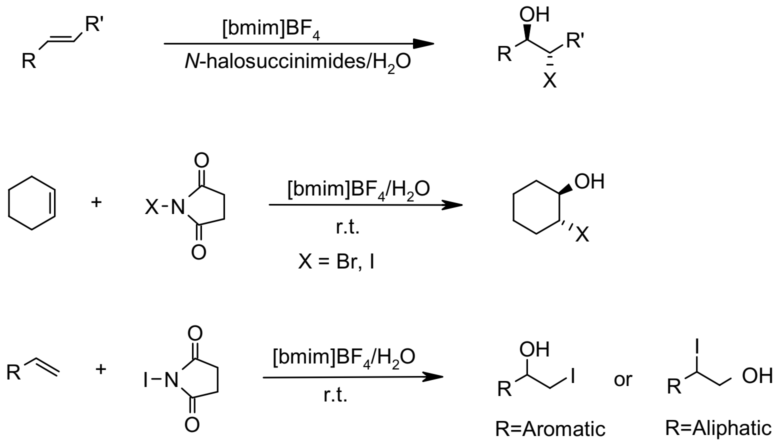
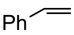
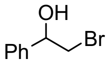
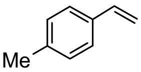
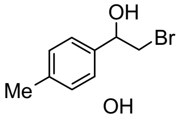
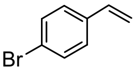
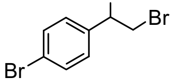
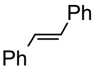
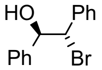
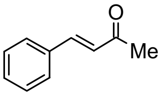
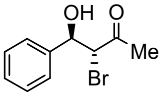
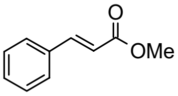
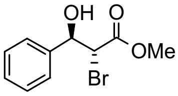
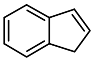
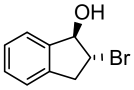
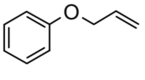
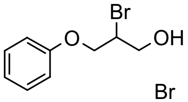
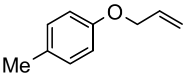
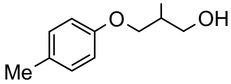
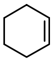
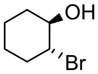
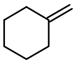
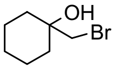
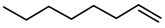
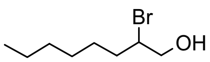
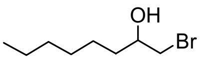


Scheme 1.

Table 1. Synthesis of bromohydrins from olefins using [bmim]BF_4–water/NBS

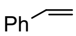
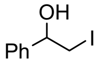
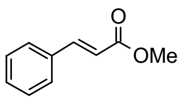
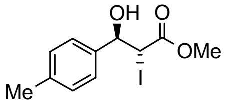
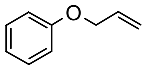
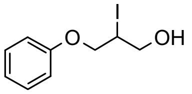
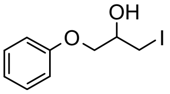
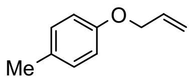
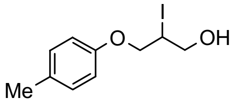
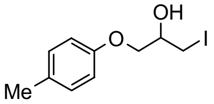
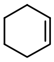
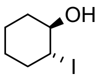
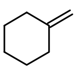
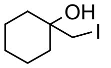
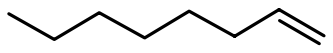
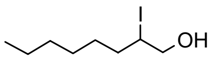
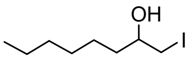
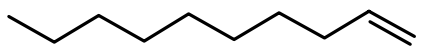
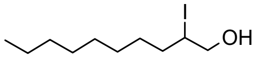
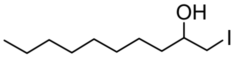
Entry	Olefin	Bromohydrin[a]	Time (h)	Yield (%)[b]
a			2.0	92
b			1.5	93
c			3.0	89
d			1.5	80[12c]
e			1.0	81
f			2.0	92[12d]
g			1.5	90
h			3.0	88
i			1.5	85
j			1.0	87
k			2.0	84
l		 	1.0	78 (14)[c]

[a] All products were characterized by ^{1}H NMR, IR spectra and mass spectrometry and are reported in the literature.[5,6,12]

[b] Isolated yield obtained after column chromatography.

[c] Yield in parentheses indicates the minor regioisomer.

Table 2. Synthesis of iodohydrins from olefins using [bmim]BF_4–water/NIS

Entry	Olefin	Iodohydrins		Time (h)	Yield[b]
		Main product[a]	Minor product[a]		
a			—	0.5	96
b			—	0.5	98[12d]
c				1.5	76 (20)[c]
d				2.0	72 (22)[c]
e			—	2.5	97
f			—	1.5	96
g				2.0	70 (26)[c]
h				2.5	71 (24)[c]

[a] All products were characterized by ^{1}H NMR, IR spectra and mass spectrometry and are reported in the literature.[5,6,12]

[b] Isolated yield obtained after column chromatography.

[c] Yield in parentheses indicates the minor regioisomer.

ionic liquid was diluted with water and extracted with ethyl acetate to recover the ionic liquid and to leave the succinimide in the water layer. The ionic liquid was activated at 80 °C under reduced pressure (3–4 Torr) and recycled in further runs without any loss of activity. To compare the efficiency of other ionic liquids, the reactions were also carried out in various quaternary ammonium salts such as 1-butyl-3-methylimidazolium chloride [bmim]Cl and *n*-tetrabutylammonium chloride. High temperature reaction conditions (60 °C) and longer reaction times (5–8 h) were typical in these ILs to achieve comparable yields to those obtained in room temperature ionic liquids. The scope and generality of this process is illustrated with respect to various alkenes and *N*-halosuccinimides and the results are presented in Tables 1 and 2.

In summary, the [bmim]BF_4–water system is an efficient alternative for the synthesis of bromo- and iodohydrins from alkenes and *N*-bromo- and *N*-iodosuccinimides, respectively. The ionic liquid plays a dual role as solvent and activator of the *N*-halosuccinimides thereby avoiding the use of environmentally unfavourable organic solvents. The simple experimental and product isolation procedures combined with ease of recovery and reuse of this novel reaction media is expected to contribute to the development of green strategies for the halohydroxylation of alkenes.

Acknowledgements

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11. *General procedure*: A mixture of aromatic or aliphatic alkene (1 mmol) and *N*-halosuccinimide (1.2 mmol) in [bmim]BF_4/water (2 mL:0.5 mL) was stirred at 27 °C for the appropriate time (see Tables 1 and 2). After completion of the reaction, as indicated by TLC, the reaction mixture was extracted with diethyl ether (3×10 mL). The combined organic extracts were concentrated in vacuo and the residue was charged onto a small silica gel column and eluted with a mixture of ethyl acetate: *n*-hexane (1:9) to afford the pure halohydrins. The remaining [bmim]BF_4 ionic liquid was diluted with water and extracted into ethyl acetate, leaving behind the water-soluble succinimide. All known compounds were confirmed by comparison of their IR, NMR and mass spectra and physical data with those of authentic samples.[5,6,12] Physical data for selected compounds and spectroscopic data for new compounds. Compound **3d** (Table 1): *erythro*-2-bromo-1,2-diphenylethanol: solid, mp = 84–86 °C (lit. mp = 86 °C[12c]). Compound **3f** (Table 1): *erythro*-methyl-3-hydroxy-2-bromo-3-phenylpropanoate: solid, mp = 62–64 °C (lit. mp = 63 °C[12d]). Compound **3g** (Table 1): 2-bromoindan-1-ol: solid, mp = 124–126 °C. Compound **3b** (Table 2): *erythro*-methyl-3-hydroxy-2-iodo-3-phenylpropanoate: white solid, mp = 62–63 °C (lit. mp = 63 °C[12d]). Compound **3h** (Table 1): 2-bromo-3-phenoxypropanol: liquid, IR (KBr): ν_{max}: 3450, 3055, 2930, 1492, 1120, 820, 662 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.38–7.20 (m, 2H), 6.98–6.78 (m, 3H), 4.22–4.19 (m, 1H), 4.10–4.05 (m, 1H), 3.98 (d, $J = 5.4$ Hz, 2H), 3.52–3.48 (m, 1H), 2.95–2.50 (br s, 1H, OH). EIMS: *m*/*z*: 230 (M^+). Compound **3c** (Table 2, major): 2-iodo-3-phenoxypropanol: liquid, IR (KBr): ν_{max}: 3422, 3040, 2970, 2927, 1452, 1380, 1113, 980, 820 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.30–7.25 (m, 2H), 6.95–6.85 (m, 3H), 4.41 (m, 1H), 4.30 (t, $J = 6.8$ Hz,2H), 3.92 (t, $J = 6.8$ Hz, 2H), 2.20 (t, $J = 7.5$ Hz, 1H). EIMS: *m*/*z*: 278 (M^+). Compound **3d** (Table 2, major): 2-iodo-3-(*p*-tolyloxy)propanol: liquid, IR (KBr): ν_{max}: 3420, 3029, 2876, 1446, 1380, 1123 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.04 (d, $J = 7.8$ Hz, 2H), 6.71 (d, $J = 8.2$ Hz, 2H), 4.40 (m, 1H), 4.35-4.22 (m, 2H), 3.90 (d, $J = 7.8$ Hz, 2H), 2.30 (s, 3H). EIMS: *m*/*z*: 292 (M^+).

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