Intramolecular aryl transfer to thionium ions in an approach to α-arylacetamides

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**General Experimental**

All reactions were carried out under an inert nitrogen atmosphere unless otherwise stated. Tetrahydrofuran was dried over sodium wire and benzophenone. Dichloromethane was dried over calcium hydride. Triethylamine was distilled from calcium hydride and stored over KOH. DMSO was distilled from calcium hydride, under reduced pressure, and stored over molecular sieves. All other solvents and reagents were purchased from commercial sources and used as supplied.

NMR spectra were recorded on 300, 400 and 500 MHz spectrometers. All chemical shift values are reported in ppm, with coupling constants in Hz. NMR assignments were performed with the aid of COSY, HMQC, HMBC, DEPT 135 and DEPT 90 experiments. The notation of signals is: -

\[ \delta_{\text{H}}: \text{chemical shift in ppm (multiplicity, J value(s), number of protons, rotamer/diasteromer assignment [if relevant], proton assignment)} \]

\[ \delta_{\text{C}}: \text{chemical shift in ppm (carbon assignment)} \]

For fluorine-containing compounds, carbon-fluorine couplings are reported with the carbon assignment. If assignment is ambiguous, for example in the case of overlapping aromatic signals, a range of shifts is reported.

\[ \text{R}^\text{F} = -\text{CH}_2\text{CH}_2\text{C}_8\text{F}_{17} \]

Routine TLC analysis was carried out on aluminium sheets coated with silica gel 60 F254, 0.2 mm thickness. Solvent systems were either 40-60\(^\circ\) petroleum ether/EtOAc mixtures or methanol/dichloromethane mixtures. Plates were viewed with a 254 nm ultraviolet lamp and stained with aqueous potassium permanganate, anisaldehyde or DNP.

Flash column chromatography was carried out on 35 – 70 \(\mu\), 60A silica gel. Fluorous solid phase extraction (FSPE) was performed using fluorous silica gel packed in a glass column or with FSPE pre-packed cartridges.
Low-resolution mass spectra were obtained using electron impact ionisation (EI) and chemical ionisation (CI) techniques, or positive electrospray ionisation (ES$^+$).

Melting points were measured on a variable heater apparatus and are uncorrected.

IR spectra were recorded on an FTIR spectrometer as evaporated films (from dichloromethane) or neat, using sodium chloride windows.

**Preparation of samarium (II) iodide$^1$**

Samarium metal (1.00 g, 6.62 mmol, 1.2 eq) was added to a dry 100 mL flask under a nitrogen atmosphere. THF (55 mL) was added and the mixture was degassed with N$_2$ for 5 minutes. I$_2$ (1.41 g, 5.52 mmol, 1 eq) was added, the flask was wrapped in aluminium foil and the mixture was degassed with N$_2$ for a further 5 minutes. The mixture was heated at 60 °C for 18 hours to give a dark blue-black solution of SmI$_2$.

**Fluorous solid phase extraction (FSPE)**

A glass column was packed with fluorous silica gel using 80% aqueous MeCN. The mixture to be purified was dry loaded onto silica gel and transferred onto the fluorous silica gel. Elution with 80% aqueous MeCN (2-3 column volumes) separated the non-fluorous components of the mixture. Elution with 100% MeCN (2-3 column volumes) provided the fluorous components of the mixture. The fluorous column could be recycled by rinsing with 3 column volumes of Et$_2$O and drying with compressed air. The mixture could also be loaded onto the column in 80% aqueous MeCN, although sonication was usually necessary to aid dissolution.

General procedure A: Preparation of α-Hydroxy amides

To the secondary benzylamine (1 eq) in CH₂Cl₂ (5 mL/mmol) was added acetoxyacetic acid (1.2 eq), 1-hydroxybenzotriazole hydrate (0.2 eq) and EDCI (1.2 eq) and the mixture stirred at room temperature for 6-20 hours. The reaction mixture was washed with 1M HCl (×3) and the organic layer dried (Na₂SO₄) and concentrated in vacuo to give the crude amide. To the resulting acetoxyacetamide (1 eq) in 2:1 MeOH/H₂O (6 mL/mmol) was added K₂CO₃ (4 eq) and the resulting mixture stirred at room temperature for 2-20 hours. MeOH was removed in vacuo and the residue taken up in H₂O and extracted with EtOAc (×3). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo to afford the α-hydroxyamide.

General procedure B: Intramolecular aryl migration to give α-aryl acetamides

To oxalyl chloride (1.1 eq) in CH₂Cl₂ (4 mL/mmol) was added DMSO (2 eq) in CH₂Cl₂ (1 mL/mmol) via cannula at -78 °C. The mixture was stirred for 30 minutes at -78 °C. α-Hydroxyamide (1 eq) in CH₂Cl₂ (4 mL/mmol) was added via cannula at -78 °C and the mixture was stirred at this temperature for 1 hour. Triethylamine (5 eq) was added and the mixture allowed to warm to room temperature. The resulting yellow solution was stirred at room temperature for 3-15 hours. The organic layer was washed with aqueous saturated NaHCO₃ (×3), dried (Na₂SO₄) and concentrated in vacuo to yield the crude glyoxamide, usually as a yellow foam. To the crude glyoxamide (1 eq) in CH₂Cl₂ (12 mL/mmol) was added 1H,1H,2H,2H-perfluorodecane-1-thiol (0.7 eq) and the mixture was stirred at room temperature for 12-15 hours. Trifluoroacetic anhydride (9 eq) was added and the mixture was stirred at room temperature for 1 hour before the addition of BF₃·OEt₂ (5 eq). After 3-8 hours stirring at room temperature, during which time the solution adopted an intense colour, aqueous saturated NaHCO₃ was added resulting in vigorous effervescence. The aqueous layer was extracted with CH₂Cl₂ (×3). The combined organic layers were washed with aqueous saturated NaHCO₃ (×3), dried (Na₂SO₄) and concentrated in vacuo to yield crude α-arylacetamide. Purification was achieved by FPSE or column chromatography on silica gel.
**General procedure C: Alkylation of tagged α-aryl acetamides**

Alkyl bromide (5 eq) was added to a solution of α-aryl amide (1 eq) in THF (0.03 mL/mmol). Sodium hydride (5 eq) was added and the reaction mixture was heated at reflux for 3-48 hours. EtOAc and H₂O were added and the layers separated. The aqueous layer was extracted with EtOAc (×2). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. Purification by FSPE or column chromatography on silica gel afforded the alkylated α-aryl acetamide.

**General procedure D: Reductive cleavage of the fluorous tag from α-aryl acetamides**

To a degassed solution of fluorous-tagged α-aryl acetamide (1 eq) in THF (0.5 mL/mmol) was added SmI₂ (0.1 M solution in THF, 2.2 – 4.0 eq). The dark blue coloured reaction mixture was stirred for 12-24 hours at room temperature until a colour change to yellow indicated consumption of SmI₂. TLC analysis was used to determine if a further addition of SmI₂ was required (2.2 – 4.0 eq). Saturated aqueous NaHCO₃ was added and the solution was extracted with Et₂O (×3). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. Purification by FSPE or flash column chromatography on silica gel afforded the detagged α-aryl acetamide.

**General procedure E: Palladium-catalysed Suzuki couplings of α-aryl acetamides**

To a solution of fluorous-tagged α-aryl acetamide (1 eq), boronic acid (4 eq) and aqueous Na₂CO₃ (2 M, 7 eq) in a toluene:ethanol mix (2:1, 0.01 mL/mmol relative to Pd) was added Pd(PPh₃)₄ (20 mol%). The reaction was stirred at 90 °C for 18 hours and subsequently purified using FSPE to afford the cross-coupled product.
General procedure F: Reductive cleavage of the fluorous tag from modified α-aryl acetamides

To a degassed solution of the fluorous-tagged α-aryl acetamide (1 eq) in THF (0.05 mL/mmol) was added SmI$_2$ (0.1 M solution in THF, 4.0 eq). The dark blue coloured reaction mixture was stirred for 24 hours at room temperature. Saturated aqueous Na$_2$S$_2$O$_3$ was added and the solution was extracted with Et$_2$O (×3). The combined organic extracts were dried (Na$_2$SO$_4$) and concentrated in vacuo. Purification by FSPE afforded the detagged α-aryl acetamide.

$N$-(2-Fluoro-6-methoxy-benzyl)-2-hydroxy-$N$-iso-propylacetamide

Following general procedure A: (2-Fluoro-6-methoxy-benzyl)-iso-propyl-amine (1.03 g, 5.24 mmol, 1 eq) was stirred with acetoxyacetic acid (0.742 g, 6.29 mmol, 1.2 eq), HOBT (0.142 g, 1.05 mmol, 0.2 eq) and EDCI (1.21 g, 6.29 mmol, 1.2 eq). The resulting crude amide (1.45 g, 4.88 mmol, 1 eq) was stirred with K$_2$CO$_3$ (2.70 g, 19.5 mmol, 4 eq). Work-up afforded $N$-(2-fluoro-6-methoxy-benzyl)-2-hydroxy-$N$-iso-propyl-acetamide as a yellow oil (0.990 g, 3.88 mmol, 74% over two steps). No further purification was required.

$\delta_{\text{H}}$ (400 MHz, CDCl$_3$, rotamer ratio 3:1) 1.10 (d, J = 6.8 Hz, major, 6H, 2 × CH$_3$CH and minor, 6H, 2 × CH$_3$CH), 3.68 (septet, J = 6.8 Hz, minor, 1H, CH(CH$_3$)$_2$), 3.82 (s, major, 3H, CH$_3$O and minor, 3H, CH$_3$O), 4.03 (septet, J = 6.8 Hz, major, 1H, CH(CH$_3$)$_2$), 4.20 (s, minor, 2H, CH$_2$OH), 4.29 (s, major, 2H, CH$_2$N), 4.33 (s, major, 2H, CH$_2$OH), 4.77 (s, minor, 2H, CH$_2$N), 6.61-6.71 (m, major, 2H, 2 × ArH and minor, 2H, 2 × ArH), 7.17 (apparent q, J = 7.5 Hz, minor, 1H, ArH), 7.25 (apparent q, J = 7.8 Hz, 1H, ArH); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$, major rotamer only) 19.4 (2 × CH$_3$CH), 36.9 (d, J = 5 Hz, CH$_2$N), 49.3 (CH(CH$_3$)$_2$), 55.9 (CH$_3$O), 60.5 (CH$_2$OH), 106.4 (d, J = 3 Hz, ArCH), 108.2 (d, J = 23 Hz, ArCH), 112.1 (d, J = 16 Hz, ArC), 129.9 (d, J =
11 Hz, ArC), 159.1 (d, J = 7 Hz, ArCOCH$_3$), 161.7 (d, J = 246 Hz, ArC), 171.7 (NCO); IR (neat/cm$^{-1}$) 3408 (broad, O-H), 2972, 2940 and 2843 (C-H), 1644 (C=O), 1615 and 1587 (Ar C=C); m/z (ES$^+$) 278 (MNa$^+$, 100%), 256 (MH$^+$, 73%); HRMS for C$_{13}$H$_{19}$NO$_3$F (MH$^+$) found 256.1343, expected 256.1343.

**N-(2-Fluoro-6-methoxy-benzyl)-2-hydroxy-N-methylacetamide**

Following general procedure A: N-(2-Fluoro-6-methoxy-benzyl)-N-methyl-amine (0.875 g, 5.18 mmol, 1 eq) was stirred with acetoxy acetic acid (0.734 g, 6.21 mmol, 1.2 eq), HOBt (0.140 g, 1.04 mmol, 0.2 eq) and EDCI (1.19 g, 6.21 mmol, 1.2 eq). The resulting crude amide (1.39 g, 5.18 mmol, 1 eq) was stirred with K$_2$CO$_3$ (2.86 g, 20.7 mmol, 4 eq). The crude acetamide was purified by column chromatography on silica gel (50% EtOAc/petroleum ether) to afford N-(2-fluoro-6-methoxy-benzyl)-2-hydroxy-N-methyl- acetamide as a white solid (0.745 g, 3.28 mmol, 63% over two steps).

$\delta_h$ (400 MHz, CDCl$_3$, rotamer ratio 3:2) 2.72 (s, minor, 3H, CH$_3$N), 2.87 (s, major, 3H, CH$_3$N), 3.71 (t, J = 4.3 Hz, major, 1H, CH$_2$OH), 3.73 (t, J = 4.3 Hz, minor, 1H, CH$_2$OH), 3.84 (s, minor, 3H, CH$_3$O), 3.85 (s, major, 3H, CH$_3$O), 4.12 (d, J = 4.3 Hz, minor, 2H, CH$_2$OH), 4.35 (d, J = 1.3 Hz, major, 2H, CH$_2$N), 4.44 (d, J = 4.3 Hz, major, 2H, CH$_2$OH), 4.77 (d, J = 1.3 Hz, minor, 2H, CH$_3$N), 6.68-6.76 (m, major, 2H, 2 × ArH and minor, 2H, 2 × ArH) 7.23-7.32 (m, major, 1H, ArH and minor, 1H, ArH); $\delta_c$ (100 MHz, CDCl$_3$, major rotamer only) 32.2 (CH$_3$N), 39.3 (d, J = 5 Hz, CH$_2$N), 56.0 (CH$_3$O), 60.0 (CH$_2$OH), 106.4 (d, J = 3 Hz, ArCH), 107.9 (d, J = 3 Hz, ArCH), 110.7 (d, J = 17 Hz, ArC), 130.3 (d, J = 11 Hz, ArCH), 159.0 (d, J = 7 Hz, ArCOCH$_3$), 162.2 (d, J = 247 Hz, ArCF), 171.8 (NCO); IR (CH$_2$Cl$_2$ evaporated film/cm$^{-1}$) 3409 (broad, O-H), 2939 and 2843 (C-H), 1650 (C=O), 1616 and 1587 (Ar C=C); m/z (ES$^+$) 250 (MNa$^+$, 100%), 228 (MH$^+$, 51%); HRMS for C$_{11}$H$_{15}$NO$_3$F (MH$^+$) found 228.1040, expected 228.1030; anal. calcd. for C$_{11}$H$_{14}$NO$_3$F: C (58.14%), H (6.21%), N (6.16%), found C (58.07%), H (6.07%), N (5.94%); mp (CHCl$_3$) 68.7-72.3 °C.
2-Hydroxy-N-iso-propyl-N-(2,6-dimethoxy-benzyl)acetamide

Following general procedure A: N-iso-Propyl-N-(2,6-dimethoxy-benzyl)-amine (1.36 g, 6.51 mmol, 1 eq) was stirred with acetoxyacetic acid (0.920 g, 7.81 mmol, 1.2 eq), HOBt (0.176 g, 1.30 mmol, 0.2 eq) and EDCI (1.50 g, 7.81 mmol, 1.2 eq). The resulting crude amide (1.81 g, 5.86 mmol, 1 eq) was stirred with K$_2$CO$_3$ (3.24 g, 23.4 mmol, 4 eq) to afford 2-hydroxy-N-iso-propyl-N-(2,6-dimethoxy-benzyl)-acetamide as a cream solid (2.57 g, 3.75 mmol, 85% over two steps). No further purification was required.

δ$_H$ (500 MHz, CDCl$_3$, rotamer ratio 8:1) 1.03 (d, $J = 6.6$ Hz, minor, 6H, 2 × CH$_3$CH), 1.09 (d, $J = 6.9$ Hz, major, 6H, 2 × CH$_3$CH), 3.61 (septet, $J = 6.6$ Hz, minor, 1H, CH(CH$_3$)$_2$), 3.80 (s, minor, 6H, 2 × CH$_3$O), 3.81 (s, major, 6H, 2 × CH$_3$O), 3.90 (septet, $J = 6.9$ Hz, major, 1H, CH(CH$_3$)$_2$), 3.92 (t, $J = 4.1$ Hz, major, 1H, CH$_2$OH), 4.18 (d, $J = 5.8$ Hz, minor, CH$_2$OH), 4.32 (s, major, 2H, CH$_2$N), 4.35 (d, $J = 4.1$ Hz, major, 2H, CH$_2$OH), 4.87 (s, minor, 2H, CH$_2$N), 6.53 (d, $J = 8.5$ Hz, minor, 2H, 2 × ArH) 6.55 (d, $J = 8.5$ Hz, major, 2H, 2 × ArH) 7.20 (t, $J = 8.5$ Hz, minor, 1H, ArH), 7.24 (t, $J = 8.5$ Hz, major, 1H, ArH); δ$_C$ (125 MHz, CDCl$_3$, major rotamer only) 19.5 (2 × CH$_3$CH), 37.4 (CH$_2$N), 49.4 (CH(CH$_3$)$_2$), 55.6 (2 × CH$_3$O), 60.6 (CH$_2$OH), 103.7 (2 × ArCH), 112.2 (ArC), 129.6 (ArCH), 159.0 (2 × ArCOCH$_3$), 171.6 (NCO); IR (CH$_2$Cl$_2$ evaporated film/cm$^{-1}$) 3400 (broad, O-H), 3103, 2992, 2967 and 2842 (C-H), 1643 (C=O), 1595 (Ar C=C); m/z (ES$^+$) 290 (MNa$^+$, 14%), 210 (8%); HRMS for C$_{14}$H$_{22}$NO$_4$ (MH$^+$) found 268.1546, expected 268.1543; anal. calcd. for C$_{14}$H$_{21}$NO$_4$: found C (63.22%), H (8.29%), N (5.24%); expected C (62.90%), H (7.92%), N (5.24%); mp (iso-propanol) 64.1-65.2 °C.

2-Hydroxy-N-(2,6-dimethyl-benzyl)-N-iso-propylacetamide

δ$_H$ (500 MHz, CDCl$_3$, rotamer ratio 8:1) 1.03 (d, $J = 6.6$ Hz, minor, 6H, 2 × CH$_3$CH), 1.09 (d, $J = 6.9$ Hz, major, 6H, 2 × CH$_3$CH), 3.61 (septet, $J = 6.6$ Hz, minor, 1H, CH(CH$_3$)$_2$), 3.80 (s, minor, 6H, 2 × CH$_3$O), 3.81 (s, major, 6H, 2 × CH$_3$O), 3.90 (septet, $J = 6.9$ Hz, major, 1H, CH(CH$_3$)$_2$), 3.92 (t, $J = 4.1$ Hz, major, 1H, CH$_2$OH), 4.18 (d, $J = 5.8$ Hz, minor, CH$_2$OH), 4.32 (s, major, 2H, CH$_2$N), 4.35 (d, $J = 4.1$ Hz, major, 2H, CH$_2$OH), 4.87 (s, minor, 2H, CH$_2$N), 6.53 (d, $J = 8.5$ Hz, minor, 2H, 2 × ArH) 6.55 (d, $J = 8.5$ Hz, major, 2H, 2 × ArH) 7.20 (t, $J = 8.5$ Hz, minor, 1H, ArH), 7.24 (t, $J = 8.5$ Hz, major, 1H, ArH); δ$_C$ (125 MHz, CDCl$_3$, major rotamer only) 19.5 (2 × CH$_3$CH), 37.4 (CH$_2$N), 49.4 (CH(CH$_3$)$_2$), 55.6 (2 × CH$_3$O), 60.6 (CH$_2$OH), 103.7 (2 × ArCH), 112.2 (ArC), 129.6 (ArCH), 159.0 (2 × ArCOCH$_3$), 171.6 (NCO); IR (CH$_2$Cl$_2$ evaporated film/cm$^{-1}$) 3400 (broad, O-H), 3103, 2992, 2967 and 2842 (C-H), 1643 (C=O), 1595 (Ar C=C); m/z (ES$^+$) 290 (MNa$^+$, 14%), 210 (8%); HRMS for C$_{14}$H$_{22}$NO$_4$ (MH$^+$) found 268.1546, expected 268.1543; anal. calcd. for C$_{14}$H$_{21}$NO$_4$: found C (63.22%), H (8.29%), N (5.24%); expected C (62.90%), H (7.92%), N (5.24%); mp (iso-propanol) 64.1-65.2 °C.
Following general procedure A: (2,4-Dimethyl-benzyl)-iso-propyl-amine (1.77 g, 10.0 mmol, 1 eq) was stirred with acetoxyacetic acid (1.42 g, 12.0 mmol, 1.2 eq), HOBT (0.270 g, 2.00 mmol, 0.2 eq) and EDCI (2.30 g, 12.0 mmol, 1.2 eq). The resulting crude amide (2.05 g, 7.40 mmol, 1 eq) was stirred with K$_2$CO$_3$ (4.09 g, 29.6 mmol, 4 eq). Purification by column chromatography on silica gel afforded 2-hydroxy-N-(2,4-dimethyl-benzyl)-N-iso-propyl-acetamide as a cream solid (0.968 g, 4.12 mmol, 41% over two steps).

δ$_H$ (400 MHz, d$_6$-DMSO, 100 ºC) 1.12 (d, $J$ = 6.8 Hz, 6H, 2 × CH$_3$CH), 2.33 (s, 6H, 2 × ArCH$_3$), 3.00 (br s, 1H, OH), 3.45 (septet, $J$ = 6.8 Hz, 1H, CH(CH$_3$)$_2$), 4.19 (s, 2H, CH$_2$OH), 4.56 (s, 2H, CH$_2$N), 7.03-7.05 (m, 2H, 2 × ArH), 7.10 (dd, $J$ = 8.5 Hz, 6.3 Hz, 1H, ArH); δ$_C$ (100 MHz, d$_6$-DMSO, 100 ºC) 19.5 (2 × ArC$_3$H$_3$), 19.7 (2 × CH$_3$CH), 42.4 (CH$_2$N), 48.0 (CH(CH$_3$)$_2$), 60.8 (CH$_2$OH), 127.3 (ArCH), 128.5 (2 × ArCH), 133.4 (ArC), 137.3 (2 × ArC), 171.8 (NCO); IR (neat/cm$^{-1}$) 3399 (broad, O-H), 3066, 2967 and 2935 (C-H), 1641 (C=O), 1595 (Ar C=C); m/z (ES$^+$) 258 (MNa$^+$, 100%), 236 (MH$^+$, 28%); HRMS for C$_{14}$H$_{21}$NO$_2$Na (MNa$^+$) found 258.1465, expected 258.1465; anal. calcd. for C$_{14}$H$_{21}$NO$_2$: C (71.46%), H (8.99%), N (5.95%), found C (71.81%), H (9.04%), N (5.86%), mp (CHCl$_3$) 96.6-97.4 ºC.

$N$-(2-Fluoro-4-methoxy-benzyl)-2-hydroxy-$N$-iso-propylacetamide

Following general procedure A: $N$-(2-Fluoro-4-methoxy-benzyl)-$N$-iso-propylamine (2.00 g, 10.2 mmol, 1 eq) was stirred with acetoxyacetic acid (1.44 g, 12.2 mmol, 1.2 eq), HOBT (0.274 g, 2.03 mmol, 0.2 eq) and EDCI (2.34 g, 12.2 mmol, 1.2 eq). The resulting crude amide (3.27 g, 11.0 mmol, 1 eq) was stirred with K$_2$CO$_3$ (6.09 g, 44.0 mmol, 4 eq). Purification by column chromatography on silica gel (3:3:1 petroleum ether/CH$_2$Cl$_2$/EtOAc) afforded $N$-(2-fluoro-4-methoxy-benzyl)-2-hydroxy-$N$-iso-propylacetamide as an orange oil (1.99 g, 7.80 mmol, 76% over two steps).

δ$_H$ (500 MHz, CDCl$_3$, rotamer ratio 4:3) 1.08 (d, $J$ = 6.9 Hz, minor, 6H, CH$_3$CH), 1.09 (d, $J$ = 6.6 Hz, major, 6H, CH$_3$CH), 2.65-3.05 (br s, major, 1H, OH and minor, 1H, OH), 3.67-3.75 (m, minor, 1H, CH(CH$_3$)$_2$), 3.71 (s, major, 3H, CH$_3$O), 3.73 (s,
minor, 3H, CH$_3$O), 4.04 (s, minor, 2H, CH$_2$OH), 4.22 (s, major, 2H, CH$_3$OH and minor, 2H, CH$_2$N), 4.52 (s, major, 2H, CH$_2$N), 4.61 (septet, $J = 6.6$ Hz, major, 1H, CH(CH$_3$)$_2$), 6.47-6.64 (m, major, 2H, 2 × ArH and minor, 2H, 2 × ArH), 6.98 (apparent t, $J = 8.8$ Hz, minor, 1H, ArH), 7.12 (apparent t, $J = 8.8$ Hz, major, 1H, ArH); $\delta$C (125 MHz, CDCl$_3$, major rotamer only) 20.8 (2 × CH$_3$CH), 36.8 (CH$_2$N), 47.5 (CH(CH$_3$)$_2$), 55.5 (CH$_3$O), 60.1 (CH$_2$OH), 101.3 (d, $J = 25$ Hz, ArCH), 110.1 (d, $J = 3$ Hz, ArCH), 117.4 (d, $J = 14$ Hz, ArC), 129.9 (d, $J = 6$ Hz, ArCH), 159.9 (d, $J = 11$ Hz, ArCOCH$_3$), 160.3 (d, $J = 245$ Hz, ArC=F), 172.0 (NCO); IR (neat/cm$^{-1}$) 3412 (broad, O-H), 2975 and 2938 (C-H), 1642 (C=O), 1588 (Ar C=C); m/z (ES$^+$) 278 (MNa$^+$, 100%), 256 (MH$^+$, 4%), 211 (26%), 139 (11%); HRMS for C$_{13}$H$_{18}$NO$_3$FNa (MNa$^+$) found 278.1174, expected 278.1163.

**N-(2-Fluoro-4-methoxy-benzyl)-2-hydroxy-N-methylacetamide**

Following general procedure A: (2-Fluoro-4-methoxy-benzyl)-methylamine (0.959 g, 5.67 mmol, 1 eq) was stirred with acetoxyacetic acid (0.804 g, 6.81 mmol, 1.2 eq), HOBt (153 mg, 1.13 mmol, 0.2 eq) and EDCI (1.31 g, 6.81 mmol, 1.2 eq). The resulting crude amide (1.52 g, 5.65 mmol, 1 eq) was stirred with K$_2$CO$_3$ (3.12 g, 22.6 mmol, 4 eq). The crude acetamide was purified by column chromatography on silica gel (50% EtOAc/petroleum ether) to afford **N-(2-fluoro-4-methoxy-benzyl)-2-hydroxy-N-methylacetamide** as an orange oil (1.02 g, 4.49 mmol, 79% over two steps).

$\delta$H (400 MHz, CDCl$_3$, rotamer ratio 2:1) 2.69 (s, major, 3H, CH$_3$N), 2.81 (s, minor, 3H, CH$_3$N), 3.64 (s, major, 3H, CH$_3$O), 3.65 (s, minor, 3H, CH$_3$O), 3.64-3.70 (m, major, 1H, OH and minor, 1H, OH), 4.03 (d, $J = 2.8$ Hz, major, 2H, CH$_2$OH), 4.16 (d, $J = 2.8$ Hz, minor, 2H, CH$_2$OH), 4.17 (s, minor, 2H, CH$_2$N), 4.47 (s, major, 2H, CH$_2$N), 6.46-6.58 (m, major, 2H, 2 × ArH and minor, 2H, 2 × ArH), 6.93 (t, $J = 8.6$ Hz, minor, 1H, ArH) 7.10 (t, $J = 8.6$ Hz, major, 1H, ArH); $\delta$C (75 MHz, CDCl$_3$, major rotamer) 32.3 (d, $J = 2$ Hz, CH$_3$N), 44.3 (d, $J = 3$ Hz, CH$_2$N), 55.4 (CH$_3$O), 59.8 (CH$_2$OH), 101.3 (d, $J = 26$ Hz, ArCH), 110.1 (d, $J = 3$ Hz, ArCH), 114.9 (d, $J = 16$ Hz, ArC).
Hz, ArC), 131.3 (d, J = 6 Hz, ArCH), 160.4 (d, J = 11 Hz, ArCOCH3), 161.5 (d, J = 246 Hz, ArCF), 171.6 (NCO); IR (neat/cm\(^{-1}\)) 3419 (broad, O-H), 3075, 2938 and 2840 (C-H), 1652 (C=O), 1626, 1587 and 1511 (Ar C=C); m/z (ES\(^+\)) 477 (dimer+Na, 98%), 335 (56%), 250 (MNa\(^+\), 100%), 228 (MH\(^+\), 71%); HRMS for C\(_{11}\)H\(_{15}\)NO\(_3\)F (MH\(^+\)) found 228.1039, expected 228.1030.

\[\text{N-(4-Bromo-2-methoxy-benzyl)-2-hydroxy-N-iso-propylacetamide}\]

Following general procedure A: N-(4-Bromo-2-methoxy-benzyl)-N-iso-propylamine (0.942 g, 3.65 mmol, 1 eq) was stirred with acetoxy acetic acid (0.517 g, 4.38 mmol, 1.2 eq), HOBt (99 mg, 0.730 mmol, 0.2 eq) and EDCI (0.840 g, 4.38 mmol, 1.2 eq). The resulting crude amide (1.16 g, 3.24 mmol, 1 eq) was stirred with K\(_2\)CO\(_3\) (1.79 g, 13.0 mmol, 4 eq) to afford N-(4-bromo-2-methoxy-benzyl)-2-hydroxy-N-iso-propylacetamide as a colourless oil (0.877 g, 2.78 mmol, 76% over two steps). No further purification was required.

\[\delta H (400 MHz, CDCl_3, \text{rotamer ratio 1.1:1}), 1.14 (\text{apparent t, } J = 6.4 \text{ Hz, major, } 6H, 2 \times CH_3CH \text{ and minor, } 6H, 2 \times CH_3CH), 3.81 (\text{septet, } J = 6.6 \text{ Hz, minor, CH(CH}_3)_2), 3.86 (s, major, 3H, CH_3O and minor, 3H, CH_3O), 4.04 (s, major, 2H, CH_3OH), 4.22 (s, major, 2H, CH_2N), 4.33 (s, minor, 2H, CH_2OH), 4.51 (s, minor, 2H, CH_2N), 4.76 (septet, J = 6.8 Hz, major, 1H, CH(CH}_3)_2), 6.92-7.10 (m, major, 3H, 3 \times ArH and minor, 3H, 3 \times ArH); \delta C (100 MHz, CDCl_3) 19.9 (major, 2 \times CH_3CH), 20.8 (minor, 2 \times CH_2CH), 38.6 (minor, CH_2N), 40.1 (major, CH_2N), 47.1 (minor, CH(CH}_3)_2), 47.3 (major, CH(CH}_3)_2), 55.6 (major, CH_3O and minor CH_3O), 60.1 (minor, CH_2OH), 60.3 (major, CH_2OH), 113.7 (minor, ArCH), 113.9 (major, ArCH), 121.0 (minor, ArC), 121.8 (major, ArC), 123.5 (minor, ArCH), 123.6 (major, ArCH), 124.3 (major, ArC), 125.5 (minor, ArC), 127.6 (major, ArCH), 128.6 (minor, ArCH), 156.8 (minor, ArCOCH_3), 157.0 (major, ArCOCH_3), 171.9 (minor, NCO), 172.5 (major, NCO); IR (CHCl_3 evaporated film/cm\(^{-1}\)) 3413 (broad, O-H), 2974 m/z (ES\(^+\)) 340 (\text{81Br, MNa}^+, 32%), 338 (\text{79Br, MNa}^+, 31%), 318 (\text{81Br, MH}^+, 94%), 316 (\text{79Br, MH}^+, 100%); HRMS for C\(_{13}\)H\(_{19}\)NO\(_3\)\(^{79}\)Br (MH\(^+\)) found 316.0545, expected 316.0543.

S11
**N-(5-Bromo-2-methoxy-benzyl)-2-hydroxy-N-iso-propyl-acetamide**

Following general procedure A: (5-Bromo-2-methoxy-benzyl)-iso-propylamine (2.59 g, 10.0 mmol, 1 eq) was stirred with acetoxyacetic acid (1.42 g, 12.0 mmol, 1.2 eq), HOBt (0.271 g, 2.01 mmol, 0.2 eq) and EDCI (2.31 g, 12.0 mmol, 1.2 eq). The resulting crude amide (3.58 g, 10.0 mmol, 1 eq) was stirred with K₂CO₃ (5.53 g, 40.0 mmol, 4 eq). Purification by column chromatography on silica gel (gradient elution 10-50% EtOAc/petroleum ether) afforded N-(5-bromo-2-methoxy-benzyl)-2-hydroxy-N-iso-propylacetamide as a colourless oil (1.85 g, 5.85 mmol, 59% over two steps).

δ_H (400 MHz, CDCl₃, 1:1 rotamer ratio) 1.13-1.15 (m, one rotamer, 6H, 2 × CH₃CH and one rotamer, 6H, 2 × CH₃CH), 3.65 (t, J = 4.3 Hz, one rotamer, 1H, OH), 3.78-3.85 (m, one rotamer, 1H, OH and one rotamer, 1H, CH(CH₃)₂), 3.83 (s, one rotamer, 3H, CH₃O and one rotamer, 3H, CH₃O), 4.03 (d, J = 3.5 Hz, one rotamer, 2H, CH₂OH), 4.24 (s, one rotamer, 2H, CH₂N), 4.33 (d, J = 3.3 Hz, one rotamer, 2H, CH₂OH), 4.54 (s, one rotamer, 2H, CH₂N), 4.74 (septet, J = 6.8 Hz, one rotamer, 1H, CH(CH₃)₂), 6.71 (d, J = 8.6 Hz, one rotamer, 1H, ArH), 6.74 (d, J = 8.6 Hz, one rotamer, 1H, ArH), 7.12 (s, one rotamer, 1H, ArH), 7.17 (s, one rotamer, 1H, ArH), 7.29 (d, J = 8.6 Hz, one rotamer, 1H, ArH), 7.35 (d, J = 8.6 Hz, one rotamer, 1H, ArH), 7.39 (one rotamer, 1H, ArH), 8.03 (one rotamer, 2 × CH₃CH), 20.8 (one rotamer, 2 × CH₃CH), 38.5 (one rotamer, CH₂N), 40.1 (one rotamer, CH₂N), 47.1 (one rotamer, CH(CH₃)₂), 47.3 (one rotamer, CH(CH₃)₂), 55.5 (both rotamers, CH₂O), 60.1 (one rotamer, CH₂OH), 60.3 (CH₂OH), 111.7 (one rotamer, ArCH), 111.8 (one rotamer, ArCH), 112.9 (one rotamer, ArC), 113.0 (one rotamer, ArC), 127.4 (one rotamer, ArC), 128.7 (one rotamer, ArC), 129.0 (one rotamer, ArCH), 129.9 (one rotamer, ArCH), 130.5 (one rotamer, ArCH), 131.2 (one rotamer, ArCH), 155.2 (one rotamer, ArCOCH₃), 155.5 (one rotamer, ArCOCH₃), 171.9 (one rotamer, NCO), 172.4 (one rotamer, NCO); IR (neat/cm⁻¹) 3411 (broad, O-H), 3072, 2971, 2937 and 2838 (C-H), 1645 (C=O), 1593 (Ar C=C); m/z (ES⁺) 340 (⁸¹Br, MNa⁺, 28%), 338 (⁷⁹Br, MNa⁺,
29%), 318 ($^{81}$Br, MH$^+$, 79%), 316 ($^{79}$Br, MH$^+$, 77%), 259 (75%), 174 (100%); HRMS for C$_{13}$H$_{19}$NO$_3$($^{79}$Br (MH$^+$) found 316.0540, expected 316.0543.

**rac-2-(2-Fluoro-6-methoxy-phenyl)-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decylsulfanyl)-N-methylacetamide 8**

 Following general procedure B: Treatment of the crude glyoxamide 5 (0.1337 g, 0.487 mmol, 1 eq) with 1H,1H,2H,2H-perfluorodecane-1-thiol (0.10 mL, 0.341 mmol, 0.7 eq), TFAA (0.62 mL, 4.38 mmol, 9 eq) and BF$_3$·OEt$_2$ (0.30 mL, 0.244 mmol, 5 eq) gave a colourless oil and purification by FSPE afforded acetamide 8 as a yellow oil (0.153 g, 0.218 mmol, 64% over two steps).

$\delta$H (400 MHz, CDCl$_3$) 1.19 (d, $J = 6.6$ Hz, 6H, 2 × CH$_3$CH), 2.33-2.50 (m, 2H, CH$_2$CH$_2$C$_8$F$_{17}$), 2.78-2.83 (m, 2H, CH$_2$CH$_2$C$_8$F$_{17}$), 3.84 (s, 3H, CH$_3$O), 4.06-4.18 (m, 1H, CH(CH$_3$)$_2$), 6.68-6.74 (m, 2H, 2 × ArH), 6.85 (d, $J = 8.1$ Hz, 1H, NH), 7.23 (td, $J = 8.4$ Hz, 6.7 Hz, 1H, ArH); $\delta$C (100 MHz, CDCl$_3$) 22.4 (2 × CH$_3$CH), 23.9 (CH$_2$CH$_2$C$_8$F$_{17}$), 32.0 (t, $J = 22$ Hz, CH$_2$CH$_2$C$_8$F$_{17}$), 42.0 (CH(CH$_3$)$_2$), 44.1 (CHS), 55.9 (CH$_3$O), 106.8 (d, $J = 3$ Hz, ArCH), 108.5 (d, $J = 23$ Hz, ArCH), 114.8 (d, $J = 17$ Hz, ArC), 129.6 (d, $J = 11$ Hz, ArCH), 157.8 (d, $J = 7$ Hz, ArCOCH$_3$), 161.0 (d, $J = 246$ Hz, ArCF), 167.4 (NCO); IR (CH$_2$Cl$_2$ evaporated film/cm$^{-1}$) 3370 (N-H), 3318, 2879, 2941 and 2972 (C-H), 1667 (C=O) 1584 and 1613 (Ar C=C); m/z (ES$^+$) 726 (MNa$^+$, 100%), 278 (17%); HRMS for C$_{24}$H$_{19}$NO$_2$F$_{18}$SNa (MNa$^+$) found 726.0732, expected 726.0741.

**rac-2-(2-Fluoro-6-methoxy-phenyl)-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decylsulfanyl)-N-methylacetamide 16**
Following general procedure B: Treatment of the crude glyoxamide 9 (0.117 g, 0.521 mmol, 1 eq) with 1H,1H,2H,2H-perfluorodecane-1-thiol (0.11 mL, 0.469 mmol, 9 eq) and TFAA (0.66 mL, 4.69 mmol, 9 eq) and BF₃·OEt₂ (0.32 mL, 2.61 mmol, 5 eq) and purification by FSPE afforded acetamide 16 as a cream amorphous solid (0.126 g, 0.187 mmol, 51% over two steps).

δ_H (400 MHz, CDCl₃) 2.34-2.49 (m, 2H, CH₂C₈F₁₇), 2.81-2.85 (m, 2H, CH₂CH₂C₈F₁₇), 2.90 (d, J = 5.0 Hz, 3H, CH₃NH), 3.86 (s, 3H, CH₃O), 4.98 (s, 1H, CHS), 6.71-6.76 (m, 2H, 2 × ArH), 6.95-7.01 (br q, 1H, NH), 7.25 (dt, J = 8.3, 6.8 Hz, 1H, ArH); δ_C (75 MHz, CDCl₃) 24.0 (C₆H₅CH₂C₈F₁₇), 27.0 (C₆H₅N), 32.0 (t, J = 22 Hz, CH₂CH₂C₈F₁₇), 43.9 (d, J = 2 Hz, CHS), 56.0 (CH₃O), 107.0 (d, J = 3 Hz, ArCH), 108.6 (d, J = 23 Hz, ArCH), 114.8 (d, J = 16 Hz, ArC), 129.7 (d, J = 11 Hz, ArCH), 157.8 (d, J = 8 Hz, ArCOCH₃), 161.0 (d, J = 247 Hz, ArC₂F), 169.1 (NCO); IR (evaporated film/cm⁻¹) 3334 (N-H), 3048, 2844 and 2846 (C-H), 1660 (C=O), 1615, 1588 and 1531 (Ar C=C); m/z (ES⁺) 698 (MNa⁺, 49%), 693 (MNH₄⁺, 42%), 676 (MH⁺, 100%); HRMS for C₂₀H₁₆NO₂F₁₈S (MH⁺) found 676.0609, expected 676.0609.

rac-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-Heptadecfluorodecylsulfanyl)-2-(2,6-dimethoxy-phenyl)-N-iso-propylacetamide 17

Following general procedure B: Treatment of crude glyoxamide 10 (0.190 g, 0.720 mmol, 1 eq) with 1H,1H,2H,2H-perfluorodecane-1-thiol (0.15 mL, 0.504 mmol, 7 eq), TFAA (0.91 mL, 6.45 mmol, 9 eq) and BF₃·OEt₂ (0.45 mL, 3.58 mmol, 5 eq) and purification by column chromatography on silica gel (35% EtOAc/petroleum ether) afforded acetamide 17 as a yellow solid (0.171 g, 0.239 mmol, 48% over two steps).

δ_H (500 MHz, CDCl₃) 1.18 (d, J = 6.6 Hz, 6H, 2 × CH₃CH), 2.33-2.56 (m, 2H, CH₂CH₂C₈F₁₇), 2.78 (t, J = 8.2 Hz, 2H, CH₂CH₂CH₂C₈F₁₇), 3.82 (s, 6H, 2 × CH₃O), 4.10 (m, 1H, CH(CH₃)₂), 5.05 (s, 1H, CHS), 5.56 (d, J = 8.2 Hz, 2H, 2 × ArH), 6.74 (d, J = 7.9 Hz, 1H, NH), 7.23 (t, J = 8.2 Hz, 1H, ArH); δ_C (125 MHz, CDCl₃) 22.7 (2 × CH₃CH), 23.9 (CH₂CH₂C₈F₁₇), 32.3 (t, J = 23 Hz, CH₂CH₂CH₂C₈F₁₇), 41.8 (CH(CH₃)₂), 13.3 (C₆H₅)}
44.7 (CHS), 55.7 (2 × CH₃O), 104.2 (2 × ArCH), 115.3 (ArC), 129.4 (ArCH), 157.6 (2 × ArCOCH₃), 168.8 (NCO); IR (CH₂Cl₂ evaporated film/cm⁻¹) 3369 (N-H), 2970, 2936 and 2841 (C-H), 1665 (C=O), 1594 and 1516 (Ar C=C); m/z (ES⁺) 738 (MNa⁺, 100%), 426 (42%); HRMS for C₂₃H₂₂NO₃SNa (MNa⁺) found 738.0942, expected 738.0941; mp (CH₂Cl₂) 90.8-93.0 °C.

**rac-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-Heptadecafluoro-decylsulfanyl)-2-(2,6-dimethyl-phenyl)-N-iso-propylacetamide 18**

Following general procedure B: Treatment of the crude glyoxamide 11 (0.340 g, 1.46 mmol, 1 eq) with 1H,1H,2H,2H-perfluorodecane-1-thiol (0.30 mL, 1.02 mmol, 0.7 eq), TFAA (1.85 mL, 13.1 mmol, 9 eq) and BF₃·OEt₂ (0.90 mL, 7.30 mmol, 5 eq) and purification by column chromatography on silica gel (5% EtOAc/petroleum ether) afforded acetamide 18 as a yellow amorphous solid (0.526 g, 0.770 mmol, 75% over two steps).

δ_H (400 MHz, CDCl₃) 1.13 (d, J = 6.6 Hz, 6H, 2 × CH₃CH), 2.18-2.49 (m, 2H, CH₂C₈F₁₇), 2.38 (s, 6H, 2 × CH₃Ar), 2.78-2.95 (m, 2H, CH₂CH₂C₈F₁₇), 4.12 (m, 1H, CH(CH₃)₂), 4.97 (s, 1H, CHS), 5.94 (d, J = 7.6 Hz, 1H, NH), 7.05-7.07 (m, 2H, 2 × ArH), 7.11-7.15 (m, 1H, ArH); δ_C (100 MHz, CDCl₃) 20.6 (2 × CH₃Ar), 22.4 (2 × CH₃CH), 24.1 (t, J = 4 Hz, CH₂CH₂C₈F₁₇), 31.9 (t, J = 22 Hz, CH₂C₈F₁₇), 42.1 (CH(CH₃)₂), 50.8 (CHS), 128.2 (2 × ArCH), 129.4 (ArCH), 134.3 (2 × ArC), 137.1 (ArC), 168.4 (NCO); IR (CH₂Cl₂ evaporated film/cm⁻¹) 3294 (N-H), 3036, 2973, 2937 and 2877 (C-H), 1652 (C=O), 1520 (Ar C=C); m/z (ES⁺) 706 (MNa⁺, 100%), 684 (MH⁺, 25%), 402 (13%); HRMS for C₂₃H₂₃NOF₁₇S (MH⁺) found 684.1231, expected 684.1223.
rac-2-(2-Fluoro-4-methoxyphenyl)-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-
heptadecafluorodecylsulfanyl)-N-iso-propylacetamide 19

Following general procedure B: Treatment of crude glyoxamide 12 (0.550 g, 2.17
mmol, 1 eq) with 1H,1H,2H,2H-perfluorodecane-1-thiol (0.45 mL, 1.52 mmol, 0.7
eq), TFAA (2.76 mL, 19.6 mmol, 9 eq) and BF3·OEt2 (1.43 mL, 10.9 mmol, 5 eq) and
purification by FSPE afforded acetamide 19 as a yellow foam (0.650 g, 0.925 mmol,
61% over two steps).

δH (500 MHz, CDCl3) 1.15 (d, J = 6.6 Hz, 3H, CH3CH), 1.18 (d, J = 6.6 Hz, 3H,
CH3CH), 2.28-2.45 (m, 2H, CH2CH2C8F17), 2.72-2.82 (m, 2H, CH2CH2C8F17), 3.79
(s, 3H, CH3O), 4.10 (m, 1H, CH(CH3)2), 4.77 (s, 1H, CHS), 6.36 (d, J = 7.9 Hz, 1H,
NH), 6.63 (dd, J = 11.7 Hz, 2.5 Hz, 1H, ArH), 6.70 (dd, J = 8.5 Hz, 2.5 Hz, 1H, ArH),
7.36 (t, J = 8.5 Hz, 1H, ArH); δC (125 MHz, CDCl3) 22.5 (2 × (CH3)2CH), 23.0
(CH2CH2C8F17), 31.5 (t, J = 21 Hz, CH2CH2C8F17), 42.1 (CH(CH3)2), 47.0 (CHS),
55.6 (CH3O), 101.9 (d, J = 26 Hz, ArH), 110.6 (d, J = 3 Hz, ArH), 115.7 (d, J = 5
Hz, ArC), 129.8 (ArCH), 159.9 (d, J = 11 Hz, ArCOCH3), 161.8 (d, J = 246 Hz,
ArCF), 167.6 (NCO); IR (CH2Cl2 evaporated film/cm⁻¹) 3306 (N-H), 3063, 2977,
2940 and 2840 (C-H), 1651 (C=O), 1634, 1585 and 1538 (Ar C=C); m/z (ES⁺) 726
(MNa⁺, 100%), 704 (MH⁺, 22%); HRMS for C22H20NO2F18S (MH⁺) found 704.0919,
expected 704.0922.

rac-2-(2-Fluoro-4-methoxy-phenyl)-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-
heptadecafluoro-decylsulfanyl)-N-methylacetamide 20

δH (500 MHz, CDCl3) 1.15 (d, J = 6.6 Hz, 3H, CH3CH), 1.18 (d, J = 6.6 Hz, 3H,
CH3CH), 2.28-2.45 (m, 2H, CH2CH2C8F17), 2.72-2.82 (m, 2H, CH2CH2C8F17), 3.79
(s, 3H, CH3O), 4.10 (m, 1H, CH(CH3)2), 4.77 (s, 1H, CHS), 6.36 (d, J = 7.9 Hz, 1H,
NH), 6.63 (dd, J = 11.7 Hz, 2.5 Hz, 1H, ArH), 6.70 (dd, J = 8.5 Hz, 2.5 Hz, 1H, ArH),
7.36 (t, J = 8.5 Hz, 1H, ArH); δC (125 MHz, CDCl3) 22.5 (2 × (CH3)2CH), 23.0
(CH2CH2C8F17), 31.5 (t, J = 21 Hz, CH2CH2C8F17), 42.1 (CH(CH3)2), 47.0 (CHS),
55.6 (CH3O), 101.9 (d, J = 26 Hz, ArH), 110.6 (d, J = 3 Hz, ArH), 115.7 (d, J = 5
Hz, ArC), 129.8 (ArCH), 159.9 (d, J = 11 Hz, ArCOCH3), 161.8 (d, J = 246 Hz,
ArCF), 167.6 (NCO); IR (CH2Cl2 evaporated film/cm⁻¹) 3306 (N-H), 3063, 2977,
2940 and 2840 (C-H), 1651 (C=O), 1634, 1585 and 1538 (Ar C=C); m/z (ES⁺) 726
(MNa⁺, 100%), 704 (MH⁺, 22%); HRMS for C22H20NO2F18S (MH⁺) found 704.0919,
expected 704.0922.
Following general procedure B: Treatment of the crude glyoxamide 20 (0.130 g, 0.455 mmol, 1 eq) with 1H,1H,2H,2H-perfluorodecane-1-thiol (0.09 mL, 0.319 mmol, 0.7 eq), TFAA (0.58 mL, 4.10 mmol, 9 eq) and BF$_3$·OEt$_2$ (0.28 mL, 2.28 mmol, 5 eq) and purification by FSPE removed all non-fluorous impurities. Subsequent column chromatography of the fluorous fraction on silica gel (10% EtOAc/petroleum ether) afforded acetamide 20 as white needles (0.084 g, 0.124 mmol, 39% over two steps).

δ$_H$ (300 MHz, CDCl$_3$) 2.26-2.45 (m, 2H, CH$_2$C$_8$F$_{17}$), 2.74-2.81 (m, 2H, CH$_2$CH$_2$C$_8$F$_{17}$), 2.88 (d, J = 4.9 Hz, 3H, NCH$_3$), 3.81 (s, 3H, CH$_3$O), 4.82 (s, 1H, CHS), 6.43-6.51 (br s, 1H, NH), 6.64 (dd, J = 12.0 Hz, 2.5 Hz, ArH), 7.40 (t, J = 8.7 Hz, 1H, ArH); δ$_C$ (75 MHz, CDCl$_3$) 23.0 (CH$_3$N), 26.8 (C$_8$F$_{17}$), 31.6 (t, J = 22 Hz, C$_8$F$_{17}$), 46.8 (d, J = 2 Hz, CHS), 55.6 (CH$_3$O), 101.7 (d, J = 26 Hz, ArCH), 110.7 (d, J = 3 Hz, ArCH), 115.7 (d, J = 16 Hz, ArC), 130.0 (d, J = 4 Hz, ArCH), 159.6 (ArCOCH$_3$), 160.7 (d, J = 246 Hz, ArCF), 169.2 (NCO); IR (CH$_2$Cl$_2$ evaporated film/cm$^{-1}$) 3253 (N-H), 3055 and 2988 (C-H), 1644 (C=O), 1577 and 1506 (Ar C=C); m/z (ES$^+$) 698 (MNa$^+$, 100%), 693 (M+18, 93%), 676 (MH$^+$, 43%); HRMS for C$_{20}$H$_{16}$NO$_2$F$_{18}$S (MH$^+$) found 676.0603, expected 676.0603; anal. calcd. for C$_{20}$H$_{15}$NO$_2$F$_{18}$: C (35.57%), H (2.24%), N (2.07%), found C (36.00%), H (2.26%), N (2.02%); mp (CHCl$_3$) 100.1-102.4 °C.

**rac-2-(4-Bromo-2-methoxy-phenyl)-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decylsulfanyl)-N-iso-propylacetamide 21**

Following general procedure B: Treatment of the crude glyoxamide 14 (0.609 g, 1.94 mmol, 1 eq) with 1H,1H,2H,2H-perfluorodecane-1-thiol (0.40 mL, 1.36 mmol, 0.7 eq), TFAA (2.47 mL, 17.5 mmol, 9 eq) and BF$_3$·OEt$_2$ (1.20 mL, 9.70 mmol, 5 eq) and purification by column chromatography on silica gel (20% EtOAc/petroleum ether) afforded acetamide 21 as a white amorphous solid (0.683 g, 0.894 mmol, 66% over two steps).
rac-2-(5-Bromo-2-methoxyphenyl)-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-heptadecafluoro-decylsulfanyl)-N-iso-propylacetamide 22

Following general procedure B: Treatment of the crude glyoxamide 15 (0.428 g, 1.36 mmol, 1 eq) with 1H,1H,2H,2H-perfluorodecane-1-thiol (0.28 mL, 0.954 mmol, 0.7 eq), TFAA (1.73 mL, 12.3 mmol, 9 eq) and BF₃·OEt₂ (0.84 mL, 6.82 mmol, 5 eq) and purification by column chromatography on silica gel (10% EtOAc/petroleum ether) afforded acetamide 22 as a white amorphous solid (0.464 g, 0.607 mmol, 64% over two steps).

δ_H (400 MHz, CDCl₃) 1.16 (d, J = 6.6 Hz, 3H, CH₃CH), 1.20 (d, J = 6.6 Hz, 3H, CH₃CH), 2.34-2.47 (m, 2H, CH₂C₈F₁₇), 2.70-2.83 (m, 2H, CH₂CH₂C₈F₁₇), 3.85 (s, 3H, CH₃O), 4.04-4.16 (m, 1H, CH(CH₃)₂), 4.86 (s, 1H, CHS), 6.35 (br d, J = 7.8 Hz, 1H, NH), 6.78 (d, J = 8.8 Hz, 1H, ArH), 7.39 (dd, J = 8.8 Hz, 2.5 Hz, 1H, ArH), 7.50 (d, J = 2.5 Hz, 1H, ArH); δ_C (75 MHz, CDCl₃) 22.5 (C₃H₃CH), 22.7 (C₃H₃CH), 33.2 (C₈H₁₇), 31.7 (t, J = 22 Hz, C₈H₁₇), 42.1 (C₈H₁₇), 47.8 (C₈H₁₇), 55.8 (CH₃O), 114.5 (ArC₈H₄), 124.3 (ArC₈H₄), 124.5 (ArC₈H₄), 129.9 (ArC₈H₄), 157.1 (ArCOCH₃), 167.9 (NCO); IR (CH₂Cl₂ evaporated film/cm⁻¹) 3297 (N-H), 2930 and 2972 (C-H), 1651 (C=O), 1587 and 16828 (Ar C=C); m/z (ES⁺) 788 (MNa⁺, 58%), 786 (MNa⁺, 51%), 766 (MH⁺, 23%), 764 (MH⁺, 21%), 627 (57%), 625 (100%); HRMS for C₂₂H₁₉NO₂F₁₇SBrNa (MNa⁺) found 785.9941, expected 785.9941.
Following general procedure C: Benzyl bromide (0.04 mL, 0.341 mmol, 5 eq) and sodium hydride (8 mg, 0.341 mmol, 5 eq) were heated at reflux with α-aryl acetamide 19 (48 mg, 0.068 mmol, 1 eq) for 18 hours. Purification of the crude product by column chromatography on silica gel (10% EtOAc/petroleum ether) gave 23 as a yellow oil (39 mg, 0.042 mmol, 71%).

δH (400 MHz, CDCl3) 0.98 (d, J = 6.6 Hz, 3H, CH3CH), 1.11 (d, J = 6.6 Hz, 3H, CH3CH), 2.09-2.35 (m, 2H, CH2C8F17), 2.63-2.80 (m, 2H, CH2CH2C8F17), 3.56 (s, 2H, CH2Ph), 3.81 (s, 3H, CH3O), 4.02-4.10 (m, 1H, CH(CH3)2), 5.97 (d, J = 8.1 Hz, 1H, NH), 6.61-6.69 (m, 2H, 2 × ArH), 6.95-6.98 (m, 2H, 2 × ArH), 7.14-7.20 (m, 4H, 4 × ArH); δC (75 MHz, CDCl3) 20.6 (CH2CH2C8F17), 22.2 (CH3CH), 22.5 (CH3CH), 31.1 (t, J = 22 Hz, CH2C8F17), 41.9 (CH2CH3CH2), 42.3 (CHN), 55.6 (CH3O), 59.4 (d, J = 3 Hz, CH3), 102.4 (d, J = 27 Hz, ArCH), 109.7 (d, J = 3 Hz, ArCH), 119.1 (d, J = 11 Hz, Ar), 126.9 (ArCH), 127.6 (2 × ArCH), 130.0 (d, J = 5 Hz, ArCH), 130.9 (2 × ArCH), 135.7 (Ar), 160.8 (d, J = 11 Hz, ArCOCH3), 160.7 (d, J = 249 Hz, ArCF), 169.7 (NCO); IR (CH2Cl2 evaporated film/cm⁻¹) 3367 (N-H), 3064, 3032, 2974, 2939, 2877 and 2843 (C-H), 1668 (C=O), 1622, 1580 and 1505 (Ar C=C); m/z (ES⁺) 991 (49%), 816 (MNa⁺, 100%); HRMS for C29H26NO2F18S (MH⁺) found 794.1393, expected 794.1391.
2-(2-Fluoro-4-methoxy-phenyl)-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decylsulfanyl)-pent-4-enoic acid isopropylamide 24

Following general procedure C: Allyl bromide (0.11 mL, 1.21 mmol, 5 eq) and sodium hydride (48 mg, 1.21 mmol, 5 eq) were heated at reflux with α-aryl acetamide 19 (0.17 g, 0.242 mmol, 1 eq) for 18 hours. Purification of the crude product by FSPE gave 24 as a yellow oil (0.1526 g, 0.177 mmol, 73 %).

δ_H (400 MHz, CDCl_3) 1.15 (d, J = 2.3 Hz, 3H, CHCH_3), 1.14 (d, J = 2.3 Hz, 3H, CHCH_3), 2.16 - 2.34 (m, 2H, CH_2CF_2), 2.65 - 2.79 (m, 2H, SCH_2), 3.01 (t, J = 6.4 Hz, 2H, CH_2CH=CH_2), 3.83 (s, 3H, OCH_3), 4.06 - 4.20 (m, 1H, CH(CH_3)_2), 5.03 - 5.11 (m, 2H, CH_2=CH), 5.59 - 5.72 (m, 1H, CH_2=CH), 5.92 (d, J = 8.1 Hz, 1H, NH), 6.65 (dd, J = 13.4, 2.5 Hz, 1H, ArCH), 6.73 (dd, J = 8.7, 2.6 Hz, 1H, ArCH), 7.41 (t, J = 9.0 Hz, 1H, ArCH); δ_C (101 MHz, CDCl_3) 20.2 (SCH_2), 22.4 (CHCH_3), 22.5 (CHCH_3), 31.1 (t, J = 22 Hz, CH_2CF_2), 40.7 (CH_2CH=CH_2), 42.0 (CH(CH_3)_2), 55.6 (OCH_3), 57.8 (SC), 102.7 (ArCH), 109.6 (ArCH), 118.8 (ArC), 119.0 (CH=CH_2), 129.5 (ArCH), 132.6 (CH=CH_2), 157.6 (t, J = 249 Hz, ArCF), 160.8 (ArC), 170.1 (C=O); IR (CHCl_3 evaporated film/cm\(^{-1}\)) 3306 (NH), 2928 (C-H), 1669 (C=O), 1623 (-C=C-), 1507 (-C=C-); m/z (ES\(^{+}\)) 766 (MNa\(^{+}\), 100%), 264 (80%); HRMS for C\(_{25}\)H\(_{23}\)NO\(_2\)F\(_{18}\)S (MNa\(^{+}\)) found 766.1066, expected 766.1054.

rac-2-(4-Bromo-2-methoxy-phenyl)-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decylsulfanyl)-2-(2-naphthylmethyl)-N-iso-propylacetamide 25

rac-2-(4-Bromo-2-methoxy-phenyl)-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decylsulfanyl)-2-(2-naphthylmethyl)-N-iso-propylacetamide 25
Following general procedure C: 2-Naphthyl bromide (9 mg, 0.406 mmol, 5 eq) and sodium hydride (10 mg, 0.406 mmol, 5 eq) were heated at reflux with α-aryl acetamide 21 (62 mg, 0.812 mmol, 1 eq) for 48 hours. FSPE removed non-fluorous impurities then purification by column chromatography on silica gel (15% EtOAc/petroleum ether) gave 25 as a yellow oil (33 mg, 0.037 mmol, 44%).

δ_H (400 MHz, CDCl_3) 0.98 (d, J = 6.6 Hz, 3H, CH_3CH), 1.09 (d, J = 6.6 Hz, 3H, CH_3CH), 2.23-2.42 (m, 2H, CH_2C_8F_17), 2.75-2.82 (m, 1H, CHHCH_2C_8F_17), 2.85-2.92 (m, 1H, CHHCH_2C_8F_17), 3.60 (d, J = 14.0 Hz, 1H, CHH(Np)), 3.79 (d, J = 14.0 Hz, 1H, CH(Np)), 3.84 (s, 3H, CH_3O), 4.02-4.09 (m, 1H, CH(CH_3)_2), 5.48 (d, J = 7.8 Hz, 1H, NH), 6.84 (dd, J = 8.6 Hz, 1.8 Hz, 1H, ArH), 6.97 (dd, J = 8.3 Hz, 1.8 Hz, 1H, ArH), 7.02 (d, J = 8.3 Hz, 1H, ArH), 7.10 (d, J = 1.8 Hz, 1H, ArH), 7.28 (s, 1H, ArH), 7.39-7.44 (m, 2H, 2 × ArH), 7.56 (d, J = 8.6 Hz, 1H, ArH), 7.64-7.68 (m, 1H, ArH), 7.73-7.76 (m, 1H, ArH); δ_C (75 MHz, CDCl_3) 20.6 (CH_2CH_2C_8F_17), 22.3 (CH_3CH), 22.6 (CH_3CH), 31.1 (t, J = 21 Hz, CH_2C_8F_17), 40.5 (CH_2(Np)), 41.8 (CH(CH_3)_2), 55.6 (CH_3O), 59.8 (CH_2(Np)), 114.9 (ArCH), 123.0 (ArC), 123.7 (ArCH), 125.5 (ArCH), 125.7 (ArCH), 126.7 (ArCH and ArC), 127.5 (ArCH), 127.7 (ArCH), 129.0 (ArCH), 129.7 (ArCH), 130.8 (ArCH), 132.2 (ArC), 132.8 (ArC), 133.7 (ArC), 157.2 (ArCOCH_3), 170.3 (NCO); IR (CHCl_3 evaporated film/cm^-1) 3399 (NH), 1667 (C=O), 1651 (C=C); m/z (ES^+) 906 (^{81}Br, MH^+, 63%), 904 (^{79}Br, MH^+, 100%), 516 (21%); HRMS for C_{33}H_{28}NO_2F_17S^{79}Br (MH^+) found 904.0749, expected 904.0747.

2-Benzyl-2-(4-Bromo-2-methoxy-phenyl)-2-(3,3,4,4,5,5,6,6,6,7,7,7,8,8,8,9,9,10,10,10-heptadecafluoro-decylsulfanyl)-pent-4-enoic acid isopropylacetamide 26

Following general procedure C: Allyl bromide (0.09 mL, 0.78 mmol, 5 eq) and sodium hydride (30 mg, 0.78 mmol, 5 eq) were heated at reflux with α-aryl acetamide 21 (0.109 g, 0.156 mmol, 1 eq) for 18 hours. Purification of the crude product by FSPE gave 26 as a yellow oil (67 mg, 0.056 mmol, 51%).
δ_H (400 MHz, CDCl_3) 0.94 (d, J = 6.8 Hz, 3H, CHCH_3), 1.01 (d, J = 6.6 Hz, 3H, CHCH_3), 2.13 - 2.32 (m, 2H, CH_2CF_2), 2.62 - 2.82 (m, 2H, SCH_2), 3.35 (d, J = 13.9 Hz, 1H, CHHPh), 3.55 (d, J = 13.9 Hz, 1H, CHHPh), 3.75 (s, 3H, OCH_3), 3.91 - 4.02 (m, 1H, CH(CH_3)_2), 5.38 (d, J = 7.8 Hz, 1H, NH), 6.68 - 6.73 (m, 2H, CH = CH), 6.89 - 6.97 (m, 2H, CH = CH), 6.99 (d, J = 1.5 Hz, 1H, ArCH), 7.00 - 7.10 (m, 3H, CH = CH); δ_C (101 MHz, CDCl_3) 20.5 (SCH_2), 22.3 (CHCH_3), 22.7 (CHCH_3), 31.0 (t, J = 22 Hz, CH_2CF_2), 40.2 (CH_2Ph), 41.8 (CH(CH_3)_2), 55.6 (OCH_3), 59.6 (SC), 114.9 (ArCH), 123.0 (ArCH), 123.7 (ArC), 126.6 (ArC), 127.4 (ArCH), 130.7 (ArCH), 130.8 (ArCH), 136.1 (ArC), 157.1 (ArCH), 170.3 (C=O); IR (CHCl_3 evaporated film/cm\(^{-1}\)) 3377 (NH), 2971 (C-H), 1667 (C=O); m/z (ES\(^+\)) 878 (\(^{81}\)Br, 60%), 876 (\(^{79}\)Br, MNa\(^+\), 100%), 856 (\(^{81}\)Br, MH\(^+\), 18%), 854 (\(^{79}\)Br, MH\(^+\), 20%); HRMS for C_{29}H_{25}NO_2F_17S_{79}Br (MNa\(^+\)) found 876.0416, expected 876.0402.

2-(4-Bromo-2-methoxy-phenyl)-pent-4-enoic acid isopropylamide 27

Following general procedure C: Allyl bromide (0.04 mL, 0.454 mmol, 5 eq) and sodium hydride (18 mg, 0.454 mmol, 5 eq) were heated at reflux with \(\alpha\)-aryl acetamide 21 (68 mg, 0.091 mmol, 1 eq) for 18 hours and purification of the crude product by FSPE gave 27 as a yellow oil (37 mg, 0.046 mmol, 51%).

δ_H (400 MHz, CDCl_3) 1.00 (d, J = 6.6 Hz, 3H, CHCH_3), 1.02 (d, J = 6.6 Hz, 3H, CHCH_3), 2.11 - 2.30 (m, 2H, CH_2CF_2), 2.63 - 2.71 (m, 2H, SCH_2), 2.81 - 2.90 (m, 1H, CHCH=CH_2), 2.92 - 3.02 (m, 1H, CHCH=CH=CH_2), 3.71 (s, 3H, OCH_3), 3.94 - 4.01 (m, 1H, CH(CH_3)_2), 4.88 - 4.92 (m, 2H, CH=CH_2), 5.35 (d, J = 8.1 Hz, 1H, NH), 5.38 - 5.51 (m, 1H, CH=CHH), 6.95 (d, J = 2.0 Hz, 1H, ArCH), 7.07 (dd, J = 8.3, 2.0 Hz, 1H, ArCH), 7.30 (d, J = 8.3 Hz, 1H, ArCH); δ_C (101 MHz, CDCl_3) 21.1 (SCH_2), 22.5 (CHCH_3), 22.6 (CHCH_3), 31.1 (CH_2CF_2), 38.6 (CH_2CH=CH_2), 41.8 (CH(CH_3)_2), 55.6 (OCH_3), 58.2 (SC), 115.1 (ArCH), 118.3 (CH=CH_2), 123.0 (ArC), 123.7 (ArCH), 126.8 (ArC), 130.2 (ArCH), 133.4 (CH=CH_2), 157.1 (ArC), 170.5 (C=O); IR (CHCl_3 evaporated film/cm\(^{-1}\)) 3378 (NH), 2971 (C-H), 1671 (C=O); m/z (ES\(^+\)) 828.
(\textsuperscript{81}Br, M\textsubscript{Na}+, 62%), 826 (\textsuperscript{79}Br, M\textsubscript{Na}+, 100%) HRMS for C\textsubscript{25}H\textsubscript{24}NO\textsubscript{2}\textsuperscript{79}BrF\textsubscript{17} (MH\textsuperscript{+})

found 804.0435, expected 804.0440.

\textit{rac-2-Benzyl-2-(3-bromo-6-methoxy-phenyl)-2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decylsulfanyl)-N-iso-

propylacetamide 28}

Following general procedure C: Benzyl bromide (0.04 mL, 0.332 mmol, 5 eq) and sodium hydride (13 mg, 0.332 mmol, 5 eq) were heated at reflux with \(\alpha\)-aryl acetamide 22 (0.05 g, 0.0067 mmol, 1 eq) for 18 hours. Purification of the crude product by FSPE gave 28 as a yellow oil (34.4 mg, 0.0041 mmol, 61%).

\(\delta\textsubscript{H} (400 MHz, CDCl\textsubscript{3})\) 0.99 (d, \(J = 6.6\) Hz, 3H, CH\textsubscript{3}CH), 1.08 (d, \(J = 6.6\) Hz, 3H, CH\textsubscript{3}CH), 2.20-2.37 (m, 2H, CH\textsubscript{2}C\textsubscript{8}F\textsubscript{17}), 2.73-2.86 (m, 2H, CH\textsubscript{2}CH\textsubscript{2}C\textsubscript{8}F\textsubscript{17}), 3.44 (d, \(J = 13.9\) Hz, 1H, CHHPh), 3.63 (d, \(J = 13.9\) Hz, 1H, CHHPh), 3.79 (s, 3H, CH\textsubscript{3}O), 3.97-4.06 (m, 1H, CH(CH\textsubscript{3})\textsubscript{2}), 5.58 (d, \(J = 7.8\) Hz, 1H, NH), 6.80-6.85 (m, 3H, 3 \times ArH)), 7.11-7.20 (m, 3H, 3 \times ArH)), 7.31 (d, \(J = 2.5\) Hz, 1H, ArH), 7.42 (dd, \(J = 8.6\) Hz, 2.5 Hz, 1H, ArH); \(\delta\textsubscript{C} (75 MHz, CDCl\textsubscript{3})\) 20.6 (CH\textsubscript{2}CH\textsubscript{2}C\textsubscript{8}F\textsubscript{17}), 22.3 (CH\textsubscript{3}CH), 22.6 (CH\textsubscript{3}CH), 31.2 (t, \(J = 22\) Hz, CH\textsubscript{2}C\textsubscript{8}F\textsubscript{17}), 40.9 (PhCH\textsubscript{2}), 41.7 (CH(CH\textsubscript{3})\textsubscript{2}), 55.5 (CH\textsubscript{2}O), 59.5 (CS) 113.1 (2 \times ArCH), 113.2 (ArC), 126.8 (ArCH), 127.4 (2 \times ArCH), 130.0 (ArC), 130.8 (ArCH), 132.2 (2 \times ArCH), 135.9 (ArC), 155.8 (ArCOCH\textsubscript{3}), 170.0 (NCO); IR (CH\textsubscript{2}Cl\textsubscript{2} evaporated film/cm\textsuperscript{-1}) 3376 (N-H), 3064, 3032, 2973, 2939 and 2845 (C-H), 1653 (C=O), 1591, 1515 and 1505 (Ar C=C); \(m/z\) (ES\textsuperscript{+}) 878 (\textsuperscript{81}Br, M\textsubscript{Na}+, 100%), 876 (\textsuperscript{79}Br, M\textsubscript{Na}+, 50%), 487 (13%); HRMS for C\textsubscript{29}H\textsubscript{24}NO\textsubscript{2}\textsuperscript{79}BrF\textsubscript{17}S (MH\textsuperscript{+}) found 852.0556, expected 852.0445.

\textit{2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-decylsulfanyl)-N-isopropyl-2-(2-methoxy-4-trimethylsilanylethynyl-phenyl)acetamide 29}

2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-Heptadecafluoro-decylsulfanyl)-N-isopropyl-2-(2-methoxy-4-trimethylsilanylethynyl-phenyl)acetamide 29
To a solution of α-aryl acetamide 21 (0.104 g, 0.138 mmol, 1 eq), trimethylsilylacetylene (0.19 mL, 1.38 mmol, 10 eq) and copper iodide (0.011 g, 0.055, 0.4 eq) in toluene:NEt$_3$ (0.3 mL, 2:1) was added Pd(PPh$_3$)$_4$ (0.032 g, 0.028 mmol, 0.2 eq) and the reaction mixture stirred at 110 °C for 18 h. The resulting reaction mixture was purified using FSPE to give 29 as brown solid (0.107 g, 1.38 mmol, 100%).

δ$_H$ (400 MHz, CDCl$_3$) 0.16 (s, 9 H, 3 × SiCH$_3$), 1.03 (d, $J = 6.6$ Hz, 3H, CHCH$_3$), 1.07 (d, $J = 6.6$ Hz, 3H, CHCH$_3$), 2.31 (m, 3H, CH$_2$CF$_2$), 2.53 - 2.74 (m, 3H, SCH$_2$), 3.77 (s, 3H, OCH$_3$), 3.94 – 4.03 (m, 1H, CH(CH$_3$)$_2$), 4.82 (s, 1H, SCH), 6.07 (d, $J = 7.8$ Hz, 1H, NH), 6.89 (d, $J = 1.5$ Hz, 1H, ArCH), 7.00 (dd, $J = 7.8$, 1.5 Hz, 1H, ArCH), 7.17 (d, $J = 7.8$ Hz, 1H, ArCH); δ$_C$ (75 MHz, CDCl$_3$) 22.6 (CHCH$_3$), 22.7 (CHCH$_3$), 23.1 (SCH$_2$), 31.9 (t, 22 Hz, CH$_2$CF$_2$), 42.1 (CH(CH$_3$)$_2$), 48.0 (SCH), 55.8 (OCH$_3$), 95.1 (C≡CSi(CH$_3$)$_3$), 104.6 (ArC=C), 114.2 (ArCH), 124.3 (ArC), 125.2 (ArCH), 128.8 (ArCH), 129.9 (ArC), 156.3 (ArC), 168.2 (C=O); IR (CHCl$_3$ evaporated film/cm$^{-1}$) 3297 (NH), 2970 (C-H), 2159 (-C≡C-), 1653 (C=O); m/z (ES$^+$) 804 (MNa$^+$, 40%), 782 (MH$^+$, 10%), 462 (10%), 353 (55%), 293 (100%) HRMS for C$_{27}$H$_{29}$NO$_2$F$_{17}$Si (MH$^+$) found 782.1417, expected 782.1411; mp (CHCl$_3$) 65.2-66.0 °C.

2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-Heptadecafluoro-decylsulfanyl)-N-isopropyl-2-(2-methoxyl-5-(4-methylphenyl)phenyl)acetamide 30
Following general procedure E: p-Tolyl boronic acid (0.09 g, 0.66 mmol, 4 eq), α-aryl acetamide 22 (0.125 g, 0.166 mmol, 1 eq), aqueous Na$_2$CO$_3$ (0.58 mL, 2 M, 1.16 mmol, 7 eq) and Pd(PPh$_3$)$_4$ (38 mg, 0.033 mmol, 0.2 eq) were stirred in toluene (2 mL) and ethanol (1 mL) at 90 °C for 18 hours. The resulting reaction mixture was purified using FSPE to give 30 as a white solid (0.057 g, 0.101 mmol, 61%).

δ$_H$ (500 MHz, CDCl$_3$) 1.08 (d, $J = 6.6$ Hz, 3H, CH$_3$CH), 1.12 (d, $J = 6.6$ Hz, 3H, CH$_3$CH), 2.27 - 2.42 (m, 5H, SCH$_2$ and ArCH$_3$), 2.64 - 2.78 (m, 2H, C$_8$F$_{17}$CH$_2$), 4.00 - 4.09 (m, 1H, CH$_2$(CH$_3$)$_2$), 4.91 (s, 3H, ArOCH$_3$), 6.29 (d, $J = 8.2$ Hz, 1H, NH), 6.89 (d, $J = 8.5$ Hz, 1H, ArH), 7.15 (d, $J = 7.9$ Hz, 2H, 2 × ArH), 7.35 (d, $J = 7.9$ Hz, 2H, 2 × ArH), 7.43 (dd, $J = 8.5, 1.9$ Hz, 1H, ArH), 7.53 (d, $J = 1.9$ Hz, 1H, ArH); δ$_C$ (125 MHz, CDCl$_3$) 21.1 (ArC$_H$$_3$), 22.5 (CHC$_H$$_3$), 22.7 (CH$_2$CH$_3$), 23.3 (SCH$_2$), 31.8 (t, $J = 22$ Hz, CH$_2$CF$_2$), 42.0 (CH(CH$_3$)$_2$), 48.4 (SCH), 56.6 (OCH$_3$), 111.3 (ArCH), 125.5 (ArC), 126.6 (2 × ArCH), 127.4 (ArCH), 127.8 (ArCH), 129.5 (2 × ArCH), 134.3 (ArC), 136.7 (ArC), 137.4 (ArC), 155.9 (ArC), 168.5 (C=O); IR (CHCl$_3$ evaporated film/cm$^{-1}$) 3322 (NH), 2932 (C-H), 1653 (C=O), 1647 (C=C); m/z (ES$^+$) 798 (MNa$^+$, 100%), 797 (80%), 774 (10%); HRMS for C$_{29}$H$_{25}$NO$_2$F$_{17}$S (M - H) found 774.1334, expected 774.1340; mp (Hexane) 107.8-109.1 °C

2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-Heptadecafluoro-decylsulfanyl)-N-isopropyl-2-(2-methoxy-5-thiophen-2'-yl-phenyl)acetamide 31
OCH₃), 4.05 - 4.29 (m, 1H, CH(CH₃)₂), 4.97 (s, 1H, C(O)CH), 6.44 (d, J = 7.9 Hz, 1H, NH), 6.94 (d, J = 8.5 Hz, 1H, ArCH), 7.07 (dd, J = 5.0, 3.5 Hz, 1H, ArCH), 7.22 (d, J = 3.5 Hz, 1H, ArCH), 7.25 (d, J = 5.5 Hz, 1H, ArCH), 7.55 (dd, J = 8.5, 2.5 Hz, 1H, ArCH), 7.63 (d, J = 2.5 Hz, 1H, ArCH); δC (125 MHz, CDCl₃) 22.5 (CHC₃H), 22.8 (CHC₃H), 23.6 (SC₂H), 31.5 (t, J = 22 Hz, CH₂CF₂), 42.0 (CHCH), 48.3 (SCH), 55.8 (OCH₃), 111.4 (ArCH), 122.6 (ArCH), 124.3 (ArCH), 125.8 (ArC), 126.5 (ArCH), 127.1 (ArCH), 127.9 (ArC), 128.0 (ArCH), 143.7 (ArC), 156.1 (ArC), 168.3 (C=O); IR (CHCl₃ evaporated film/cm⁻¹) 3311 (NH), 2929 (C-H), 1653 (C=O), 1212 (C-N); m/z (ES⁺) 790 (MNa⁺, 30%), 768 (MH⁺, 100%), 443 (10%); HRMS for C₂₆H₂₃NO₂F₁₇S₂ (MH⁺) found 768.0882, expected 768.0893; mp (CHCl₃) 116.4-118.9 °C.

2-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-Heptadecafluoro-decylsulfanyl)-N-isopropyl-2-(2-methoxy-4-thiophen-2'-yl-phenyl)acetamide 32

Following general procedure E: 2-Thienylboronic acid (0.15 g, 1.19 mmol, 4 eq), α-aryl acetamide 21 (0.224 g, 0.3 mmol, 1 eq), aqueous Na₂CO₃ (1.04 mL, 2 M, 2.09 mmol, 7 eq) and Pd(PPh₃)₄ (69 mg, 0.06 mmol, 0.2 eq) were stirred in toluene (4 mL) and ethanol (2 mL) at 90 °C for 18 hours. The resulting reaction mixture was purified using FSPE to give 32 as a yellow solid (0.145 g, 0.75 mmol, 63%).

δH (400 MHz, CDCl₃) 1.08 (d, J = 6.6 Hz, 3H, CHCH₃), 1.11 (d, J = 6.6 Hz, 3H, CHCH₃), 2.22 - 2.45 (m, 2H, SCh₂), 2.61 - 2.81 (m, 2H, CH₂CF₂), 3.85 (s, 3H, OCH₃), 3.95 - 4.11 (m, 1H, CH(CH₃)₂), 4.87 (s, 1H, SCH), 6.22 (d, J = 8.1 Hz, 1H, NH), 7.00 - 7.04 (m, 2H, 2 × ArCH), 7.15 (dd, J = 8.1, 1.8 Hz, 1H, ArCH), 7.21 - 7.25 (m, 2H, 2 × ArCH), 7.32 (d, J = 8.1 Hz, 1H, ArCH); δC (101 MHz, CDCl₃) 22.5 (CHCH₃), 22.7 (CHCH₃), 23.1 (SCh₂), 31.8 (CH₂CF₂), 42.0 (CH(CH₃)₂), 47.9 (SCH), 55.6 (OCH₃), 108.5 (ArCH), 119.0 (ArCH), 123.6 (ArCH), 124.4 (ArC), 125.3 (ArCH), 128.1 (ArCH), 129.2 (ArCH), 135.8 (ArC), 143.8 (ArC), 156.8 (ArC), 168.3 (C=O); IR (CHCl₃ evaporated film/cm⁻¹) 3292 (NH), 2973 (C-H), 1682 (C=O); m/z
(ES⁺) 806 (100%), 790 (MNa⁺, 20%) HRMS for C₂₆H₂₂NO₂NaS₂F₁₇ (MNa⁺) found 790.0710, expected 790.0718; mp (CHCl₃) 117.4-118.3 °C.

2-(2-Fluoro-6-methoxy-phenyl)-N-iso-propylacetamide 33

Following general procedure D: Acetamide 8 (0.153 g, 0.218 mmol, 1 eq) and SmI₂ (4.79 mL, 0.479 mmol, 2.2 eq) were stirred at room temperature for 48 hours. Purification by FSPE afforded 33 as a brown oil (30 mg, 0.133 mmol, 61%). Starting material (6%) was also recovered.

δH (400 MHz, CDCl₃) 1.08 (d, J = 6.6 Hz, 6H, 2 × CH₃CH), 3.56 (d, J = 1.5 Hz, 2H, ArCH₂), 3.86 (s, 3H, CH₃O), 4.00-4.11 (m, 1H, CH(CH₃)₂), 5.30-5.37 (br s, 1H, NH), 6.70-6.76 (m, 2H, 2 × ArH), 7.23 (td, J = 8.3 Hz, 6.8 Hz, 1H, ArH); δC (100 MHz, CDCl₃) 22.6 (2 × C₂H₃CH), 30.9 (6, J = 3 Hz, ArCH₂), 41.3 (CH(CH₃)₂), 106.3 (d, J = 3 Hz, ArCH), 108.0 (ArCH), 111.4 (ArC), 128.8 (d, J = 11 Hz, ArCH), 158.6 (ArC), 161.6 (d, J = 244 Hz), IR (CHCl₃ evaporated film/cm⁻¹) 3292 (N-H), 2969 and 2932 (C-H), 1651 (C=O), 1617, 1587 and 1545 (Ar C=C); m/z (ES⁺) 248 (MNa⁺, 62%), 226 (MH⁺, 100%), 173 (19%); HRMS for C₁₂H₁₇NO₂F (MH⁺) found 226.1232, expected 226.1238.

2-(2,6-Dimethyl-phenyl)-N-iso-propylacetamide 34

Following general procedure D: Acetamide 18 (150 mg, 0.220 mmol, 1 eq) and SmI₂ (4.83 mL, 0.483 mmol, 2.2 eq) were stirred at room temperature for 30 hours. Purification by FSPE afforded 34 as a yellow amorphous solid (39 mg, 0.190 mmol, 87%).

δH (400 MHz, CDCl₃) 1.02 (d, J = 6.6 Hz, 6H, 2 × CH₃CH), 2.28 (s, 6H, 2 × ArCH₃), 3.60 (s, 2H, ArCH₂), 4.03-4.12 (m, 1H, CH(CH₃)₂), 5.01-5.11 (br s, 1H, NH), 7.06-7.15 (m, 3H, 3 × ArH); δC (100 MHz, CDCl₃) 20.1 (2 × ArCH₃), 22.5 (2 × CH₃CH),
Following general procedure D: Acetamide 19 (40 mg, 0.057 mmol, 1 eq) and SmI₂ (1.25 mL, 0.125 mmol, 2.2 eq) were stirred at room temperature for 24 hours. SmI₂ (0.57 mL, 0.057 mmol, 1 eq) was added and the reaction mixture stirred at room temperature for 6 hours. Purification using FSPE afforded 35 as a yellow waxy solid (8 mg, 0.036 mmol, 63%, 77% based on recovered starting material).

δ_H (400 MHz, CDCl₃, 3:2 rotamer ratio) 1.06 (d, J = 6.6 Hz, minor, 3H, CH₃CH), 1.10 (d, J = 6.6 Hz, major, 6H, 2 × CH₃CH), 1.18 (d, J = 6.6 Hz, minor, 3H, CH₃CH), 3.48 (s, major, 2H, ArCH₂ and minor, 2H, ArCH₂), 3.79 (s, minor, 3H, CH₃O), 3.80 (s, major, 3H, CH₃O), 4.02-4.11 (m, major, 1H, CH(CH₃)₂ and minor, 1H, CH(CH₃)₂), 5.20-5.29 (br s, major, 1H, NH), 5.47 (br d, minor, 1H, NH), 6.61-6.71 (m, major, 2H, 2 × ArH and m, minor, 2H, 2 × ArH), 7.19 (apparent t, J = 8.8 Hz, major, 1H, ArH), 7.19 (apparent t, J = 8.8 Hz, minor, 1H, ArH); δ_C (100 MHz, CDCl₃, major rotamer only) 22.2 (CH₃CH), 22.7 (CH₃CH), 36.5 (ArCH₂), 41.5 (CH(CH₃)₂), 55.6 (CH₃O), 101.08 (ArCH), 110.3 (ArCH), 114.0 (ArC), 131.9 (ArC), 160.1 (ArCOCH₃), 161.5 (d, J = 230 Hz, ArCF), 173.1 (NCO); IR (CH₂Cl₂ evaporated film/cm⁻¹) 3289 (N-H), 3080, 2973 and 2935 (C-H), 1627 (C=O), 1586, 1549 and 1510 (Ar C=C); m/z (ES⁺) 228 (MNa⁺, 62%), 226 (MH⁺, 100%), 173 (19%); HRMS for C₁₃H₂₀NO (MH⁺) found 206.1538, expected 206.1545.

(4-Bromo-2-methoxy-phenyl)-N-iso-propylacetamide 36

δ_H (400 MHz, CDCl₃, 3:2 rotamer ratio) 1.06 (d, J = 6.6 Hz, minor, 3H, CH₃CH), 1.10 (d, J = 6.6 Hz, major, 6H, 2 × CH₃CH), 1.18 (d, J = 6.6 Hz, minor, 3H, CH₃CH), 3.48 (s, major, 2H, ArCH₂ and minor, 2H, ArCH₂), 3.79 (s, minor, 3H, CH₃O), 3.80 (s, major, 3H, CH₃O), 4.02-4.11 (m, major, 1H, CH(CH₃)₂ and minor, 1H, CH(CH₃)₂), 5.20-5.29 (br s, major, 1H, NH), 5.47 (br d, minor, 1H, NH), 6.61-6.71 (m, major, 2H, 2 × ArH and m, minor, 2H, 2 × ArH), 7.19 (apparent t, J = 8.8 Hz, major, 1H, ArH), 7.19 (apparent t, J = 8.8 Hz, minor, 1H, ArH); δ_C (100 MHz, CDCl₃, major rotamer only) 22.2 (CH₃CH), 22.7 (CH₃CH), 36.5 (ArCH₂), 41.5 (CH(CH₃)₂), 55.6 (CH₃O), 101.08 (ArCH), 110.3 (ArCH), 114.0 (ArC), 131.9 (ArC), 160.1 (ArCOCH₃), 161.5 (d, J = 230 Hz, ArCF), 173.1 (NCO); IR (CH₂Cl₂ evaporated film/cm⁻¹) 3289 (N-H), 3080, 2973 and 2935 (C-H), 1627 (C=O), 1586, 1549 and 1510 (Ar C=C); m/z (ES⁺) 228 (MNa⁺, 62%), 226 (MH⁺, 100%), 173 (19%); HRMS for C₁₃H₂₀NO₂F (MH⁺) found 226.1232, expected 226.1238.
Following general procedure D: Acetamide 21 (80 mg, 0.105 mmol, 1 eq) and SmI$_2$ (2.30 mL, 0.230 mmol, 2.2 eq) were stirred at room temperature for 20 hours. Purification by FSPE afforded 36 as a white amorphous solid (23 mg, 0.080 mmol, 77%).

$\delta$$_H$ (400 MHz, CDCl$_3$) 1.07 (d, $J = 6.6$ Hz, 6H, $2 \times$ CH$_3$CH), 3.45 (s, 2H, CH$_2$Ar), 3.84 (s, 3H, CH$_3$O), 4.03 (m, 1H, CH(CH$_3$)$_2$), 5.31-5.44 (br s, 1H, NH), 7.03 (s, 1H, ArH), 7.09-7.11 (m, 2H, $2 \times$ ArH); $\delta$$_C$ (100 MHz, CDCl$_3$), 22.7 ($2 \times$ CH$_3$CH), 38.5 (CH$_2$Ar), 55.7 (CH$_3$O), 114.3 (ArCH), 121.8 (ArC), 123.0 (ArC), 124.0 (ArCH), 132.3 (ArCH), 157.8 (ArCOCH$_3$), 169.6 (NCO); IR (CH$_2$Cl$_2$ evaporated film/cm$^{-1}$) 3306 (N-H), 2973 and 2931 (C-H), 1644 (C=O), 1595 and 1579 (Ar C=C); m/z (ES$^+$) 310 ($^{81}$Br, MNa$^+$, 49%), 308 ($^{79}$Br, MNa$^+$, 53%), 288 ($^{81}$Br, MH$^+$, 71%), 286 ($^{79}$Br, MH$^+$, 76%); HRMS for C$_{12}$H$_{17}$NO$_2$ (MH$^+$) found 286.0445, expected 286.0437.

2-(5-Bromo-2-methoxy-phenyl)-N-iso-propylacetamide 37

Following general procedure F: Acetamide 28 (0.150 g, 0.196 mmol, 1 eq) and SmI$_2$ (4.32 mL, 0.432 mmol, 2.2 eq) were stirred at room temperature for 24 hours. SmI$_2$ (0.78 mL, 0.078 mmol, 0.4 eq) was added and the reaction mixture stirred at room temperature for 24 hours. Purification by FSPE afforded 37 as a cream amorphous solid (39 mg, 0.136 mmol, 69%). Starting material (10%) was also recovered.

$\delta$$_H$ (400 MHz, CDCl$_3$, 12:1 rotamer ratio) 1.03 (d, $J = 6.6$ Hz, minor, 3H, CH$_3$CH), 1.08 (d, $J = 6.6$ Hz, major, 6H, $2 \times$ CH$_3$CH), 1.16 (d, $J = 6.6$ Hz, minor, 3H, CH$_3$CH), 3.45 (s, major, 2H, ArCH$_2$ and minor, 2H, ArCH$_2$), 3.82 (s, major, 3H, CH$_3$O), 3.83 (s, minor, 3H, CH$_3$O), 3.97-4.09 (m, major, 1H, CH(CH$_3$)$_2$ and minor, 1H, CH(CH$_3$)$_2$), 5.42-5.51 (br s, major, 1H, NH), 5.59-5.64 (br d, $J = 7.6$ Hz, minor, 1H, NH), 6.75-6.78 (m, major, 1H, ArH and minor, 1H, ArH), 7.33-7.38 (m, major, 2H, 2
× ArH and minor, 2H, 2 × ArH); δC (100 MHz, CDCl₃, major rotamer only) 22.7 (2 × CH₃CH), 38.7 (ArCH₂), 41.4 (CH(CH₃)₂), 55.6 (CH₃O), 112.3 (ArCH), 113.1 (ArC), 126.2 (ArC), 131.3 (ArCH), 133.8 (ArCH), 156.4 (ArCOCH₃), 169.5 (NCO); IR (CH₂Cl₂ evaporated film/cm⁻¹) 3287 (N-H), 2972 and 2936 (C-H), 1644 (C=O), 1593 and 1551 (Ar C=C); m/z (ES⁺) 310 (⁸¹Br, MNa⁺, 89%), 308 (⁷⁹Br, MNa⁺, 91%), 288 (⁸¹Br, MH⁺, 98%), 286 (⁷⁹Br, MH⁺, 100%), 179 (11%), 101 (20%); HRMS for C₁₂H₁₇NO₂⁷⁹Br (MH⁺) found 286.0425, expected 286.0437.

**rac-2-Benzyl-2-(4-bromo-2-methoxy-phenyl)-N-*iso*-propylacetamide 38**

![Chemical Structure](image)

Following general procedure F: Acetamide 26 (0.150 g, 0.196 mmol, 1 eq) and SmI₂ (7.2 mL, 0.712 mmol, 4 eq) were stirred at room temperature for 24 hours. Purification by FSPE afforded 38 as a cream solid (48 mg, 0.133 mmol, 68%).

δH (400 MHz, CDCl₃) 0.98 (d, J = 4.3 Hz, 3H, CHCH₃), 1.00 (d, J = 4.3 Hz, 3H, CHCH₃), 2.91 (dd, J = 13.6, 6.3 Hz, 1H, C(O)CH), 3.44 - 3.53 (m, 1H, PhCHH), 3.80 (s, 3H, OCH₃), 3.91 - 4.03 (m, 2H, CH(CH₃)₂ and PhCHH), 5.27 (d, J = 7.8 Hz, 1H, NH), 6.99 (d, J = 1.8 Hz, 1H, ArCH), 7.11 (dd, J = 8.2, 1.9 Hz, 1H, ArCH), 7.15 - 7.21 (m, 3H, 3 × ArCH), 7.22 - 7.28 (m, 2H, 2 × ArCH), 7.31 (d, J = 8.3 Hz, 1H, ArCH); δC (125 MHz, CDCl₃) 22.5 (CH₂CH₃), 22.7 (CH₂CH₃), 37.8 (CH₂Ph), 41.3 (CH(CH₃)₂), 47.2 (C(O)CH), 55.7 (OCH₃), 114.2 (ArCH), 124.1 (ArCH), 126.1 (ArCH), 127.5 (ArC), 128.2 (ArCH), 129.0 (ArCH), 129.8 (ArCH) 134.6 (ArC), 139.9 (ArC), 159.5 (ArC), 171.3 (C=O); IR (CH₂Cl₂ evaporated film/cm⁻¹) 3317 (NH), 2968 (C-H), 1643 (C=O); m/z (ES⁺) 400 (⁸¹Br, MNa⁺, 43%), 398 (⁷⁹Br, MNa⁺, 45%), 377 (⁸¹Br, MH⁺, 32%), 375 (⁷⁹Br, MH⁺, 30%), 320 (30%), 293 (30%), 257 (25%) HRMS for C₁₉H₂₃NO₂⁷⁹Br (MH⁺) found 376.0893, expected 376.0907, mp (CHCl₃) 143.9-144.5 °C.

**2-(4-Bromo-2-methoxy-phenyl)-pent-4-enoic acid N-*iso*-propylamide 39**

S30
Following general procedure F: Acetamide 27 (0.124 g, 0.156 mmol, 1 eq) and SmI₂ (6.3 mL, 0.626 mmol, 4 eq) were stirred at room temperature for 24 hours. Purification by FSPE afforded 39 as a white solid (38 mg, 0.121 mmol, 78%).

δ_H (500 MHz, CDCl₃) 0.94 (d, J = 6.3 Hz, 3H, CHCH₃), 2.37 (dt, J = 14.3, 7.2 Hz, 1H, CH₂=CHCHH), 2.75 - 2.85 (m, 1H, CH₂=CHCHH), 3.69 (t, J = 7.6 Hz, 1H, C(O)CH), 3.78 (s, 3H, OCH₃), 3.89 - 4.00 (m, 1H, CH(CH₃)₂), 4.89 (d, J = 10.4 Hz, 1H, CHH=CH), 4.97 (dd, J = 17.0, 1.6 Hz, 1H, CHH=CH), 5.32 (d, J = 6.9 Hz, 1H, NH), 5.65 (m, J = 17.0, 10.4, 6.9, 6.9 Hz, 1H, CH₂=CH), 6.93 (d, J = 1.9 Hz, 1H, ArCH), 7.02 (dd, J = 8.2, 1.9 Hz, 1H, ArCH), 7.13 (d, J = 8.2 Hz, 1H, ArCH); δ_C (75 MHz, CDCl₃) 22.6 (CHCH₃), 22.9 (CHCH₃), 35.4 (CH₂=CHCH₂), 41.3 (CH(CH₃)₂), 44.8 (OCH₃), 55.7 (OCH₃), 114.2 (ArCH), 116.5 (CH₂=CH), 121.3 (ArC), 124.2 (ArCH), 127.2 (ArC), 129.7 (ArCH), 136.1 (CH₂=CH), 157.2 (ArC), 171.5 (C=O); IR (CHCl₃ evaporated film/cm⁻¹) 3303 (NH), 2969 (C-H), 1636 (C=O); m/z (ES) 362 (⁺₁¹^Br, M + Cl⁻, 100%), 360 (⁺⁷^Br, M + Cl⁻, 70%), 349 (25%), 258 (15%), 239 (35%), 183 (20%) HMRS for C₁₅H₂₀NO₂⁺⁷^BrCl found 360.0357, expected 360.0366; mp (CHCl₃) 108.4-110.2 °C.

rac-2-Benzyl-2-(5-bromo-2-methoxy-phenyl)-N-iso-propylacetamide 40

Following general procedure F: Acetamide 28 (0.097 g, 0.114 mmol, 1 eq) and SmI₂ (4.54 mL, 0.454 mmol, 4 eq) were stirred at room temperature for 24 hours. Purification by FSPE afforded 40 as a cream amorphous solid (33 mg, 0.088 mmol, 77%).

δ_H (400 MHz, CDCl₃) 0.98 (apparent t, J = 6.5 Hz, 6H, 2 × CH₃CH), 2.90 (dd, J = 13.3 Hz, 5.6 Hz, 1H, CHHPh), 3.48 (dd, J = 13.3 Hz, 9.0 Hz, 1H, CHHPh), 3.78 (s, 3H, CH₃O), 3.92 - 4.00 (m, 2H, CH(CH₃)₂ and CHC(O)Ph), 5.26 (d, J = 7.3 Hz, 1H,
NH), 6.73 (d, J = 8.8 Hz, 1H, ArH), 7.17-7.19 (m, 3H, 3 × ArH), 7.22-7.24 (m, 2H, 2 × ArH), 7.32 (dd, J = 8.8 Hz, 1H, ArH), 7.56 (d, J = 2.5 Hz, 1H, ArH); δC (100 MHz, CDCl₃) 22.5 (CH(CH₃)₂), 22.7 (CH₂CH), 37.8 (CH₂Ph), 41.2 (CH(CH₃)₂), 47.3 (CH(O)Ph), 55.6 (CH₃O), 112.1 (ArCH), 113.5 (ArC), 126.2 (ArCH), 128.2 (2 × ArCH), 129.0 (2 × ArCH), 130.6 (ArC), 130.7 (ArCH), 131.2 (ArCH), 139.9 (ArC), 155.5 (ArC=OCH₃), 171.1 (NCO); IR (CHCl₃ evaporated film/cm⁻¹) 3318 (NH), 1648 (C=O); m/z (ES⁺) 400 ([⁸¹Br, MNa⁺, 90%] 398 ([⁷⁹Br, MNa⁺, 100%]), 377 ([⁸¹Br, M, 12%] 375 ([⁷⁹Br, M, 10%]), 183 (20%); HRMS for C₁₉H₂₃NO₂⁷⁹Br (MH⁺) found 376.0912, expected 376.0909.

2-(2-Fluoro-4-methoxy-phenyl)-pent-4-enoic acid N-isopropylamide 41

Following general procedure F: Acetamide 24 (0.14 g, 0.188 mmol, 1 eq) and SmI₂ (7.54 mL, 0.754 mmol, 4 eq) were stirred at room temperature for 24 hours. Purification by FSPE afforded 42 as a brown oil (35.4 mg, 0.133 mmol, 71%).

δH (500 MHz, CDCl₃) 1.06 (d, J = 6.6 Hz, 3H, CHCH₃), 1.14 (d, J = 6.3 Hz, 3H, CHCH₃), 2.41 - 2.57 (m, 1H, CH₂=CHCH₂), 2.82 - 2.96 (m, 1H, CH₂=CHCH₂), 3.64 (t, J = 7.6 Hz, 1H, C(O)CH), 3.81 (s, 3H, OCH₃), 4.06 (m, 1H, CH(CH₃)₂), 5.00 (d, J = 10.4 Hz, 1H, CHH=CH), 5.07 (dd, J = 16.9, 1.4 Hz, 1H, CHH=CH), 5.31 (d, J = 7.06 Hz, 1H, NH), 5.74 (m, 1H, CHH=CH), 6.63 (dd, J = 12.1, 2.7 Hz, 1H, ArCH), 6.72 (dd, J = 8.2, 2.8 Hz, 1H, ArCH), 7.34 (t, J = 8.2 Hz, 1H, ArCH); δC (100 MHz, CDCl₃) 22.5 (CHCH₃), 22.8 (CHCH₃), 36.3 (CH₂CH=CH₂), 41.5 (CH(CH₃)₂), 44.3 (SCH), 55.6 (OCH₃), 101.5 (ArCH), 110.3 (ArCH), 116.9 (ArC), 118.4 (CH=CH₂), 129.5 (ArCH), 135.7 (CH=CH₂), 159.8 (ArC), 160.1 (d, J = 223 Hz, ArC-F), 171.4 (C=O); IR (CHCl₃ evaporated film/cm⁻¹) 3313 (NH), 2967 (C-H), 1647 (C=O); m/z (ES⁺) 288 (MNa⁺, 50%), 287 (80%), 266 (MH⁺, 100%), 238 (10%); HRMS for C₁₉H₂₁NOF found 266.1561, expected 266.1556.

N-isopropyl-2-(2-methoxy-4-trimethylsilanylethynyl-phenyl)acetamide 42

S32
Following general procedure F: Acetamide 31 (0.08 g, 0.104 mmol, 1 eq) and SmI$_2$ (4.16 mL, 0.416 mmol, 4 eq) were stirred at room temperature for 24 hours. Purification by FSPE afforded 41 as a white solid (27.5 mg, 0.090 mmol, 87%).

δ$^H$ (500 MHz, CDCl$_3$) 0.19 (s, 9 H, Si(CH$_3$)$_3$), 0.97 (d, $J = 6.6$ Hz, 6H, CH(CH$_3$)$_2$), 3.43 (s, 2H, C(O)CH$_2$), 3.78 (s, 3H, OCH$_3$), 3.90 - 3.99 (m, 1H, CH(CH$_3$)$_2$), 5.29 (br. s., 1H, NH), 6.92 (d, $J = 1.3$ Hz, 1H, ArCH), 7.01 (dd, $J = 7.6$, 1.6 Hz, 1H, ArCH), 7.08 (d, $J = 7.9$ Hz, 1H, ArCH); δ$^C$ (75 MHz, CDCl$_3$) 0.0 (Si(CH$_3$)$_3$), 22.7 (CH(CH$_3$)$_2$), 39.0 (CH(CH$_3$)$_2$), 41.3 (C(O)CH$_2$), 55.5 (OCH$_3$), 94.4 (C≡CSi(CH$_3$)$_3$), 104.8 (ArC=C), 114.0 (ArCH), 123.4 (ArC), 125.0 (ArCH), 125.1 (ArCH), 131.1 (ArC), 156.8 (ArC), 169.8 (C=O); IR (CHCl$_3$ evaporated film/cm$^{-1}$) 3267 (NH), 2969), 1640 (C=O); m/z (ES$^+$) 326 (MNa$^+$, 100%), 304 (MH$^+$, 45%), 220 (10%) HRMS for C$_{17}$H$_{26}$NO$_2$Si found 304.1720, expected 304.1727; mp (Hexane) 141.7-142.9 °C.

$N$-iso-propyl-2-(2-methoxy-5-thiophen-2'-yl-phenyl)-3-phenyl-propionamide 43

To a suspension of propionamide 32 (0.10 g, 0.130 mmol, 1 eq) and NaH (60% in mineral dispersion, 0.026 g, 0.652 mmol, 5 eq) in dry THF (4 ml), benzyl bromide (0.08mL, 0.652 mmol, 5 eq) was added dropwise at room temperature, heated at reflux and stirred for 18 hours. The reaction was quenched with water (5 mL) and the organic layer extracted with Et$_2$O (3 x 5 mL). The combined organic layers were dried (Na$_2$SO$_4$) and concentrated in vacuo. Purification by FSPE and subsequently by column chromatography afforded an inseparable mixture of benzyl propionamide and 43 (49 mg).
The mixture was dissolved in dry, degassed THF (2 mL) and SmI$_2$ (2.23 mL, 0.223 mmol, approx. 4 eq) was added. The reaction was stirred at room temperature for 24 hours. Saturated aqueous Na$_2$S$_2$O$_3$ (5 mL) was added and the organic layer extracted with Et$_2$O (3 × 5 mL). The combined organic layers were dried (Na$_2$SO$_4$) and concentrated in vacuo. Purification by column chromatography (15:85 ethyl acetate:petroleum ether 60/40) gave 43 (19 mg, 0.052 mmol, 38% over 2 steps, approx. 94% for SmI$_2$ reaction) as a white solid.

δ$_H$ (400 MHz, CDCl$_3$) 0.90 (d, $J = 6.6$ Hz, 3H, CHCH$_3$), 0.91 (d, $J = 6.5$ Hz, 3H, CHCH$_3$), 2.88 (dd, $J = 13.6, 6.3$ Hz, 1H, CHHPPh), 3.47 (dd, $J = 13.5, 8.7$ Hz, 1H, CHHPPh), 3.78 (s, 3H, OCH$_3$), 3.86 - 3.97 (m, 2H, CH(CH$_3$)$_2$ and CH(O)), 5.27 (d, $J = 7.8$ Hz, 1H, NH), 6.98 - 7.03 (m, 2H, 2 × ArCH), 7.05 - 7.24 (m, 8H, 8 × ArCH), 7.32 (d, $J = 7.8$ Hz, 1H, ArCH); δ$_C$ (101 MHz, CDCl$_3$) 22.5 (CHCH$_3$), 22.7 (CHCH$_3$), 37.7 (CH$_2$Ph), 41.3 (CH(CH$_3$)$_2$), 47.5 (CHC(O)), 55.5 (OCH$_3$), 108.3 (ArCH), 118.9 (ArCH), 123.2 (ArCH), 124.9 (ArCH), 126.1 (ArC), 127.7 (ArC), 128.0 (ArCH), 128.2 (ArCH), 129.0 (ArCH), 129.1 (ArCH), 134.4 (ArC), 140.3 (ArC), 144.2 (ArC), 156.8 (ArC), 171.7 (C=O); IR (CHCl$_3$ evaporated film/cm$^{-1}$) 3320 (NH), 2971 (C-H), 1640 (C=O); $m/z$ (ES$^+$) 380 (MH$^+$, 100%), 210 (10%), 204 (12%), 173 (18%), 115 (14%) HRMS for C$_{23}$H$_{26}$NO$_2$S (MH$^+$) found 380.1681, expected 380.1684; mp (Hexane) 141.7-142.9 °C.

$N$-iso-propyl-2-(2-methoxy-5-(4'-methylphenyl)-phenyl)acetamide 44

Following general procedure F: Acetamide 29 (0.057 g, 0.0735 mmol, 1 eq) and SmI$_2$ (2.94 mL, 0.294 mmol, 4 eq) were stirred at room temperature for 24 hours. Purification by FSPE afforded 43 as a cream solid (14.6 mg, 0.049 mmol, 67%).

δ$_H$ (400 MHz, CDCl$_3$) 1.00 (d, $J = 6.6$ Hz, 6H, 2 × CHCH$_3$), 2.32 (s, 3H, ArCH$_3$), 3.50 (s, 2H, C(O)CH$_2$), 3.82 (s, 3H, OCH$_3$), 3.98 (m, 1H, CH(CH$_3$)$_2$), 5.46 (d, $J = 6.3$ Hz, 1H, NH), 6.89 (d, $J = 8.3$ Hz, 1H, ArCH), 7.16 (d, $J = 7.8$ Hz, 2H, 2 × ArCH), 7.51 (d, $J = 8.3$ Hz, 2H, 2 × ArCH), 7.64 (d, $J = 8.3$ Hz, 2H, 2 × ArCH).
7.34 - 7.51 (m, 3H, 3 × ArCH), 7.57 - 7.70 (m, 1H, ArCH); $^{13}$C NMR (101 MHz, CDCl$_3$) δ ppm 21.1 (ArCH$_3$), 22.7 (2 × CH$_2$CH$_3$), 39.3 (C(O)CH), 41.3 (CH(CH$_3$)$_2$), 55.5 (OCH$_3$), 111.0 (ArCH), 124.2 (ArC), 126.6 (ArCH), 128.5 (ArCH), 129.5 (ArCH), 129.9 (ArCH), 132.1 (ArC), 136.6 (ArC), 137.5 (ArC), 156.6 (ArC), 170.3 (C=O); IR (CHCl$_3$ evaporated film/cm$^{-1}$) 3269 (NH), 2970 (C-H), 1641 (C=O); m/z (ES$^+$) 320 (MNa$^+$, 100%), 298 (MH$^+$, 5%), 229 (7%) HRMS for C$_{19}$H$_{22}$NO$_2$ (MH$^+$) found 298.1796, expected 298.1807; mp (Hexane) 110.2-112.0 °C.
NMR spectra: α-hydroxyamides

400 MHz (CDCl₃)

100 MHz (CDCl₃)
400 MHz (CDCl₃)

100 MHz (CDCl₃)
500 MHz (CDCl₃)

125 MHz (CDCl₃)
400 MHz (d$_6$-DMSO, 100 °C)

100 MHz (d$_6$-DMSO, 100 °C)
400 MHz (CDCl₃)

100 MHz (CDCl₃)
400 MHz (CDCl₃)

100 MHz (CDCl₃)
NMR data for aryl transfer products

400 MHz (CDCl₃)

100 MHz (CDCl₃)
500 MHz (CDCl₃)

125 MHz (CDCl₃)
300 MHz (CDCl₃)

![NMR spectrum of compound 20 at 300 MHz in CDCl₃.](image)

75 MHz (CDCl₃)

![NMR spectrum of compound 20 at 75 MHz in CDCl₃.](image)
400 MHz (CDCl₃)

75 MHz (CDCl₃)
NMR data for modified aryl transfer products:

400 MHz (CDCl₃)

75 MHz (CDCl₃)
400 MHz (CDCl₃)

100 MHz (CDCl₃)
400 MHz (CDCl₃)

75 MHz (CDCl₃)
400 MHz (CDCl₃)

100 MHz (CDCl₃)
400 MHz (CDCl₃)

75 MHz (CDCl₃)
400 MHz (CDCl$_3$)

75 MHz (CDCl$_3$)
400 MHz (CDCl₃)

75 MHz (CDCl₃)
NMR spectra: Tag cleaved products

400 MHz (CDCl₃)

100 MHz (CDCl₃)
400 MHz (CDCl₃)

35

100 MHz (CDCl₃)
400 MHz (CDCl₃)

100 MHz (CDCl₃)
$400 \text{ MHz (CDCl}_3\text{)}$

$100 \text{ MHz (CDCl}_3\text{)}$
$400 \text{ MHz (CDCl}_3\text{)}$

$100 \text{ MHz (CDCl}_3\text{)}$
400 MHz (CDCl₃)

100 MHz (CDCl₃)