Triethylborane-Induced Radical Reactions in Ionic Liquids

Hideki Yorimitsu and Koichiro Oshima*

Department of Material Chemistry,
Graduate School of Engineering, Kyoto University,
Yoshida, Sakyo-ku, Kyoto 606-8501

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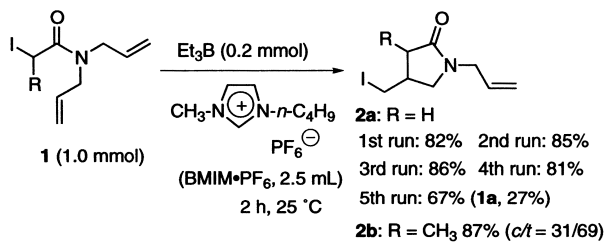
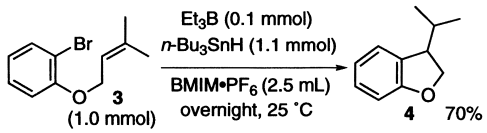
Some triethylborane-induced radical reactions were found to proceed in ionic liquids. The reactions include atom transfer radical cyclization, hydrostannylation of alkyne, and atom transfer radical addition. Benzyl bromoacetate participated in the bromine atom transfer addition reaction to 1-octene in 1-ethyl-3-methylimidazolium tetrafluoroborate to afford the corresponding adduct in excellent yield. The facile bromine atom transfer addition in the ionic liquid indicates that the ionic liquid may have a highly polar nature. The ionic liquid used was recyclable in one case, but was not in the other case.

Room temperature ionic liquids have proved to be good solvents for many reactions, such as the Diels–Alder reaction, transition metal-catalyzed reactions, and the Friedel–Crafts reactions.[1,2] However, radical reactions in ionic liquids have been poorly investigated.[3] We have been interested in solvent effects on radical reactions.[4] Here we wish to report the results of some radical reactions in ionic liquids.

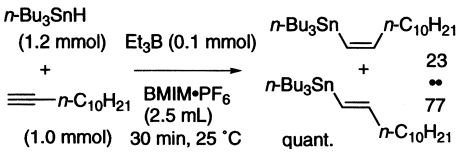
We first examined radical cyclization reaction of *N*,*N*-diallyl-2-iodoacetamide (**1a**). Triethylborane was added to amide **1a** in 1-butyl-3-methylimidazolium hexafluorophosphate (BMIM·PF_6). After stirring under air at 25 °C for 2 h, ether (15 mL) was added to the reaction flask, and the product was extracted (four times). Concentration and silica gel column purification provided γ-lactam **2a** in 82% yield. The reaction was homogeneous. 2-Iodopropanamide **1b** underwent cyclization similarly to afford **2b** in 87% yield. We investigated the number of times that we could reuse the solvent. After extraction, the ionic liquid was dried at 80 °C in vacuo (0.5 Torr) for recycling (1 Torr≈133.322 Pa). As shown in Scheme 1, a decreasing yield was observed in the fifth run. Although we did



Scheme 1.

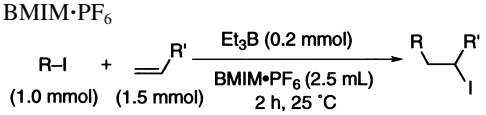


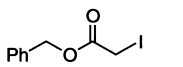
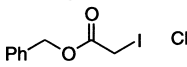
Scheme 2.



Scheme 3.

Table 1. Iodine Atom-Transfer Radical Addition in BMIM·PF_6



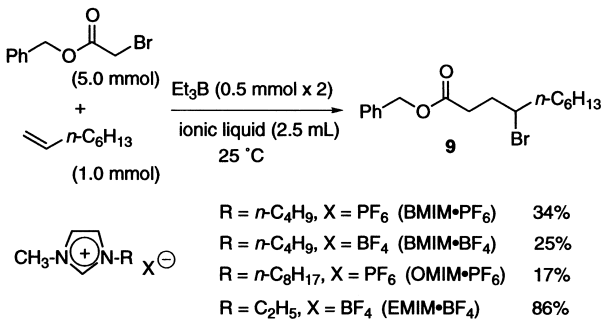
R–I	R'	yield/%
	n-C_6H_{13}	**5:** 87
	CH_2CH_2OH	**6:** 64
n-C_4F_9–I	n-C_6H_{13}	**7:** 94
n-C_4F_9–I	CH_2CH_2OH	**8:** 74

NMR measurements of fresh ionic liquid and the ionic liquid used five times, no meaningful difference was observed in the NMR charts. The reason for the decreasing yield is not clear.

Tributyltin hydride effected reductive cyclization of the prenyl ether of *o*-bromophenol **3**, although the reaction required a longer reaction time (Scheme 2). In this case, the system was heterogeneous, and the layer of tributyltin hydride floated on the ionic liquid.

We then focused on intermolecular radical addition reactions. Hydrostannylation of 1-dodecyne yielded the corresponding 1-alkenylstannane (*E*/*Z* = 77/23) quantitatively (Scheme 3). A similar reaction was also successful in hexane or without solvent. In regard to the stereoselectivity of the alkenylstannane, no difference was observed among these three reactions.

Finally, halogen atom-transfer addition was examined. Perfluoroalkyl iodide and benzyl iodoacetate underwent radical addition smoothly to yield the corresponding adducts (Table 1). The reaction appeared to proceed in a homogeneous phase. On the other hand, addition of benzyl bromoacetate was less efficient (Scheme 4), where a heterogeneous phase, arising from an excess of benzyl bromoacetate, was formed. The reaction in BMIM·PF_6 gave **9** in 34% yield. Several kinds of ionic liquid were surveyed to improve the yield. The use of 1-methyl-3-octylimidazolium hexafluorophosphate (MOIM·PF_6) that has a longer side chain resulted in the lowest yield of **9**. In contrast, reaction in 1-ethyl-3-methylimidazolium tetrafluoroborate (EMIM·BF_4) proceeded very efficiently. The adduct **9** was obtained in 86% yield upon treatment of a mixture of 1-



Scheme 4.

octene and benzyl bromoacetate with triethylborane (0.50 mL×2) for 6 h. Bromine atom transfer reaction of bromoacetate is usually difficult and requires high temperature. We have reported that the reaction proceeded quite efficiently in water, and have concluded that the improvement is partly due to the polar nature of solvent.[4b,5] Thus, the facile bromine atom transfer addition in EMIM·BF_4 indicates that the ionic liquid would have a highly polar nature. Disappointingly, reuse of the ionic liquid was unsuccessful. The second run led to a lower yield (56%).

Experimental

Most of the substrates and the products are known.[4,6] BMIM·PF_6 and BMIM·BF_4 were prepared according to the literature.[7,2d] MOIM·PF_6 was prepared in a similar fashion.[7] EMIM·BF_4 and neat triethylborane were purchased from Aldrich.

Radical Cyclization of *N*,*N*-Diallyl-2-iodoacetamide in BMIM·PF_6 and Recycling of the Ionic Liquid. *N*,*N*-Diallyl-2-iodoacetamide (**1a**, 265 mg, 1.0 mmol) was placed in a 20-mL reaction flask. BMIM·PF_6 (2.5 mL) was added, and the reaction flask was filled with argon. Triethylborane (0.03 mL, 0.2 mmol) was added to the homogeneous reaction mixture, and the resulting mixture was stirred for 2 h under air at 25 °C. Ether (15 mL) for extraction was added with vigorous stirring. After stirring for 1 min, the upper layer was decanted. This extraction procedure was repeated four times. The combined ethereal solution was evaporated. Purification on silica gel with hexane/AcOEt = 2/1 provided γ-lactam (**2a**, 216 mg, 82% yield). The ionic liquid used was dried in vacuo (0.5 Torr) at 80 °C for 3 h. For the second run, the substrate **1a** was added to the ionic liquid in the reaction flask. Amide **1a** was then treated with triethylborane similarly to furnish γ-lactam (225 mg, 85%).

Radical Addition of Benzyl Bromoacetate to 1-Octene in EMIM·PF_6. Benzyl bromoacetate (0.79 mL, 5.0 mmol) and 1-octene (0.16 mL, 1.0 mmol) were placed in a 20-mL reaction flask. EMIM·PF_6 (2.5 mL) was added with stirring. The flask was then flushed with argon. Triethylborane (0.07 mL, 0.5 mmol) was added with stirring under argon, and air (10 mL) was introduced to the reaction flask. After stirring for 3 h under air at 25 °C, additional triethylborane (0.07 mL, 0.5 mmol) was added. The resulting mixture was further stirred for 3 h under air. Ether (15 mL) was added to the reaction mixture, and products were extracted (three times). The combined ethereal layer was concentrated in vacuo. Silica gel column purification of the crude oil (hexane/AcOEt = 20/1) provided benzyl 4-bromodecanoate (**9**, 294 mg, 86%).

Benzyl 4-Iododecanoate (5): IR (neat) 2928, 1738, 1167 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 6.6 Hz, 3H), 1.20–1.56 (m, 8H), 1.63–1.75 (m, 1H), 1.81–1.94 (m, 1H), 2.05–2.13 (m, 2H), 2.47–2.70 (m, 2H), 4.06–4.16 (m, 1H), 5.13 (s, 2H), 7.32–7.38 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 13.85, 22.36, 28.22, 29.21, 31.43, 34.20, 35.23, 38.02, 40.52, 66.21, 128.18, 128.23, 128.53, 135.84, 172.46. Found: C, 52.74; H, 6.39%. Calcd for $C_{17}H_{25}IO_2$: C, 52.59; H, 6.49%.

Benzyl 6-Hydroxy-4-iodohexanoate (6): IR (neat) 3427, 2891, 1732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.7 (bs, 1H), 1.89–2.19 (m, 4H), 2.49–2.72 (m, 2H), 3.70–4.00 (m, 2H), 4.23–4.33 (m, 1H), 5.13 (s, 2H), 7.28–7.42 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 33.33, 34.26, 35.46, 42.75, 62.10, 66.46, 128.23, 128.28, 128.56, 135.70, 172.47. Found: C, 45.03; H, 5.09%. Calcd for $C_{13}H_{17}IO_3$: C, 44.85; H, 4.92%.

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