Electronic Supporting Information

2,2,2-Trifluoroethanol as a Tool to Control Nucleophilic Peptide Arylation

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Materials and general methods

All chemicals and solvents were analytical grade and used without further purification. Liquid chromatography-mass spectrometry (LC/MS; ESI+ mode) analyses were performed on a Acquity UPLC BEH C18 column (1.7 μm 2.1 mm x 50 mm) using a Waters Acquity UPLC system equipped with a photodiode array detector, providing absorbance data from 210 nm to 400 nm. A gradient with eluent I (0.1% HCOOH in water) and eluent II (0.1% HCOOH in acetonitrile) rising linearly from 5 to 95% of II during t=0.2–4.0 min was applied at a flow rate of 0.6 ml/min after 0.2 min of 95% solvent I initial equilibration. High-resolution QToF-LC/MS and QToF-MS/MS analyses were performed in a Acquity UPLC BEH C18 column (1.7 μm, 2.1 mm x 50 mm) using a Waters Acquity UPLC system coupled to Micromass QToF Premier mass spectrometer, also equipped with a photodiode array detector providing absorbance data from 210 nm to 400 nm. A gradient with eluent I (0.1% HCOOH in water) and eluent II (0.1% HCOOH in acetonitrile) rising linearly from 0 to 99% of II during t=0.0–5.0 min was applied at a flow rate of 0.6 ml/min. $^{19}$F NMR spectra studies were recorded at 376MHz in a Bruker Advance spectrometer at 298 K, using 8 scans with a relaxation delay of 1s. All data has been processed using Mestrenova® software.

Peptides (pep1-4) were prepared using conventional Fmoc/tBu SPSS procedures. Full experimental details and characterisation of pep1-4 are given in -

Model peptide tagging and stapling with perfluoroaromatics:

General procedure for solution phase peptide tagging and stapling

Solid crude peptides pep1-3 (2 mg, approx. 2.5 µmol) were dissolved in the DMF or TFE (0.5 mL) in a 1.5 mL plastic Eppendorf tube, to which a Cs$_2$CO$_3$ or DIPEA stock solution (50 mM in appropriate solvent, 0.5 mL) was added. Pentafluoropyridine (1) or hexafluorobenzene (3) was added in 5 equivalents and the tube was shaken vigorously at room temperature for 4.5 h. After removal of volatiles under vacuum, all products were redissolved in an 8:1:1 mixture of DMF/H$_2$O/MeCN (1mL) and characterised by LC/MS (ESI+). When formation of novel compounds was observed, 10-fold scaled reactions were employed in all cases for product isolation and purification in order to afford a complete characterisation. Scaled reactions were run under exactly the same conditions but in argon-flushed syringes, to avoid air bubbles where volatile aromatic compounds could concentrate. LC/MS data for crude reactions is provided next.

LC/MS analysis of small scale reactions 1-22

Effect of the solvent: DMF vs. TFE, using DIPEA. Entries 1-12 from Table 1 (main article)

Entry 1: Ac-YCGGGCAL- NH$_2$ + HEXAFLUOROBENZENE in DMF/DIPEA:

![LC/MS traces at λ= 280 (middle panel) and λ= 220 nm (lower panel) of crude reaction of peptide pep1 with hexafluorobenzene when using DIPEA as a base in DMF.](image)

Figure SI01. LC/MS traces at λ= 280 (middle panel) and λ= 220 nm (lower panel) of crude reaction of peptide pep1 with hexafluorobenzene when using DIPEA as a base in DMF.
Entry 2: Ac-YSGGGSAL-NH$_2$ + HEXAFLUOROBENZENE in DMF/DIPEA:

![Figure SI02](image)

**Figure SI02.** LC/MS traces at $\lambda=220$ nm of crude reaction of peptide pep2 with hexafluorobenzene when using DIPEA as a base in DMF.

Entry 3: Ac-YKGGGKAL- NH$_2$ + HEXAFLUOROBENZENE in DMF/DIPEA:

![Figure SI03](image)

**Figure SI03.** LC/MS traces $\lambda=220$ nm of crude reaction of peptide pep3 with hexafluorobenzene when using DIPEA as a base in DMF.
**Entry 4:** Ac-YCGGGCAL- NH₂ + PENTAFLUOROPYRIDINE in DMF/DIPEA:

<table>
<thead>
<tr>
<th>Peak</th>
<th>Retention time (min)</th>
<th>m/z</th>
<th>Identity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.946</td>
<td>820</td>
<td>Starting peptide [M+MeCN]⁺</td>
</tr>
<tr>
<td>2</td>
<td>2.706</td>
<td>1082</td>
<td>Double ArF addition [M+2ArF]⁺</td>
</tr>
<tr>
<td>3</td>
<td>3.074</td>
<td>1138</td>
<td>[M+2ArF⁺+TFA]²⁺</td>
</tr>
<tr>
<td>4</td>
<td>3.175</td>
<td>1231</td>
<td>Triple ArF addition [M+3ArF]⁺</td>
</tr>
</tbody>
</table>

*Figure SI04.* LC/MS traces at λ=280 nm of crude reaction of peptide pep1 with pentafluoropyridine when using DIPEA as a base in DMF.

**Entry 5:** Ac-YSGGGSAL- NH₂ + PENTAFLUOROPYRIDINE in DMF/DIPEA:

*Figure SI05.* LC/MS traces at λ=220 nm of crude reaction of peptide pep2 with pentafluoropyridine when using DIPEA as a base in DMF.
**Entry 6:** Ac-YKGGGKAL-\(\text{NHz}_2\) + PENTAFLUOROPYRIDINE in DMF/DIPEA:

**Figure SI6.** LC/MS traces at \(\lambda=220\) nm of crude reaction of peptide pep3 with pentafluoropyridine when using DIPEA as a base in DMF.

**Entry 7:** Ac-YCGGGCAL-\(\text{NHz}_2\) + HEXAFLUOROBENZENE in TFE/DIPEA:

**Figure SI7.** LC/MS traces at \(\lambda=220\) nm of crude reaction of peptide pep1 with hexafluorobenzene when using DIPEA as a base in TFE.
**Entry 8:** Ac-YSGGSAL- NH$_2$ + HEXAFLUOROBENZENE in TFE/DIPEA:

**Figure SI8.** LC/MS traces at $\lambda=220$ nm of crude reaction of peptide pep2 with hexafluorobenzene when using DIPEA as a base in TFE.

**Entry 9:** Ac-YKGGGKAL- NH$_2$ + HEXAFLUOROBENZENE in TFE/DIPEA:

**Figure SI9.** LC/MS traces at $\lambda=220$ nm of crude reaction of peptide pep3 with hexafluorobenzene when using DIPEA as a base in TFE.
Entry 10: Ac-YCGGGCAL-NH₂ + PENTAFLUOROPYRIDINE in TFE/DIPEA:

```
783 Da  →  +115 Da /[M+TFA]⁺  →  898 Da
Starting

+149 Da (4F-Pyr)  →
932 Da  →  +57 Da /[2M+TFA]²⁺  →  989 Da
1-ArF

+149 Da (4F-Pyr)  →
1081 Da
2-ArF
```

Figure SI10. LC/MS traces at λ=220 nm of crude reaction of peptide pep1 with pentafluoropyridine when using DIPEA as a base in TFE. Upper figure showing the scheme corresponding to adduct formation on the basis of the observed masses.
**Entry 11:** Ac-YSGGGSAL-NH$_2$ + PENTAFLUOROPYRIDINE in TFE/DIPEA:

![Figure SI11](C:/Users/pcnf5...DG024A_1501.raw) Injection 1 MS ES+ MS+ spectrum 1.85..2.24

**Figure SI11.** LC/MS traces at $\lambda=220$ nm of crude reaction of peptide pep2 with pentafluoropyridine when using DIPEA as a base in TFE.

**Entry 12:** Ac-YKGGGKAL-NH$_2$ + PENTAFLUOROPYRIDINE in TFE/DIPEA:

![Figure SI12](C:/Users/pcnf5...rated_water.raw) Injection 1 PDA - Chromatogram 220 nm

**Figure SI12.** LC/MS traces at $\lambda=220$ nm of crude reaction of peptide pep3 with pentafluoropyridine when using DIPEA as a base in TFE
Effect of the base: DIPEA vs Cs₂CO₃. **Entries 13-18 from Table 1 (main article)**

**Entry 13:** Ac-YCGGCal- NH₂ + HEXAFLUOROBENZENE in TFE/Cs₂CO₃:

**Figure S113.** LC/MS traces at λ=220 nm of crude reaction of peptide pep1 with hexafluorobenzene when using Cs₂CO₃ as a base in TFE.

**Entry 14:** Ac-YSGGSAL- NH₂ + HEXAFLUOROBENZENE in TFE/Cs₂CO₃:

**Figure S114.** LC/MS traces at λ=220 nm of crude reaction of peptide pep2 with hexafluorobenzene when using Cs₂CO₃ as a base in TFE.
Entry 15: Ac-YKGGKAL- NH$_2$ + HEXAFLUOROBENZENE in TFE/Cs$_2$CO$_3$:

**Figure S115.** LC/MS traces at λ=220 nm of crude reaction of peptide pep3 with hexafluorobenzene when using Cs$_2$CO$_3$ as a base in TFE.
**Entry 16:** Ac-YCGGCal-NH₂ + Pentafluoropyridine in TFE/C₅O₃₂:

- **Starting:** 783 Da
- **1-ArF:** 932 Da + 57 Da /[2M+TFA]²⁺ → 989 Da +149 Da (4F-Pyr)
- **2-ArF:** 1081 Da + 57 Da /[2M+TFA]²⁺ → 1138 Da +149 Da (4F-Pyr)
- **3-ArF:** 1230 Da

**Figure SI16.** LC/MS traces at λ=220 nm of crude reaction of peptide pep1 with pentafluoropyridine when using Cs₂CO₃ as a base in TFE. Upper figure showing the scheme corresponding to adduct formation on the basis of the observed masses.
**Entry 17:** Ac-YSGGSAL- NH$_2$ + PENTAFUOROPYRIDINE in TFE/CS$_2$CO$_3$

**Figure SI17.** LC/MS traces at $\lambda$=220 nm of crude reaction of peptide pep2 with pentafluoropyridine when using CS$_2$CO$_3$ as a base in TFE.

**Entry 18:** Ac-YKGGGKAL- NH$_2$ + PENTAFUOROPYRIDINE in TFE/CS$_2$CO$_3$

**Figure SI18.** LC/MS traces at $\lambda$=220 nm of crude reaction of peptide pep3 with pentafluoropyridine when using CS$_2$CO$_3$ as a base in TFE.
Selective tagging of **pep4**. Entries 19-22 from Table 2 (main article)

**Entry 19**: Ac-FKACGKGCA - NH₂ + HEXAFLUOROBENZENE in DMF/DIPEA

**Figure SI19**. LC/MS traces at λ=220 nm of crude reaction of peptide **pep4** with hexafluorobenzene when using DIPEA as a base in DMF.

**Entry 20**: Ac-FKACGKGCA - NH₂ + HEXAFLUOROBENZENE in TFE/DIPEA

**Figure SI20**. LC/MS traces at λ=220 nm of crude reaction of peptide **pep4** with hexafluorobenzene when using DIPEA as a base in TFE.
Entry 21: Ac-FKACGKGCA - NH₂ + PENTAFLUOROPYRIDINE in DMF/DIPEA

Figure SI21. LC/MS traces at λ=220 nm of crude reaction of peptide pep4 with pentafluoropyridine when using DIPEA as a base in DMF.

Entry 22: Ac-FKACGKGCA - NH₂ + PENTAFLUOROPYRIDINE in TFE/DIPEA

Figure SI22. LC/MS traces at λ=220 nm of crude reaction of peptide pep4 with pentafluoropyridine when using DIPEA as a base in TFE.

Electronic Supporting Information [17]
**Isolation and characterization of compounds 4-14**

*General methods:*

Products from large-scale reactions were purified and isolated by semi-preparative reverse phase HPLC performed on a Discovery Bio wide pore C₁₈-5 column from Supelco (5 μm, 25 cm × 10 mm), using a Pelkin-Elmer 200 LC pump coupled to a Waters 486 tuneable absorbance detector set at $\lambda=220$ nm. A gradient with eluent A (95:5:0.1% H₂O:ACN:TFA) and eluent B (5:95:0.1% H₂O:ACN:TFA) was applied, where solvent B was firstly rose linearly from 0 to 100% during $t=60$ min and finally maintained isocratically for 5 min at a flow rate of 2 mL/min. Purified pooled fractions were then freeze-dried and the identity of the different compounds verified by LC/MS. The desired pure compounds were then further characterised by $^{19}$F NMR (2 mg/mL in H₂O/CD₃CN 50:50, unless otherwise stated), high resolution LC/MS-QToF and ion directed tandem mass spectrometry (MS/MS), allowing to obtain the characteristic rupture profile for each product. In MS/MS fragmentation analysis we have made use of the accepted nomenclature for fragment ions firstly proposed by Roepstorff and Fohlman (P. Roepstorff and J. Fohlman, *Biol. Mass Spectrom*. 1984, 11, 601–601.), and subsequently modified by Johnson et al. (R. S. Johnson, S. A. Martin, K. Biemann J. T. Stults and J. T. Watson, *Anal. Chem.*, 1987, 59, 2621–2625). Note that, in peptides and proteins, ions arising from fragmentation series $\gamma$ or $b$ are expected to be predominant.
Product 4.

Figure S123. Structure, high resolution QToF-LC/MS trace at λ=280 nm and composition of isolated compound 4.

Figure S124. $^{19}$F NMR spectrum of compound 4 as recorded in D$_2$O/MeCN 1:1 at room temperature.
Product 5.

QToF LC/MS: Calculated \( m/z \): 1230.27, observed \( m/z \): 1231.28 \([M+H]^+\). Retention time: 3.442 min. Elemental composition: C\(_{47}\)H\(_{46}\)F\(_{12}\)N\(_{12}\)O\(_{10}\)S\(_{2}\).

QToF-MS/MS: Calculated \( m/z \): 1103.18 \([b7+H]^+\), 1032.81 \([b6+H]^+\), 780.14 \([b5+H]^+\), 722.11 \([b4+H]^+\), 665.09 \([b3+H]^+\), 608.07 \([b2+H]^+\), 356.07 \([b1+H]^+\), 495.15 \([z4+H]^+\) Da.

Observed \( m/z \): 1103.22 \([b7+H]^+\), 1032.18 \([b6+H]^+\), 780.17 \([b5+H]^+\), 722.14 \([b4+H]^+\), 665.12 \([b3+H]^+\), 608.13 \([b2+H]^+\), 355.08 \([b1+H]^+\), 495.14 \([z4+H]^+\) Da.

\(^{19}\)F NMR (376 MHz, DMSO-\(d_6\)) \( \delta \) -91.20 (m, 2F), -93.42 (m, 4F), -137.49 (m, 4F), -155.63 (m, 2F).

**Figure S125.** Structure, high resolution QToF-LC/MS trace at \( \lambda = 220 \) nm and composition of isolated compound 5.
Figure SI26. MS/MS analysis of compound 5 showing its characteristic rupture pattern and the assignation of the main ions observed.

Figure SI27. $^{19}$F NMR spectrum of compound 5 as recorded in DMSO-d$_6$ at room temperature.
Product 6.

QToF LC/MS: Calculated \( m/z \): 900.34, observed \( m/z \): 901.34 [M+H]+. Retention time: 2.375 min. Elemental composition: C\(_{37}\)H\(_{48}\)F\(_4\)N\(_{10}\)O\(_{12}\).

QToF-MS/MS: Calculated \( m/z \): 771.24 [b\(_7\)+H]+, 700.20 [b\(_6\)+H]+, 613.17 [b\(_5\)+H]+, 499.12 [b\(_3\)+H]+, 442.35 [b\(_2\)+H]+, 355.07 [b\(_1\)+H]+, 530.26 [z\(_7\)+H]+, 443.23 [z\(_6\)+H]+ Da.

Observed \( m/z \): 771.27 [b\(_7\)+H]+, 700.24 [b\(_6\)+H]+, 613.19 [b\(_5\)+H]+, 449.10 [b\(_3\)+H]+, 442.08 [b\(_2\)+H]+, 355.11 [b\(_1\)+H]+, 530.26 [z\(_7\)+H]+, 442.08 [z\(_6\)+H]+ Da.

\(^{19}\)F NMR (376 MHz, H\(_2\)O/MeOD 1:1) \( \delta \) -91.32 (m, 2F), -155.98 (m, 2F).

Figure S128. Structure, high resolution QToF-LC/MS trace at \( \lambda = 220 \) nm and composition of isolated compound 6.
Figure SI29. MS/MS analysis of compound 6 showing its characteristic rupture pattern and the assignment of the main ions observed.

Figure SI30. $^{19}$F NMR spectrum of compound 6 as recorded in H$_2$O/MeOD 1:1 at room temperature.
Product 7.

QToF LC/MS: Calculated $m/z$: 1280.44, observed $m/z$: 1281.45 [M+H]$^+$. Retention time: 3.492 min. Elemental composition: C$_{53}$ H$_{60}$ F$_{12}$ N$_{14}$ O$_{10}$.

QToF-MS/MS:

Calculated $m/z$: 1152.34 [b7+H]$^+$, 1081.30 [b6+H]$^+$, 804.22 [b5+H]$^+$, 691.2337 [b3+H]$^+$, 747.20 [b4+H]$^+$, 911.36 [z7+H]$^+$, 634.28 [z6+H]$^+$, 520.23 [z4+H]$^+$ Da.


$^{19}$F NMR (376 MHz, H$_2$O/MeOD 1:1) $\delta$ -91.66 (m, 2F), -98.17 (m, 4F), -156.29 (m, 4F), -165.54 (m, 2F).

Figure SI31. Structure, high resolution QToF-LC/MS trace at $\lambda=220$ nm and composition of isolated compound 7.
**Figure SI32.** MS/MS analysis of compound 7 showing its characteristic rupture pattern and the assignation of the main ions observed.

**Figure SI33.** $^{19}$F NMR spectrum of compound 7 as recorded in H$_2$O/MeOD 1:1 at room temperature.
Product 8.

\[
\text{O} \quad \text{N} \quad \text{H} \quad \text{N} \\
\text{O} \quad \text{O} \quad \text{O} \quad \text{N} \quad \text{H} \\
\text{O} \quad \text{N} \quad \text{H} \quad \text{N} \quad \text{O} \\
\text{S} \quad \text{N} \quad \text{F} \quad \text{F} \quad \text{F} \\
\text{F} \quad \text{F} \quad \text{F} \quad \text{F} \quad \text{F} \\
\text{OH}
\]

QToF LC/MS: Calculated \( m/z \): 1081.28, observed \( m/z \): 1082.19 \([\text{M+H}]^+\). Retention time: 3.017 min. Elemental composition: \( \text{C}_{42}\text{H}_{47}\text{F}_{8}\text{N}_{11}\text{O}_{10}\text{S}_{2} \).

QToF-MS/MS:

Calculated \( m/z \): 953.18 \([\text{b7+H}]^+\), 882.14 \([\text{b6+H}]^+\), 630.56 \([\text{b5+H}]^+\), 573.51 \([\text{b4+H}]^+\), 516.46 \([\text{b3+H}]^+\) Da.

Observed \( m/z \): 954.22 \([\text{b7+H}]^+\), 883.18 \([\text{b6+H}]^+\), 630.16 \([\text{b5+H}]^+\), 573.16 \([\text{b4+H}]^+\), 517.06 Da.

\(^{19}\text{F} \text{NMR (376 MHz, H}_2\text{O/ MeCN-d}_3 \text{ 1:1)} \delta -94.02 (\text{m, 2F}), -94.16 (\text{m, 2F}), -138.01 (\text{m, 2F}), -138.32 (\text{m, 2F}).

Figure SI34. Structure, high resolution QToF-LC/MS trace and composition of isolated compound 8.
Figure S135. MS/MS analysis of compound 8 showing its characteristic rupture pattern and the assignation of the main ions observed.

Figure S136. 19F NMR spectrum of compound 8 as recorded in H2O/ MeCN-d3 1:1 at room temperature.
Product 9. (Mixture of regioisomers)

QToF LC/MS: Calculated m/z: 932.96, observed m/z: 989.36 [2M+TFA+H]^2+. Retention time: 2.842 min. Elemental composition: C_{37}H_{48}F_{4}N_{10}O_{10}S_{2}.

QToF-MS/MS:


^{19}F NMR (376 MHz, H_{2}O/ MeCN-d_{3} 1:1) δ -94.05 (m, 2F), -94.18 (m, 2F), -138.01 (m, 2F), -138.31 (m, 2F).

Figure SI37. Structure, high resolution QToF-LC/MS trace at λ=220 nm and composition of isolated compound 9.
**Figure SI38.** MS/MS analysis of compound 9 showing its characteristic rupture pattern and the assignment of the main ions observed.

**Figure SI39.** $^{19}$F NMR spectrum of compound 9 as recorded in H$_2$O/ MeCN-$d_3$ 1:1 at room temperature.
**Product 10.** (Mixture of regioisomers)

QToF LC/MS: Calculated $m/z$: 1081.28, observed $m/z$: 1138.35 [2M+TFA+2H$^+$]$^{2+}$.
Retention time: 3.300 min. Elemental composition: C$_{42}$H$_{47}$F$_8$N$_{11}$O$_{10}$S$_2$.

QToF-MS/MS:


$^{19}$F NMR (376 MHz, H$_2$O/ MeCN-$d_3$ 1:1) $\delta$ -91.57 (m, 2F), -93.40 (m, 2F), -137.69 (m, 2F), -156.12 (m, 2F).

Figure S140. Structure, high resolution QToF-LC/MS trace at $\lambda=220$ nm and composition of isolated compound 10.
Figure S141. MS/MS analysis of compound 10 showing its characteristic rupture pattern and the assignment of the main ions observed.

Figure S142. $^{19}$F NMR spectrum of compound 10 as recorded in H$_2$O/ MeCN-$d_3$ 1:1 at room temperature.

Electronic Supporting Information [31]
Product 11.

QToF LC/MS: Calculated m/z: 1070.41, observed m/z: 1071.41 [M+H]⁺, 536.39 [M+2H]²⁺. Retention time: 1.875 min. Elemental composition: C₄₅ H₆₂ F₄ N₁₂ O₁₀ S₂.

QToF-MS/MS:
Calculated m/z: 881.32 [y₈+H]⁺, 753.23 [y₇+H]⁺, 536.22 [M+2H]²⁺, 492.67 [b₈+2H]²⁺, 441.16 [y₈+2H]²⁺ Da.


¹⁹F NMR (376 MHz, H₂O/ MeCN-d₃ 1:1) δ -134.53 (m, 4F).
**Figure SI43.** Structure, high resolution QToF-LC/MS trace at \(\lambda=220\) nm and composition of isolated compound 11.

**Figure SI44.** MS/MS analysis of compound 11 showing its characteristic rupture pattern and the assignation of the main ions observed.
**Figure SI45.** $^{19}$F NMR spectrum of compound 11 as recorded in H$_2$O/ MeCN-$d_3$ 1:1 at room temperature.

**Product 12.**

![Chemical structure of Product 12](image)

QToF LC/MS: Calculated $m/z$: 1520.39, observed $m/z$: 1521.41 [M+H]$^+$. Retention time: 4.033 min. Elemental composition: C$_{59}$H$_{60}$F$_{16}$N$_{16}$O$_{10}$S$_2$.

QToF MS/MS:

Calculated $m/z$: 753.18 [M-NH$_2$+2H]$^{2+}$, 717.66 [b8+2H]$^{2+}$ Da.

Observed 754.18 [M-NH$_2$+2H]$^{2+}$, 718.15 [b8+2H]$^{2+}$ Da.

$^{19}$F NMR (376 MHz, H$_2$O/ MeCN-$d_3$ 1:1) $\delta$ -93.99 (m, 4F), -98.06 (m, 4F), -138.14 (m, 4F), -165.38 (m, 4F).
Figure SI46. Structure, high resolution QToF-LC/MS trace at $\lambda=220$ nm and composition of isolated compound 12.

Figure SI47. MS/MS analysis of compound 12 showing its characteristic rupture pattern and the assignation of the main ions observed.
**Figure S148.** $^{19}$F NMR spectrum of compound 12 as recorded in H$_2$O/ MeCN-d$_3$ 1:1 at room temperature.

**Product 13.**

![Chemical structure of Product 13](image)

QToF LC/MS: Calculated $m/z$: 1222.41, observed $m/z$: 1223.41 [M+H]$^+$, 612.20 [M+2H]$^{2+}$. Retention time: 2.200 min. Elemental composition: C$_{49}$ H$_{62}$ F$_8$ N$_{14}$ O$_{10}$ S$_2$.

QToF-MS/MS:

Calculated $m/z$: 1135.35 [b8+H]$^+$, 1033.32 [y8+H]$^+$, 905.23 [y7+H]$^+$, 834.19 [y6+H]$^+$, 612.05 [M+2H]$^{2+}$, 518.16 [y8+2H]$^+$, 389.22 [b3+H]$^+$ Da.


$^{19}$F NMR (376 MHz, H$_2$O/ MeCN-d$_3$ 1:1) $\delta$ -94.01 (m, 4F), -137.98 (m, 4F).
Figure S149. Structure, high resolution QToF-LC/MS trace at $\lambda=220$ nm and composition of isolated compound 13.

Figure S150. MS/MS analysis of compound 13 showing its characteristic rupture pattern and the assignation of the main ions observed.
**Figure SI51.** $^{19}$F NMR spectrum of compound 13 as recorded in H$_2$O/ MeCN-$d_3$ 1:1 at room temperature.

**Product 14.** (Mixture of regioisomers)

QToF LC/MS: Calculated $m/z$: 1073.42, observed $m/z$: 1130.49 [2M+TFA+H]$^{2+}$. Retention time: 2.167 min. Elemental composition: C$_{44}$ H$_{63}$ F$_4$ N$_{13}$ O$_{10}$ S$_2$.

QToF-MS/MS:


$^{19}$F NMR (376 MHz, H$_2$O/ MeCN-$d_3$ 1:1) $\delta$ -93.39 (m, 2F), -138.12 (m, 2F).
Figure S152. Structure, high resolution QToF-LC/MS trace at \( \lambda = 220 \) nm and composition of isolated compound 14.

Figure S153. MS/MS analysis of compound 14 showing its characteristic rupture pattern and the assignation of the main ions observed.
**Figure SI54.** $^{19}$F NMR spectrum of compound 14 as recorded in H$_2$O/ MeCN-$d_3$ 1:1 at room temperature.