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The first Cu(I)-mediated nucleophilic trifluoromethylation reactions using (trifluoromethyl)trimethylsilane in ionic liquids

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The new ionic liquids (**5a–8a**) were used as reaction media for nucleophilic trifluoromethylation reactions of trifluoromethyl(trimethyl)silane with (1) aryl, allyl, benzyl, and alkyl halides in Cu(I)-mediated C–C bond formation reactions, and (2) carbonyl functionalities catalyzed with Ph_3P or CsF. In addition, conversion of benzyl bromide as a model compound to benzyl fluoride was examined in **6a** using CsF as the fluorinating reagent. The morpholinium-based ionic liquid (**6a**) stood out as an efficient solvent system comparable to organic solvents and superior to the other new ionic liquids prepared in this work as well as to $[bmim]^+[PF_6]^-$. Neat reactions of *N*-methyloxazolidine (**1**), *N*-methylmorpholine (**2**), *N*-methylimidazole (**3**) or *N*-methyltriazole (**4**) with 2-(2-ethoxyethoxy)ethyl bromide ($BrCH_2CH_2OCH_2CH_2OCH_2CH_3$, **9**) or 2-bromoethyl methyl ether ($BrCH_2CH_2OCH_3$, **10**) at 75 or 105 °C gave the *N*-(2-ethoxyethoxy)ethyl- or *N*-methoxyethyl-substituted oxazolidinium, morpholinium, imidazolium and triazolium quaternary bromides (**1a–4a**, **1b–4b**) which were metathesized with $LiN(SO_2CF_3)_2$ to form the respective room-temperature liquid bis(trifluoromethanesulfonyl)amides **5a–8a** and **5b–8b** in high yields with transition or melting points <−78 °C as determined by DSC. All of the ionic liquids are thermally stable to >310 °C as determined by thermogravimetric analyses (TGA). Densities range between 1.29 and 1.53 g cm^{-3} at 25 °C.

Introduction

The introduction of fluorine and fluorinated groups into organic and inorganic molecules is interesting due to the resulting dramatic changes in physical and chemical properties.[1–2] The presence of the trifluoromethyl group influences the lipophilicity of pharmaceutical and agrochemical compounds, thus, improving transport characteristics *in vivo* and facilitates lower dose rates.[1a,2d,3] Since trifluoromethyl(trimethyl)silane ($TMSCF_3$) was first synthesized in 1984 and demonstrated to be a powerful trifluoromethylating reagent with aldehydes and ketones, extensive research has led to the introduction of the trifluoromethyl group into a very large number of organic and inorganic molecules.[1,4] Recently, very effective nucleophilic trifluoromethylation reactions using $TMSCF_3$ in the presence of fluoride ions with carbonyl compounds, such as ketones, aldehydes, enones, esters and diketo compounds, were reported.[1,5–10] Some effort has been focused on generating a (trifluoromethyl)copper species for use for the trifluoromethylation of organic halides.[11] For example, such a species was generated for reaction of aryl halides with trifluoromethyl iodide in the presence of activated copper at 130–140 °C in DMF,[11a] and, also, by heating bis(trifluoromethyl)-mercury with activated copper powder in NMP or DMAC at 140 °C for 2 h.[11c] However, using the CuI/KF system with $TMSCF_3$ under mild conditions is apparently a more convenient method for introducing a trifluoromethyl group into organic halides.[12] The trifluoromethylation of allyl halides is much more difficult than that of benzyl and aryl bromides.[11,12]

In a highly efficient manner, caesium fluoride was shown to fluorinate alkyl mesylate or alkyl halides in ionic liquids.[13] In these fluorination experiments, ionic liquids played a critical role in increasing the reactivity of metal fluorides as well as reducing the number of byproducts. Also, the commercially available ionic liquid, $[bmim][PF_6]$, has been shown to be a useful medium for electrophilic fluorination reactions.[14]

In general, ionic liquids based on the *N*-alkyl-3-methylimidazolium cation have been evaluated extensively as alternatives to organic solvents. There are a few examples of the use of ionic liquids as solvents for fluorination reactions as well as of non-imidazolium based ionic liquids for this purpose.[13–15] To the best of our knowledge, ionic liquids have not been used as solvents for trifluoromethylation reactions.

In this work, we report the synthesis of several new *N*-methyloxazolidinium (**5a–b**), *N*-methylmorpholinium (**6a–b**), *N*-methylimidazolium (**7a–b**) and *N*-methyltriazolium (**8a–b**) based ionic liquids where the cations contain either 2-(2-ethoxyethoxy)ethyl or methoxyethyl substituents. The relative efficiency of the nucleophilic trifluoromethylation of benzyl bromide with $TMSCF_3$ was determined in the presence of a Cu(I) catalyst in various ionic liquids. The trifluoromethylation of carbonyl functionalities with $TMSCF_3$ using a catalytic amount of CsF or Ph_3P as well as fluorination reactions using CsF was examined.

Results and discussion

Recently we have reported a variety of fluorinated oxazolidinium, morpholinium, imidazolium, pyridinium, bipyridinium, pyrazinium, pyridazinium, pyrimidinium, 1,4-dimethylpiperazinium, and triazolium ionic liquids.[16–20] *N*-Alkoxyalkyl and *N*-fluoroalkoxyalkyl substituted morpholinium ionic liquids, when compared with alkyl or fluoroalkyl substituted analogues, display increasing thermal stabilities and decreasing viscosities which are independent of the number of fluorine atoms.[19] Because of these interesting changes in physical and thermal properties, the chemistry of *N*-methoxyethyl- and *N*-(ethoxyethoxy)ethyl-substituted oxazolidinium, morpholinium, imidazolium and triazolium based ionic liquids were examined more extensively (Scheme 1).

Initially, *N*-methyltriazole was heated with 2-(2-ethoxyethoxy)ethyl bromide (**9**) in THF at 75 °C for several days, but no reaction occurred. Neither increased reaction temperature (105 °C) nor extended reaction time altered this result. However, the neat reaction at 105 °C for 24 h led to the formation of the quaternary salt (**4a**) in excellent yield (95%). Similarly, although *N*-methylmorpholine and *N*-methylimidazole with **9** in THF at 75 °C for 2 days gave the corresponding quaternary salts (**2a, 3a**) in low yields, 15 and 45%, respectively, neat reactions at 105 °C resulted in significantly enhanced yields (95%). The reactions of *N*-methyloxazolidine with **9** or **10** (2-(2-ethoxyethoxy)ethyl bromide) in THF or without solvent at 70 °C for 1 day resulted in high yields (99%) of **1a** and **1b**. Each of the bromides (**1a–4a, 1b–4b**) was metathesized with lithium bis(trifluoromethanesulfonyl)amide using either acetone or water as solvent at 25 °C

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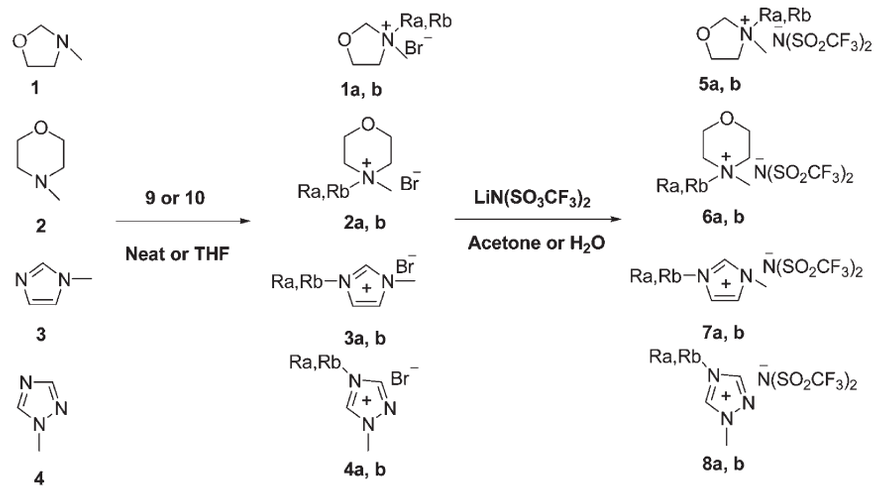


Ra = $CH_2CH_2OCH_2CH_2OCH_2CH_3$
Rb = $CH_2CH_2OCH_3$
9 = $BrCH_2CH_2OCH_2CH_2OCH_2CH_3$
10 = $BrCH_2CH_2OCH_3$

Scheme 1

Table 1 Physical and thermal properties of *N*-alkoxy-substituted oxazolidinium (**5a**,**b**), morpholinium (**6a**,**b**), imidazolium (**7a**,**b**) and triazolium salts (**8a**,**b**)

Compd	Density[a]	Yield[b]	T_m (T_g)[c]	T_d[d]
5a	1.29	99	[e]	318
6a	1.39	93	[e]	340
7a	1.35	95	[e]	358
8a	1.38	97	(−53)	308
5b	1.53	95	[e]	321
6b	1.42	97	[e]	350
7b	1.41	95	[e]	386
8b	1.53	98	[e]	310

[a] g cm^{-3}, 25 °C, pycnometer. [b] Isolated (%). [c] Phase transition temperature (°C). [d] Thermal decomposition temperature TGA (°C). [e] <−78 °C.

Table 2 Dynamic viscosities (η/cP) of *N*-alkoxy-substituted oxazolidinium (**5a**,**b**), morpholinium (**6a**,**b**), imidazolium (**7a**,**b**) and triazolium salts (**8a**,**b**) with bis(trifluoromethanesulfonyl)amide as anion at various temperatures (°C)

Compd	η_{25}	η_{45}	η_{65}	η_{85}	η_{100}
5a	66.7	28.1	14.7	10.7	7.31
6a	210	70.6	30.6	16.2	12.8
7a	64.2	28.3	15.4	9.42	7.16
8a	117	39.9	19.2	9.11	8.42
5b	107	46.5	23.2	13.6	9.80
6b	284	85.9	36.6	20.6	13.0
7b	49.7	23.2	13.1	8.42	6.39
8b	122	43.1	20.3	12.0	8.98

to form the corresponding new ionic liquids, **5a–8a** and **5b–8b**, in excellent yields. The physical and thermal properties of these new quaternary salts are presented in Table 1.

Phase transition temperatures were studied using differential scanning calorimetry (DSC). With the exception of **8a** with a glass transition temperature of −53 °C, the T_g values of the quaternary salts were <−78 °C as determined by DSC. The thermal stabilities of those compounds were determined by thermogravimetric analyses (TGA). The new ionic liquids are thermally stable to >310 °C. Based on DSC and TGA measurements, the *N*-methylmorpholinium (**6a**,**b**) and *N*-methylimidazolium (**7a**,**b**) bis(trifluoromethanesulfonyl)amide salts have higher thermal stabilities than the corresponding oxazolidinium and triazolium salts. In general, there appears to be little difference between the thermal stabilities of the *N*-methoxyethyl (**5b–8b**) and *N*-2-(2-ethoxyethoxy)ethyl derivatives (**5a–8a**). The densities of the *N*-methoxyethyl derivatives (1.41–1.53 g cm^{-3}) were slightly higher than those of *N*-2-(2-ethoxyethoxy)ethyl derivatives (1.29–1.39 g cm^{-3}).

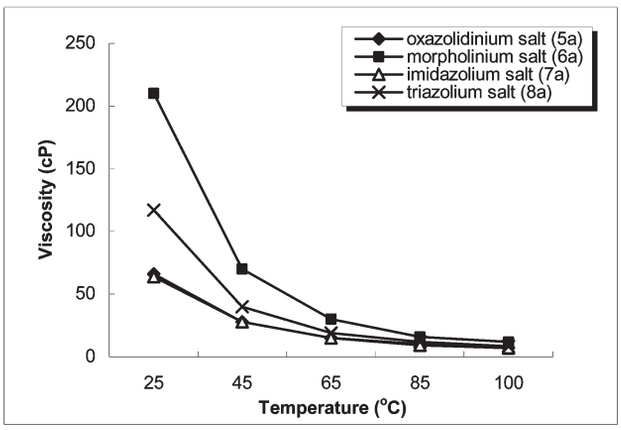
The viscosity data are given in Fig. 1 and Table 2. For all of the ionic liquids, the viscosities decreased remarkably as the temperature increased in the range of 25–100 °C, and are very similar to each other at 100 °C. While the imidazolium ionic liquids (**7a–b**) are least viscous, the morpholinium analogues (**6a–b**) are significantly more viscous than others regardless of the chain length of the substituents. Interestingly, oxazolidinium **5a** and imidazolium **7a** salts show very similar trends in viscosity between 25 and 100 °C. This suggests that the presence of oxygen or nitrogen in the ring or the degree of saturation of the ring has essentially no effect on the inter-ring interactions. However, little similarity between the two-quaternized groups was observed when the substituent was the monoether (**5b**,**7b**).

Cu(I)-catalyzed trifluoromethylation of benzyl bromide in various ionic liquids

Although extensive research has not been reported, Cu(I)-mediated trifluoromethylation reactions of aryl, vinyl, benzylic and allyl halides in organic solvents have been studied.[11,12] However, no trifluoromethylation reactions of $TMSCF_3$ have been examined in ionic liquids as solvents.

Utilizing benzyl bromide (**11**) as a model compound, the efficacy of $TMSCF_3$ in forming the trifluoromethylated compound **12** was examined in several ionic liquids (**5a–8a**) (IL). These results are summarized in Table 3. When the triazolium ionic liquid (**8a**) was employed as solvent, after 12 h, **12** was obtained in 70% yield (entry 4). 30% of **11** was recovered. When glyme was introduced as co-solvent, the yield was reduced. However, when **6a** was the solvent, the yield of **12** was 90% after 8 h (entry 2). Surprisingly, the reaction did not occur in **5a** or **7a** even when longer reaction times were employed (entries 1 and 3). In comparison, when the commercially available imidazolium ionic liquid, [bmim][PF_6], from two different sources was used as a solvent, it was found not to be suitable for Cu(I)-mediated trifluoromethylation reactions. It is not clear why the product yields (which are very reproducible) varied from solvent to solvent. They are not greatly different in that (1) the viscosities of **5a–8a** are essentially identical at 80 °C, and (2) the solubilities of the reactants are approximately the same in each ionic liquid.

Based on these results, **6a** was selected as the solvent of choice for further studies. The CuI/KF catalyzed trifluoromethylation of benzyl bromide was examined in **6a** and in organic solvents



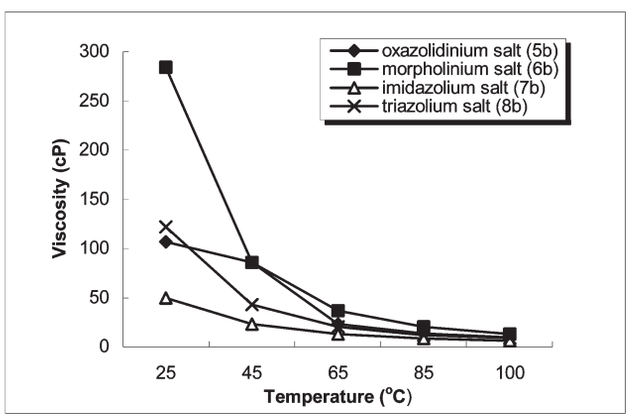


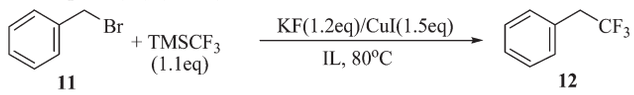
Fig. 1 Dynamic viscosities (η/cP) of *N*-2-(2-ethoxyethoxy)ethyl-substituted and *N*-methoxyethyl-substituted oxazolidinium (**5a**,**b**), morpholinium (**6a**,**b**), imidazolium (**7a**,**b**) and triazolium salts (**8a**,**b**) with bis(trifluoromethanesulfonyl)amide as anion at various temperatures.

under various conditions (Table 4). Trifluoromethylation of **11** did not occur in CH_3CN even at 80 °C after 24 h (entry 5). This was also the case using other organic solvents, such as glyme and THF. However, using **6a** as solvent under the same conditions for 8 h, the reaction occurred smoothly to give **12** in excellent yields with no byproducts. While the reaction proceeded smoothly on this scale, *i.e.*, when 1 mmol of **6a** was used as solvent for trifluoromethylation of **11** (entries 1 and 2), the reaction yield was markedly decreased when 0.5 mmol of **6a** was used under the same conditions (entry 4). Also, adding THF or CH_3CN as a co-solvent seriously decreased the efficiency of trifluoromethylation of **11** (entry 3).

In Table 5, the results for the Cu(I)-mediated trifluoromethylation of alkyl, benzyl, aryl and allyl halides in the presence of **6a** for 8 h at 80 °C are shown. The trifluoromethylated products are formed in yields comparable to those obtained *via* other methods.[11,12] Trifluoromethylation of primary bromoalkanes under these conditions gave the trifluoromethylated products in only low yields (36 and 27%, respectively, entries 1 and 5). The trifluoromethylation of allyl and benzyl bromides (entries 2 and 3) proceeded with DMF as co-solvent affording the corresponding trifluoromethyl compounds in medium to good yields (42% and 81%, respectively). However, the trifluoromethylation reactions of these two compounds (entries 2 and 3) did not occur in **6a** without DMF. Even with longer reaction times and at high temperatures, the reaction in **6a** with glyme, THF or CH_3CN as co-solvent did not give the desired product.

The trifluoromethylation of reactions of ketones and aldehydes are solvent and catalyst dependent.[1] A very large number of papers have appeared that report successful trifluoromethylation using $TMSCF_3$ catalyzed by KF, CsF and TBAF.[1b,c,4–10] In our work, **6a** was employed as solvent for the trifluoromethylation reactions of carbonyl compounds in the

Table 3 Cu(I)-mediated trifluoromethylation of benzyl bromide in ionic liquids (IL) (**5a**–**8a**)[a]

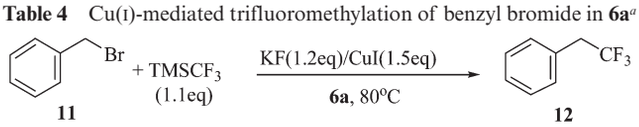


11 **12**

Entry	Ionic liquid	Solvent	Reaction time/h	Yield[b] (%)
1	**5a**	—	24	0
2	**6a**	—	8	90
3	**7a**	—	24	0
4	**8a**	—	12	70
5	[bmim][PF_6]	—	24	0
6	**8a**	Glyme	24	0

[a] 1 mmol each of **11** and IL. [b] Isolated yield.

Table 4 Cu(I)-mediated trifluoromethylation of benzyl bromide in **6a**[a]



11 **12**

Entry	**6a** (mmol)	Solvent (1 mL)	Reaction time/h	Yield of product[b] (%)
1	2	—	8	89
2	1	—	8	90
3	1	[c]	8	0
4	0.5	—	24	65
5	—	CH_3CN	8	0

[a] 1.0 mmol each of **11** and **6a**. [b] Isolated yield. [c] THF, glyme or CH_3CN.

presence of catalytic amounts of CsF or Ph_3P (Table 6). While 6 h required to complete the CsF-catalyzed trifluoromethylation of benzaldehyde (88% yield) under neat conditions,[5] the reaction of benzaldehyde with $TMSCF_3$ (CsF catalyst) at 25 °C in **6a** for 3 h led to the product in essentially the same yield (entry 1). With Ph_3P as the catalyst, trifluoromethylation of benzaldehyde gave 91% yield but did not proceed as rapidly. Although demanding longer reaction times, triphenylphosphine was as effective as CsF in catalyzing the trifluoromethylation of the enone and ketone at 35 °C in excellent yields (entries 4 and 6). In the case of cyclohexenone, with either CsF or Ph_3P as catalyst, only the 1,2-addition product is obtained in excellent yield (entries 5[6] and 6). Interestingly, a novel method is reported for the regioselective 1,4-trifluoromethylation of α, β-enones by treating the substrate protected with a bulky aluminium Lewis acid with $TMSCF_3$ and a threefold excess of a variety of different nucleophilic initiators.[23,24]

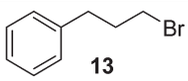
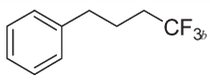
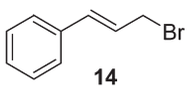
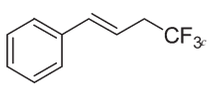
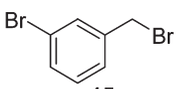
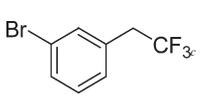
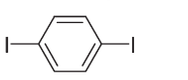
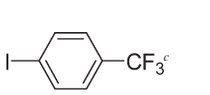
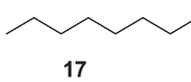
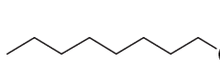
However, **6a** was not an effective alternative to organic solvents for trifluoromethylation of *N*-methylcaprolactam (entries 7 and 8).

Not surprisingly the trifluoromethylation reactions of lactams are very sluggish since the carbonyl group in these systems is deactivated by the electron-donating nitrogen atom.[1c] Based on our experimental results, Ph_3P-catalyzed trifluoromethylation reactions of ketone, enone and aldehyde are slower than CsF- and TBAF-catalyzed reactions but give equivalent product yields and the reagent is less expensive.

As shown in Scheme 2, the nucleophilic fluorination of benzyl bromide with CsF at 65 °C for 4 h in **6a** gave **15** (89%). Our results are comparable to those previously reported.[14b] However, when THF or CH_3CN was used as co-solvent, the reaction was very sluggish and gave low yields (40%).

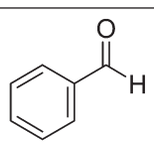
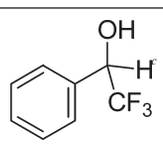
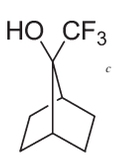
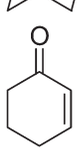
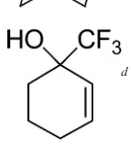
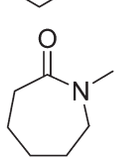
Increasing temperature and lengthening the reaction time did not improve the yield of **15.** Both CsF and **6a** were dried at 200 °C before reaction. While CsF was not appreciably soluble in **6a**, the color of the reaction solution began to change after 2 h. After reaction the ionic liquid was washed with dichloromethane and water, dried *in vacuo* at 70 °C, and three equivalents of CsF were added. However, the efficiency of fluorination in

Table 5 Cu(I)-mediated trifluoromethylation of alkyl, allyl, aryl and benzyl halides in **6a** (1 mmol)

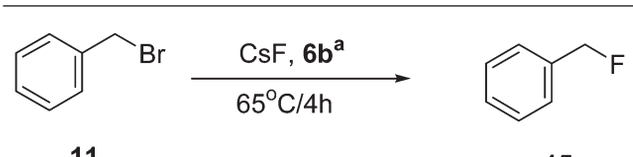
Entry	Substrate	Product	Cosolvent (mL)	Yield[a] (%)
1	 **13**	 [b]	—	36
2	 **14**	 [c]	[d]	42
3	 **15**	 [c]	[d]	81
4	 **16**	 [c]	—	38
5	 **17**	 [e]	—	27

[a] Determined by GC/MS. [b] Ref. 21. [c] Ref. 12. [d] DMF. [e] Ref. 22.

Table 6 CsF- or Ph_3P-catalyzed trifluoromethylation reactions of aldehyde, ketone, enone and lactam with $TMSCF_3$ in **6a** as solvent[a]

Entry	Substrate	Product	Catalyst	Temp./°C	Time/h	Yield [b] (%)
1		 [f]	CsF	25	3	88
2			Ph_3P	35	24	91
3		 [c]	CsF	25	1	94
4			Ph_3P	35	24	95
5		 [d]	CsF	25	0.5	98
6			Ph_3P	35	24	98
7		—	CsF	45	24	0
8		—	CsF	45	24	0

[a] (1) 1.1 mmol $TMSCF_3$, 1 mmol **6a**, 0.1 mmol CsF or Ph_3P; (2) aq. HCl. [b] Isolated yield. [c] Ref. 5. [d] Ref. 6. [e] THF 1 mL co-solvent.



Scheme 2

the recycled ionic liquid decreased. Our inability to recycle **6a** successfully is similar to results reported after the fluorination of **11** using CsF in [bmim][PF_6], which suggests that recycling of ionic liquids is limited for nucleophilic fluorination reactions using alkali metal fluorides.[14b] This system was not investigated in detail but it indicates that ionic liquids cannot be recycled effectively when reaction is carried out under highly basic conditions and higher temperatures.

Conclusion

In summary, the morpholinium ionic liquid (**6a**) acts as a useful solvent for Cu(I)-mediated C–C bond formation reactions of trifluoromethyl(trimethyl)silane with aryl, benzyl, vinyl and primary halides to give products in varying yields. Also, Ph_3P- or CsF-catalyzed reactions of carbonyl functionalities with trifluoromethyl(trimethyl)silane proceeded smoothly in **6a** with enhanced nucleophilic reactivity. The conversion of benzyl bromide to benzyl fluoride with CsF in **6a** gave good isolated yields, but the reactivity decreased when the ionic liquid was recycled. Trifluoromethylation and fluorination reactions in the new ionic liquids were very effective with short reaction times and easy purification. Furthermore, Ph_3P-catalyzed trifluoromethylation is cost effective compared to previously demonstrated methodologies.[7,10] *N*-Methoxyethyl- and *N*-(2-ethoxyethoxy)ethyl-substituted oxazolidinium, morpholinium, imidazolium and triazolium-based ionic liquids with bis(trifluoromethanesulfonyl)amide as anion were synthesized and characterized. Although overall the imidazolium and morpholinium quaternary salts have higher thermal stabilities than oxazolidinium and triazolium ionic liquids, all of the ionic liquids reported in this paper have wide liquid ranges and are thermally stable to >310 °C. The viscosities of the imdazolium

quaternary salts are lowest regardless of the chain length of the substituent and the morpholinium quaternary salts are most viscous.

Experimental

General methods

^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded using a Bruker spectrometer operating at 300, 282, 75 MHz, respectively, in acetone-d_6 unless otherwise stated. Chemical shifts are reported in ppm relative to the appropriate standard. IR spectra were recorded using KBr plates on a BIO-RAD FTS 3000 Infrared spectrometer. Mass spectra were obtained at 70 eV with a Shimadzu QP5050A GC/MS spectrometer and for ionic solids, the solids probe was utilized. Fragmentation is reported only for the cation in the ionic liquids. Elemental analyses were obtained from the Shanghai Institute of Organic Chemistry, China. Products were sometimes purified by silica-gel chromatography. DSC was measured at a heating rate of 10 °C min^{-1} over the range between −78 and 400 °C on a TA Instruments DSC Q10. Thermogravimetric analysis measurements were made using a TA Instrument TA 50. Densities and viscosities of the ionic liquids were measured by using a pycnometer and a viscometer (Minivis II, Grabner Instruments), respectively. Tetrahydrofuran and glyme were dried with sodium and distilled over a purple solution of benzophenone immediately before use. Chemicals were purchased from Sigma-Aldrich, Acros, Lancaster, Synquest and Fluka. During the experiments, a Schlenk line system was used for handling the air- and moisture-sensitive reactions under nitrogen.

General procedure for the preparation of quaternary salts (1–4a, 1–4b)

In a typical reaction, *N*-methyloxazolidine (0.87 g, 10 mmol) and 2-(2-ethoxyethoxy)ethyl bromide (20.69 g, 10.5 mmol) were placed in a 20 mL Pyrex glass tube which was evacuated, sealed and then heated for 24 h at 70 °C. All of the volatile materials were removed at reduced pressure and the residue was subjected to dynamic vacuum for 1 day leaving the pure quaternary salt. The product (**1a**) was obtained in 93% yield. The compounds which were used in further synthetic reactions were not subjected to elemental analyses.

***N*-2-(2-Ethoxyethoxy)ethyl-*N*-methyloxazolidinium bromide (1a).** 93% yield, yellow viscous liquid; IR (KBr): 2994, 2915, 1483, 1390, 1284, 1198, 1132, 1053, 943, 893, 810 cm^{-1}; ^{1}H NMR: δ 1.12 (t, J = 7.09, 3H), 3.17 (s, 3H), 3.53 (q, J = 7.08 Hz, 2H), 3.62–3.82 (m, 8H), 3.90 (br s, 2H), 4.31 (m, 2H), 4.93 (d, J = 5.87 Hz, 1H), 4.81 (d, J = 5.87 Hz, 1H); ^{13}C NMR: δ 94.52, 70.96, 69.93, 66.87, 65.69, 64.72, 64.49, 61.31, 48.51 (br), 15.02; MS (solid probe) (EI) m/z (%) 204 (M$^+$, 34).

***N*-2-(2-Ethoxyethoxy)ethyl-*N*-methylmorpholinium bromide (2a).** 90% yield, yellow viscous liquid; IR (KBr) 3104, 2931, 2901, 2860, 1739, 1640, 1520, 1304, 1284, 1017, 951 cm^{-1}; ^{1}H NMR: δ 1.14 (t, J = 7.01 Hz, 3H), 3.49 (q, J = 7.00 Hz, 2H), 3.59 (m, 2H), 3.62 (s, 3H), 3.72 (m, 2H), 3.87 (m, 4H), 4.15 (br s, 8H); ^{13}C NMR: δ 71.20, 70.18, 66.78, 65.06, 63.89 (br s), 61.52, 61.28, 49.50 (br s), 15.21; MS (solid probe) (EI) m/z (%) 218 (M$^+$, 100).

***N*-2-(2-Ethoxyethoxy)ethyl-*N*-methylimidazolium bromide (3a).** 93% yield, yellow viscous liquid; IR (KBr): 3428, 2995, 1592, 1520, 1472, 1395, 1260, 996, 921, 883 cm^{-1}; ^{1}H NMR: δ 1.13 (t, J = 6.99 Hz, 3H), 3.47 (q, J = 7.00 Hz, 3H), 3.55 (m, 2H), 3.67 (m, 2H), 3.95 (br t, J = 5.03, 2H), 4.13 (s, 3H), 4.66 (br t, J = 4.78, 2H), 7.89 (t, J = 1.16, 1H) 7.98 (t, J = 1.64, 1H), 10.05 (s, 1H); ^{13}C NMR: δ 132.04, 124.07, 123.93, 70.95, 70.35, 69.56, 66.78, 50.18, 36.20, 15.56; MS (solid probe) (EI) m/z (%) 199 (M$^+$, 45).

***N*-2-(2-Ethoxyethoxy)ethyl-*N*-methyltriazolium bromide (4a).** 95% yield, yellow viscous liquid; IR (KBr): 3103, 3021, 2952, 2870, 1794, 1625, 1529, 1508, 1427, 1379, 1320, 1165, 953 cm^{-1}; ^{1}H NMR: δ 1.15 (t, J = 6.99 Hz, 3H), 3.49 (q, J = 6.99, 2H), 3.58 (m, 2H), 3.71 (m, 2H), 4.00 (t, J = 4.95, 2H), 4.29 (s, 3H), 4.82 (t, J = 4.75, 2H), 9.39 (s, 1H), 11. 16 (s. 1H); ^{13}C NMR: δ 145.78, 144.55, 70.83, 70.27, 68.77, 66.76, 48.83, 39.48, 15.57; MS (solid probe) (EI) m/z (%) 200 (M$^+$, 42).

***N*-Methoxyethyl-*N*-methyloxazolidinium bromide (1b).** 93% yield, yellow viscous liquid; IR (KBr): 3472, 2998, 2732, 1623, 1521, 1321, 970, 882, 762 cm^{-1}; ^{1}H NMR (D_2O): δ 3.10 (s, 3H), 3.20 (s, 3H), 3.58–3.81 (m, 6H), 4.21 (m, 2H), 4.71 (d, J = 5.97 Hz, 1H), 4.84 (d, J = 5.97 Hz, 1H); ^{13}C NMR (D_2O): δ 94.02, 66.64, 66.55, 62.05 (t, J = 3.51 Hz), 61.80 (t, J = 2.64 Hz), 59.22, 48.37 (t, J = 3.56 Hz); MS (solid probe) (EI) m/z (%) 146 (M$^+$, 100).

***N*-Methoxyethyl-*N*-methylmorpholinium bromide (2b).** 90% yield, white solid; IR (KBr): 3421, 2189, 1694, 1453, 1321, 1286, 1109, 1015, 889 cm^{-1}; ^{1}H NMR (D_2O): δ 3.22 (s, 3H), 3.34 (s, 3H), 3.52 (m, 4H), 3.68 (m, 2H), 3.88 (br m, 2H), 3.99 (br m, 4H); ^{13}C NMR (D_2O): δ 66.42, 64.92, 62.04, 60.10, 59.19, 48.90; MS (solid probe) (EI) m/z (%) 160 (M$^+$, 100).

***N*-Methoxyethyl-*N*-methylimidazolium bromide (3b)[25].** 90% yield, yellow viscous liquid; IR (KBr): cm^{-1}; ^{1}H NMR (D_2O): δ 3.31 (s, 3H), 3.70 (t, J = 4.99 Hz, 2H), 3.82 (s, 3H), 4.32 (t, J = 5.07 Hz, 2H), 7.38 (s, 1H), 7.43 (s, 1H) ^{13}C NMR: δ 137.70, 124.13, 123.28, 71.01, 59.12, 51.01, 37.19; MS (solid probe) (EI) m/z (%); 161 (M$^+$, 54)

***N*-Methoxyethyl-*N*-methyltriazolium bromide (4b).** 90% yield, yellow viscous liquid; IR (KBr): 3480, 2948, 2832, 2309, 1629, 1424, 1293, 981 cm^{-1}; ^{1}H NMR (D_2O): δ 3.39 (s, 3H), 3.84 (t, J = 4.71 Hz, 2H), 4.13 (s, 3H), 4.52 (t, J = 4.87 Hz, 2H), 8.85 (s, 1H); ^{13}C NMR (D_2O): δ 145.58, 143.24, 70.04, 59.40, 48.79, 39.86; MS (solid probe) (EI) m/z (%) 142 (M$^+$, 60).

General procedure for the preparation of 5a–8a and 5b–8b

Lithium bis(trifluoromethanesulfonyl)amide (10.50 mmol) was added to magnetically stirred solution of bromide **1a** (10.00 mmol) in water (5 mL). After 3 h at room temperature, the oily liquid was separated and washed with a small amount of water (3 × 20 mL) and evaporated *in vacuo* to give **5a** in 97% yield.

***N*-2-(2-Ethoxyethoxy)ethyl-*N*-methyloxazolidinium bis(trifluoromethanesulfonyl)amide (5a).** 97% yield, colorless viscous liquid; IR (KBr): 3421, 2987, 2379, 1377, 1120, 1090, 965, 889 cm^{-1}; ^{1}H NMR: δ 1.15 (t, J = 7.00, 3H), 3.44 (s, 3H), 3.51 (q, J = 7.00 Hz, 2H), 3.60 (m, 2H), 3.72 (m, 2H), 3.94–4.16 (m, 6H), 4.47 (m, 2H), 5.08 (d, J = 5.79 Hz), 5.20 (d, J = 5.79 Hz, 1H); ^{13}C NMR 120.99 (q, J_{C-F} = 320.93), 94.67, 71.16, 70.13, 66.77, 66.69, 65.58 (t, J = 3.51 Hz) 65.28, 62.32 (t, J = 3.00 Hz), 48.26 (t, J = 3.34 Hz); ^{19}F NMR: δ −79.88 (s, 6F); MS (solid probe) (EI) m/z (%) 204 (M$^+$, 100). Anal. Found: C, 29.60; H, 4.50; N, 5.91. $C_{13}H_{24}F_6N_2O_7S_2$ requires C, 29.75; H, 4.54; N, 5.79%.

***N*-2-(2-Ethoxyethoxy)ethyl-*N*-methylmorpholinium bis(trifluoromethanesulfonyl)amide (6a).** 90% yield, yellow viscous liquid; IR (KBr) 3467, 2082, 1641, 1423, 1411, 1234, 1116, 883 cm^{-1}; ^{1}H NMR: δ 1.14 (t, J = 7.00 Hz, 3H), 3.49 (q, J = 7.00 Hz, 2H), 3.50 (s, 3H), 3.58 (m, 2H), 3.69 (m, 2H), 3.73 (br t, 2H), 3.80 (br t, 2H), 3.96 (m, 2H), 4.13 (br s, 6H); ^{13}C NMR: δ 120.99 (q, J_{C-F} = 321.16 Hz) 71.04, 70.16, 66.77, 64.87, 64.33 (br s), 61.72, 61.72 (t, J = 2.30 Hz) 61.24, 49.35 (br s); ^{19}F NMR: δ −79.86 (s, 6F); MS (solid probe) (EI) m/z (%) 218 (M$^+$, 100). Anal. Found: C, 31.09; H, 4.81; N, 5.60. $C_{13}H_{24}F_6N_2O_7S_2$ requires C, 31.13; H, 4.81; N, 5.62%.

***N*-2-(2-Ethoxyethoxy)ethyl-*N*-methylimidazoliumbis(trifluoromethanesulfonyl)amide (7a).** 98% yield, yellow viscous liquid; IR (KBr): 3475, 3124, 2987, 2981, 1698, 1578, 1528, 1433, 1387, 1196, 1135, 894 cm^{-1}; ^1H NMR: δ 1.15 (t, J = 7.01 Hz, 3H), 3.48 (q, J = 7.00 Hz, 2H), 3.55 (m, 2H), 3.66 (m, 2H), 3.94 (br t, J = 4.75, 2H), 4.09 (s, 3H), 4.55 (br t, J = 4.89, 2H), 7.71 (t, J = 1.70, 1H) 7.79 (t, J = 1.78, 1H), 9.04 (s, 1H); ^{13}C NMR: δ 137.83, 124.35, 124.07, 120.99 (q, J = 321.56 Hz), 70.97, 70.30, 69.34, 66.79, 50.49, 36.65, 15.51; ^{19}F NMR: δ −79.86 (s, 6F); MS (solid probe) (EI) m/z (%) 199 (M^+, 100). Anal. Found: C, 29.82; H, 3.94; N, 8.95. $C_{12}H_{19}F_6N_3O_6S_2$ requires C, 30.06; H, 3.97; N, 8.77%.

***N*-2-(2-Ethoxyethoxy)ethyl-*N*-methyltriazolium bis(trifluoromethanesulfonyl)amide (8a).** 95% yield, yellow viscous liquid; IR (KBr): 3476, 3147, 3033, 2985, 1570, 1519, 1438, 1298, 1165, 990, 901 cm^{-1}; ^1H NMR: δ 1.17 (t, J = 7.00 Hz, 3H), 3.49 (q, J = 7.00, 2H), 3.58 (m, 2H), 3.69 (m, 2H), 3.98 (br t, J = 3.98, 2H), 4.28 (s, 3H), 4.69 (t, J = 4.67, 2H), 9.10 (s, 1H), 9.97 (s. 1H); ^{13}C NMR: δ 145.87, 143.92, 120.95, (q, J = 321.19 Hz), 70.81, 70.20, 68.55, 66.81, 49.81, 39.55, 15.52; ^{19}F NMR: δ −79.96 (s, 6F); MS (solid probe) (EI) m/z (%) 200 (M^+, 100). Anal. Found: C, 27.50; H, 3.87; N, 11.55. $C_{11}H_{18}F_6N_4O_6S_2$ requires C, 27.50; H, 3.75; N, 11.67%.

***N*-Methoxyethyl-*N*-methyloxazolidinium bis(trifluoromethanesulfonyl)amide (5b).** 95% yield, colorless viscous liquid; IR (KBr): 3219, 3128, 2839, 2890, 1569, 1467, 1198, 1040, 901, 893 cm^{-1}; ^1H NMR: δ 3.43 (s, 3H), 3.44 (s, 3H), 3.98–4.11 (m, 6H), 4.46 (m, 2H), 5.03 (d, J = 5.71 Hz, 1H), 5.17 d, J = 5.71 Hz, 1H); ^{13}C NMR: δ 206.81, 120.90 (q, J = 321.16 Hz), 94.50, 66.76, 66.69, 62.33 (t, J = 3.64 Hz), 62.19 (t, J = 2.74 Hz), 48. 31 (t, J = 3.61 Hz); ^{19}F NMR: δ −79.78 (s, 6F); MS (solid probe) (EI) m/z (%) 146 (M^+, 100). Anal. Found: C, 25.23; H, 3.75; N, 6.62. $C_9H_{16}F_6N_2O_6S_2$ requires C, 25.35; H, 3.78; N, 6.57%.

***N*-Methoxyethyl-*N*-methylmorpholinium bis(trifluoromethanesulfonyl)amide (6b).** 97% yield, white solid; IR (KBr): 3449, 2956, 2937, 2879, 1867, 1487, 1341, 1059, 956, 790 cm^{-1}; ^1H NMR: δ 3.40 (s, 3H), 3.50 (s, 3H), 3.74 (m, 4H), 3.97 (br m, 2H), 4.01 (br m, 2H), 4.12 (br m, 4H); ^{13}C NMR: δ 120.97 (q, J = 321.08), 66.22, 64.67 (br s), 61.66 (t, J = 2.61), 61.20, 58.98, 49.06 (br s); ^{19}F NMR: δ −79.89 (s, 6F); MS (solid probe) (EI) m/z (%) 160 (M^+, 100). Anal. Found: C, 27.03; H, 4.07; N, 6.38. $C_{10}H_{18}F_6N_2O_6S_2$ requires C, 27.27; H, 4.09; N, 6.36%.

***N*-Methoxyethyl-*N*-methylimidazolium bis(trifluoromethanesulfonyl)amide (7b)[26].** 95% yield, yellow viscous liquid; IR (KBr): 2978, 2956, 1685, 1490, 1321, 1284, 1153, 1032, 958, 743, 706 cm^{-1}; ^1H NMR: δ 3.36 (s, 3H), 3.82 (t, J = 4.56 Hz, 2H), 4.09 (s, 3H), 4.55 (t, J = 4.87 Hz, 2H), 7.38 (s, 1H), 7.43 (s, 1H), 9.02 (s, 1H); ^{13}C NMR: δ 137.70, 124.43, 123.88 120.93 (q, J = 321.18), 70.69, 58.82, 50.39, 36.60; ^{19}F NMR: δ −79.49 (s, 6F); MS (solid probe) (EI) m/z (%); 161 (M^+, 100).

***N*-Methoxyethyl-*N*-methyltriazolium bis(trifluoromethanesulfonyl)amide (8b).** 98% yield, yellow viscous liquid; IR (KBr): 3124, 3071, 2980, 2872, 1772, 1593,1440, 1320, 1035, 841 cm^{-1}; ^1H NMR: δ 3.39 (s, 3H), 3.87 (t, J = 4.78 Hz, 2H), 4.29 (s, 3H), 4.70 (t, J = 4.96 Hz, 2H), 9.06 (s, 1H), 9.98 (s, 1H); ^{13}C NMR: δ 146.21, 144.72, 120.91 (q, J = 322.01) 70.14, 64.10, 48.71, 39.50; ^{19}F NMR: δ −79.09 (s, 6F); MS (solid probe) (EI) m/z (%) 142 (M^+, 100). Anal. Found: C, 22.83; H, 2.93; N, 13.42. $C_8H_{12}F_6N_4O_5S_2$ requires C, 22.75; H, 2.84; N, 13.27%.

Typical procedure for trifluoromethylation in Tables 3–5

Copper(I) iodide (0.286 g, 1.5 mmol) and KF (0.068 g, 1.2 mmol) were added to the mixture of benzyl bromide (0.17 g, 1 mmol), ionic liquid **6a** and $TMSCF_3$ (0.156 g, 1.1 mmol). The mixture was heated to 80 °C with stirring for 8 h. Reactions were monitored by GC-MS. The products were extracted from reaction mixture with diethyl ether (3 × 3 mL). The ether layer was dried with magnesium sulfate and evaporated under reduced press. The product was purified with flash column chromatography using silica gel.

Typical procedure for trifluoromethylation reactions displayed in Table 6

The ionic liquid (0.498 g, 1 mmol) **6a** was transferred to 20 ml flask, and a catalytic amount of CsF (0.1 equiv) or Ph_3P (0.1 equiv), the required $TMSCF_3$ (0.156 g, 1.1 mmol) and 1 equiv of various substrates were added sequentially under nitrogen. The mixture was stirred at room temperature and was monitored by ^{19}F NMR. After complete disappearance of the $TMSCF_3$ ^{19}F NMR resonance (−67.4 ppm), the reaction mixture was extracted with ethyl ether (3 × 3 mL). For hydrolysis, 3 M HCl was added to ether layer and stirred for 3 h at room temperature. The volatile compounds were removed under reduced pressure and the product was extracted with ethyl ether. Purification was accomplished with flash column chromatography.

Typical procedure for the fluorination reported in Scheme 2

The ionic liquid (0.498 g, 1 mmol) **6a** was transferred to 20 ml Schlenk tube and then benzyl bromide (0.17 g, 1 mmol) and CsF (0.1 equiv) were added under nitrogen. The reaction mixture was stirred for 8 h at 65 °C and was extracted with diethyl ether (3 × 3 mL). The reaction was monitored by GC-MS.

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