SUPPLEMENTARY INFORMATION

Initial development of a cytotoxic amino-seco-CBI warhead for delivery by prodrug systems

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Synthetic methods for 31-33,37

Naphthalene-1,4-dione (14). KNO₃ (35.5 mg, 0.35 mmol) was added to 13 (67.6 mg, 0.35 mmol) in CF₃CO₂H (10 mL) at -20°C. The mixture was stirred at -20°C for 35 min and poured onto ice. Extraction (EtOAc), drying and chromatography (CH₂Cl₂ / EtOAc 3:2) gave 14 (41.4 mg, 75%) as a pale buff solid: mp 124-126°C (lit.¹ 125-127°C); ¹H NMR ((CD₃)₂SO) (COSY) δ 7.14 (2 H, s, 2,3-H₂), 7.93 (2 H, m, 6,7-H₂), 8.04 (2 H, m, 5,8-H₂); ¹³C NMR ((CD₃)₂SO) δ 125.83 (5,8-C₂), 131.53 (4a,8a-C₂), 134.18 (6,7-C₂), 138.70 (2,3-C₂), 184.80 (1,4-C₂); MS m/z 159.0466 (M + H)⁺ (C₁₀H₇O₂ requires 159.0446).

4-Amino-2-nitronaphthalen-1-ol (16). SnCl₂.2H₂O (15.0 g, 67 mmol) in EtOH (20 mL) was added to 15 (5.04 g, 22 mmol) in aq. HCl (9 M, 20 mL) and EtOH (10 mL) during 1 h at < 35°C. The mixture was stirred for 17 h at 20°C. The suspension was filtered and the solid was washed with EtOH / aq. HCl (9 M) (3:2). The yellow solid was partitioned between EtOAc and water. The aqueous layer was extracted (EtOAc, 3×). The combined extracts were washed (brine) and dried. Evaporation and chromatography (CH₂Cl₂) gave 16 (3.11 g, 71%) as a pale pink solid: mp 160-161°C (lit.² mp 160°C); IR νmax 3148, 3337 cm⁻¹; ¹H NMR δ 3.98 (2 H, s, NH₂), 7.26 (1 H, s, 3-H), 7.64 (1 H, dd, J = 8.1, 7.0 Hz, 7-H), 7.74 (1 H, dd, J = 8.3, 6.9 Hz, 6-H), 7.83 (1 H, d, J = 8.4 Hz, 5-H), 8.53 (1 H, dd, J = 8.3, 0.6 Hz, 8-H), 11.92 (1 H, s, OH); ¹³C NMR δ 100.54 (3-C), 121.42 (5-C), 125.65 (8a-C), 125.92 (8-C), 127.15 (7-C), 127.90 (2-C), 129.56 (4a-C), 130.87 (6-C), 135.18 (4-C), 150.11 (1-C); MS m/z 203.0466 (M - H)⁻ (C₁₀H₇N₂O₂ requires 203.0457).

4-Amino-2-nitronaphthalen-1-yl 1,1-dimethylcarbamate (17). Compound 16 (54 mg, 0.26 mmol) was stirred with Boc₂O (60 mg, 0.28 mmol) and 4-dimethylaminopyridine (25 mg, 0.20 mmol) in CH₂Cl₂ (17 mL) for 30 min under N₂. The mixture was washed (water, brine) and dried. Evaporation and chromatography (CH₂Cl₂) gave 17 (14 mg, 17%) as a yellow solid, which decomposed on heating: ¹H NMR δ 1.60 (9 H, s, Bu'), 4.34 (2 H, s, NH₂), 7.29 (1 H, s, 3-H), 7.62-7.66 (2 H, m, 6,7-H₂), 7.81 (1 H, m, 5-H), 8.15 (1 H, m, 8-H); ¹³C NMR δ 27.60 (CMe₂), 84.87 (CMe₃), 102.48 (3-C), 121.22 (5-C), 124.15 (8-C), 126.12 (4a-C), 128.14 (6-C), 128.20 (8a-C), 128.67 (7-C), 133.79 (4-C), 137.91 (2-C), 141.07 (1-C), 150.94 (C=O).

1,1-Dimethylcarbonyl (4-hydroxy-3-nitronaphthalen-1-yl)carbamate (18). Compound 16 (560 mg, 2.7 mmol) was stirred with Boc₂O (3.04 g, 14 mmol) in dry THF (25 mL) under N₂ under reflux for 20 h. The mixture was cooled. The evaporation residue, in CH₂Cl₂, was washed (water, brine). Drying, evaporation and chromatography (petroleum ether / EtOAc 9:1) gave 18 (740 mg, 89%) as an orange solid: mp 175-177°C; IR νmax 3338, 3259, 1687, 1525 cm⁻¹; ¹H NMR (NOESY) δ 1.55 (9 H, s, Bu'), 6.59 (1 H, br s, NH), 7.65 (1 H, ddd, J = 8.2, 7.0, 1.1 Hz,
Me + 2C + 2\degree 2\degree 3Me + 3

The evaporation and chromatography (CH₂Cl₂ → CH₂Cl₂ / EtOAc 1:1 → EtOAc) gave 19 (942 mg, 81%) as a yellow solid: mp 110-111\degree C; IR νmax 3435, 1737 cm⁻¹; ¹H NMR (NOESY) δ 1.59 (9 H, s, Bu'), 7.19 (1 H, s, NH), 7.78-7.82 (2 H, m, 6,7-H₂), 7.96 (1 H, d, J = 8.0 Hz, 5-H), 8.29 (1 H, d, J = 8.2-8.8 Hz), 8.73 (1 H, s, 3-H); ¹³C NMR δ 28.20 (CMe₂), 82.54 (CMe₃), 110.52 (3-C), 118.42 (q, J = 321.2 Hz, CF₃), 121.34 (5-C), 125.19 (8-C), 127.13 (8a-C), 127.51 (4a-C), 129.35 (6-C or 7-C), 130.12 (7-C or 6-C), 132.72 (2-C), 134.61 (4-C), 143.02 (1-C), 152.20 (C=O). ¹⁹F NMR (CDCl₃) δ -72.55 (s, CF₃); MS m/z 459.0484 (M + Na)⁺ (C₁₅H₁₅F₃Na₂O₇S requires 459.0450).

1,1-Dimethylethyl N-(3-amino-4-oxonaphthalen-1-ylidene)carbamate (21). Compound 18 (66 mg, 0.22 mmol) was stirred vigorously with Pd/C (36.5 mg) in MeOH (20 mL) under H₂ for 1.5 h. Filtration (Celite) and evaporation gave 21 (51 mg, 84%) as a dark buff solid: mp 155-156\degree C; IR νmax 3331, 1704 cm⁻¹; ¹H NMR δ 1.61 (9 H, s, Bu'), 5.06 (2 H, s, NH₂), 6.10 (1 H, s, 2-H), 7.58 (1 H, t, J = 7.2 Hz, 6-H), 7.65 (1 H, t, J = 6.9 Hz, 7-H), 8.09 (1 H, d, J = 7.6 Hz, 5-H), 8.29 (1 H, d, J = 7.7 Hz, 8-H); ¹³C NMR δ 28.23 (CMe₂), 82.26 (CMe₃), 99.01 (2-C), 125.78 (8-C), 126.33 (5-C), 130.41 (4a-C), 131.27 (6-C), 133.62 (7-C), 134.84 (8a-C), 144.84 (3-C), 157.13 (1-C), 162.94 (Boc C=O), 180.70 (4-C); MS m/z 567.2262 (2 M + Na)⁺ (C₃₀H₃₂N₄NaO₆ requires 567.2220), 295.1052 (M + Na)⁺ (C₁₅H₁₆Na₂O₃S requires 295.1059).

1,1-Dimethylethyl N-(4-oxo-3-(2,2,2-trifluoroacetamido)napthalen-1-ylidene)carbamate (22). K₂CO₃ (178 mg, 1.3 mmol) and Na₂S₂O₄ (198 mg, 1.1 mmol) in water (4.0 mL) were added dropwise to 18 (75 mg, 0.25 mmol) in CH₂Cl₂ (8.0 mL) and water (1.0 mL) under N₂. Stirring was continued for 16 h at 35\degree C. The organic phase was separated, dried and filtered. The filtrate was cooled to 0\degree C. Pr₂NEt (580 mg, 4.5 mmol) was added, followed by dropwise addition of (F₃CCO)₂O (315 mg, 1.5 mmol). The mixture was stirred at 0\degree C for 15 min then at 20\degree C for 2 h, before being washed with (water, brine) and dried. Evaporation and chromatography (petroleum ether / EtOAc 9:1) gave 22 (39 mg, 42%) as a yellow solid: mp 122-123\degree C; IR νmax 3290, 3097, 1744 cm⁻¹; ¹H NMR δ 1.66 (9 H, s, Bu'), 7.71 (1 H, ddd, J = 9.0, 7.7, 1.9 Hz, 6-H), 7.78 (1 H, ddd, J = 8.9, 7.4, 1.5 Hz, 7-H), 8.13 (1 H, s, 2-H), 8.19 (1 H, dd, J = 7.7, 1.1, Hz, 5-H), 8.36 (1 H, dd, J = 7.8, 0.9 Hz, 8-H), 9.17 (1 H, s, NH); ¹³C NMR δ 28.13 (CMe₂), 81.22 (CMe₃), 114.57 (2-C), 114.72 (q, J = 288.4 Hz, CF₃), 126.11 (8-C), 127.12 (5-C), 129.40 (4a-C), 132.45 (6-C), 133.67 (3-C), 134.80 (7-C), 135.00 (8a-C), 155.28 (Boc C=O), 155.57 (q, J = 39.2 Hz, CF₂C=O), 161.36 (1-C), 178.63 (4-C); ¹⁹F NMR (CDCl₃) δ -75.76 (s, CF₃); MS m/z 367.0941 (M - H)⁺ (C₁₇H₁₄F₃N₂O₄ requires 367.0906).

Ethyl 5-hydroxyindole-2-carboxylate (31). 5-Hydroxyindole-2-carboxylic acid 30 (1.53 g, 8.6 mmol) was boiled under reflux in EtOH (100 mL) saturated with HCl under N₂ for 4 h. The evaporation residue, EtOAc, was washed (water, brine). Drying, evaporation and chromatography (CH₂Cl₂ → CH₂Cl₂ / EtOAc 4:1) gave 31 (1.64 g, 92%) as a white solid: mp
152-154°C (lit.3 146-148°C); IR νmax 3316, 3209, 1696 cm⁻¹; 1H NMR ((CD3)2SO) δ 1.38 (3 H, t, J = 7.1 Hz, Me), 4.37 (2 H, q, J = 7.1 Hz, CH₂), 6.86 (1 H, dd, J = 8.8, 2.4 Hz, 6-H), 6.97 (1 H, d, J = 2.3 Hz, 4-H), 7.00 (1 H, dd, J = 2.1, 0.8 Hz, 3-H), 7.32 (1 H, d, J = 8.8 Hz, 7-H), 8.93 (1 H, s, OH). 13C NMR ((CD3)2SO) δ 14.29 (Me), 60.17 (CH₂), 104.43 (4-C), 106.66 (3-C), 113.07 (7-C), 116.15 (6-C), 127.36 (2-C or 3a-C), 127.44 (3a-C or 2-C), 132.21 (7a-C), 151.34 (5-C), 161.30 (C=O).

**Ethyl 5-(2-Dimethylaminoethoxy)indole-2-carboxylate (32).** Me₂N(CH₂)₂Cl.HCl (1.77 g, 12 mmol), K₂CO₃ (3.40 g, 25 mmol) and water (8 mL) were added to 31 (1.68 g, 8.2 mmol) in CHCl₃ (40 mL). The stirred solution was placed in an oil bath at 65°C. The temperature was slowly raised to 80°C during 65 min and the mixture was stirred for 16 h at 80°C. The organic phase was separated and the solvent was evaporated to 25% of its original volume. This solution was combined with the aqueous phase and diluted with water and tolune. The organic layer was separated, washed with water and extracted with aq. HCl (1.0 M). The acidic phase was washed (toluene), cooled to 0°C, basified (~pH 12) by addition of aq. NaOH (4.0 M) and extracted (toluene). The extract was washed (water, brine) and dried. Evaporation gave 32 (1.81 g, 80%) as a white solid: mp 108-109 (lit.3 mp 110°C); IR νmax 3315, 1687; 1H NMR δ 1.39 (3 H, t, J = 7.1 Hz, OCH₂), 2.35 (6 H, s, NMe₂), 2.76 (2 H, t, J = 5.8 Hz, Me₂NCH₂CH₂), 4.00 (2 H, q, J = 7.1 Hz, OCH₂CH₃), 4.10 (2 H, t, J = 5.8 Hz, Me₂NCH₂CH₂), 4.39 (2 H, q, J = 7.1 Hz, OCH₂CH₃), 6.99 (1 H, dd, J = 8.9, 2.4 Hz, 6-H), 7.07 (1 H, d, J = 2.4 Hz, 4-H), 7.12 (1 H, dd, J = 2.1, 0.8 Hz, 3-H), 7.28 (1 H, d, J = 8.9 Hz, 7-H), 9.30 (1 H, s, NH); 13C NMR δ 14.32 (OCH₂CH₃), 45.83 (NMe₂), 58.38 (Me₂NCH₂CH₂), 60.82 (OCH₂CH₃), 66.57 (Me₂NCH₂CH₂), 103.67 (4-C), 108.13 (3-C), 112.69 (7-C), 117.37 (6-C), 127.74 (2-C), 127.89 (3a-C), 132.42 (7a-C), 153.83 (5-C), 162.01 (C=O).

**Ethyl 5-(2-Dimethylaminoethoxy)indole-2-carboxylate (33).** Ester 32 (609 mg, 2.2 mmol) was heated with Cs₂CO₃ (2.50 g, 7.7 mmol) in MeOH (12 mL) and water (6 mL) at reflux for 2 h. The evaporation residue, in water, was adjusted to pH 6.5 with aq. HCl (1.0 M). The mixture was cooled to 4°C for 18 h. The crystals were collected by filtration, washed (ice-cold water, acetone) to give 33 (419 mg, 77%) as white crystals. A sample of the product was treated with HCl in 1,4-dioxane (4.0 M) and EtOAc. Filtration gave 33.HCl as a white solid: mp 238-239°C (lit.4 mp 237-239°C); IR νmax 3380, 3240, 1593 cm⁻¹; 1H NMR ((CD₃)₂SO) δ 2.37 (6 H, s, NMe₂), 2.81 (2 H, t, J = 5.7 Hz, NCH₂), 4.12 (2 H, t, J = 5.8 Hz, OCH₂), 6.91 (1 H, dd, J = 8.9, 2.4 Hz, 6-H), 6.95 (1 H, d, J = 1.5 Hz, 3-H), 7.14 (1 H, d, J = 2.3 Hz, 4-H), 7.35 (1 H, d, J = 8.9 Hz, 7-H), 11.50 (1 H, s, NH); 13C NMR ((CD₃)₂SO) δ 45.04 (NMe₂), 57.39 (NCH₂), 65.66 (OCH₂), 103.18 (4-C), 106.06 (3-C), 113.21 (7-C), 115.50 (6-C), 127.27 (3a-C), 130.33 (2-C), 132.39 (7a-C), 152.69 (5-C), 163.30 (C=O).

**S-Oxiran-2-ylmethyl 4-nitrobenzenesulfonate (37).** 4-Nitrobenzenesulfonyl chloride (3.16 g, 14 mmol) was added portionwise to Et₃N (2.3 mL, 1.67 g, 16 mmol) and R-oxiranylmethanol 36 (1.00 g, 14 mmol) in toluene at 0°C. The mixture was stirred at 20°C for 30 min. The suspension was filtered (Celite®). The evaporation residue, in CH₂Cl₂, was washed (aq. H₂SO₄, 2%), sat. aq. NaHCO₃, brine. Drying, evaporation and recrystallisation (toluene / hexane) gave 37 (1.69 g, 40%) as a white solid: mp 82-83°C (lit.5 mp 84-86°C); [α]D¹⁸ (c = 6.5, CHCl₃) + 33.3° (lit.6 [α]D²⁰ + 26.5° (c 2.45, CHCl₃, 82% e.e.)); 1H NMR δ 2.60 (1 H, dd, J = 4.7, 2.5 Hz, 3-H), 2.83 (1 H, t, J = 4.4 Hz, 3-H), 3.20 (1 H, m, 2-H), 4.02 (1 H, dd, J = 11.6, 6.4 Hz, SOCH), 4.46 (1 H, dd, J = 11.6, 2.9 Hz, SOCH), 8.12 (2 H, m, Ph 2,6-H₂), 8.40 (2 H, m, Ph 3,5-H₂); 13C NMR (CDCl₃) δ 44.42 (3-C), 48.61 (2-C), 71.62 (SOCH₂), 124.43 (Ph 3,5-C₂), 129.24 (Ph 2,6-C₂), 141.59 (Ph 1-C), 150.84 (Ph 4-C).
1,1-Dimethylethyl N-(R-1-iodo-2-(N-(oxiranylmethyl)-2,2,2-trifluoroacetamido)naphthalen-4-yl)carbamate (diastereomeric atropisomers 38A & 38B). Compound 29 (21 mg, 43 \mu mol) was stirred with 37 (17 mg, 66 \mu mol) and K$_2$CO$_3$ (26 mg, 0.19 mmol) in acetone (20 mL) at 50°C under N$_2$ for 3 d. Sat. aq. NaHCO$_3$ was added to the mixture, which was extracted with EtOAc. The extract was washed (brine) and dried. Evaporation and chromatography (petroleum ether / EtOAc 19:1 → 9:1) gave 38A (7.8 mg, 34%) as a yellow oil: $^1$H NMR (NOESY) δ 1.56 (5.4 H, s, Bu rotamer a), 1.56 (3.6 H, s, Bu' rotamer b), 2.45 (0.4 H, dd, $J = 4.6, 2.4$ Hz, oxirane-3-C rotamer b), 2.56 (0.6 H, dd, $J = 4.8, 2.5$ Hz, oxirane-3-H rotamer a), 2.84 (1 H, m, oxirane-3-H rotamers a,b), 3.17 (0.6 H, dd, $J = 14.3, 7.1$ Hz, CHNOCOF$_3$ rotamer a), 3.34 (0.4 H, m, oxirane-2-H rotamer b), 3.38 (0.4 H, dd, $J = 13.6, 5.8$ Hz, CHNOCOF$_3$ rotamer b), 3.44 (0.6 H, m, oxirane-2-H rotamer a), 4.55 (0.4 H, dd, $J = 13.8, 4.6$ Hz, CHNOCOF$_3$ rotamer b), 4.63 (0.6 H, dd, $J = 14.3, 3.9$ Hz, CHNOCOF$_3$ rotamer a), 6.99 (1 H, s, NH rotamers a,b), 7.63-7.67 (2 H, m, 6-H$_2$ rotamers a,b), 7.86 (1 H, m, 5-H rotamers a,b), 8.06 (0.4 H, s, 3-H rotamer b), 8.18 (0.6 H, s, 3-H rotamer a), 8.31 (1 H, m, 8-H rotamers a,b); $^{13}$C NMR δ 28.30 (CMe$_3$ rotamer b), 28.33 (CMe$_3$ rotamer a), 45.67 (oxirane-3-C rotamer a), 46.70 (oxirane-3-C rotamer b), 48.02 (oxirane-2-C rotamer b), 49.31 (oxirane-2-C rotamer a), 53.29 (CH$_2$NOCOF$_3$ rotamer b), 54.66 (CH$_2$NOCOF$_3$ rotamer a), 81.64 (CMe$_2$ rotamer a), 81.68 (CMe$_2$ rotamer b), 99.03 (1-C rotamer a), 99.45 (1-C rotamer b), 115.88 (q, $J = 288.4$ Hz, CF$_3$ rotamers a,b), 118.47 (3-C rotamers a,b), 120.55 (5-C rotamer b), 120.59 (5-C rotamer a), 125.80 (4a-C rotamers a,b), 128.05 (6-C rotamer a), 128.13 (6-C rotamer b), 128.78 (7-C rotamer a), 128.86 (7-C rotamer b), 134.42 (8-C rotamer a), 134.55 (8-C rotamer b), 135.06 (8a-C rotamer a,b), 135.09 (4-C rotamers a,b), 135.11 (8a-C rotamer b), 140.32 (2-C rotamer b), 140.80 (2-C rotamer a), 152.43 (Boc C=O rotamers a,b), 157.09 (q, $J = 36.5$ Hz, F$_3$CC=O rotamer a), 157.20 (q, $J = 38.1$ Hz, F$_3$CC=O rotamer b); $^{19}$F NMR δ -68.40 (0.4 F, s, CF$_3$ rotamer b), -68.52 (0.6 F, s, CF$_3$ rotamer a); MS m/z 537.0504 (M + H)$^+$ (C$_{30}$H$_{33}$F$_3$IN$_2$O$_4$ requires 537.0498). Further elution gave 38B (9.1 mg, 39%) as a pale yellow oil: $^1$H NMR (NOESY) δ 1.55 (9 H, s, Bu'), 2.78 (1 H, dd, $J = 4.7, 2.6$ Hz, oxirane-3-H), 2.95 (1 H, t, $J = 4.5$ Hz, oxirane-3-H), 3.49 (1 H, m, oxirane-2-H), 4.30 (1 H, dd, $J = 12.2, 6.2$ Hz, CHNOCOF$_3$), 4.71 (1 H, dd, $J = 12.2, 2.8$ Hz, CHNOCOF$_3$), 6.70 (1 H, s, NH), 7.47 (1 H, t, $J = 7.7$ Hz, 6-H), 7.57 (1 H, m, 7-H), 7.63 (1 H, s, 3-H), 7.76 (1 H, d, $J = 8.4$ Hz, 5-H); 8.19 (1 H, d, $J = 8.5$ Hz, 8-H); $^{13}$C NMR δ 28.29 (CMe$_3$), 44.85 (oxirane-3-C), 48.89 (oxirane-2-C), 69.29 (CH$_2$NOCOF$_3$), 81.25 (CMe$_3$), 85.75 (1-C), 110.89 (3-C), 115.72 (q, $J = 284.6$ Hz, CF$_3$), 120.33 (5-C), 123.42 (4a-C), 125.48 (6-C), 128.25 (7-C), 132.53 (8-C), 134.43 (4-C), 134.95 (8a-C), 145.08 (2-C), 152.71 (C=O Boc); $^{19}$F NMR δ -75.62 (s, CF$_3$); MS m/z 537.0504 (M + H)$^+$ (C$_{30}$H$_{33}$F$_3$IN$_2$O$_4$ requires 537.0498).

1,1-Dimethylethyl S,N-(1-iodo-2-(oxiran-2-ylmethylamino)naphthalen-4-yl)carbamate (40). MeLi in Et$_2$O (1.6 M, 0.24 mL, 0.39 mmol) was added dropwise (~5 min) to a stirred suspension of CuCN (17.4 mg, 0.19 mmol) in dry THF (0.6 mL) at -78°C under N$_2$ and the mixture was stirred for 5 min. The mixture was brought to 40°C and stirred for 30 min. After being cooled to -78°C, compound 38 (65.6 mg, 0.12 mmol) in dry THF (0.6 mL) was added dropwise and stirring was continued at -78°C. The mixture was stirred at 25°C for 3 d. Water was added. The mixture was extracted (EtOAc). The extract was washed (brine). Drying, evaporation and chromatography (petroleum ether / EtOAc 19:1) gave 40 (39 mg, 73%) as a yellow solid: mp 127-128°C; IR $\nu_{\text{max}}$ 3389, 3336, 3082, 1699 cm$^{-1}$; $^1$H NMR (NOESY) δ 1.56 (9 H, s, Bu' conformers a,b), 2.77 (0.45 H, d, $J = 2.6$ Hz, oxirane-3-H conformer B), 2.78 (0.55 H, d, $J = 2.7$ Hz, oxirane-3-H conformer A), 2.84 (0.45 H, d, $J = 2.6$ Hz, oxirane-3-H conformer B), 2.86 (1 H, d, $J = 4.0$ Hz, oxirane-3-H conformer A), 3.27 (1 H, m, oxirane-2-H conformers a,b), 3.51 (0.55 H, dd, $J = 6.2, 4.6$ Hz, NCH/CH conformer A), 3.55 (0.45 H, dd, $J = 6.2, 4.6$ Hz, NCH/CH conformer B), 3.71 (0.45 H, dd, $J = 5.7, 3.5$ Hz, NHCH/CH conformer...
B), 3.75 (0.55 H, dd, J = 5.7, 3.5 Hz, NCH/H conformer A), 4.87 (1 H, t, J = 5.8 Hz, NHCH₂ conformers A,B), 6.93 (1 H, s, Boc NH conformers A,B), 7.26 (1 H, ddd, J = 8.1, 6.8, 1.1 Hz, 6-H conformers A,B), 7.45 (1 H, ddd, J = 8.1, 6.8, 1.2 Hz, 7-H conformers A,B), 7.62 (1 H, d, J = 8.2 Hz, 5-H conformers A,B), 7.74 (1 H, s, 3-H conformers A,B), 7.99 (1 H, dd, J = 8.6, 0.6 Hz, 8-H conformers A,B); ¹³C NMR δ 28.32 (CMe₂), 45.38 (NCH₂), 45.44 (oxirane 3-C), 50.82 (oxirane 2-C), 78.88 (1-C), 80.91 (CMe₃), 105.08 (3-C), 120.13 (5-C), 120.74 (4a-C), 122.63 (6-C), 128.10 (7-C rotamer a), 131.02 (8-C), 135.03 (4-C), 135.59 (8a-C), 145.84 (2-C), 152.84 (C=O); MS m/z 463.0522 (M + Na⁺) (C₁₉H₂₁N₂NaO₃ requires 463.0495).

1,1-Dimethylethyl N-(1-iodo-2-(N-(prop-2-enyl)-2,2,2-trifluoroacetamido)naphthalene-4-yI)-N-(prop-2-enyl)carbamate (41). Compound 29 (99.4 mg, 0.21 mmol), K₂CO₃ (119 mg, 0.83 mmol) and 3-bromopropene (84 mg, 0.69 mmol) in acetone (15 mL) were stirred at 50°C under N₂ for 16 h. Sat. aq. NaHCO₃ was added and mixture was extracted (EtOAc). Washing (brine), drying and evaporation gave 41 (115 mg, 99%) as a yellow oil: IR ν max 1698 cm⁻¹; ¹H NMR (COSY) δ 1.23 (0.6 H, br, Bu' conformers A,B), 3.71 (0.6 H, dd, J = 14.4, 8.3 Hz, CF₃CONCH conformer A), 3.76 (0.4 H, dd, J = 14.4, 8.0 Hz, CF₃CONCH conformer B), 3.83 (0.6 H, dd, J = 14.9, 7.4 Hz, BocNCH conformer A), 3.95 (0.4 H, dd, J = 14.7, 7.1 Hz, BocNCH conformer B), 4.53 (0.4 H, m, BocNCH conformer B), 4.64 (0.6 H, m, BocNCH conformer A), 4.98-5.21 (5 H, m, 2 × propenyl 3-H, CF₃CONCH conformers A,B), 5.85-5.94 (2 H, m, 2 × propenyl 2-H conformers A,B), 7.11 (1 H, s, 3-H conformers A,B), 7.61-7.68 (2 H, m, 6,7-H₂ conformers A,B), 7.83 (1 H, m, 5-H conformers A,B), 8.31 (1 H, m, 8-H conformers A,B); ¹³C NMR δ 27.88 (CMes conformer A), 28.11 (CMes conformer B), 52.45 (BocNCH₂ conformers A,B), 53.69 (CF₃CONCH₂ conformer A), 80.78 (CMes conformers A,B), 105.48 (1-C conformers A,B), 115.94 (q, J = 289.4 Hz, CF₃ conformers A,B), 118.46 (BocNCH₂CHCH₂ conformers A,B), 120.92 (CF₃CONCH₂CHCH₂ conformers A,B), 123.42 (5-C conformer A), 123.57 (5-C conformer B), 127.79 (3-C conformer A), 128.11 (3-C conformer B), 128.52 (6-C or 7-C conformers A,B), 128.91 (7-C or 6-C conformers A,B), 130.31 (CF₃CONCH₂CHCH₂ conformers A,B), 130.99 (4a-C conformers A,B), 133.37 (BocNCH₂CHCH₂ conformers A,B), 133.87 (8-C conformers A,B), 135.71 (8a-C conformers A,B), 139.39 (2-C conformers A,B), 139.86 (4-C conformers A,B), 154.53 (Boc C=O conformers A,B), 156.42 (q, J = 36.0 Hz, CF₃C=O conformer B); 19F NMR δ -68.58 (1.2 F, s, CF₃ conformer B), -68.65 (1.8 F, s, CF₃ conformer A); MS m/z 583.0804 (M + Na⁺) (C₂₃H₂₄F₃N₂NaO₃ requires 583.0681).

References for Supplementary Information


