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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 159.0446 (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 νₘₚₙ 3418, 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) (C₁₀H₇N₂O requires 203.0457).

4-Amino-2-nitronaphthalen-1-yl 1,1-dimethylethyl carbonate (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-Dimethylethyl (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 νₘₚₙ 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, dd, J = 8.2, 7.0, 1.1 Hz,
6-H), 7.77 (1 H, ddd, J = 8.2, 6.9, 1.2 Hz, 7-H), 7.87 (1 H, d, J = 8.4 Hz, 8-H), 8.33 (1 H, s, 2-H), 8.56 (1 H, dd, J = 8.4, 0.5 Hz, 5-H), 12.11 (1 H, s, OH); $^{13}$C NMR δ 28.31 (CMe$_2$), 81.31 (CMe$_3$), 112.82 (2-C), 121.46 (8-C), 125.45 (8a-C), 125.83 (4-C), 125.91 (4a-C), 127.25 (6-C), 127.55 (3-C), 131.56 (7-C), 152.98 (4-C), 153.50 (C=O); MS m/z 327.0966 (M + Na)$^+$ (C$_{15}$H$_{16}$N$_2$NaO$_3$ requires 327.0957).

4-(1,1-Dimethylethoxycarbonylamino)-2-nitronaphthalen-1-yl trifluoromethanesulfonate (19). (F$_3$CSO$_2$)$_2$O (1.20 g, 4.2 mmol) was added dropwise during 45 min to 18 (808 mg, 2.7 mmol) in dry pyridine (20 mL) under N$_2$ at 0°C and the mixture was stirred for 30 min at 0°C. The mixture was then warmed to 20°C during 10 min. Water was added and the mixture was extracted (EtOAc). Drying, evaporation and chromatography (CH$_2$Cl$_2$ → CH$_2$Cl$_2$ / EtOAc 1:1 → EtOAc) gave 19 (942 mg, 81%) as a yellow solid: mp 110-111°C; IR $\nu$$_{max}$ 3435, 1737 cm$^{-1}$; $^1$H NMR (NOESY) δ 1.59 (9 H, s, Bu$^t$), 7.19 (1 H, s, NH), 7.78-7.82 (2 H, m, 6.7-H$_2$), 7.96 (1 H, d, J = 8.0 Hz, 5-H), 8.29 (1 H, d, J = 8.2 Hz, 8-H), 8.73 (1 H, s, 3-H); $^{13}$C NMR δ 28.20 (CMe$_2$), 82.54 (CMe$_3$), 110.52 (3-C), 118.42 (q, J = 321.2 Hz, CF$_3$), 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). $^{19}$F NMR (CDCl$_3$) δ -72.55 (s, CF$_3$); MS m/z 459.0484 (M + Na)$^+$ (C$_{18}$H$_{15}$F$_3$N$_2$NaO$_7$S requires 459.0450).

1,1-Dimethyl 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 H$_2$ for 1.5 h. Filtration (Celite$^b$) and evaporation gave 21 (51 mg, 84%) as a dark buff solid: mp 155-156°C; IR $\nu$$_{max}$ 3331, 1704 cm$^{-1}$; $^1$H NMR δ 1.61 (9 H, s, Bu$^t$), 5.06 (2 H, s, NH$_2$), 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); $^{13}$C NMR δ 28.23 (CMe$_2$), 82.26 (CMe$_3$), 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)$^+$ (C$_{30}$H$_{32}$N$_4$NaO$_6$ requires 567.2200), 295.1052 (M + Na)$^+$ (C$_{18}$H$_{16}$N$_2$NaO$_3$ requires 295.1059).

1,1-Dimethyl N-(4-oxo-3-(2,2,2-trifluorooacetamido)naphthalen-1-ylidene)carbamate (22). K$_2$CO$_3$ (178 mg, 1.3 mmol) and Na$_2$S$_2$O$_4$ (198 mg, 1.1 mmol) in water (4.0 mL) were added dropwise to 18 (75 mg, 0.25 mmol) in CH$_2$Cl$_2$ (8.0 mL) and water (1.0 mL) under N$_2$. Stirring was continued for 16 h at 35°C. The organic phase was separated, dried and filtered. The filtrate was cooled to 0°C. Pr$_2$NEt (580 mg, 4.5 mmol) was added, followed by dropwise addition of (F$_3$CCO)$_2$O (315 mg, 1.5 mmol). The mixture was stirred at 0°C for 15 min then at 20°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°C; IR $\nu$$_{max}$ 3290, 3097, 1744 cm$^{-1}$; $^1$H NMR δ 1.66 (9 H, s, Bu$^t$), 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); $^{13}$C NMR δ 28.13 (CMe$_2$), 84.22 (CMe$_3$), 114.57 (2-C), 114.72 (q, J = 288.4 Hz, CF$_3$), 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, CF$_3$C=O), 161.36 (1-C), 178.63 (4-C); $^{19}$F NMR (CDCl$_3$) δ -75.76 (s, CF$_3$); MS m/z 367.0941 (M - H)$^+$ (C$_{17}$H$_{14}$F$_3$N$_2$O$_4$ 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 N$_2$ for 4 h. The evaporation residue, EtOAc, was washed (water, brine). Drying, evaporation and chromatography (CH$_2$Cl$_2$ → CH$_2$Cl$_2$ / EtOAc 4:1) gave 31 (1.64 g, 92%) as a white solid: mp
152-154°C (lit. 3 146-148°C); IR ν_max 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 toluene. 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 ν_max 3315, 1687; ¹H NMR δ 1.39 (3 H, t, J = 7.1 Hz, OCH₂CH₃), 2.35 (6 H, s, NMe₂), 2.76 (2 H, t, J = 5.8 Hz, Me₂NCH₂CH₂), 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 ν_max 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-Nitrobenzenesulfonfyl 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]D⁰ (c = 6.5, CHCl₃) +33.3° (lit. 6 [α]D⁰ + 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 μmol) was stirred with 37 (17 mg, 66 μmol) and K₂CO₃ (26 mg, 0.19 mmol) in acetone (20 mL) at 50°C under N₂ for 3 d. Sat. aq. NaHCO₃ 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: ¹H 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, CHNOCOF₃ 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, CHNOCOF₃ 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, CHNOCOF₃ rotamer b), 4.63 (0.6 H, dd, J = 14.3, 3.9 Hz, CHNOCOF₃ rotamer a), 6.99 (1 H, s, NH rotamers a,b), 7.63-7.67 (2 H, m, 6-H 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); ¹³C NMR δ 28.30 (CMe₂ rotamer b), 28.33 (CMe₂ 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 b), 53.29 (CH₂NOCOF₃ rotamer b), 54.66 (CH₂NOCOF₃ rotamer a), 81.64 (CMε₂ rotamer a), 81.68 (CMε₂ rotamer b), 99.03 (1-C rotamer a), 99.45 (1-C rotamer b), 115.88 (q, J = 288.4 Hz, CF₃ 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), 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, F₃CC=O rotamer a), 157.20 (q, J = 38.1 Hz, F₃CC=O rotamer b); ¹⁹F NMR δ -68.40 (0.4 F, s, CF₃ rotamer b), -68.52 (0.6 F, s, CF₃ rotamer a); MS m/z 537.0504 (M + H)⁺ (C₂₀H₂₃F₃InN₂O₄ requires 537.0498). Further elution gave 38B (9.1 mg, 39%) as a pale yellow oil: ¹H 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, CHNOCOF₃), 4.71 (1 H, dd, J = 12.2, 2.8 Hz, CHNOCOF₃), 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), 7.66 (1 H, d, J = 8.4 Hz, 5-H), 8.19 (1 H, d, J = 8.5 Hz, 8-H); ¹³C NMR δ 28.29 (CMe₂), 44.85 (oxirane 3-C), 48.89 (oxirane 2-C), 69.29 (CH₂NOCOF₃), 81.25 (CMe₂), 85.75 (1-C), 110.89 (3-C), 115.72 (q, J = 284.6 Hz, CF₃), 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); ¹⁹F NMR δ -75.62 (s, CF₃); MS m/z 537.0504 (M + H)⁺ (C₂₀H₂₁F₃InN₂O₄ requires 537.0498).

1,1-Dimethylethyl S-N-(1-iodo-2-(oxiran-2-ylmethylamino)naphthalen-4-yl)carbamate (40). MeLi in Et₂O (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 N₂ 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 9:1) gave 40 (39 mg, 73%) as a yellow solid: mp 127-128°C; IR v_max 3389, 3336, 3082, 1699 cm⁻¹; ¹H 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/H conformer A), 3.55 (0.45 H, dd, J = 6.2, 4.6 Hz, NHC/H conformer B), 3.71 (0.45 H, dd, J = 5.7, 3.5 Hz, NHCH/H conformer.
1,1-Dimethylethyl N-(1-iodo-2-(N-(prop-2-enyl)-2,2,2-trifluoroacetamido)naphthalene-4-yl)-N-(prop-2-enyl)carbamate (41). Compound 29 (99.4 mg, 0.21 mmol), K$_2$CO$_3$ (119 mg, 0.83 mmol) and 3-bromopropene (84 mg, 0.69 mmol) in acetone (15 mL) were stirred at 50°C under N$_2$ for 16 h. Sat. aq. NaHCO$_3$ was added and mixture was extracted (EtOAc). Washing (brine), drying and evaporation gave 41 (115 mg, 99%) as a yellow oil: IR $\nu$ 1698 cm$^{-1}$; $^1$H NMR (COSY) $\delta$ 1.23 (0.6 H, br, Bu$'$ conformers A,B), 3.71 (0.6 H, dd, J = 14.4, 8.3 Hz, CF$_3$CONCH conformer A), 3.76 (0.4 H, dd, J = 14.4, 8.0 Hz, CF$_3$CONCH 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-C, CF$_3$CONCH 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-H$_2$ conformers A,B), 7.83 (1 H, m, 5-H conformers A,B), 8.31 (1 H, m, 8-H conformers A,B); $^{13}$C NMR $\delta$ 27.88 (CMes conformer A), 28.11 (CMes conformer B), 52.45 (BocNCH$_2$ conformers A,B), 53.69 (CF$_3$CONCH$_2$ conformer A), 80.78 (CMes conformers A,B), 105.48 (1-C conformers A,B), 115.94 (q, J = 289.4 Hz, CF$_3$ conformers A,B), 118.46 (BocNCH$_2$CHCH$_2$ conformers A,B), 120.92 (CF$_3$CONCH$_2$CHCH$_2$ conformers A,B), 123.42 (5-C conformer B), 123.57 (5-C conformer A), 127.79 (3-C conformer B), 128.11 (3-C conformer A), 128.52 (6-C or 7-C conformers A,B), 128.91 (7-C or 6-C conformers A,B), 130.31 (CF$_3$CONCH$_2$CHCH$_2$ conformers A,B), 130.99 (4a-C conformers A,B), 133.37 (BocNCH$_2$CHCH$_2$ 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, CF$_3$C=O conformer B); 156.50 (q, J = 35.0 Hz, CF$_3$C=O conformer A); $^{19}$F NMR $\delta$ -68.58 (1.2 F, s, CF$_3$ conformer B); -68.65 (1.8 F, s, CF$_3$ conformer A); MS m/z 583.0804 (M + Na)$^+$ (C$_{23}$H$_{24}$F$_3$IN$_2$NaO$_3$ requires 583.0681).

References for Supplementary Information