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Transformations of Organic Molecules with F-TEDA-BF₄ in Ionic Liquid Media

Jasminka Pavlinac ¹, Marko Zupan ² and Stojan Stavber ¹,*

¹ Department of Physical and Organic Chemistry, ‘Jožef Stefan’ Institute, Jamova 39, 1000 Ljubljana, Slovenia; E-mail: jasminka.pavlinac@ijs.si (J.P.)
² Faculty for Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, 1000 Ljubljana, Slovenia; E-mail: marko.zupan@fkkt.uni-lj.si (M.Z.)

* Author to whom correspondence should be addressed; E-mail: stojan.stavber@ijs.si; Tel.: +386 1 477 3660; Fax: +386 1 251 93 85

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Abstract: The transformations of organic molecules with F-TEDA-BF₄ (1) were investigated in the hydrophilic ionic liquid (IL) 1-butyl-3-methyl-imidazolium tetrafluoroborate ([bmim][BF₄], 2) and the hydrophobic IL 1-butyl-3-methyl-imidazolium hexafluorophosphate ([bmim][PF₆], 3). The range of substrates included alkyl substituted phenols 4a-c, 9, 13, 1,1-diphenylethene (15), alkyl aryl ketones 19-22, aldehydes 23-25 and methoxy-substituted benzene derivatives 26-30. The evaluation of the outcome of reactions performed in IL media in comparison to those of the corresponding reactions in conventional organic solvents revealed that the transformations in IL are less efficient and selective. The effect of the presence of a nucleophile (MeOH, H₂O, MeCN) on the course of reaction was also studied.

Keywords: F-TEDA-BF₄; fluorination; ionic liquids; green chemistry

1. Introduction

The last decade has witnessed a rapidly growing interest in various aspects of ionic liquids (ILs), with great emphasis being placed on their potential utility in chemical synthesis as recyclable solvents, reagents and catalysts [1,2]. Prime features that have made ILs so attractive include their low vapour
pressure, high thermal and chemical stability, wide liquid-state temperature range, large
electrochemical window, favourable solvation behavior and their potential for recyclability, all of
which lead to their recognition as ‘greener’ alternative media to volatile and often toxic organic
solvents [3-6]. Additionally, their highly diverse chemical and physical properties resulting from the
infinite possibilities for combining cations and anions to form ILs are also considered promising
advantages for their various applications, e.g. in synthetic transformations, catalysis, electrochemistry,
spectroscopy, extraction and separation processes [7-10]. However, a full understanding of their
physical and chemical behavior is still lacking and data on their environmental effects have only just
started to appear [11-14], so one should be extremely careful before claiming that a certain
transformation is advantageous and environmentally friendlier if performed in ILs rather than in
conventional organic solvents.

Owing to its unique properties (e.g. small size, high electronegativity, low polarizability, strong C-F
bond), the incorporation of fluorine into organic molecules may bring about a dramatic change in their
physical, chemical and biological properties [15]. An increased demand for fluorinated compounds for
diverse applications, such as pharmaceuticals, agrochemicals, solvents, liquid crystals, dyestuffs,
polymers and novel materials, has been notable in recent decades and consequently, fluorination of
organic molecules has become a very important target in various sectors [16,17]. Although substantial
effort has been devoted to the development of methods for the selective introduction of fluorine into
target molecules, mild, selective and environmentally more acceptable fluorination procedures still
continue to remain a significant challenge to organofluorine chemists. Due to the lack of appropriate
reagents at the beginning of the 20th century, fluorination of organic compounds represented an
extremely demanding area of organic chemistry. Reactions employing molecular fluorine are, due to
the weak F-F bond and strong C-F bond formed, characterized by high exothermicity, and thus its
handling requires working at very low temperatures and pressure, using special laboratory equipment
and exceptional safety precautions. Further developments included reagents such as XeF2 and O-F
reagents, while a breakthrough was achieved with the introduction of N-F reagents. The latter have
been recognized as mild and efficient electrophilic fluorinating reagents, whose handling does not
require special safety measures. Among them 1-chloromethyl-4-fluoro-1,4-
diazeniabicyclo[2.2.2]octane bis(tetrafluoroborate), F-TEDA-BF4 (1), known under the commercial
name of Selectfluor™, has been highlighted as an efficient and selective fluorinating reagent for a
wide variety of organic compounds, in addition to possessing oxidative properties and as such being
utilized also as a mediator or a catalyst for other functionalizations [18-21]. This reagent has been
extensively studied for various transformations in conventional organic solvents, while in ILs it has
been investigated only for a limited series of compounds [22-26].

The present study aimed to investigate transformations of alkyl substituted phenols 4a-c, 9, 13,
1,1-diphenylethene (15) as a model alkene molecule, methoxy substituted alkyl aryl ketones 19-22,
aldehydes 23-25 and methoxy-substituted aromatic substrates 26-30, and to compare the results
obtained in IL media with the outcomes of the corresponding reactions in conventional organic
solvents. Especially for alkyl substituted phenols [27-30], alkenes [31-33] and aryl alkyl ketones [34],
it has been previously established that the reaction conditions may play a significant role on the course
of the transformation, while many examples display the dramatic effect of ionic liquids on the
selectivity and efficiency of reaction. This study was performed using the hydrophilic IL 1-butyl-3-
methylimidazolium tetrafluoroborate ([bmim][BF_4], 2) and hydrophobic 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF_6], 3). The effect of a nucleophile on the course of reaction was additionally investigated (Scheme 1).

**Scheme 1.** Effect of reaction conditions on the course of transformation of organic molecules with F-TEDA-BF_4 in the presence of a nucleophile.

**2. Results and Discussion**

First of all we performed a blank experiment by stirring solutions of 0.24 mmol of F-TEDA-BF_4 in 1 mL of ILs [bmim][BF_4] or [bmim][PF_6] at 70°C for 24 h and established that no reaction between the fluorinating reagent and either IL occurred. The fluorinating reagent F-TEDA-BF_4 remained active, while no transformation of [bmim][BF_4] or [bmim][PF_6] could be observed from NMR spectra.

The study of fluoro transformations of alkyl substituted phenols with F-TEDA-BF_4 (1) in the ILs [bmim][BF_4] and [bmim][PF_6] revealed that the properties of the IL have a considerable effect on the course of transformation, as well as on its efficiency. Likewise, in conventional organic solvents, depending upon the substrate structure and reaction conditions, the following products may be present in the reaction mixture when employing IL media: (a) 2-fluoro-4-alkylphenols 5, as a consequence of electrophilic substitution at the ortho position with respect to the phenolic group; (b) difluorocyclohexadiene (6) after further fluorination of ortho-fluoro substituted phenolic product 5; (c) 4-alkyl-4-fluoro-cyclohexa-2,5-dienone (7) after the addition-elimination process following an attack at the para position with respect to the phenolic group, and (d) 4-fluorophenol (8) as a result of ipso substitution after dealkylation at the para position (Scheme 2). However, their distribution in ILs (Table 1) differs from the corresponding product distribution obtained in MeCN or in MeOH [27].

A typical experiment was performed in the following way: 0.24 mmol of F-TEDA-BF_4 was vigorously stirred in 1 mL IL until the reagent was completely dissolved. Then, 0.2 mmol of substrate was added and the reaction mixture was continued to be stirred at temperature similar to the
corresponding reaction in an organic solvent. After reaction ceased, the reaction mixture was extracted with t-BuOMe, the organic phase washed with water and after drying, filtered, concentrated in vacuo and the crude reaction mixture analysed by TLC, $^1$H- and $^{19}$F-NMR.

**Scheme 2.** Transformation of 4-alkyl substituted phenols with F-TEDA-BF$_4$.

In the case of 4-methylphenol (4a), the transformation was less efficient in both studied ILs than in MeCN or MeOH [27], since the formation of a complex reaction mixture or low transformation of starting material was observed (entries 1-3; Table 1). Compared to 4a, 4-i-propyl phenol (4b) and 4-t-butyl phenol (4c) were transformed more efficiently in IL media (Table 1, entries 4-6), but still less efficiently compared to the reaction carried out in an organic solvent [27]. In a 24 h reaction between 4b and F-TEDA-BF$_4$ carried out at 70 °C in [bmim][BF$_4$], the substrate was 71% converted into a mixture of fluorinated products, with 2-fluoro-4-i-propyl phenol (5b) as the major product and 2,2-difluoro-4-i-propyl-3,5-cyclohexadienone (6b) and 4-fluorophenol (8) as minor ones. Under comparable reaction conditions in the hydrophilic IL [bmim][PF$_6$], only the ortho-fluoro substituted product 5b was formed, however with a modest conversion (36%). The transformation proceeded more efficiently in hydrophilic [bmim][BF$_4$] than in [bmim][PF$_6$], as was the case of 4-t-butylphenol (4c) (Table 1, entries 5, 6). In the reaction between 4c and F-TEDA-BF$_4$ carried out at 70 °C for 4 h in [bmim][BF$_4$], 69% of the substrate was converted into a mixture of 3 products, namely 2-fluoro-4-t-butylphenol (5c, 37%), 4-fluorophenol (8, 28%) and 2,2-difluoro-4-t-butyl-3,5-cyclohexadienone (6c, 4%), while 31% of the substrate remained unchanged (Table 1, entry 5). Under the same reaction conditions applied to the reaction between 4c and F-TEDA-BF$_4$ in [bmim][PF$_6$], 86% of the substrate remained unreacted, the rest corresponding to ortho-fluoro substituted product 5c (10%) and 4-fluorophenol (8, 4%). Prolonging the reaction time to 24 h increased to the efficiency of the transformation (entry 6). In [bmim][PF$_6$] 46% of 4c was converted into a 2:1 mixture of 2-fluoro-4-t-butylphenol (5c) and 4-fluorophenol (8) (Table 1, entry 6). Comparing the outcome of reactions for these substrates with F-TEDA-BF$_4$ performed in organic solvents (MeCN, MeOH) or in IL media ([bmim][BF$_4$], [bmim][PF$_6$]), a more efficient and faster reaction was observed to take place in organic
solvents than in ILs, while the distribution of products were also found to be considerably different (Figure 1).

Table 1. Transformations of 4-alkyl substituted phenols with F-TEDA-BF4 in ILs.

| Entry | R       | Substrates: | Products: |
|-------|---------|-------------|-----------|
|       | IL a    | R=Me        | 4a        |
|       | [bmim][BF4] T, t | 70 °C, 4 h  | complex reaction mixture |
|       | [bmim][PF6] | 22 °C, 22 h | 10% 6 : 0 : 4 : 0 |
| 1     | Me      | (4a)        | 22 °C, 22 h | 71% 59 : 2 : 0 : 10 |
| 2     | 2       | i-Pr        | 70 °C, 24 h | 69% 37 : 4 : 0 : 28 |
| 3     | 3       | t-Bu        | 70 °C, 24 h | 87% 44 : 11 : 0 : 32 |
| 4     | 4       | t-Bu        | 70 °C, 4 h  | complex reaction mixture |
| 5     | 5       | 4a          | 70 °C, 4 h  | complex reaction mixture |
| 6     | 6       | 4b          | 70 °C, 24 h | complex reaction mixture |
|       | a       | Ionic liquid; b Conversion of substrate determined by 1H- and 19F-NMR; c Unreacted substrate; d The presence of 6b and 8 in traces; e The presence of 6c in traces.

Figure 1. Comparison of product distribution obtained in reaction of 4-i-propyl phenol (4b) or 4-t-butyl phenol (4c) with F-TEDA-BF4 in ILs and organic solvents a.

In the case of a sterically hindered alcohol, namely 2,4,6-tri-t-butylphenol (9, Scheme 3), the reaction with F-TEDA-BF4 in [bmim][PF6] did not proceed at all in 5 h either at room temperature or at 70 °C. After 2 h reaction carried out at 70 °C in [bmim][BF4], 60% of the substrate remained unreacted, while 31% of oxidized quinone product 10 was formed along with 9% 2-fluoro-4,6-di-t-
butylphenol (11). This result is different from the outcome of the reaction performed in MeCN or MeOH, where as earlier established, the polarity of the solvent and reaction temperature greatly affected the course of reaction [28,29]. In MeCN, the substrate 9 was quantitatively transformed into the fluoro-dealkylated product 11 at 80 °C, while a mixture of MeCN/MeOH (9/1 ratio) at 30 °C proved to be suitable for the quantitative formation of 4-methoxy-2,4,6-tri-t-butyl-cyclohexa-2,5-dienone (12).

Scheme 3. Effect of reaction conditions on the reaction of 2,4,6-tri-t-butyl phenol (9) with F-TEDA-BF₄.

3,4,5-Trimethylphenol (13) in [bmim][BF₄] was quantitatively converted into 4-fluoro-3,4,5-trimethyl-2,5-cyclohexadienone (14) when it was reacted with F-TEDA-BF₄ for 22 h at room temperature or for 4 h at 70 °C (Scheme 4). On the contrary, the reaction carried out in [bmim][PF₆] at room temperature was inefficient, while at elevated temperature a polymeric material was formed. Likewise for the previously discussed substrates, MeCN seems to be an advantageous solvent for this transformation, since the product 14 was obtained efficiently in a reaction performed for 4.5 hours at room temperature [30].

Scheme 4. Transformation of 3,4,5-trimethylphenol (13) with F-TEDA-BF₄ in the hydrophilic IL [bmim][BF₄].

Furthermore, we investigated the effect of a nucleophile on the transformation of 4-t-butylphenol (4c) and the sterically more hindered 2,4,6-tri-t-butylphenol (9) in reaction with F-TEDA-BF₄ performed in an IL. After F-TEDA-BF₄ was completely dissolved in the IL, the substrate (4c or 9) was added to the reaction mixture, followed by the addition of approximately 5 molar equivalents of MeOH or MeCN and the reaction mixture continued to be stirred at an optimized reaction temperature. In the case of 4-t-butylphenol (4c), the presence of MeOH or MeCN in [bmim][BF₄] did not have a substantial effect on the course of the reaction as transformation of the substrate, as well as the
distribution of products 5c, 8 and 6c, were comparable to the results of reactions performed in the absence of the nucleophile. In the case of 2,4,6-tri-t-butylphenol (9), the substrate still prevailed (50-66%) in the reaction mixture when the reaction with F-TEDA-BF₄ was performed in [bmim][BF₄] and in the presence of 4-5 equivalents of a nucleophile (MeCN or MeOH), where 2,6-di-t-butyl-p-benzoquinone (10, 26-45%) was formed as the major product. In addition to the quinonic product 10, the presence of a minor amount of dealkylated methoxy substituted di-t-butylphenols (2-methoxy-4,6-di-t-butylphenol and 4-methoxy-2,6-di-t-butylphenol) could be noticed from the NMR spectra if the reaction was carried out at 70 °C; however, these products were present in small quantities. Since in the mixture of MeCN/MeOH (9/1) the substrate 9 was converted with high yield into 4-methoxy-2,4,6-tri-t-butyl-cyclohexa-2,5-dienone (12) at 30 °C in few hours, one can conclude that an organic solvent is more advantageous for these transformations than the use of ILs (Scheme 3).

The effect of the presence of a nucleophile in IL media was further investigated for the fluorofunctionalization of 1,1-diphenylethene (15) as a model alkene substrate, with F-TEDA-BF₄. The reaction between the substrate 15 and F-TEDA-BF₄ performed in [bmim][PF₆] at room temperature for 24 h did not provide any product, while under similar reaction conditions applied in [bmim][BF₄] a modest transformation occurred, yielding 1,1-diphenyl-1-hydroxy-2-fluoroethane (16b, 25%) and 1,1-diphenyl-2-fluoroethene (17, 17%) (Table 2). Raising the temperature to 50 °C resulted in the almost complete conversion of the substrate in the hydrophilic IL [bmim][BF₄] (Table 2, entry 7), while in [bmim][PF₆] the conversion yield of the reaction performed at 50 °C and in the absence of a nucleophile was still modest (Table 2, entry 2). The experimental data indicate a difference in the selectivity of fluorotransformation obtained in an IL with [BF₄] as the anionic part from the outcome of the reaction carried out in [bmim][PF₆] (Scheme 5). In the latter, which forms a two-phase system with water, the substrate was converted to addition-elimination product 1,1-diphenyl-2-fluoroethene (17) with high selectivity, regardless of the presence of a nucleophile (MeOH, H₂O, MeCN) (Table 2, entries 3-5). On the other hand, the addition product, namely vicinal hydroxy- or methoxyfluoroalkane 16b, 16a, prevailed in the reaction mixture when [bmim][BF₄] was used as the reaction medium (Table 2, entries 8, 9).

**Scheme 5.** The selectivity of fluorotransformation of 1,1-diphenyl ethene (15) in reaction with F-TEDA-BF₄ in an IL.
Table 2. Effect of reaction conditions on fluorotransformation of 1,1-diphenyl ethene (15) with F-TEDA-BF$_4$ in ILs$^a$.

| Entry | IL$^b$   | NuH$^c$ | T [°C] | Product distribution$^d$ | 15 | 16a | 16b | 17 | 18a | 18b |
|-------|----------|---------|--------|--------------------------|----|-----|-----|----|-----|-----|
| 1     | [bmim][PF$_6$] | /       | 22     |                          | 100% | / | / | / | / | / |
| 2     | /         | 50      | 64%    |                          | 36% | 22% | 17% | / | / | / |
| 3     | MeOH      | 50      | 7%     |                          | 60% | 22% | 12% | / | / | / |
| 4     | H$_2$O    | 50      | 13%    |                          | 78% | 9%  | / | / | / | / |
| 5     | MeCN      | 50      | 30%    |                          | 70% | / | / | / | / | / |
| 6     | [bmim][BF$_4$] | /       | 22     |                          | 58% | 25% | 17% | / | / | / |
| 7     | /         | 50      | 2%     |                          | 65% | 14% | 19% | / | / | / |
| 8     | MeOH      | 50      | /      |                          | 76% | 6%  | 1%  | 17% | / | / |
| 9     | H$_2$O    | 50      | 3%     |                          | 76% | / | / | / | 21% | / |

$^a$ Reaction conditions: 0.2 mmol substrate, 0.24 mmol F-TEDA-BF$_4$, 1 mL IL, 24h; $^b$ Ionic liquid; $^c$ nucleophile (5 molar equivalents); $^d$ The distribution of products determined from $^1$H- and $^{19}$F-NMR spectra of the crude reaction mixture.

Additionally, we investigated the effect of various amounts of a nucleophile (MeOH or H$_2$O; 5, 10, 20 and 50 molar equivalents) on the fluorination of 1,1-diphenylethene (15) with F-TEDA-BF$_4$ in both studied ILs (Figure 2). We found that the presence of 10-20 molar equivalents of MeOH or H$_2$O in [bmim][PF$_6$] considerably enhanced the efficiency of transformation of 15 into 1,1-diphenyl-2-fluoroethene (17). Furthermore, 1,1-diphenylethene (15) with F-TEDA-BF$_4$ and in the presence of 5-50 equivalents of MeOH was completely converted after 24 h at 50 °C if the reaction was carried out in [bmim][BF$_4$], thus highlighting the improved efficiency of the transformation in the presence of a nucleophile in this hydrophilic IL. In these cases, the major product corresponded to 1,1-diphenyl-1-methoxy-2-fluoroethane (16a), while 1,1-diphenyl-2-fluoroethene (17), 1,1-diphenyl-1-hydroxy-2-fluoroethene (16b) and 1,1-diphenyl-1-methoxy-2,2-difluoroethane (18a) could be detected in minor amounts from the NMR spectra as well. In cases where H$_2$O was used as the source of the external nucleophile in [bmim][BF$_4$], 1,1-diphenyl-1-hydroxy-2-fluoroethene (16b) formed as the major product, while the addition-elimination product 17 and 1,1-diphenyl-1-hydroxy-2,2-difluoroethane (18b) were present as minor products. Vicinal methoxy- or hydroxy-fluoroalkane (16a or 16b) were produced most efficiently in [bmim][BF$_4$] when the reaction was performed at 50 °C and in the presence of 50 equivalents of the corresponding nucleophile.

Evaluating the experimental results obtained for fluororotransformations of 1,1-diphenylethene (15) with F-TEDA-BF$_4$ as fluorinating reagent in the presence of a nucleophile in ILs, in comparison with published results carried out in organic solvents (a mixture MeCN/MeOH, their ratio corresponding to 9/1) [31], preference should be given to the use of organic solvents. This can be ascribed to the fact that in a mixture of MeCN/MeOH (9/1 ratio) substrates of alkenic moiety were quantitatively converted into the corresponding vicinal methoxyfluoroalkanes, following Markovnikov type of
regioselectivity at room temperature and for this transformation required a considerably shorter reaction time, while authors do not report on the formation of side products [31]. On the other hand, for the formation of vicinal hydroxyfluoroakanes priority should be given to water [33] as reaction medium over ILs.

**Figure 2.** Effect of the amount of nucleophile on the product distribution for fluorination of 1,1-diphenyl ethane (15) with F-TEDA-BF4 in [bmim][BF4] and [bmim][PF6]a,b.

\[ \begin{align*}
\text{a) [bmim][BF4]} \\
\begin{array}{c}
\text{Amount of nucleophile (mol equiv.)} \\
\text{MeOH} & 5 & 10 & 20 & 50 \\
\text{H2O} & 5 & 10 & 20 & 50
\end{array}
\end{align*} \]

\[ \begin{align*}
\text{b) [bmim][PF6]} \\
\begin{array}{c}
\text{Amount of nucleophile (mol equiv.)} \\
\text{MeOH} & 5 & 10 & 20 & 50 \\
\text{H2O} & 5 & 10 & 20 & 50
\end{array}
\end{align*} \]

\[ \begin{align*}
\text{Reaction conditions: } 0.2 \text{ mmol substrate (15), 0.24 mmol F-TEDA-BF4, nucleophile (MeOH or H2O; 5, 10, 20 or 50 molar equivalents), 1 mL IL ([bmim][BF4] or [bmim][PF6]), 50 °C, 24 h; } \]

The investigation of fluorination with F-TEDA-BF4 in IL media was further expanded to methoxy substituted benzene derivatives. During previous studies in our laboratory, we already reported regulation of the regioselectivity of fluorination of aryl alkyl ketones with N-F reagents by the proper choice of organic solvent. While in acetonitrile fluorofunctionalization took place efficiently and regioselectively onto the aromatic ring, α-alkyl position next to the carbonyl group was selectively fluorinated when MeOH was used as reaction solvent [34]. In an attempt to fluorinate some aryl alkyl ketones (19, 20, 21, 22) with F-TEDA-BF4 in ILs, we found that in addition to the substantially lower efficiency of fluorotransformations of these substrates in IL media also the aryl/alkyl selectivity failed to be controlled (Table 3).
Table 3. Transformations of aryl alkyl ketones with F-TEDA-BF₄ in ILs.<sup>a</sup>

| Entry | Substrate | Ionic liquid | t (h) | Conv. | Products | Product distribution<sup>c</sup> |
|-------|-----------|--------------|-------|-------|----------|-------------------------------|
| 1     |            |              |       |       | [COCH₃] | 19a: 9%, 19: 90%<sup>d</sup> |
| 2     | [bmim][BF₄] |              | 5     | 10%   | [COCH₃] | 19a: 11%, 19b: 2%, 19: 86%<sup>d</sup> |
| 3     | [bmim][BF₄] |              | 5     | 6%    | [COCH₃] | 19a: 6%, 19: 94% |
| 4     | [bmim][BF₄] |              | 5     | 10%   | [COCH₃] | 19a: 9%, 19: 90%<sup>d</sup> |
| 5     |            |              | 20    | 28%   | [COCH₃] | 20a: 28%, 20: 72% |
| 6     | [bmim][BF₄] |              | 20    | 7%    | [COCH₃] | 20a: 7%, 20: 93% |
| 7     |            |              | 5     | 29%   | [COCH₃] | 21a: 17%, 21b: 5%, 21c: 7%, 21: 71% |
| 8     |            |              | 18    | 47%   | [COCH₃] | 21a: 27%, 21b: 7%, 21c: 13%, 21: 53% |
| 9     | [bmim][BF₄] |              | 5     | 18%   | 21a: X₁=F, X₂=X₃=H, 21b: X₂=F, X₁=X₃=H, 21c: X₃=F, X₁=X₂=H |
| 10    | [bmim][BF₄] |              | 18    | 10%   | 21a: 12%, 21b: 3%, 21c: 3%, 21: 82% |
| 11    | [bmim][BF₄] |              | 5     | 49%   | 21a: X₁=F, X₂=X₃=H, 21b: X₂=F, X₁=X₃=H, 21c: X₃=F, X₁=X₂=H |
| 12    | [bmim][BF₄] |              | 18    | 61%   | 22a: X₁=F, X₂=X₃=H, 22b: X₂=F, X₁=X₃=H, 22c: X₃=F, X₁=X₂=H |
| 13    | [bmim][BF₄] |              | 5     | 22%   | 22a: X₁=F, X₂=X₃=H, 22b: X₂=F, X₁=X₃=H, 22c: X₃=F, X₁=X₂=H |
| 14    | [bmim][BF₄] |              | 18    | 11%   | 22a: X₁=X₃=F, X₂=H, 22b: X₂=F, X₁=X₃=H, 22c: X₃=F, X₁=X₂=H |

<sup>a</sup> Reaction conditions: 0.2 mmol substrate, 0.24 mmol F-TEDA-BF₄, 1 mL ionic liquid, 70 °C;<sup>b</sup> Conversion of substrate determined from ³¹H- and ¹⁹F-NMR spectra of the crude reaction mixture;<sup>c</sup> The distribution of compounds in the reaction mixture was determined from ³¹H- and ¹⁹F-NMR spectra;<sup>d</sup> Also the presence of 1% of 4-fluoroanisole.

The substituted benzaldehydes (23: 4-methoxybenzaldehyde, 24: 3,4-(methylenedioxy)benzaldehyde, and 25: 4-hydroxybenzaldehyde) remained unchanged in the reactions with F-TEDA-BF₄, performed in the investigated ILs. A slight transformation was noticed only in the case of the reaction of 4-methoxybenzaldehyde (23) with F-TEDA-BF₄, carried out for 20 h at 70 °C in [bmim][BF₄], where the substrate was converted into 3-fluoro-3-methoxybenzaldehyde (23a, 9%).
In the cases of dimethoxy- and trimethoxy-substituted benzenes, the fluorotransformation with F-TEDA-BF\(_4\) in IL media proved to be crucially dependent on the structure of the substrate. In the case of 1,3-dimethoxybenzene (26) and 1,3,5-trimethoxybenzene (27), which are both highly activated toward electrophilic substitution, the corresponding reaction mixture in [bmim][BF\(_4\)], as well as in [bmim][PF\(_6\)], contained at least 4 different products after 3 h reaction performed at 70 °C (Figure 3). On the other hand, the substrates 1,2-dimethoxybenzene (28), 1,4-dimethoxybenzene (29) and 1,2,3-trimethoxybenzene (30) remained mostly unreacted or fluoro-functionalization occurred only to a minor extent. 1,3-Dimethoxybenzene (26) in a reaction performed for 3 h at 70 °C in [bmim][BF\(_4\)] was over 80% converted into a mixture of fluorinated products, with the formation of 4-fluoro-1,3-dimethoxybenzene (26a) as the major product, while from the \(^{19}\text{F}\)-NMR spectra the presence of the minor products 4,6-difluoro-1,3-dimethoxybenzene (26b), 2-fluoro-1,3-dimethoxybenzene (26c) and 4,6,6-trifluoro-3-methoxy-2,4-cyclohexadienone (26c) was established. The substrate 26 subjected to similar reaction conditions in [bmim][PF\(_6\)] was 60% converted into a mixture of products 26a, 26b, 26c and 26d, with 4-fluoro-1,3-dimethoxybenzene (26a) prevalent. The efficiency of transformation and the distribution of the fluorinated products formed resembled the outcomes of reactions which occur under comparable reaction conditions in MeCN or in MeOH. The reaction of another reactive substrate, namely 1,3,5-trimethoxybenzene (27) with F-TEDA-BF\(_4\) in the studied IL media after 4 h at 70 °C provided a mixture of the products: 2-fluoro-1,3,5-trimethoxybenzene (27a, >50%) and in smaller quantities 2,4-difluoro-1,3,5-trimethoxybenzene (27b, ~5%), 4,4-difluoro-3,5-dimethoxy-2,5-cyclohexadienone (27c, 10-20%) and 2,2-difluoro-3,5-dimethoxy-3,5-cyclohexadienone (27d, <5%). Regarding the efficiency and the product distribution of the reaction, this was a similar result to the case when fluorination with F-TEDA-BF\(_4\) was carried out in MeCN [35] or in MeOH.

**Figure 3.** The mixture of products obtained in reaction of 1,3-dimethoxybenzene (26) or 1,3,5-trimethoxybenzene (27) with F-TEDA-BF\(_4\) in the IL [bmim][BF\(_4\)] or [bmim][PF\(_6\)] (70 °C, 3-4 h).
3. Experimental

3.1. General

The reactions were performed in 5-mL round bottom flasks with 1 mL of IL ([bmim][BF₄] or [bmim][PF₆]) as reaction medium. Firstly, F-TEDA-BF₄ (0.24 mmol) was vigorously stirred in the IL at 70 °C until its complete dissolution. Then, substrate (0.2 mmol) was added and the reaction mixture continued to be stirred at the appropriate reaction temperature (22-70 °C). After the reaction had ceased, the products were extracted with t-BuOMe (4x2 mL), the combined organic phase was washed with water and after drying of the organic phase over anhydrous Na₂SO₄, the insoluble material was filtered off, while the reaction mixture was concentrated in vacuo. The crude reaction mixture was analyzed by TLC, ¹H-NMR, ¹⁹F-NMR and MS and the products identified on the basis of comparison of their spectroscopic data with literature values [27-30,33-51].

4. Conclusions

The transformations of organic molecules with F-TEDA-BF₄ investigated in the hydrophilic IL [bmim][BF₄] and in the hydrophobic IL [bmim][PF₆] and their evaluation in comparison to the corresponding reactions carried out in organic solvents revealed that these ILs are less convenient media for the fluoro-functionalization of alkyl substituted phenols (4a, 4b, 4c, 9, 13), 1,1-diphenylethene (15) and methoxy-substituted aryl alkyl ketones (19, 20, 21, 22) than MeCN or MeOH. Reactions of alkyl substituted phenols, namely 4-methylphenol (4a), 4-i-propylphenol (4b), 4-t-butylphenol (4c), 2,4,6-tri-t-butylphenol (9) and 3,4,5-trimethylphenol (13), with F-TEDA-BF₄, depending on the substrate structure and reaction conditions, lead to the formation of either of the following fluorofunctionalised products: the corresponding ortho-fluorosubstituted product 5 as a result of electrophilic substitution at the ortho position of the phenol, difluorocyclohexadienone 6 formed following another fluorine introduction into 5, 4-alkyl-4-fluoro-cyclohexa-2,5-dienone (7) as a consequence of the addition-elimination process after fluorine attack at the para position of 4-alkyl phenol, while 4-fluorophenol (8) was produced through ipso substitution and dealkylation at the para position. The transformations were higher in the hydrophilic IL [bmim][BF₄] than in the hydrophobic [bmim][PF₆]; however, compared to the published results of reactions performed in MeOH or in MeCN they were considerably less efficient and with a different distribution of products. Also for a substrate with an aromatic alkene moiety, namely 1,1-diphenylethene (15), when reacted with F-TEDA-BF₄ a higher conversion was obtained in the hydrophilic IL than in the hydrophobic one. In addition, a markedly different selectivity of product formation was observed in the studied ILs. In [bmim][PF₆], which with water forms a two-phase system, the substrate 15 was, regardless of the nucleophile present (MeOH, H₂O or MeCN), transformed into an addition-elimination product, namely 1,1-diphenyl-2-fluoroethene (17), with high selectivity. On the other hand, when the reaction was performed in [bmim][BF₄] the major product corresponded to vicinal hydroxy- or methoxy fluoroalkane (16b or 16a). In an attempt to fluorofunctionalize some methoxy substituted aryl alkyl ketones using F-TEDA-BF₄ in ILs, we found that in addition to the very low efficiency of the transformation, the reactions also proved unselective, thus giving preference to MeOH or MeCN for these fluoro-functionalizations. The efficiency of fluorination and the distribution of products in the
cases of the reactions of 1,3-dimethoxybenzene (26) and 1,3,5-trimethoxybenzene (27) with F-TEDA-BF₄ in the studied ILs was similar to the outcome of the reactions performed in MeCN or MeOH. Finally, we would like to point out that a small variation in reaction conditions may severely affect the outcome. Moreover, due to the lack of data on their physico-chemical properties, as well as long-term environmental influence of ILs one should be very cautious before proclaiming them as ‘greener’ alternative to organic solvents.

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