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Significantly Enhanced Reactivities of the Nucleophilic Substitution Reactions in Ionic Liquid

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We have investigated the reactivities of various metal fluorides in the nucleophilic fluorination of 2-(3-methanesulfonyloxypropyl)naphthalene (**1**) as a model compound in the presence of 1-*n*-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]). The higher periodic alkali metal fluorides demonstrate greater reactivity. The fluorination using CsF among the alkali metal fluorides was completed in 20 min, affording the desired product 2-(3-fluoropropyl)naphthalene (**2a**, 95%) without any byproducts. However, the fluorinations using alkali earth, transition, and low periodic alkali metal fluorides under the same conditions occurred rarely or not at all. We have also carried out the various facile nucleophilic substitutions such as halogenations, acetoxylation, nitrilation, and alkoxylations of mesyloxyalkane **1** and 2-(3-bromopropyl)naphthalene (**6**) at the primary aliphatic position using the potassium halides, acetate, cyanide, and alkoxides, respectively, in the presence of ionic liquids. These reactions provided the desired products, such as 2-(3-halopropyl)naphthalenes **5**−**7** (95% for Cl, 96% for Br, and 93% for I), 2-(3-acetoxypropyl)naphthalene (**8**, 95%), 2-(3-cyanopropyl)naphthalene (**9**, 93%), and 2-(3-methoxypropyl)naphthalene (**10**, 92%).

Introduction

Metal salts consisting of alkali metal cations and certain anions are generally stable, economical, and easy to obtain and are traditional nucleophile sources in nucleophilic substitution processes. However, their limited solubility and low nucleophilicity in organic solvents can make the process of nucleophilic substitution difficult.[1] Generally, the polar aprotic solvents,[2] particularly dimethyl sulfoxide (DMSO),[2b] hexamethylphosphoric triamide (HMPA),[2c] and *N*-methylpyrrolidinone (NMP), etc., are good solvents for the nucleophilic substitution using metal salts. However, the high water solubility of these solvents and their high boiling points create problems in the separation and purification of organic product from these polar aprotic solvents. The reactions using polar aprotic solvents are generally less efficient in the absence of crown ether derivatives[3] or phase-transfer catalysts.[4] The crown ether derivatives such as 18-crown-6 and Kryptofix[2.2.2] and the phase-transfer catalysts such as quaternary ammonium or phosphonium salts have been widely used to enhance the solubility and nucleophilicity of alkali metal salts not only in polar aprotic solvents but in nonpolar solvents, consequently increasing the reaction rate.[3,4] Solid-supported phase-transfer and crown ether derivative catalysts also have been used in such reactions to facilitate the recovery of the catalysts.[5] However, in case of the use of tight ion pair salts, such as KF, as a nucleophile, this reaction still requires generally vigorous conditions. Recently, we reported a highly efficient method[6] for the nucleophilic fluorination of alkyl mesylate or alkyl halide to generate fluoroalkanes using KF in the presence of an ionic liquid such as [bmim][X][7] compared with the previous fluorination methods.[8,9] In this method, ionic liquids enhanced not only the reactivity of KF significantly but reduced the formation of byproducts such as alkenes and/or alcohol. There has

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(1) See: Smith, M. D.; March, J. *Advanced Organic Chemistry*, 5th ed.; Wiley-Interscience: New York, 2001; pp 389−674.

(2) (a) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; VCH (UK) Ltd.: Cambridge, U.K., 1998. (b) Martin, D.; Weise, A.; Niclas, H. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 318−334. (c) Normant, H. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 1046−1067. (d) Parker, A. J. *Chem. Rev.* **1969**, *69*, 1−32. (e) Sowinski, A. F.; Whitesides, G. M. *J. Org. Chem.* **1979**, *44*, 2369−2376. (f) Hutchins, R. O.; Taffer, I. M. *J. Org. Chem.* **1983**, *48*, 1360−1362.

(3) (a) Gokel, G. W. *Crown Ethers and Cryptands*; Royal Society of Chemistry: Cambridge, 1991. (b) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017−7036. (c) Liotta, C. L.; Harris, H. P. *J. Am. Chem. Soc.* **1974**, *96*, 2250−2252. (d) Sam, D. J.; Simmons, H. E. *J. Am. Chem. Soc.* **1974**, *96*, 2252−2253.

(4) (a) Dehmlow, E. V.; Dehmlow, S. S. *Phase Transfer Catalysis*, 3rd ed.; VCH Ltd.: New York, 1993. (b) Dehmlow, E. V. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 493−505. (c) Starks, C. M. *J. Am. Chem. Soc.* **1971**, *93*, 195−199. (d) Starks, C. M.; Owens, R. M. *J. Am. Chem. Soc.* **1973**, *95*, 3613−3617.

(5) (a) Regen, S. L.; Lee, D. P. *J. Am. Chem. Soc.* **1974**, *96*, 294−296. (b) Regen, S. L. *J. Am. Chem. Soc.* **1975**, *97*, 5956−5957; *J. Am. Chem. Soc.* **1976**, *98*, 6270−6274; *J. Org. Chem.* **1977**, *42*, 875−879.

(6) Kim, D. W.; Song, C. E.; Chi, D. Y. *J. Am. Chem. Soc.* **2002**, *124*, 10278−10279.

(7) 1-*n*-Butyl-3-methylimidazolium cation [bmim] and its counteranions—tetrafluoroborate [BF_4], hexafluorophosphate [PF_6], hexafluoroantimonate [SbF_6], triflate [OTf], bis(trifluoromethanesulfonyl)imide [NTf_2], and acetate [OAc]—are used.

(8) For reviews on nucleophilic fluorination, see: (a) Gerstenberger, M. R. C.; Haas, A. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 647−667. (b) Mascaretti, O. A. *Aldrichim. Acta* **1993**, *26*, 47−58.

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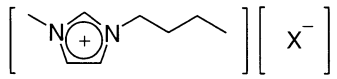


[bmim][X] {X = BF_4, PF_6, SbF_6, OTf, NTf_2, OAc}

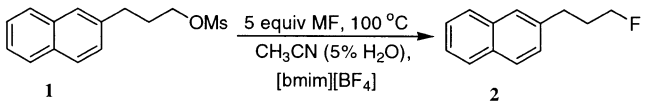
FIGURE 1. Ionic liquids.

also been much attention for ionic liquids[10] acting as powerful media in some catalytic organic reactions for facilitating catalyst recovery, accelerating reaction rate, and improving selectivity.[11] The nucleophilicity of an ionic liquid anion itself, such as chloride, bromide, and iodide of [bmim][X] (X = Cl, Br and I), has been reported.[12] Wheeler et al. reported the rate of the nucleophilic substitution reaction of only benzyl chloride using potassium cyanide in [bmim][PF_6], depending on temperature.[13] Recently, Lourenco and Afonso also reported that recycling and reuse of the ionic liquids were demonstrated for the azide formation.[14] The immiscibility of some ionic liquids with some solvents, such as ether, benzene, hexane, etc. and water, provides a bi- or triphasic system that affords facile extraction of the desired products from ionic liquids.[10a,15] In this paper, we present the reactivity of various metal fluorides, especially alkali, alkali earth, and transition-metal fluorides in the presence of various ionic liquids for nucleophilic fluorination and record the various nucleophilic substitutions of mesyloxyalkane or bromoalkane such as halogenation, acetoxylation, nitrilation, and alkoxylation using the potassium halides, acetate, cyanide, and alkoxides, respectively, in the presence of ionic liquid. In this method, the ionic liquid significantly enhanced the reactivity of various metal salts compared with the use of conventional methods.[2−5]

Results and Discussion

Table 1 illustrates the nucleophilic fluorination of 2-(3-methanesulfonyloxypropyl)naphthalene (**1**) as a model compound with various metal fluorides as fluoride sources in the presence of [bmim][BF_4]. To investigate the reactivity of various alkali metal fluorides from the second to sixth periodic, we carried out the fluorination with lithium fluoride, sodium fluoride, potassium fluoride, rubidium fluoride, and cesium fluoride under the conditions described in our previous report of this fluorination method.[6] Whereas the same reaction with KF was completed in 1.5 h, affording 2-(3-fluoropropyl)-naphthalene (**2**, 94%, entry 3), the fluorination of the mesylate **1** with LiF and NaF in the presence of [bmim]-[BF_4] at 100 °C did not proceed at all even after 48 h (entries 1 and 2). Entry 4 shows that the use of RbF, the fifth periodic alkali metal fluoride, made this fluorination proceed much faster than that of KF, presumably due to less tightness of ion pairs of RbF than KF. Moreover, the fluorination using CsF that is the most reactive in this method proceeded over the shortest reaction time among the other alkali metal fluorides, affording the desired product **2** (95%) without byproducts such as alkenes and alcohol (entry 5). These results mean that the reactivities of alkali metal fluorides in this reaction depend on the tightness of ion pairs and the size of alkali metals.[16] We also performed the fluorination with CaF_2 and AgF to investigate the reactivity of alkali earth and transition metal fluorides. However, the fluorination with CaF_2 did not take place (entry 6), and it was found that AgF was not a proper fluorination source, giving a poor yield (5%, entry 7).

TABLE 1. Fluorination of Mesylate 1 with Various Metal Fluorides in [bmim][BF_4][a]



1 2

entry	MF	reaction time (h)	yield[b] (%)
1	LiF	48	
2	NaF	48	
3	KF	1.5	93
4	RbF	30 min	93
5	CsF	20 min	95
6	CaF_2	24	
7	AgF	48	5[c]

[a] All reactions were carried out on a 1.0 mmol reaction scale of mesylate **1** using 5 mmol of MF in 3 mL of [bmim][BF_4] and 3 mL of CH_3CN (5% H_2O) at 100 °C. [b] Isolated yield. [c] Determined by ^1H NMR.

As a further study of entry 5 in Table 1 in detail, Table 2 illustrates the fluorination of mesylate **1** with CsF in the presence or absence of [bmim][BF_4] under various reaction conditions. Whereas the mesylate **1** was converted to the fluoroalkane **2** (58%) at 25 °C for 48 h via fluorination using CsF in the presence of [bmim][BF_4] (entry 2), the same reaction in an organic solvent such as acetonitrile without an ionic liquid did not proceed at all (entry 3). Even though we have carried out the fluorination in acetonitrile at 100 °C for 48 h, the reaction converted only the 16% of mesylate **1** to the fluoroalkane **2** (entry 4). A comparison of entries 1 and 5 demonstrates that fluorination in the ionic liquid [bmim][BF_4] not only proceeded remarkably faster but provided fluoroalkane **2** in higher yield (95%) without any byproducts compared

(9) (a) Colonna, S.; Re, A.; Gelbard, G.; Cesarotti, E. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2248−2252. (b) Ishikawa, N.; Kitazume, T.; Yamazaki, T.; Mochida, Y.; Tatsumo, T. *Chem. Lett.* **1981**, 761−764. (c) Clark, J. H.; Hyde, A. J.; Smith, D. K. *J. Chem. Soc., Chem. Commun*. **1986**, 791−793. (d) Ichihara, J.; Matsuo, T.; Hanafusa, T.; Ando, T. *J. Chem. Soc., Chem. Commun*. **1986**, 793−794. (e) Cox, D. P.; Terpinsky, J.; Lawrynowicz, W. *J. Org. Chem*. **1984**, *49*, 3216−3219. (f) Chi, D. Y.; Kilbourn, M. R.; Katzenellenbogen, J. A.; Welch, M. J. *J. Org. Chem*. **1987**, *52*, 658−664. (g) Pilcher, A. S.; Ammon, H. L.; DeShong, P. *J. Am. Chem. Soc*. **1995**, *117*, 5166−5167. (h) Garayt, M.; Le Boulaire, V.; Gree, D.; Gree, R.; Schanen, V.; Spindler, J.-F. PCT Int. Appl. PIXXD2 WO 0292608, 2002, 59 pp.

(10) For recent reviews on ionic liquids, see: (a) Sheldon, R. *Chem. Commun*. **2001**, 2399−2407. (b) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed. Engl*. **2000**, *39*, 3772−3789. (c) Welton, T. *Chem. Rev*. **1999**, *99*, 2071−2083.

(11) (a) Song, C. E.; Shim, W. H.; Roh, E. J.; Lee, S.-g.; Choi, J. H. *Chem. Commun*. **2001**, 1122−1123. (b) Song, C. E.; Shim, W. H.; Roh, E. J.; Choi, J. H. *Chem. Commun*. **2000**, 1695−1696. (c) Song, C. E.; Roh, E. J. *Chem. Commun*. **2000**, 837−838.

(12) (a) Lancaster, N. L.; Welton, T.; Young, G. B. *J. Chem. Soc., Perkin Trans. 2* **2001**, 2267−2270. (b) Lancaster, N. L.; Salter, P. A.; Welton, T.; Young, G. B. *J. Org. Chem*. **2002**, *67*, 8855−8861.

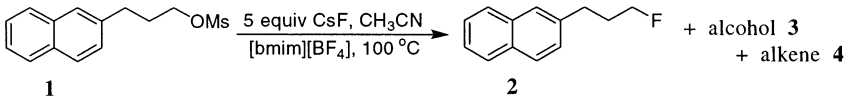
(13) Wheeler, C.; West, K. N.; Liotta, C. L.; Eckert, C. A. *Chem. Commun*. **2001**, 887−888.

(14) Lourenco, N. M. T.; Afonso, C. A. M. *Tetrahedron* **2003**, *59*, 789−794.

(15) Carmichael, A. J.; Earle, M. J.; Holbrey, J. D.; McCormac, P. B.; Seddon, K. R. *Org. Lett*. **1999**, *1*, 977−979.

(16) Dijkstra, G.; Kruizinga, W. H.; Kellog, R. H. *J. Org. Chem*. **1987**, *52*, 4230−4234.

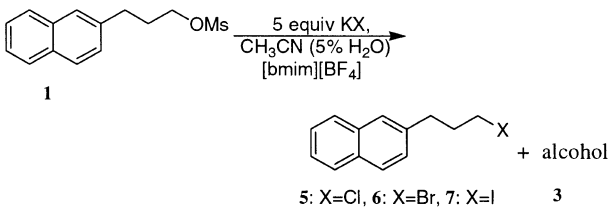
TABLE 2. Fluorination of Mesylate 1 with CsF under Various Reaction Conditions[a]



entry	[bmim][BF_4] (mL) [equiv]	CH_3CN (mL)	*T* (°C)	reaction time (h)	yield of product[b] (%) 1	2	3	4
1	3	3	100	20 min		95		
2	3	3	25	48	35	58	trace	
3		6	25	48	94			
4		6	100	48	79	16		
5	18-crown-6 [2]	6	100	5	trace	88		7[c]

[a] All reactions were carried out on a 1.0 mmol reaction scale of mesylate **1** using 5 mmol of CsF. [b] Isolated yield. [c] Determined by ^1H NMR.

TABLE 3. Various Halogenations of Mesylate 1 with Potassium Halides in [bmim][BF_4][a]



entry	KX	time (min)	*T* (°C)	yield of product[b] (%) 1	5−7	3
1	KCl	30	100		95	
2	KBr	30	100		96	
3	KI	15	100	trace	93	trace
4	KI	24 h	25	45	50	5[c]

[a] All reactions were carried out on a 1.0 mmol reaction scale of mesylate **1** using 5 mmol of KX in 3 mL of [bmim][BF_4] and 3 mL of CH_3CN (5% H_2O) at 100 °C. [b] Isolated yield. [c] Determined by ^1H NMR.

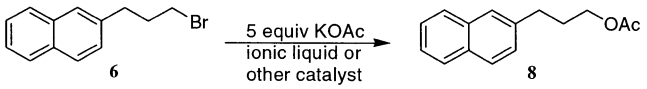
to the fluorination using 2 equiv of 18-crown-6, which afforded the fluoroalkane **2** (88%) with alkene (7%) after a 15 times longer reaction time.

As shown in Table 3, we have also carried out the various nucleophilic halogenations—chlorination, bromination, and iodination—of mesylate **1** with the corresponding potassium halides instead of KF in the presence of [bmim][BF_4] under the same conditions as for entry 3 in Table 1. Entries 1−3 show the chlorination, bromination, and iodination using KCl, KBr, and KI in the presence of [bmim][BF_4] were completed within 30 min, providing 2-(3-chloropropyl)naphthalene (**5**, 95%), 2-(3-bromopropyl)naphthalene (**6**, 96%), and 2-(3-iodopropyl)-naphthalene (**7**, 93%), respectively. A comparison of nucleophilic substitution reactions with potassium halides in an ionic liquid shows that the reaction times are shortened by the increase of nucleophilicity of the halides.

To determine whether an ionic liquid enhanced the reactivity and selectivity significantly in other S_N2 reactions, we have performed the nucleophilic acetoxylation of bromoalkane **6** to 2-(3-acetoxypropyl)naphthalene (**8**) using potassium acetate at 25 °C under the various conditions as shown in entries 1−5 in Table 4. In general, although the transformations of alkyl alcohols to alkyl chlorides or bromides are quite easy, the reverse transformations are not. Therefore, the acetoxylations of alkyl chlorides or bromides would be an important step to prepare alkyl alcohols. The acetoxylation using [bmim]-[BF_4] and CH_3CN as a cosolvent system was completed within 2 h at 25 °C, affording the desired product **8** in high yield (95%, entry 1), while the same reaction in only acetonitrile without an ionic liquid did not occur even after 48 h (entry 2). In entry 3, the acetoxylation in polar aprotic solvent such as DMSO-d_6, as monitored by NMR, proceeded for 6 h. In entry 4, the use of 2 equiv of 18-crown-6 as a phase-transfer catalyst gave a similar result with the use of DMSO as a solvent. However, a comparison of entries 3, 4, and 1 demonstrates that DMSO and 18-crown-6 enhance the nucleophilicity of KOAc in the reaction media less than ionic liquid [bmim][BF_4] does. In entry 5, the acetoxylation with 2 equiv of tetrabutylammonium bromide as a phase-transfer catalyst in benzene/water system at 25 °C occurred to only a small extent, affording only 5% of **8**. We have also carried out the acetoxylations of **6** using six other ionic liquids at 50 °C to investigate the reactivity of KOAc under various ionic liquids. Acetoxylation in [bmim][BF_4] was completed within 30 min, affording **8** in high yield (entry 6, 96%). In entry 7, with [bmim][OAc], we obtained a similar result in [bmim][BF_4]. These reactions in [bmim][OTf], [bmim][PF_6], and [bmim][SbF_6] also provided **8** in good yield (95, 94, and 89%, respectively) but required longer reaction times (12, 24, and more than 24 h, entries 8−10). When we carried out the same reaction with entry 9 at 90 °C in the presence of [bmim][PF_6] in CH_3CN (entry 12) or 1,4-dioxane (entry 13) as a cosolvent, the reaction rate increased significantly compared with reaction rate at 50 °C. Low solubility of KOAc in [bmim][PF_6]/CH_3CN reaction media at 50 °C makes the reaction rate slow. In entry 11, when the acetoxylation in [bmim][NTf_2] was carried out over 24 h, bromoalkane **6** still remained.

Table 5 illustrates the nucleophilic nitrilation using 5 equiv of potassium cyanide in the presence or absence of [bmim][BF_4] and the alkoxylation using 5 equiv of potassium alkoxides in [bmim][BF_4] and corresponding alcohols as cosolvents. Whereas the nitrilation of **6** in the absence of [bmim][BF_4] did not occur (entry 2), the same reaction in the presence of [bmim][BF_4] was completed within 1 h, affording 2-(3-cyanopropyl)naphthalene (**9**, 93%, entry 1). In entry 3, the methoxylation of **6** with potassium methoxide in the presence of [bmim][BF_4] at 25 °C provided 2-(3-methoxypropyl)naphthalene (**10**, 92%) without any byproduct. However, bromoalkane **6**

TABLE 4. Acetoxylation of Bromoalkane 6 with KOAc under Various Reaction Conditions[a]

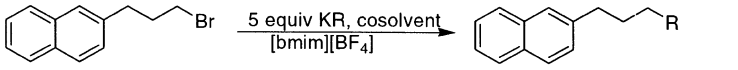


6 8

entry	ionic liquid (mL) or catalyst (2 equiv)	solvent (mL)	*T* (°C)	time (h)	yield[b] (%) 6	yield[b] (%) 8
1	[bmim][BF_4] (3.0)	CH_3CN (3.0)	25	2		95
2		CH_3CN (6.0)	25	48	97	0
3[c]		DMSO-d_6 (0.6)	25	6	trace	99[d]
4	18-crown-6	CH_3CN (6.0)	25	6		92
5	*n*-Bu_4NBr	benzene/H_2O [5/1]	25	48	91	5[d]
6	[bmim][BF_4] (3.0)	CH_3CN (3.0)	50	0.5		96
7	[bmim][OAc] (3.0)	CH_3CN (3.0)	50	1		95
8	[bmim][OTf] (3.0)	CH_3CN (3.0)	50	12		95
9	[bmim][PF_6] (3.0)	CH_3CN (3.0)	50	24		94
10	[bmim][SbF_6] (3.0)	CH_3CN (3.0)	50	24	5[d]	89
11	[bmim][NTf_2] (3.0)	CH_3CN (3.0)	50	24	24	67
12	[bmim][PF_6] (3.0)	CH_3CN (3.0)	90	0.5		93
13	[bmim][PF_6] (3.0)	1,4-dioxane (3.0)	90	0.5		95

[a] All reactions were carried out on a 1.0 mmol reaction scale of bromoalkane **6** using 5 mmol of KOAc. [b] Isolated yield. [c] 0.1 mmol reaction scale of **6**. [d] Determined by ^1H NMR.

TABLE 5. Nucleophilic Substitutions of Bromoalkane 6 with Various Potassium Salts in the Presence or Absence of [bmim][BF_4][a]



6 **9**: R=CN, **10**: R=OCH_3, **11**: R=O*t*Bu

entry	KR	[bmim][BF_4] (mL)	solvent (mL)	*T* (°C)	time (min)	yield[b] (%)	comment
1	KCN	3.0	CH_3CN (3.0)	50	60	93	
2	KCN		CH_3CN (6.0)	25	48 h	0	100% SM
3	$KOCH_3$	3.0	MeOH (3.0)	25	15 h	92	
4	$KOCH_3$	3.0	MeOH (3.0)	70	25	80	15% alkene
5	KO*t*-Bu	3.0	*t*-BuOH (3.0)	70	25	0	95% alkene

[a] All reactions were carried out on a 1.0 mmol reaction scale of bromoalkane **6** using 5 mmol of KR in 3 mL of [bmim][BF_4] and 3 mL of cosolvent. [b] Isolated yield.

underwent the methoxylation and elimination simultaneously under more vigorous conditions (70 °C) in the same reaction, providing the methoxyalkane (80%) with alkene (15%) as a byproduct because potassium methoxide can act not only as a nucleophile but also as a base (entry 4). When potassium *tert*-butoxide was used under the same conditions with entry 4 in Table 5, the elimination took place, but not butoxylation since potassium *tert*-butoxide acted only as a base (entry 5).

Conclusion

We have demonstrated the reactivities of various metal fluorides in the nucleophilic fluorination of the mesylalkane to the fluoroalkane in the presence of ionic liquid [bmim][BF_4]. Among alkali metal fluorides, CsF was the most reactive in this reaction since the reactivities of alkali metal fluorides depend on the tightness of ion pairs and the size of alkali metals. The presence of [bmim][BF_4] not only increased the reactivity of CsF markedly but also reduced the formation of byproducts. However, the fluorination using alkali earth and transition-metal fluorides under the same conditions occurred hardly or not at all.

We have also demonstrated the various facile nucleophilic substitutions such as halogenations, acetoxylation, nitrilation, and alkoxylations of bromo- and mesyloxyalkanes at the primary aliphatic position using the corresponding potassium salts as nucleophiles in the presence of ionic liquids. Ionic liquids could enhance the reactivity of metal salts, especially alkali metal salts, significantly in the nucleophilic substitution. This ionic liquid method was more efficient (lower reaction temperature, shorter reaction time, easier purification, etc.) than the previous methods using phase transfer catalysts or polar aprotic solvents. Further studies on the development of new designed ionic liquids for a more efficient nucleophilic substitution are in progress in our laboratories. Applications of other reaction methods using ionic liquids are also under investigations.

Experimental Section

Materials. ^1H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer, and chemical shifts were reported in δ units (ppm) relative to tetramethylsilane. TLC analysis was performed using glass plate with silica gel 60 F_{254}. Flash chromatography was performed with 230−400 mesh silica gel. All other known compounds and all ionic liquids were commercially available.

2-(3-Hydroxypropyl)naphthalene (3). Butyllithium (52.7 mmol) in hexane (21.0 mL) was added dropwise, over 30 min, to a well-stirred solution of 2-methylnaphthalene (5.0 g, 35.2

mmol) and potassium *tert*-butoxide (5.9 g, 52.7 mmol) in dried THF (150 mL) at 0 °C under nitrogen atmosphere. After 1 h at 0 °C, 1-bromo-2-*tert*-butyldimethylsilyloxyethane (12.6 g, 52.7 mmol) was added portionwise to the mixture at 0 °C. The reaction mixture was stirred at 25 °C for 3 h. The reaction mixture was poured into water (200 mL) and extracted from the aqueous phase with EtOAc (200 mL × 3). The organic layer was dried (sodium sulfate) and evaporated under reduced pressure. The residue was purified by short flash column chromatography (100% EtOAc) to obtain the crude product. The solvent was evaporated under reduced pressure. Tetrabutylammonium fluoride (16.6 g, 52.7 mmol) was added to the crude product in THF (200 mL) and stirred at 25 °C for 6 h. The reaction mixture was dissolved in water (200 mL) and extracted from the aqueous phase with EtOAc (200 mL × 3). The organic layer was dried (sodium sulfate) and evaporated under reduced pressure. The residue was purified by flash column chromatography (30% EtOAc/hexane) to yield 5.9 g (31.7 mmol, 90%) of 2-(3-hydroxypropyl)naphthalene (**3**) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (s, 1H), 1.96−2.03 (m, 2H), 2.89 (t, J = 7.6 Hz, 2H), 3.72 (t, J = 6.4 Hz, 2H), 7.34−7.37 (m, 1H), 7.41−7.48 (m, 2H), 7.65 (s, 1H), 7.77−7.82 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.17, 34.05, 62.23, 125.16, 125.92, 126.40, 127.24, 127.37, 127.58, 127.94, 131.98, 133.58, 139.28; MS (EI) 186 (M^+), 142 (100); HRMS (EI) calcd for $C_{13}H_{14}O$ (M^+) 186.1045, found 186.1049.

2-(3-Methanesulfonyloxypropyl)naphthalene (1). To alcohol **3** (5.0 g, 26.8 mmol) in methylene chloride (150 mL) were added triethylamine (4.5 mL, 32.2 mmol) and methanesulfonyl chloride (2.5 mL, 32.2 mmol) at 0 °C. The mixture was stirred at 25 °C for 3 h and evaporated under reduced pressure to remove methylene chloride. The residue was dissolved in water (200 mL) and extracted from the aqueous phase with EtOAc (200 mL × 3). The organic layer was dried (sodium sulfate) and evaporated under reduced pressure. The residue was purified by flash column chromatography (20% EtOAc/hexane) to give 6.2 g (23.6 mmol, 88%) of 2-(3-methanesulfonyloxypropyl)naphthalene (**1**) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.14−2.21 (m, 2H), 2.93 (t, J = 7.6 Hz, 2H), 2.99 (s, 3H), 4.26 (t, J = 6.4 Hz, 2H), 7.32−7.35 (m, 1H), 7.44−7.50 (m, 2H), 7.65 (s, 1H), 7.79−7.84 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.45, 31.59, 37.24, 69.10, 125.39, 126.07, 126.62, 126.92, 127.36, 127.57, 128.18, 132.06, 133.48, 137.68; MS (EI) 264 (M^+), 168 (100), 141; HRMS (EI) calcd for $C_{14}H_{16}O_3S$ (M^+) 264.0820, found 264.0831.

Typical Procedure of the Fluorination in Table 1. CsF (760 mg, 5 mmol) was added to the mixture of 2-(3-methanesulfonyloxypropyl)naphthalene (**1**, 264 mg, 1.0 mmol), [bmim]-[BF_4] (3.0 mL), and H_2O (90 μL, 5 mmol) in acetonitrile (3.0 mL). The mixture was stirred at 100 °C for 20 min. We determined the reaction time by TLC. The reaction mixture was extracted from the ionic liquid phase with ethyl ether (7 mL × 3). The ether layer was dried (sodium sulfate) and evaporated under reduced pressure. The residue was purified by flash column chromatography (5% EtOAc/hexane) to provide 179 mg (0.95 mmol, 95%) of 2-(3-fluoropropyl)naphthalene (**2**) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.07−2.20 (m, 2H), 2.95 (t, J = 7.6 Hz, 2H), 4.52 (dt, J = 47.6, 6.0 Hz, 2H), 7.37−7.39 (m, 1H), 7.45−7.53 (m, 2H), 7.68 (s, 1H), 7.84−7.87 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.41 (d, J = 5.4 Hz), 31.89 (d, J = 19.7 Hz), 83.05 (d, J = 163.7 Hz), 125.26, 125.97, 126.57, 127.17, 127.40, 127.58, 128.02, 132.03, 133.57, 138.54; MS (EI) 188 (M^+), 141 (100), 115; HRMS (EI) calcd for $C_{13}H_{13}F$ (M^+) 188.1001, found 188.1001.

Procedure for the Halogenation in Table 3. The preparation followed the typical procedure of fluorination except that KX (X = Cl, Br, or I) was used and 195 mg (0.95 mmol, 95%) of 2-(3-chloropropyl)naphthalene (**5**), 239 mg (0.96 mmol, 96%) of 2-(3-bromopropyl)naphthalene (**6**), or 275 mg (0.93 mmol, 93%) of 2-(3-iodopropyl)naphthalene (**7**) was obtained as a colorless oil, respectively.

2-(3-Chloropropyl)naphthalene (5): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16−2.23 (m, 2H), 2.97 (t, J = 7.4 Hz, 2H), 3.58 (t, J = 6.4 Hz, 2H), 7.35−7.37 (m, 1H), 7.44−7.51 (m, 2H), 7.67 (s, 1H), 7.80−7.85 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.84, 33.85, 44.20, 125.30, 126.00, 126.71, 127.14, 127.40, 127.58, 128.08, 132.06, 133.54, 138.12; MS (EI) 204 (M^+), 141 (100), 115; HRMS (EI) calcd for $C_{13}H_{13}Cl$ (M^+) 204.0706, found 204.0702.

2-(3-Bromopropyl)naphthalene (6): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24−2.31 (m, 2H), 2.97 (t, J = 7.2 Hz, 2H), 3.44 (t, J = 6.6 Hz, 2H), 7.34−7.37 (m, 1H), 7.44−7.51 (m, 2H), 7.67 (s, 1H), 7.80−7.85 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.09, 33.97, 34.20, 125.31, 126.01, 126.74, 127.12, 127.40, 127.58, 128.09, 132.07, 133.53, 137.96; MS (EI) 250 (M^+), 248 (M^+), 141, 115; HRMS (EI) calcd for $C_{13}H_{13}{}^{79}Br$ (M^+) 248.0201, found 248.0200.

2-(3-Iodopropyl)naphthalene (7): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21−2.28 (m, 2H), 2.92 (t, J = 7.2 Hz, 2H), 3.22 (t, J = 6.8 Hz, 2H), 7.34−7.37 (m, 1H), 7.45−7.52 (m, 2H), 7.68 (s, 1H), 7.80−7.85 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 6.37, 34.66, 36.28, 125.30, 126.00, 126.73, 127.11, 127.40, 127.58, 128.08, 132.07, 133.51, 137.80; MS (EI) 296 (M^+), 141 (100); HRMS (EI) calcd for $C_{13}H_{13}I$ (M^+) 296.0062, found 296.0054.

Typical Procedure for Acetoxylation. Potassium acetate (491 mg, 5 mmol) was added to the mixture of 2-(3-bromopropyl)naphthalene (**1**, 249 mg, 1.0 mmol), and [bmim][BF_4] (3.0 mL) in acetonitrile (3.0 mL). The mixture was stirred at 50 °C for 30 min. The reaction mixture was extracted from the ionic liquid phase with ethyl ether (7 mL × 3). The ether layer was dried (sodium sulfate) and evaporated under reduced pressure. The residue was purified by flash column chromatography (10% EtOAc/hexane) to yield 219 mg (0.96 mmol, 96%) of 2-(3-acetoxypropyl)naphthalene (**8**) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.04−2.11 (m, 5H), 2.88 (t, J = 7.6 Hz, 2H), 4.16 (t, J = 6.6 Hz, 2H), 7.34−7.36 (m, 1H), 7.45−7.50 (m, 2H), 7.65 (s, 1H), 7.79−7.84 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.91, 30.02, 32.26, 63.79, 125.19, 125.92, 126.39, 127.06, 127.35, 127.54, 127.96, 131.98, 133.52, 138.62, 171.09; MS (EI) 228 (M^+), 168 (100), 141, 115; HRMS (EI) calcd for $C_{15}H_{16}O_2$ (M^+) 228.1150, found 228.1156.

2-(3-Cyanopropyl)naphthalene (9). The preparation followed the typical procedure of acetoxylation except that potassium cyanide was used and 181 mg (0.93 mmol, 93%) of 2-(3-cyanopropyl)naphthalene (**9**) was obtained as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.04−2.12 (m, 2H), 2.35 (t, J = 7.2 Hz, 2H), 2.95 (t, J = 7.4 Hz, 2H), 7.31−7.33 (m, 1H), 7.44−7.51 (m, 2H), 7.65 (s, 1H), 7.79−7.84 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.36, 26.74, 34.44, 119.50, 125.55, 126.19, 126.77, 126.84, 127.44, 127.62, 128.37, 132.20, 133.51, 137.08; MS (EI) 195 (M^+), 141 (100), 115; HRMS (EI) calcd for $C_{14}H_{13}N$ (M^+) 195.1048, found 195.1049.

2-(3-Methoxypropyl)naphthalene (10). The preparation followed the typical procedure of acetoxylation except that potassium methoxide was used and 184 mg (0.92 mmol, 92%) of 2-(3-methoxypropyl)naphthalene (**10**) was obtained as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03−2.08 (m, 2H), 2.92 (t, J = 7.6 Hz, 2H), 3.42 (s, 3H), 3.47 (t, J = 6.2 Hz, 2H), 7.39−7.42 (m, 1H), 7.47−7.52 (m, 2H), 7.69 (s, 1H), 7.82−7.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.07, 32.36, 58.48, 71.79, 125.05, 125.80, 126.38, 127.28, 127.35, 127.53, 127.80, 131.94, 133.57, 139.40; MS (EI) 200 (M^+), 168, 142 (100), 115; HRMS (EI) calcd for $C_{14}H_{16}O$ (M^+) 200.1201, found 200.1204.

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