Supporting Information

for

Hydrolysis, polarity, and conformational impact of C-terminal partially fluorinated ethyl esters in peptide models

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Amide equilibrium constants (Table S1) and copies of the NMR and CD spectra

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Remark: We use the notation ✔ (checkmark)-shape for description of the log P tendencies. On our opinion, this should be distinguished from more simple notation ‘V-shape’ due to the asymmetry of both the dip position and the edge highs.

Table S1: Amide equilibrium constants for compounds 1–5 as determined by $^1$H and $^{19}$F NMR at 298 K in different solvents.

<table>
<thead>
<tr>
<th>compound</th>
<th>$K_{\text{trans/cis}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D$_2$O</td>
</tr>
<tr>
<td></td>
<td>ε 80.1</td>
</tr>
<tr>
<td>1</td>
<td>4.95±0.05</td>
</tr>
<tr>
<td>2</td>
<td>4.60±0.08</td>
</tr>
<tr>
<td>3</td>
<td>4.74±0.04</td>
</tr>
<tr>
<td>4</td>
<td>4.95±0.05</td>
</tr>
<tr>
<td>5</td>
<td>5.48±0.14</td>
</tr>
</tbody>
</table>
Copies of the NMR spectra for compounds 1–5

$^1$H NMR spectrum of 1 in deuterium oxide at 700 MHz

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Current Data Parameters
NAME: \text{wI_FI2m-esters1}
EXPNO: 492
PROCNO: 1

F2 - Acquisition Parameters
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Time: 10:33
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PROBHD: 5 mm PATXI 1H/
PULPROG: zg
TD: 65536
SOLVENT: D$_2$O
NS: 1
DS: 0
SWH: 8033.333 Hz
FIDRES: 0.127157 Hz
AQ: 3.9221599 sec
RG: 33.06
DW: 60.000 usec
DE: 10.00 usec
TE: 299.0 K
D1: 2.00000000 sec
TD0: 1

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NUC1: 1H
P1: 10.50 usec
PLW1: 16.00000000 W

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WOW: EM
SSB: 0
LB: 0.30 Hz
QE: 0
PC: 100.00
$^{13}$C-$^1$H NMR spectrum of 1 in deuterium oxide at 126 MHz
$^1$H NMR spectrum of 1 in benzene-$d_6$ at 700 MHz
$^{13}$C{\textsuperscript{1}H} NMR spectrum of 1 in benzene-d$_6$ at 176 MHz
$^1$H NMR spectrum of 2 in deuterium oxide at 700 MHz
$^{13}C\{^1H\}$ NMR spectrum of 2 in deuterium oxide at 176 MHz
$^1$H NMR spectrum of 2 in benzene-d$_6$ at 700 MHz
$^{13}$C{\textsuperscript{1}H} NMR spectrum of 2 in benzene-d$_6$ at 176 MHz
'H and \textsuperscript{19}F NMR spectra of 3 in deuterium oxide at 500 MHz
$^{13}$C\textsuperscript{[1]H} NMR spectrum of 3 in deuterium oxide at 126 MHz
$^{19}$F and $^{19}$F($^1$H) NMR spectra of 3 in deuterium oxide at 471 MHz
$^1$H NMR spectrum of 3 in benzene-d$_6$ at 700 MHz
\(^{13}\)C\(\{^1\text{H}\}\) NMR spectrum of 3 in benzene-\(d_6\) at 176 MHz
'H and 1H{19F} NMR spectra of 4 in deuterium oxide at 500 MHz
$^{19}$F and $^{19}$F($^1$H) NMR spectra of 4 in deuterium oxide at 471 MHz

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**19F spectrum**

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**19F($^1$H) spectrum**
$^1$H NMR spectrum of 4 in benzene-$d_6$ at 700 MHz
$^{13}$C{\textsuperscript{1}H} NMR spectrum of 4 in benzene-d$_6$ at 176 MHz
$^1$H NMR spectrum of 5 in deuterium oxide at 700 MHz
$^{13}$C($^1$H) NMR spectrum of 5 in deuterium oxide at 176 MHz
\(^{19}\)F and \(^{19}\)F\(^{(1)}\)H\} NMR spectra of 5 in deuterium oxide at 471 MHz
$^1$H NMR spectrum of 5 in benzene-d$_6$ at 700 MHz
$^{13}$C$^1$H NMR spectrum of 5 in benzene-d$_6$ at 176 MHz
Spectra of 5 (in methanol-d$_4$, 700 MHz) obtained after esterification via chloranhydride (bottom) and in acidic trifluoroethanol (top)
$^1$H NMR spectrum of compound 7

$^1$H NMR spectrum of compound 7 in deuterium oxide at 700 MHz
NMR spectra of 3-5 with the europium shift reagent

$^{19}$F($^1$H) NMR spectra (inverse-gated decoupling) of 3 in dichloromethane-$d_2$ upon addition of Eu$^{3+}$ shifting reagent (two enantiomers)

![NMR spectra diagram]

- 1 equiv. Eu$^{3+}$
- 1/2 equiv. Eu$^{3+}$
- 0 equiv. Eu$^{3+}$

$ppm$
$^{19}\text{F}[^1\text{H}]$ NMR spectra (inverse-gated decoupling) of 4 in dichloromethane-$d_2$ upon addition of Eu$^{3+}$ shifting reagent (single enantiomer)
$^{19}$F($^1$H) NMR spectra (inverse-gated decoupling) of 5 in dichloromethane-d$_2$ upon addition of Eu$^{3+}$ shifting reagent (two enantiomers)
NMR spectra of the peptides

$^1$H 90-pulse NMR spectra in deuterium oxide
$^1$H 1D stimulated echo NMR spectra in deuterium oxide at 700 MHz
$^{19}$F NMR spectra of the peptides in deuterium oxide at 471 MHz

10b 4 mM

9b 7 mM

8b 8 mM

-126.0 -126.5 -127.0 -127.5 -128.0 ppm
Circular dichroism spectra for the peptides

in methanol:

in aqueous buffer:
in methanol:

![Graph showing absorbance changes in methanol]

in aqueous buffer:

![Graph showing absorbance changes in aqueous buffer]
in methanol:  

in aqueous buffer:
Hydrolysis of the peptides

Starting peptide concentrations 8b – 5 mM, 9b – 5 mM, 10b – 2.5 mM

peptide 8b, series # 1

19F{1H} spectra

- 14 days
- 13 days
- 10 days
- 7 days
- 5 days
- 4.5 days
- 3 days
- 0 days

peptide 8b
difluoroethanol

ppm
peptide 9b, series # 1

19F{1H} spectra
difluoroethanol

14 days

13 days

10 days

7 days

6 days

5 days

4.5 days

3 days

0 days

ppm -126.0 -126.5 -127.0 -127.5 -128.0
peptide 10b, series # 1

19F{1H} spectra

- 14 days
- 13 days
- 10 days
- 7 days
- 6 days
- 5 days
- 4.5 days
- 3 days
- 0 days

ppm
peptide 9b, series # 2

19F{1H} spectra

9 days

8 days

5 days

3 days

2 days

1 days

0.5 days

0 days

-126.0 -126.5 -127.0 -127.5 -128.0 ppm
peptide 10b, series # 2

19F{1H} spectra

9 days

8 days

5 days

3 days

2 days

1 days

0.5 days

0 days

-126.0
-126.5
-127.0
-127.5
-128.0
ppm

difluoroethanol

peptide 10b