Tetrahedron 68 (2012) 603–607

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

# Stereoselective cyanation of β-bromo-β-fluorostyrenes using potassium cyanide and promoted by $(CH_3CN)_4Cu^+$ $BF_4^-$

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ARTICLE INFO

*Article history:*
Received 20 August 2011
Received in revised form 30 October 2011
Accepted 31 October 2011
Available online 6 November 2011

ABSTRACT

A general method for the synthesis of α-fluorocinnamonitrile based on the stereoselective reaction between β-bromo-β-fluorostyrene and potassium cyanide, promoted by $(CH_3CN)_4Cu^+$ $BF_4^-$ in 1-methyl-2-pyrrolidinone (NMP), is described.



## 1. Introduction

Very few syntheses of α-fluoro-α,β-unsaturated nitriles **2** have been described in the literature.[1] The most common access is based on the reaction of diethylcyanofluoromethanephosphonate with the corresponding aldehydes or ketones.[2] Diethylcyanofluoromethanephosphonate is synthesized either by fluorination of diethylcyanomethanephosphonate, transformation of ethyl diethylphosphonofluoroacetate into the amide by ammonia, followed by dehydration or by reaction of diethylchlorophosphate with a fluoroacetonitrile anion. These α-fluoro-α,β-unsaturated nitriles **2** may serve as fluorinated building blocks since they can be further transformed into 2-fluoroallylamines by reduction with DIBAL-H and then into C-(1-fluorovinyl)nitrones.[2i,j] The wide availability of cold-labelled ($^{13}C$ and $^{15}N$) or hot-labelled ($^{14}C$) potassium cyanide and the ease of manipulation of this reagent in small quantities in comparison with gaseous carbon dioxide strengthen the interest of the synthesis of α-fluoro-α,β-unsaturated nitriles **2** based on this reagent. However, while the transformation of bromoolefins into the corresponding cyanoolefins is a well-documented reaction, the reaction between 1-bromo-1-fluoroalkenes and potassium cyanide has received little attention. Only Nenajdenko et al. have reported the synthesis of 2-fluoroacrylonitriles starting from 1-bromo-1-fluoroalkenes by copper cyanide in DMF at 150 °C.[2k] 1-Bromo-1-fluoroalkenes are easily obtainable in several ways: (i) in configurationally pure form by the addition of bromine to the corresponding fluoroacrylate followed by dehydrogenative decarboxylation;[3] (ii) as an *E*/*Z* mixture by condensation with $LiCFBr_2$ on an aldehyde followed by water elimination;[4] or (iii) by reaction of fluorotribromethane with an aldehyde in the presence of a tertiary phosphine according to the procedure developed for the synthesis of dibromoolefins by Corey and Fuchs,[5] adapted to bromofluoroolefins by Burton et al.[6] and improved by activating the condensation step by diethylzinc as described by Pannecouke et al.[7] Recently, Shastin et al. have introduced a new version of this last reaction based on the treatment of *N*-unsubstituted hydrazones with $CFBr_3$ in the presence of a catalytic amount of CuCl.[8] The Corey–Burton strategy is particularly convenient as it is compatible with functionalized molecules like carbohydrates, nucleotides and polyphenols.[9] Furthermore, the kinetic resolution gives the pure thermodynamic *Z* product starting from an *E*/*Z* mixture since the (*Z*)-bromofluorolefin may be isomerized into the *E* isomer, which is more reactive.[10] The reaction may also be conducted on the crude *E*/*Z* mixture and stopped when all the (*E*)-bromofluorolefin is consumed, leading to pure *Z* products.[10,11] The substitution of a bromine atom located on a vinylic position by the cyanide anion was decribed since the early 70s using various organometallic catalysts based on derivatives of copper, nickel, cobalt or palladium alone or with copper (I) as co-catalyst.[12] We report a general method for the synthesis of α-fluoro-α,β-unsaturated nitriles based on the reaction between 1-bromo-1-fluoroalkenes and potassium cyanide (KCN) promoted by $(CH_3CN)_4Cu^+$ $BF_4^-$. The use of potassium cyanide as a CN source allows a potentially easy labelling of the final product without isolating copper cyanide.[13]

## 2. Results and discussion

First we tried to use the conditions originally described by Yamamura et al.[14] and recently employed for the synthesis of $^{13}C$ labelled cinnamonitrile.[14b] These conditions are based on the solubilisation of potassium cyanide by 18-crown-6 and palladium (0) ($Pd(PPh_3)_4$, $PPh_3$) as catalyst in benzene at reflux. For this

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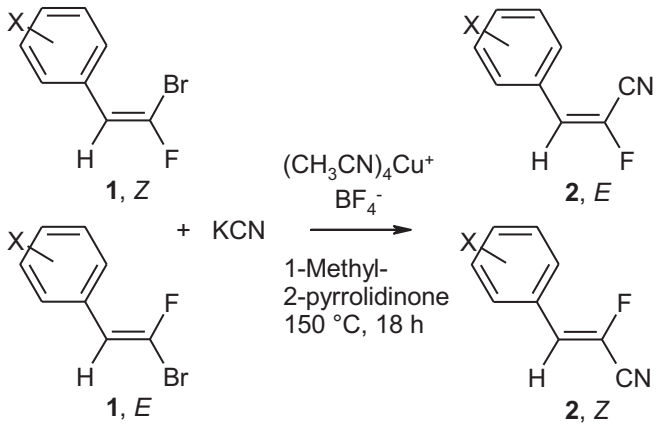
doi:10.1016/j.tet.2011.10.111

experiment we used almost stereochemically pure (*Z*)-β-bromo-β-fluorostyrene (*Z*/*E*>95/5) **1a**, *Z* obtained by dehydrogenative decarboxylation of (*Z*)-α-fluorocinnamic acid. Unfortunately, under these conditions β-bromo-β-fluorostyrene was recovered unreacted, but not isomerized and no α-fluorocinnamonitrile **2a** could be detected (Table 1, entry a). This result was rather unexpected as the conditions are close to those we previously described for the synthesis of fluorinated dienes and enynes based on the palladium catalyzed coupling of alkenes and alkynes starting from 1-bromo-1-fluoroalkenes.[3,15] The replacement of the palladium (0) catalyst by a palladium (II) precursor ($Pd(OAc)_2$, 3%; $PPh_3$, 6%) did not lead to any improvement (Table 1, entry b). Using triethylamine as a solvent, which avoids the use of 18-crown-6 for solubilising potassium cyanide, also failed (Table 1, entry c). 1-Methyl-2-pyrrolidinone (NMP) was recently used as a solvent for the uncatalyzed substitution of 1-bromo-1-fluoroolefins by sodium benzene sulfinate leading to α-fluoro conjugated sulfones in good yields.[16] But using NMP as a solvent for palladium catalyzed substitution by potassium cyanide also failed (Table 1, entry d). So we were delighted that the conditions originally described by Bouas-Laurent et al.,[12a] which are based on the use of copper (I) cyanide (CuCN) in 1-methyl-2-pyrrolidinone (NMP) led to α-fluorocinnamonitrile **2a**, *E* in good yield (94%; Table 1, entry e). In spite of the rather harsh conditions (heating at 150 °C for 6 h) the stereochemistry of the obtained α-fluorocinnamonitrile **2a** was mainly *E*, as demonstrated by the 17 Hz value for the observed $^3J_{HF}$ coupling constant. This result shows that the stereochemistry of the β-bromo-β-fluorostyrene **1a** reagent was well preserved, even when using an *E*, *Z* mixture containing in majority the less stable *Z* precursor.[10] The use of DMF as a solvent as described by Friedman and Shechter[17] also yielded the desired product. However the results were slightly lower for both yield and stereochemistry (Table 1, entry f).




**Scheme 1.** Stereoselective cyanation of β-bromo-β-fluorostyrene **1** using potassium cyanide and promoted by $(CH_3CN)_4Cu^+$ $BF_4^-$ in 1-methyl-2-pyrrolidinone (NMP).

tetrafluoroborate with KCN in 1-methyl-2-pyrrolidinone may lead to the formation of a cuprate species,[20] mostly $Cu(CN)_2^-$ and $Cu(CN)_3^{2-}$, which are able to transfer the CN group.[21] The enhanced formation of reduction products in the presence of triphenylphosphine may be explained by the reaction with water traces, which are difficult to remove from a dipolar aprotic solvent like NMP, leading to triphenylphosphine oxide and reductive hydrogen species.

These results have prompted us to ascertain the kinetics of the reaction (Table 2) and to look if the effect described by Burton for palladium catalysis, in which the (*E*)-β-bromo-β-fluorostyrene **1a** is by far more reactive, is also observed for copper catalysis. Starting from β-bromo-β-fluorostyrene **1a** richer in the kinetic isomer *Z*[10] (*E*/*Z* ratio 26/74),[3] the *E*/*Z* ratio of the remaining β-bromo-β-fluorostyrene **1a** increases steadily to 12/88. This kinetics shows that the *Z* kinetic isomer was not converted into the thermodynamic *E* isomer in these reaction conditions and that the *E* isomer also has

**Table 1**
Cyanation of β-bromo-β-fluorostyrene **1a** with *Z*/*E* geometry better than 95/5 by copper and potassium cyanide

| Entry | Catalyst and $CN^-$ source | Solvent | *T* °C | Time (h) | Recovered **1a**, *Z* %[b] | PhCH=CFCN **2a** % (*E*/*Z*)[b] |
|---|---|---|---|---|---|---|
| a | $Pd(PPh_3)_4$, 3%; KCN (2 equiv); 18-crown-6[a] (8%) | Benzene | 75 | 20 | 100 | — |
| b | $Pd(OAc)_2$, 3%; $PPh_3$, 6%; KCN (2 equiv); 18-crown-6[a] (8%) | Benzene | 75 | 36 | 100 | — |
| c | $Pd(OAc)_2$, 3%; $PPh_3$, 6%; KCN (2 equiv) | $Et_3N$ | 100 | 12 | 100 | — |
| d | $Pd(OAc)_2$, 3%; $PPh_3$, 6%; KCN (2 equiv) | NMP[a] | 150 | 18 | 100 | — |
| e | CuCN (2 equiv) | NMP | 150 | 5 | 6 | 94 (93/7) |
| f | CuCN (1.1 equiv) | DMF | 150 | 72 | 15 | 85 (80/20) |
| g | CuCN (5%); KCN (2 equiv); 18-crown-6[a] (8%) | NMP | 150 | 24 | 100 | Traces |
| h | $(PPh_3)_4Cu^+$ $BF_4^-$ (1.5 equiv); NaCN (1.5 equiv) | NMP | 150 | 24 | 37 | 63 (>95/5) |
| i | $(CH_3CN)_4Cu^+$ $BF_4^-$ (1.5 equiv); KCN (1.5 equiv) | NMP | 150 | 18 | Traces | 100 (>95/5) |

[a] Abbreviations: 18-crown-6: 1,4,7,10,13,16-hexaoxacyclooctadecane; NMP: 1-methyl-2-pyrrolidinone.
[b] Relative yield determined by GC/MS assuming the same factor response for both products and isomers.

In order to utilize labelled cyanide we tried to use a catalytic amount of copper (I) cyanide in 1-methyl-2-pyrrolidinone in the presence of potassium cyanide, but only traces of α-fluorocinnamonitrile **2a** were obtained (Table 1, entry g). The replacement of copper (I) cyanide by tetrakis(triphenylphosphine) copper (I), tetrafluoroborate[18] in 1-methyl-2-pyrrolidinone in the presence of sodium cyanide (NaCN) led to (*E*)-α-fluorocinnamonitrile **2a** in fair yield (63%) while still preserving an almost pure *E* stereochemistry (*E*/*Z* better than 95/5; Table 1, entry h). An equivalent result was obtained using potassium cyanide. However, a careful examination of the reaction mixture showed the presence of β-fluorostyrene arising from the reduction of β-bromo-β-fluorostyrene **1a**. We also found that the proportion of the reduction product increased when the reaction was performed on a substituted β-bromo-β-fluorostyrene bearing either electron-donating or electron-attracting groups. The use of tetrakis(acetonitrile)copper(I), tetrafluoroborate[19] under the same conditions (Scheme 1) gave the substitution products cleanly and in a nearly quantitative yield (Table 1, entry i). The mixing of tetrakis(acetonitrile)copper(I),

**Table 2**
Kinetics and stereochemistry of the cyanation of β-bromo-β-fluorostyrene **1a** using potassium cyanide promoted by $(CH_3CN)_4Cu^+$ $BF_4^-$ in 1-methyl-2-pyrrolidinone (NMP) at 150 °C

| Time (mn) | Starting material **1a** | | PhCH=CFCN **2a** | |
|---|---|---|---|---|
| | % Exp[a] (calcd)[b] | % *E*/*Z* exp[a] (calcd)[b] | % Exp[a] (calcd)[b] | % *E*/*Z* exp[a] (calcd)[b] |
| 0 | 100 (100) | 26/74 (26/74) | — | — |
| 30 | 80 (71) | 23/77 (22/78) | 20 (29) | 73/27 (68/32) |
| 60 | 53 (50) | 20/80 (19/81) | 47 (50) | 80/20 (72/28) |
| 120 | 28 (26) | 18/82 (14/86) | 72 (74) | 78/22 (79/22) |
| 180 | 12 (13) | 12/88 (9/91) | 88 (87) | 83/17 (85/15) |

[a] Relative yield determined by GC/MS assuming the same response factor for both products and isomers.
[b] Calculated values using the following first order kinetic constants ($mol^{-1}$ $min^{-1}$) $k_E$=0.017, $k_Z$=0.010 for the reagents; $k_{Z\rightarrow E}$=0.005 for the product (see text).

a slightly higher reactivity in the case of cyanation promoted by $(CH_3CN)_4Cu^+$ $BF_4^-$. Experimental data are well fitted by a first order reaction for both isomers ($k_E$=0.017 $mol^{-1}$ $min^{-1}$; $k_Z$=0.010 $mol^{-1}$ $min^{-1}$). The stereochemistry of the product was in majority *E* as expected for a specific substitution on each isomer of the bromine atom by the cyanide ion. However, the proportion of the *E* isomer in the α-fluorocinnamonitrile **2a** product increased with time. The final ratio in favour of the *E* isomer was slightly higher than the *Z* ratio in the starting β-bromo-β-fluorostyrene **1a**. This may be explained by an isomerisation of the formed (*Z*)-2-fluoro-3-phenyl-acrylonitrile **2a** to the *E* isomer ($k_{Z\rightarrow E}$=0.005 $mol^{-1}$ $min^{-1}$). Calculated values using this set of kinetic constants are in good agreement with experimental results and are given in brackets in Table 2.

In summary, this kinetic experiment demonstrates that (i) the stereochemistry of the starting β-bromo-β-fluorostyrene **1** is preserved and (ii) the *E* isomer corresponding to the bromine atom cis to the hydrogen atom on the less crowded part of the olefin while still fully conjugated with the aromatic ring has a greater reactivity.

We then performed preparative experiments with a series of substituted β-bromo-β-fluorostyrene **1** bearing either electron-attracting groups (Table 3, entries b–d), electron-donating groups (Table 3, entry e) or mixed groups (Table 3, entry f). In all cases the reaction proceeded very cleanly, giving only substitution products in good chemical yields and with an almost complete conservation of the stereochemistry of the starting product. The stereochemistry of the obtained unsubstituted α-fluorocinnamonitrile **2a** was mostly completely *E* (96%, Table 3, entry 1a). This higher amount when compared to the kinetic experiment described above is due to a longer heating time leading to a near complete isomerisation.

**Table 3**
Cyanation of substituted β-bromo-β-fluorostyrene **1a**–**f** using potassium cyanide promoted by $(CH_3CN)_4Cu^+$ $BF_4^-$ in 1-methyl-2-pyrrolidinone (NMP) at 150 °C

| **1** | Substituents | | **1** (*E*/*Z*)[a] | **2**, Isolated yield (%) | **2** (*E*/*Z*)[a] |
|---|---|---|---|---|---|
| | *meta* | *para* | | | |
| **1a** | H | H | 26/74 | 85 | 96/4 |
| **1b** | H | F | 74/26 | 88 | 23/77 |
| **1c** | H | Cl | 90/10 | 83 | 10/90 |
| **1d** | H | Br | 10/90 | 79 | 88/12 |
| **1e** | H | OMe | 42/58 | 91 | 43/57 |
| **1f** | Br | OMe | 73/27 | 82 | 27/73 |

[a] Relative yield of isomers determined by GC/MS assuming the same response factor for both isomers. The values obtained are consistent with those determined by $^1H$ NMR.

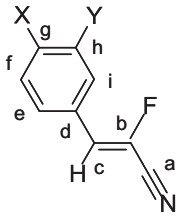
## 3. Conclusion

We report a convenient method for the conversion of β-bromo-β-fluorostyrenes **1** into the corresponding nitriles **2** using potassium cyanide enabling easy labelling of the final product. The stereochemistry of the starting 1-bromo 1-fluoroalkene is preserved: β-bromo-β-fluorostyrene **1**, *Z* gave α-fluorocinnamonitrile **2**, *E* and reciprocally **1**, *E* starting material afforded **2**, *Z* product. As α-fluoro-α,β-unsaturated nitriles **2** can be reduced into aldehydes by di-isobytylaluminium hydride[2d] this new reaction opens the way to labelled α-fluoro-2-alkenals and 2-fluoroallylic alcohols.

## 4. Experimental part

### 4.1. General

All commercially available products were purchased from Aldrich (Saint-Quentin Fallavier, France) and used as received. Deuterated solvents (99.9% or better) were purchased from Eurisо-Top (Saint-Aubain, France). Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under argon before use. Dimethylformamide (DMF) and 1-methyl-2-pyrrolidinone (NMP) were distilled at reduced pressure before use. NMR spectra were recorded on a Bruker (Wissembourg, France) AM 300 spectrometer (300, 282 and 75 MHz, for $^1H$, $^{19}F$ and $^{13}C$, respectively) using $CDCl_3$ as solvent and TMS as internal standard; chemical shifts and coupling constants J values are given in delta and hertz, respectively; C and H are assigned according to Scheme 2. MS experiments: Gas chromatography mass spectrometry experiments using electron impact ionization (EI) spectra were carried out on a Polaris-Q ion trap (Thermo Finnigan, San Jose, CA). High resolution mass spectra were recorded on a JEOL MStation 700 double focussing mass spectrometer using electron impact ionization (EI) by direct inlet introduction. Starting *E*/*Z* mixtures of unsubstituted or substituted β-bromo-β-fluorostyrenes were obtained either enriched in *E* or Z isomer by bromine addition to the corresponding fluoroacrylate followed by dehydrogenative decarboxylation,[3] or as a roughly equimolar *E*,*Z* mixture using the reaction of aromatic aldehyde with fluorotribromomethane according to the Burton protocol.[10]




**Scheme 2.** Atom numbering for the description of NMR spectra.

### 4.2. Procedure of the synthesis of 2-fluoro-3-phenyl-acrylonitrile 2a using CuCN (Table 1, entry e)

A mixture of (2-bromo-2-fluorovinyl)-benzene (201 mg, 1 mmol), copper cyanide (179 mg, 2 mmol) in 3 ml NMP (1-methyl-2-pyrrolidinone) was heated at 150 °C under argon for 5 h. After cooling, the organic phase was acidified with hydrochloric acid (1 M, 10 ml) then extracted with pentane. The pentane phase was washed with brine then dried over anhydrous $MgSO_4$ and the solvent was removed in vacuum, giving 120 mg of 2-fluoro-3-phenyl-acrylonitrile as a clear oil.

### 4.3. Procedure of the synthesis of 2-fluoro-3-phenyl-acrylonitrile 2a from NaCN using $(PPh_3)_4Cu^+$ $BF_4^-$ as catalyst (Table 1, entry h)

A mixture of (2-bromo-2-fluorovinyl)-benzene (1.05 g, 5.00 mmol), sodium cyanide (0.36 g, 7.34 mmol) and tetrakis(-triphenylphosphine)copper(I), tetrafluoroborate complex (8.94 g, 7.46 mmol) in 8 ml of 1-methyl-2-pyrrolidone was heated at 150 °C under argon for 24 h. After cooling, the organic phase was acidified with hydrochloric acid (1 M, 10 ml) then extracted with pentane. The pentane phase was washed with brine then dried over anhydrous $MgSO_4$ and then the solvent was removed in vacuum, giving 782 mg of 2-fluoro-3-phenyl-acrylonitrile as a clear oil.

### 4.4. General procedure for the preparation of of 2-fluoro-3-phenyl-acrylonitrile 2a from KCN using $(CH_3CN)_4Cu^+$ $BF_4^-$ as catalyst (Table 1, entry i)

A mixture of (2-bromo-2-fluorovinyl)-benzene (201 mg, 1.0 mmol), potassium cyanide (97.50 mg, 1.5 mmol) and tetrakis(acetonitrile)copper(I), tetrafluoroborate complex (474 mg, 1.5 mmol) in 3 ml of 1-methyl-2-pyrrolidone was heated at 150 °C under argon for 18 h. After cooling, the organic phase was acidified

with hydrochloric acid (1.0 M, 10 ml) then extracted with pentane. The pentane phase was washed with brine then dried over anhydrous $MgSO_4$ then the solvent was removed in vacuo, giving a clear oil.

*4.4.1. 2-Fluoro-3-phenyl-acrylonitrile* ***2a*** *(Table 3, entry a)*[2f,i]. (*E*) Isomer: $^1$H NMR ($CDCl_3$): 7.08 (d, $^3J_{H-F}$=16.7 Hz, 1H, H$^a$), 7.35–7.45 (m, 3H), 7.57 (m, 2H); $^{19}$F NMR ($CDCl_3$): −126.5 (d, $^3J_{H-F}$=16.7 Hz, 1F). $^{13}$C NMR ($CDCl_3$): 113.0 (d, $^2J_{C-F}$=48.6 Hz, C$^a$), 126.1 (d, $^2J_{C-F}$=24.0 Hz, C$^c$), 128.4 (d, $^4J_{C-F}$=3.2 Hz, C$^e$), 129.2 (s, C$^g$), 130.2 (d, $^3J_{C-F}$=7.7 Hz, C$^d$), 131.5 (d, $^5J_{C-F}$=1.7 Hz, C$^h$), 131.9 (d, $^1J_{C-F}$=257.1 Hz, C$^b$). (*Z*) Isomer: $^1$H NMR ($CDCl_3$) 6.47 (d, $^3J_{H-F}$=34.6 Hz, 1H, H$^c$), 7.35–7.45 (m, 3H), 7.57 (m, 2H); $^{19}$F NMR ($CDCl_3$): −125.8 (d, $^3J_{H-F}$=34.6 Hz, 1F); MS (EI) *m*/*z* (relative intensity): 147 (100, M$^+$•), 146 (15), 128 (12), 127 (45), 121 (16), 120 (50), 105 (16), 100 (15), 96 (10), 94 (10), 86 (29). HRMS (EI) (*E*/*Z*) isomer mixture (*m*/*z*): observed, 147.1548; calculated for $C_9H_6FN$, 147.1533.

*4.4.2. 2-Fluoro-3-(4-fluorophenyl)acrylonitrile* ***2b*** *(Table 3, entry b).* (*Z*) Isomer: $^1$H NMR ($CDCl_3$): 6.44 (d, $^3J_{H-F}$=34.4 Hz, 1H, H$^c$), 7.12 (dd, $^3J_{H-F}$=8.6 Hz, $^3J_{H-H}$=8.5 Hz, 2H, H$^f$), 7.56 (dd, $^3J_{H-H}$=8.6 Hz, $^4J_{H-F}$=5.4 Hz, 2H, H$^e$); $^{19}$F NMR ($CDCl_3$): −127.0 (dd, $^3J_{H-F}$=34.4 Hz, $^7J_{F-F}$=2.7 Hz, 1F), −111.9 (m, 1F); $^{13}$C NMR ($CDCl_3$): 116.3 (d, $^2J_{C-F}$=22.0 Hz, C$^f$), 116.4 (d, $^2J_{C-F}$=22.1 Hz, C$^c$), 117.4 (d, $^2J_{C-F}$=46.7 Hz, C$^a$), 130.5 (d, $^1J_{C-F}$=269.2 Hz, C$^b$), 130.8 (dd, $^3J_{C-F}$=8.6 Hz, $^4J_{C-F}$=3.2 Hz, C$^d$), 132.3 (dd, $^3J_{C-F}$=8.5 Hz, $^4J_{C-F}$=8.5 Hz, C$^e$), 163.4 (dd, $^1J_{C-F}$=253.5 Hz, $^6J_{C-F}$=2.9 Hz, C$^g$). (*E*) Isomer: $^1$H NMR ($CDCl_3$): 7.04 (d, $^3J_{H-F}$=16.5 Hz, 1H, H$^c$), 7.14 (dd, $^3J_{H-F}$=8.6 Hz, $^3J_{H-H}$=8.4 Hz, 2H, H$^f$), 7.56 (dd, $^3J_{H-H}$=8.4 Hz, $^4J_{H-F}$=5.4 Hz, 2H, H$^e$); $^{19}$F NMR ($CDCl_3$): −126.9 (dd, $^3J_{H-F}$=16.5 Hz, $^7J_{F-F}$=4.8 Hz, 1F), −111.9 (m, 1F). MS (EI) *m*/*z* (relative intensity): 165 (100, M$^+$•), 146 (13), 145 (59), 138 (38), 118 (13). HRMS (EI) (*E*/*Z*) isomer mixture (*m*/*z*): observed, 165.0388; calculated for $C_9H_5F_2N$, 165.0390.

*4.4.3. 2-Fluoro-3-(4-chlorophenyl)acrylonitrile* ***2c*** *(Table 3, entry c).* (*Z*) Isomer: $^1$H NMR ($CDCl_3$): 6.43 (d, $^3J_{H-F}$=34.2 Hz, 1H, H$^c$), 7.40 (d, $^3J_{H-H}$=8.5 Hz, 2H, H$^f$), 7.50 (d, $^3J_{H-H}$=8.5 Hz, 2H, H$^e$); $^{19}$F NMR ($CDCl_3$): −124.8 (d, $^3J_{H-F}$=34.2 Hz, 1F); $^{13}$C NMR ($CDCl_3$): 117.8 (d, $^2J_{C-F}$=46.3 Hz, C$^a$), 124.3 (d, $^2J_{C-F}$=24.9 Hz, C$^c$), 129.4 (s, C$^f$), 129.6 (d, $^3J_{C-F}$=11.2 Hz, C$^d$), 131.3 (d, $^4J_{C-F}$=8.2 Hz, C$^e$), 131.6 (d, $^1J_{C-F}$=255.1 Hz, C$^b$), 136.7 (d, $^6J_{C-F}$=3.8 Hz, C$^g$). (*E*) Isomer: $^1$H NMR ($CDCl_3$): 7.03 (d, $^3J_{H-F}$=16.3 Hz, 1H, H$^c$), 7.43 (d, $^3J_{H-H}$=8.4 Hz, 2H, H$^f$), 7.58 (d, $^3J_{H-H}$=8.4 Hz, 2H, H$^e$). $^{19}$F NMR ($CDCl_3$): −125.4 (d, $^3J_{H-F}$=16.3 Hz, 1F). MS (EI) *m*/*z* (relative intensity): 183 (24, M$^+$•, $^{37}$Cl), 181 (75, M$^+$•, $^{35}$Cl), 146 (100), 126 (28), 99 (13). HRMS (EI) (*E*/*Z*) isomer mixture (*m*/*z*): observed, 181.0088; calculated for $C_9H_5FClN$, 181.0095.

*4.4.4. 2-Fluoro-3-(4-bromophenyl)acrylonitrile* ***2d*** *(Table 3, entry d).* (*E*) Isomer: $^1$H NMR ($CDCl_3$): 6.98 (d, $^3J_{H-F}$=16.9 Hz, 1H, H$^c$), 7.32 (d, $^3J_{H-H}$=8.5 Hz, 2H, H$^f$), 7.45 (d, $^3J_{H-H}$=8.5 Hz, 2H, H$^e$); $^{19}$F NMR ($CDCl_3$): −127.7 (d, $^3J_{H-F}$=16.4 Hz, 1F); $^{13}$C NMR ($CDCl_3$): 116.5 (d, $^2J_{C-F}$=47.6 Hz, C$^a$), 122.1 (d, $^2J_{C-F}$=24.5 Hz, C$^c$), 128.8 (s, C$^f$), 129.2 (s, C$^g$), 129.4 (d, $^3J_{C-F}$=8.6 Hz, C$^d$), 130.7 (d, $^4J_{C-F}$=2.3 Hz, C$^e$), 131.2 (d, $^1J_{C-F}$=247.5 Hz, C$^b$). (*Z*) Isomer: $^1$H NMR ($CDCl_3$): 6.38 (d, $^3J_{H-F}$=34.4 Hz, 1H, H$^c$), 7.32 (d, $^3J_{H-H}$=8.6 Hz, 2H, H$^f$), 7.45 (d, $^3J_{H-H}$=8.6 Hz, 2H, H$^e$); $^{19}$F NMR ($CDCl_3$): −128.6 (d, $^3J_{H-F}$=34.4 Hz, 1F). MS (EI) *m*/*z* (relative intensity): 227 (40, M$^+$, $^{81}$Br), 225 (41, M$^+$•, $^{79}$Br), 197 (17), 195 (16), 146 (100), 126 (36), 116 (55), 99 (18), 89 (21). HRMS (EI) (*E*/*Z*) isomer mixture (*m*/*z*): observed, 226.0490; calculated for $C_9H_5BrFN$, 226.0493.

*4.4.5. 2-Fluoro-3-(4-methoxyphenyl)acrylonitrile* ***2e*** *(Table 3, entry e)*[2f,i]. (*Z*) Isomer: $^1$H NMR ($CDCl_3$): 3.79 (s, 3H, $OCH_3$), 6.35 (d, $^3J_{H-F}$=35.4 Hz, 1H, H$^c$), 6.86 (d, $^3J_{H-H}$=8.9 Hz, 2H, H$^f$), 7.46 (d, $^3J_{H-H}$=8.9 Hz, 2H, H$^e$); $^{19}$F NMR ($CDCl_3$): −130.3 (d, $^3J_{H-F}$=34.4 Hz, 1F); $^{13}$C NMR ($CDCl_3$): 55.2 ($OCH_3$), 113.8 (d, $^2J_{C-F}$=46.4 Hz, C$^a$), 114.3 (s, C$^h$), 123.2 (d, $^2J_{C-F}$=6.3 Hz, C$^d$), 125.7 (d, $^2J_{C-F}$=24.5 Hz, C$^c$), 129.6 (d, $^1J_{C-F}$=253.2 Hz, C$^b$), 131.8 (d, $^4J_{C-F}$=8.5 Hz, C$^e$), 161.7 (d, $^6J_{C-F}$=3.4 Hz, C$^g$). (*E*) Isomer: $^1$H NMR ($CDCl_3$): 3.79 (s, 3H, $OCH_3$), 6.97 (d, $^3J_{H-F}$=17.4 Hz, 1H, H$^e$), 6.88 (d, $^3J_{H-H}$=8.9 Hz, 2H, H$^f$), 7.47 (d, $^3J_{H-H}$=8.9 Hz, 2H, H$^e$); $^{19}$F NMR ($CDCl_3$): −131.2 (d, $^3J_{H-F}$=17.3 Hz, 1F). MS (EI) *m*/*z* (relative intensity): 177 (100, M$^+$•), 162 (43), 147 (10), 134 (50), 107 (36). HRMS (EI) (*E*/*Z*) isomer mixture (*m*/*z*): observed, 177.0593; calculated for $C_{10}H_8OFN$, 177.0590.

*4.4.6. 2-Fluoro-3-(3-bromo-4-methoxyphenyl)acrylonitrile* ***2f*** *(Table 3, entry f).* (*Z*) Isomer: $^1$H NMR ($CDCl_3$): 4.00 (s, 3H), 6.34 (d, $^3J_{H-F}$=34.4 Hz, 1H, H$^c$), 6.92 (d, $^3J_{H-H}$=8.7 Hz, 1H, H$^f$), 7.50 (dd, $^3J_{H-H}$=8.7 Hz, $^4J_{H-H}$=2.2 Hz, 1H, H$^e$), 7.78 (d, $^4J_{H-H}$=2.2 Hz, 1H, H$^i$); $^{19}$F NMR ($CDCl_3$): −127.8 (d, $^3J_{H-F}$=34.4 Hz, 1F); $^{13}$C NMR ($CDCl_3$): 56.4 ($OCH_3$), 112.0 (s, C$^h$), 112.3 (s, C$^f$), 118.1 (d, $^2J_{C-F}$=46.5 Hz, C$^a$), 124.3 (d, $^2J_{C-F}$=25.2 Hz, C$^c$), 128.5 (d, $^3J_{C-F}$=3.0 Hz, C$^d$), 130.4 (d, $^1J_{C-F}$=237.8 Hz, C$^b$), 133.5 (s, C$^e$), 133.8 (s, C$^i$), 161.5 (C$^g$). (*E*) Isomer: $^1$H NMR ($CDCl_3$): 3.95 (s, 3H), 6.94 (d, $^3J_{H-F}$=16.5 Hz, 1H, H$^c$), 6.98 (d, $^3J_{H-H}$=8.6 Hz, 1H, H$^f$), 7.61 (dd, $^3J_{H-H}$=8.6 Hz, $^4J_{H-H}$=2.3 Hz, 1H, H$^e$). 7.73 (d, $^4J_{H-H}$=2.3 Hz, 1H, H$^i$); $^{19}$F NMR ($CDCl_3$): −128.3 (d, $^3J_{H-F}$=16.6 Hz, 1F). MS (EI) *m*/*z* (relative intensity): 257 (100, M$^+$•, $^{81}$Br), 255 (100, M$^+$•, $^{79}$Br), 242 (56), 240 (55), 214 (37), 212 (37), 176 (11), 161 (13), 133 (65), 132 (20), 106 (10). HRMS (EI) (*E*/*Z*) isomer mixture (*m*/*z*): observed, 254.9691; calculated for $C_{10}H_7OBrFN$, 254.9695.

## Acknowledgements

This work was supported by the Conseil Régional Nord, Pas-de-Calais, France. The NMR and Mass Spectrometry facilities used in this study were funded by the European Community (FEDER), the Région Nord-Pas de Calais (France), the CNRS, and the Université de Lille 1, Sciences et Technologies. S.E. thanks the Université Cadi Ayyad, Faculté des Sciences et Techniques Guéliz, Marrakech, Morocco, for a sabbatical leave and the Region Nord, Pas-de-Calais for a position as invited professor. This work was performed in the frame of the CNRST-CNRS 'Action concertée Chimie 08/09 Synthèse de sondes fluorescentes spécifiques des glyco et phopshopeptides pour l'analyse protéomique'. The authors thank Dr. Maria van Agthoven for her help with editing this manuscript.

## Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2011.10.111. These data include MOL files and InChiKeys of the most important compounds described in this article.

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