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# One-pot α-nucleophilic fluorination of acetophenones in a deep eutectic solvent

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ABSTRACT

Two methods of nucleophilic fluorination to prepare α-fluoroacetophenones from α-bromoacetophenones by using KF with PEG-400 or TBAF with $ZnF_2$ are described. On the fundamental of nucleophilic fluorination, a novel method of one-pot fluorination to prepare α-fluoroacetophenones directly from acetophenones in DES was developed.



## 1. Introduction

Fluorinated molecules find innumerable applications in the industries or daily life and the fluorine atom endows unique properties such as some characteristic effects on bioactivity to the molecules that are extremely important in the pharmaceutical and agrochemical industries [1]. α-Fluorocarbonyl compounds that contain fluorine atom next to carbonyl group have important usage in medicinal and biological chemistry and α-fluoroacetophenones that have carbonyl group, α-fluorinated carbon and aromatic ring can be transformed into a large number of interesting molecules that have potential to constitute an important class of fluorinated intermediates in the pharmaceutical and agrochemical chemistry [2].

Generally speaking, α-fluoroacetophenones can be prepared from acetophenones through two kinds of strategies that are electrophilic and nucleophilic fluorination [3]. A wide range of reagents bearing a $R_2N$-F unit was used in the electrophilic way of preparing fluorinated carbonyl compounds and α-fluoroacetophenones were obtained from acetophenones directly by electrophilic fluorination using Selectfluor or NFSI [4]. But the N-F reagents are too expensive for large-scale preparation and elemental F, a sort of hazardous and toxic chemical, is widely used in preparing N-F reagents and electrophilic fluorination in the plant-scale production [5]. Comparing with electrophilic methods, nucleophilic processes to prepare α-fluoroacetophenones from α-bromoacetophenones by KF or tetrabutylammonium fluoride (TBAF) are more safe and cheaper and are more easily used in the large-scale fluorination [6].

In order to develop methods for preparing α-fluoroacetophenones from α-bromoacetophenones by nucleophilic strategy, KF or TBAF was respectively used in different conditions and several substrates were tested. Based on these results, a novel method to prepare α-fluoroacetophenones directly from acetophenones in one pot by nucleophilic strategy was developed in a deep eutectic solvent. Choline chloride is an important compound in the chemical and biological technology. Deep eutectic solvents (DES) prepared from choline chloride are thought to be versatile alternatives to ionic liquids and have been shown to be good solvents for many organic reactions [7]. Some good results of preparing α-fluoroacetophenones by nucleophilic strategy were reported [8] and we tried to make the fluorination more safe, cheaper and easier to handle. In this paper, we wish to report two nucleophilic processes and a new one-pot method of nucleophilic fluorination in a deep eutectic solvent to prepare α-fluoroacetophenones (Scheme 1).

## 2. Results and discussion

KF is widely used in the nucleophilic fluorination and polyethylene glycol (PEG) as a safe and cheap solvent has been reported to be used in the nucleophilic fluorination with KF to improve the yields of fluorinated products. Efficient fluorination was reported using potassium fluoride as a nucleophilic source of fluorine and PEG-400 as a solvent and the yields of the fluorinated products were 24–63% [9]. Acetonitrile was used as a solvent and PEG-400 was cosolvent. When α-bromoacetophenone **2a** was stirred and heated directly with KF and PEG-400 in acetonitrile that is frequently used as a solvent in nucleophilic fluorination reaction,

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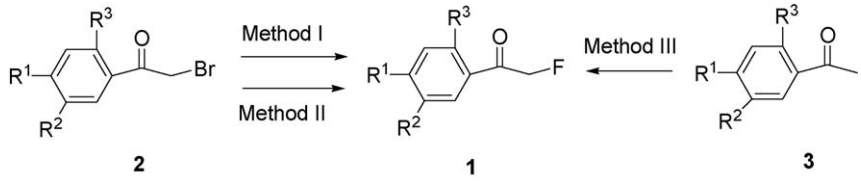



Method I: KF, PEG-400, acetonitrile, 80 °C. Yields: 55~74%.

Method II: TBAF, $ZnF_2$, KF, acetonitrile, 80 °C. Yields: 60~90%.

Method III: DES, DCDMH, TBAF, $ZnF_2$, acetonitrile, 80 °C. Yields: 32~80%.

**a**: $R^1$=H, $R^2$=H, $R^3$=H
**b**: $R^1$=$CH_3$, $R^2$=H, $R^3$=H
**c**: $R^1$=$OCH_3$, $R^2$=H, $R^3$=H
**d**: $R^1$=$OCH_3$, $R^2$=$OCH_3$, $R^3$=Br
**e**: $R^1$=Cl, $R^2$=H, $R^3$=H
**f**: $R^1$=Br, $R^2$=H, $R^3$=H
**g**: $R^1$=H, $R^2$=Br, $R^3$=H
**h**: $R^1$=$NO_2$, $R^2$=H, $R^3$=H
**i**: $R^1$=H, $R^2$=$NO_2$, $R^3$=H
**j**: $R^1$=H, $R^2$=$CH_3$, $R^3$=H
**k**: $R^1$=F, $R^2$=H, $R^3$=H
**l**: $R^1$=Cl, $R^2$=Cl, $R^3$=H
**m**: $R^1$=$OCH_3$, $R^2$=Cl, $R^3$=H

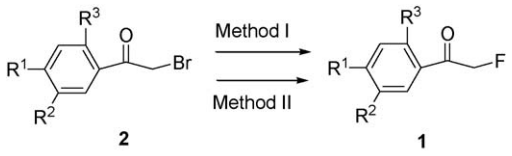
**Scheme 1.**

the yield of α-fluoroacetophenone was 50% and *trans*-1,2,3-tri-(benzoyl)cyclopropane that reduced the yield of fluorinated compound was found among the products. *trans*-1,2,3-Tri-(benzoyl)cyclopropane prepared from α-bromoacetophenone has been reported and reducing the concentration of α-bromoacetophenone in the solvent is helpful to lower the amount of *trans*-1,2,3-tri-(benzoyl)cyclopropane and to offer more fluorinated products [10]. A diluted solution of α-bromoacetophenone was slowly added drop by drop into the mixture of KF, PEG-400 and acetonitrile at 80 °C and the yield of α-fluoroacetophenone increased to 72%. After that, other substituted α-bromoacetophenones were tested and the yields were from 55% to 74% (Scheme 1, method I; Table 1). The yields of **1b**–**1d** that have electron-donating groups were close to 70% (Table 1, entry 2–4) and the yields of **1e**–**1g** that have weak deactivating groups were lower than 58% (Table 1, entry 5–7). Only trace amount of **1h** or **1i** that has strong electron-withdrawing group was obtained and **3h** or **3i** was collected as major product (Table 1, entry 8–9). 85% of **2h** was transformed into **3h** and 82% of **2i** was transferred into **3i**. α,α-Dibromoacetophenone was also used as a tested substrate and α,α-difluoroacetophenone was not found among the products while **1a** and acetophenone were obtained; the yield of **1a** was 15% and the yield of acetophenone was 75%.

In order to improve the yields of fluorinated compounds, tetrabutylammonium fluoride (TBAF) was used as the fluorinating reagent. Tetrabutylammonium hydrogen bifluoride is a nucleophilic fluorine source with good solubility property and tetrabutylammonium fluoride trihydrate that can generate reactive fluoride ions in organic solvents has also been reported as a nucleophilic reagent [11]. Tetrabutylammonium fluoride trihydrate is easy to handle and it is cheaper than tetrabutylammonium hydrogen bifluoride. Some examples using tetrabutylammonium hydrogen bifluoride were reported and the yields were 20–51% [2b]. In our research, we tried to improve the yields of the fluorinated products and tetrabutylammonium fluoride trihydrate was selected as the fluorinating reagent. When α-bromoacetophenone **2a** was heated and stirred with TBAF·$3H_2O$ in acetonitrile, the isolated yield of **1a** was 62%. When TBAF·$3H_2O$ was replaced by $ZnF_2$ in this reaction, only trace amount of **1a** was obtained. While **2a** (5 mmol) was heated with TBAF·$3H_2O$ (5 mmol) and $ZnF_2$ (5 mmol) in acetonitrile at 80 °C, the yield of **1a** was 70%. KF is cheaper than TBAF·$3H_2O$ and part of TBAF·$3H_2O$ used in the reaction was replaced by KF. A mixture of TBAF·$3H_2O$ (3.75 mmol), KF (2.5 mmol), $ZnF_2$ (5 mmol) and acetonitrile (20 ml) was stirred at 80 °C and then a solution of substrate (5 mmol) was added into the reaction mixture. After the reaction completed, the yield of **1a** was 76%. When DMSO was used as solvent, the yield of α-fluoroacetophenone **1a** declined to 66%. When $CaF_2$ was used instead of $ZnF_2$, the yield of **1a** was 72%; when $MgF_2$ was added instead of $ZnF_2$, the yield of **1a** was 70%. Other substituted substrates were tested and yields of **1a**–**1i** were 60–90% (Scheme 1, method II; Table 1). The yields of **1b**–**1d** that have electron-donating groups were from 82% to 90%, which were better than the yields of **1e**–**1i** that have deactivating groups (Table 1). Comparing with method I, the yields of method II were better. In both two methods, the yields of **1a**–**1d** were higher than the yields of **1e**–**1i**.

Deep eutectic solvents (DES) formed between choline chloride and acids are thought to be a new kind of solvents that will be closer to the principles of green chemistry and an efficient method of chlorination in DES that formed between choline chloride and *p*-TsOH has been reported [12]. Based on the nucleophilic fluorination by TBAF, we tried to combine the chlorination in DES with nucleophilic fluorination to develop a one-pot fluorination method that α-fluoroacetophenones can be prepared directly from acetophenones. Firstly, acetophenone **3a** was selected as the tested substrate. We thought more α,α-dichloroacetophenone produced in DES would reduce the yield of the fluorinated product so we tried to control the amount of chlorinating reagent. 1,3-Dichloro-5,5-dimethylhydantoin (DCDMH) is a bleaching reagent and it has also been extensively used as a disinfectant for industrial and domestic water. So DCDMH was selected as the chlorinating reagent. DES was prepared from choline chloride (1 mmol) and *p*-TsOH (1 mmol) and then **3a** (2 mmol) was added into the DES. After that, DCDMH (1.1 mmol) was added bit by bit into the reaction mixture. After the reaction mixture was stirred at room temperature for 1 h, 80% of **3a** was transformed into α-chloroacetophenone and 12% of **3a** was transformed into α,α-dichloroacetophenone. 8% of **3a** was also found in the mixture, which was determined by GC. When the amount of DCDMH increased to 1.3 or 1.5 mmol, the yield of α-chloroacetophenone determined by GC was 86% or 78%. But when **3b** was selected as the tested substrate, the yields of chlorinated products were different. When the amount of DCDMH was 1.1 mmol, the yield of α-chloro-4-methylacetophenone determined by GC was 92%. When the amount increased to 1.3 or 1.5 mmol, the yield declined to 80% or 74%. We thought that 1.1 mmol was a proper amount for **3a** and 1.3 mmol was a proper amount for **3b**. So both two amounts of DCDMH (1.1 mmol and 1.3 mmol) were tested when other

**Table 1**
Nucleophilic fluorination of α-bromoacetophenones by KF (I)[a] or TBAF (II)[b].



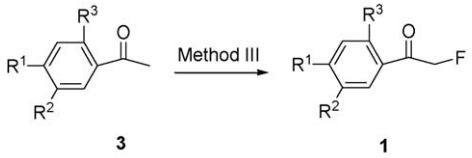

Method I: KF, PEG-400, acetonitrile, 80 °C.
Method II: TBAF, $ZnF_2$, KF, acetonitrile, 80 °C.

| Entry | Substrate | Product | Yield of I (%)[c] | Yield of II (%)[d] |
|---|---|---|---|---|
| 1 | **2a** | **1a** | 72 | 76 |
| 2 | **2b** | **1b** | 66 | 90 |
| 3 | **2c** | **1c** | 74 | 84 |
| 4 | **2d** | **1d** | 70 | 82 |
| 5 | **2e** | **1e** | 55 | 65 |
| 6 | **2f** | **1f** | 58 | 70 |
| 7 | **2g** | **1g** | 58 | 72 |
| 8 | **2h** | **1h** | /[e] | 60 |
| 9 | **2i** | **1i** | /[f] | 66 |

[a] Method I: 30 ml of acetonitrile solution of substrate (10 mmol) was added slowly dropwise into a mixture of KF (50 mmol), PEG-400 (2 ml) and acetonitrile (50 ml) at 80 °C.
[b] Method II: 5 ml of acetonitrile solution of substrate (5 mmol) was added into a mixture of TBAF·$3H_2O$ (3.75 mmol), KF (2.5 mmol), $ZnF_2$ (5 mmol) and acetonitrile (20 ml) at 80 °C.
[c] Isolated yields of method I.
[d] Isolated yields of method II.
[e] Only trace amount of **1h** was obtained and the yield of the major product **3h** was 85%.
[f] Only trace amount of **1i** was obtained and the yield of the major product **3i** was 82%.

acetophenones were used as substrates. When DES that was prepared from $ZnCl_2$ and choline chloride was used, the reaction mixture was stirred for longer time (3 h) to fully consume starting material **3a** after DCDMH was added. When DBDMH was used instead of DCDMH, both chlorinated compounds and brominated compounds were found in the reaction mixture, which made the reaction complex.

**Table 2**
One-pot fluorination of acetophenones by TBAF·$3H_2O$ in DES[a].




Method III: DES, DCDMH, TBAF, $ZnF_2$, acetonitrile, 80 °C.

| Entry | Substrate | Product | Isolated yield (%)[b] |
|---|---|---|---|
| 1 | **3a** | **1a** | 60 (72) |
| 2 | **3b** | **1b** | 80 (66) |
| 3 | **3c** | **1m** | 33 (38) |
| 4 | **3d** | **1d** | /[c] |
| 5 | **3e** | **1e** | 45 (50) |
| 6 | **3f** | **1f** | 50 (50) |
| 7 | **3g** | **1g** | 60 (60) |
| 8 | **3h** | **1h** | 32 (35) |
| 9 | **3i** | **1i** | 35 (40) |
| 10 | **3j** | **1j** | 75 (62) |
| 11 | **3k** | **1k** | 50 (55) |
| 12 | **3l** | **1l** | 40 (46) |

[a] Substrate (2 mmol) was stirred with DCDMH (1.1 mmol or 1.3 mmol) in DES (1 mmol choline chloride and 1 mmol *p*-TsOH) at room temperature for 1 h. After that, $ZnF_2$ (5 mmol) and TBAF·$3H_2O$ (6 mmol) were added and the reaction mixture was heated at 80 °C for 8 h.
[b] When the amount of DCDMH was 1.1 mmol, the yields was written out of the bracket; when the amount was 1.3 mmol, the yields was in the bracket.
[c] Only trace amount of **1d** was obtained.

After that, we tried to combine chlorination with fluorination to develop a one-pot process. To improve the fluorination in the DES, the amount of TBAF·$3H_2O$ used in the reaction was increased without KF. After **3a** was added into the DES and stirred with DCDMH, $ZnF_2$ and TBAF·$3H_2O$ were added into the reaction mixture. After the mixture was heated at 80 °C for 8 h, the fluorinated product **1a** was isolated. When the amount of DCDMH was 1.1 mmol, the yield of **1a** was 60% and the yields of the other tested substrates were from 32% to 80%. When this amount was 1.3 mmol, the yields of fluorinated products were from 35% to 72% (Table 2). When **3c** that has a $-OCH_3$ group was tested as the substrate, **1m**, a new compound, that has a $-OCH_3$ group and a chlorine atom on the aromatic ring was obtained as the major fluorinated product. Maybe **3c** was easily transformed into **3m** in the DES (Table 2-entry 3). As to the substrate **3d**, only trace amount of **1d** was obtained (Table 2-entry 4). When 1.1 mmol of DCDMH was used, the yields of **1b** and **1j** were higher than the yields when 1.3 mmol of DCDMH was used (Table 2-entry 2, 10). The yields of the other tested products when 1.1 mmol of DCDMH was used in the reaction were lower than the yields when 1.3 mmol of DCDMH was used. The substrates that have $-CH_3$ group like **3b** and **3j** were perhaps transformed into more α-chloroacetophenones in DES when 1.1 mmol of DCDMH was added. These substrates were perhaps transformed into more α,α-dichloroacetophenones when 1.3 mmol of DCDMH was added. Comparing with **3b** and **3j**, the substrates that have deactivating groups were perhaps transformed into more α-chloroacetophenones in DES when 1.3 mmol of DCDMH was added. Additionally, the yields of **3b** and **3j** were higher than the yields of the other products.

## 3. Conclusion

We tried to prepare α-fluoroacetophenones by three different methods and nucleophilic fluorination was involved in all these methods. Method I and method II using KF or TBAF·$3H_2O$ as fluorinating reagent improved the yields of α-fluoroacetophenones that prepared from α-bromoacetophenones. Method III took advantage of chlorination in DES and nucleophilic fluorination to prepare α-fluoroacetophenones directly from acetophenones in one pot and the yields of method III were higher than some examples of electrophilic fluorination using N-F reagents [2]. As far as the reactants and products were concerned, method III completed "electrophilic" fluorination by nucleophilic strategy.

## 4. Experimental

### 4.1. General procedure of method I

A mixture of KF (50 mmol), PEG-400 (2 ml) and acetonitrile (50 ml) was stirred and heated at 80 °C for 2 h and then 30 ml of acetonitrile solution of substrate (10 mmol) was added slowly dropwise into the reaction mixture. After the addition completed, the reaction mixture was heated for further 18 h. After the mixture was filtered, solvent was distilled under reduced pressure. The crude product was purified by column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate (10:1) as eluent to afford the pure product.

### 4.2. General procedure of method II

A mixture of TBAF·$3H_2O$ (3.75 mmol), $ZnF_2$ (5 mmol), KF (2.5 mmol) and acetonitrile (20 ml) was stirred and heated at

80 °C for 1 h and then 5 ml of acetonitrile solution of substrate (5 mmol) was added into the reaction mixture. After the reaction mixture was heated for further 10 h at 80 °C, the mixture was filtered and acetonitrile was distilled under reduced pressure. Water (40 ml) was added to the residue and ether (4× 40 ml) was used to extract the water layer. The combined ether layer was washed by dilute hydrochloric acid (2× 40 ml, 0.5 M) and by brine (3× 40 ml) and dried on magnesium sulfate. After that, the organic layer was filtered and solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate (10:1) as eluent to afford the pure product.

### 4.3. General procedure of method III

A mixture of choline chloride (1 mmol) and TsOH (1 mmol) was added into a flask with a magnetic stirring bar under $N_2$ atmosphere. The flask was heated in an oil bath at 100 °C for 40 min and then was cooled to room temperature slowly. After cooling down, the colorless DES was prepared in the flask. Substrate (2 mmol) and acetonitrile (3 ml) were added into DES and DCDMH (1.1 mmol or 1.3 mmol) was added bit by bit into the reaction mixture. After addition, the mixture was stirred at room temperature for 1 h and then $ZnF_2$ (5 mmol) and TBAF·$3H_2O$ (6 mmol) were added into the mixture. After the reaction mixture was heated at 80 °C for 8 h, the mixture was filtered and acetonitrile was distilled under reduced pressure. Dilute hydrochloric acid (20 ml, 0.5 M) was added to the residue and dichloromethane (2× 20 ml) was used to extract the water layer. The combined organic layer was washed by saturated aqueous sodium bicarbonate solution (2× 20 ml) and water (2× 20 ml) and dried on magnesium sulfate. The organic layer was filtered and solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate (10:1) as eluent to afford the pure product.

### 4.4. 2-Fluoro-1-phenylethanone (**1a**) [8a]

Clear oil. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 5.52 (d, $J$ = 47 Hz, 2H, $CH_2F$), 7.47–7.50 (m, 2H, ArH), 7.60–7.62 (m, 1H, ArH), 7.87–7.88 (m, 2H, ArH).

### 4.5. 2-Fluoro-1-(4-methylphenyl)ethanone (**1b**) [2d]

Clear oil. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 2.41 (s, 3H, $CH_3$), 5.50 (d, $J$ = 47 Hz, 2H, $CH_2F$), 7.26–7.29 (m, 2H, ArH), 7.77–7.79 (m, 2H, ArH).

### 4.6. 2-Fluoro-1-(4-methoxyphenyl)ethanone (**1c**) [13]

White solid. m.p.: 78–79 °C (lit: 78–79 °C). $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 3.88 (s, 3H, $OCH_3$), 5.47 (d, $J$ = 47 Hz, 2H, $CH_2F$), 6.95–6.97 (m, 2H, ArH), 7.89–7.90 (m, 2H, ArH).

### 4.7. 1-(2-Bromo-4,5-dimethoxyphenyl)-2-fluoroethanone (**1d**)

White solid. m.p.: 86–87 °C. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 3.91 (s, 3H, $OCH_3$), 3.93 (s, 3H, $OCH_3$), 5.50 (d, $J$ = 47 Hz, 2H, $CH_2F$), 7.06 (s, 1H, ArH), 7.23 (s, 1H, ArH). $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$: 56.2 ($OCH_3$), 56.4 ($OCH_3$), 84.5 ($CH_2F$), 112.3 (ArCBr), 113.1 (ArCH), 116.4 (ArCH), 129.1 (ArC), 148.5 (ArC), 152.6 (ArC), 195.0 (CO). IR (KBr, $cm^{-1}$): 2940, 1676, 1592, 1509, 1392, 1262, 1219, 1172, 1043, 880, 833, 765 and 632. Ms: 278, 267, 256, 245, 232, 216, 200, 186, 170, 158, 142, 132, 122, 109, 94, 78, 61, 50. Element Analysis: found: C, 43.4%; H, 3.6%. Calculated for $C_{10}H_{10}BrFO_3$ (277.08): C, 43.3%; H, 3.6%.

### 4.8. 1-(4-Chlorophenyl)-2-fluoroethanone (**1e**) [14]

White solid. m.p.: 51–52 °C (lit: 52–53 °C). $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 5.48 (d, $J$ = 47 Hz, 2H, $CH_2F$), 7.45–7.47 (m, 2H, ArH), 7.83–7.85 (m, 2H, ArH). Ms: 173, 155, 140, 126, 112, 100, 86, 76, 61, 50.

### 4.9. 1-(4-Bromophenyl)-2-fluoroethanone (**1f**) [15]

White solid. m.p.: 69–70 °C (lit: 71–72 °C). $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 5.47 (d, $J$ = 47 Hz, 2H, $CH_2F$), 7.64–7.66 (m, 2H, ArH), 7.77–7.79 (m, 2H, ArH).

### 4.10. 1-(3-Bromophenyl)-2-fluoroethanone (**1g**)

Clear oil. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 5.47 (d, $J$ = 47 Hz, 2H, $CH_2F$), 7.37–7.40 (m, 1H, ArH), 7.75–7.77 (m, 1H, ArH), 7.82–7.83 (m, 1H, ArH), 8.04–8.05 (m, 1H, ArH). $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$: 83.4 ($CH_2F$), 123.2 (ArC), 126.3 (ArCH), 130.4 (ArCH), 130.9 (ArCH), 135.3 (ArCH), 136.9 (ArC), 192.2 (CO). IR (KBr, $cm^{-1}$): 2933, 1716, 1568, 1424, 1227, 1095, 990, 786, 701 and 680. Ms: 217, 183, 155, 104, 76, 61, 50.

### 4.11. 2-Fluoro-1-(4-nitrophenyl)ethanone (**1h**) [15]

White solid. m.p.: 90–92 °C (lit: 96–97 °C). $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 5.52 (d, $J$ = 47 Hz, 2H, $CH_2F$), 8.08–8.11 (m, 2H, ArH), 8.35–8.37 (m, 2H, ArH).

### 4.12. 2-Fluoro-1-(4-nitrophenyl)ethanone (**1i**)

White solid. m.p.: 92–93 °C. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 5.54 (d, $J$ = 47 Hz, 2H, $CH_2F$), 7.73–7.76 (m, 1H, ArH), 8.26–8.28 (m, 1H, ArH), 8.47–8.49 (m, 1H, ArH), 8.73–8.74 (m, 1H, ArH). $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$: 83.8 ($CH_2F$), 123.1 (ArCH), 128.3 (ArCH), 130.3 (ArCH), 133.7 (ArCH), 135.0 (ArC), 148.3 (ArC), 191.9 (CO). IR (KBr, $cm^{-1}$): 2939, 1704, 1609, 1535, 1352, 1230, 1074, 974, 826, 739 and 670. Ms: 183, 167, 150, 134, 122, 104, 92, 76, 63, 50. Element Analysis: found: C, 52.6%; H, 3.3%. Calculated for $C_8H_6FNO_3$ (183.03): C, 52.5%; H, 3.3%.

### 4.13. 2-Fluoro-1-(3-methylphenyl)ethanone (**1j**) [16]

Clear oil. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 2.41 (s, 3H, $CH_3$), 5.52 (d, $J$ = 47 Hz, 2H, $CH_2F$), 7.36–7.39 (m, 1H, ArH), 7.42–7.44 (m, 1H, ArH), 7.66–7.67 (m, 1H, ArH), 7.70 (m, 1H, ArH).

### 4.14. 2-Fluoro-1-(4-fluorophenyl)ethanone (**1k**) [17]

White solid. m.p.: 47–49 °C (lit: 49–51 °C). $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 5.47 (d, $J$ = 47 Hz, 2H, $CH_2F$), 7.15–7.18 (m, 2H, ArH), 7.94–7.96 (m, 2H, ArH).

### 4.15. 1-(3,4-Dichlorophenyl)-2-fluoroethanone (**1l**)

White solid. m.p.: 52–54 °C. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 5.45 (d, $J$ = 47 Hz, 2H, $CH_2F$), 7.58–7.60 (m, 1H, ArH), 7.73–7.75 (m, 1H, ArH), 8.00–8.01 (m, 1H, ArH). $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$: 83.6 ($CH_2F$), 127.1 (ArCH), 130.1 (ArCH), 131.1 (ArCH), 133.2 (ArC), 133.8 (ArC), 138.9 (ArC), 191.7 (CO). IR (KBr, $cm^{-1}$): 2926, 1704, 1587, 1383, 1230, 1087, 1030, 983 and 835. Ms: 207, 173, 145, 109, 74, 61, 50. Element Analysis: found: C, 46.8%; H, 2.3%. Calculated for $C_8H_5Cl_2FO$ (205.97): C, 46.4%; H, 2.4%.

### 4.16. 1-(3-Chloro-4-methoxyphenyl)-2-fluoroethanone (**1m**)

White solid. m.p.: 73–74 °C. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 3.96 (s, 3H, $OCH_3$), 5.43 (d, $J$ = 47 Hz, 2H, $CH_2F$), 6.96–6.98 (m, 1H, ArH), 7.81–7.83 (m, 1H, ArH), 7.93–7.94 (m, 1H, ArH). $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$: 56.4 ($OCH_3$), 83.5 ($CH_2F$), 111.5 (ArCH), 123.3 (ArC), 125.5 (ArCH), 128.5 (ArCH), 130.2 (ArC), 159.5 (ArC), 191.2 (CO). IR (KBr, $cm^{-1}$): 2926, 1691, 1596, 1508, 1396, 1274, 1096, 1061, 1009, 861, 704 and 617. Ms: 202, 189, 169, 154, 141, 126, 111, 97, 85, 71, 57. Element Analysis: found: C, 53.3%; H, 4.0%. Calculated for $C_9H_8ClFO_2$ (202.02): C, 53.4%; H, 4.0%.

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