Supporting Information Available For:

Preparation of a Psammaplysene-Based Library

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GENERAL METHODS AND MATERIALS

^{1}H-NMR spectra of intermediates were recorded on a Varian Inova-500 NMR spectrometer (at 500 MHz), and representative examples are included. A Varian Inova-600 spectrometer was used to obtain ^{1}H-NMR (at 600 MHz), ^{13}C-NMR (at 151 MHz with complete proton decoupling) and HMQC/HMBC-NMR spectra of final products. ^{1}H-NMR spectra of all final products are included, along with ^{13}C-NMR spectra of those prepared on large scale and HMQC/HMBC spectra of those prepared on small scale. NMR data were collected at 25 ^{o}C. Chemical shifts δ are reported in parts per million (ppm) downfield relative to tetramethylsilane (δ=0.00), using the solvent residual peak in each case as a reference.

Mass spectra were obtained on a Waters Alliance LC-MS system which is a combination of a Micromass Platform LCT mass spectrometer (using ESI), a Waters 2795 separation module and a Waters 2996 photodiode array detector.

Microwave reactions were carried out using a Personal Chemistry Emrys^{TM} Optimizer.

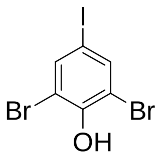
HPLC purifications were carried out using an Agilent 1100 Series HPLC system with a semi-preparative Discovery C18 column from SUPELCO.

Flash chromatography was performed using Silica Gel 60 (particle size 0.040-0.063 mm) from Fisher Scientific.

For those reactions requiring an inert atmosphere, the sealed reaction vessels/flasks containing the solids were initially purged with argon before any additions of liquids and were kept under argon at balloon pressure throughout the reaction.

All organic solvents used for reactions in this study were anhydrous or redistilled (unless otherwise stated) and came in Sure/Seal^{TM} bottles, packaged under nitrogen. All solvents and chemicals were purchased from Sigma-Aldrich, with the exception of $Pd(PPh_3)_4$ which was purchased from Strem Chemicals.

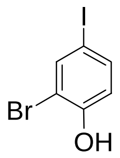
EXPERIMENTAL PROCEDURES/CHARACTERIZATION DATA



2

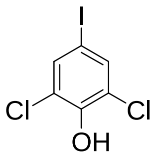
<u>2:</u> Procedure: A round-bottom flask was charged with 4.51 g (20.5 mmol) of 4-iodophenol (**1**). These were dissolved by adding 45 mL of 1,2-dichlorobenzene, and cooled at 0 ^{o}C. Under vigorous stirring, 6.54 g (43 mmol, 2.1 equiv) of freshly prepared *N*-bromo-*tert*-butylamine dissolved in 20 mL of 1,2-dichlorobenzene were added dropwise through an addition funnel at a very slow rate. The reaction was then allowed to proceed for 30 more minutes at 0 ^{o}C, during which **2** precipitated out as a white solid. The reaction mixture was filtered through a Buchner funnel while still cold and the solid was washed with a small quantity of cold 1,2-dichlorobenzene and allowed to dry under vacuum. This was followed by additional drying on a lyophilizer, after which LC-MS and NMR showed the product to be free of impurities. The solid weighted 6.47 g (17.2 mmol, 84%).

^{1}H-NMR (CDCl$_3$, 7.26 ppm)-δ (ppm): 5.88 (1H, singlet), 7.68 (2H, singlet). **MS (ESI)-*m/z*:** (M-H)$^-$-found: 374.73, (M-H)$^-$-calculated: 374.75.



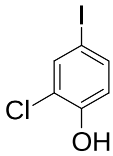
3

<u>3:</u> Procedure: A round-bottom flask was charged with 3.30 g (15 mmol) of 4-iodophenol (**1**). These were dissolved in 20 mL of MeOH, and cooled at 0 ^{o}C. Under vigorous stirring, 0.84 mL (2.61 g, 16.5 mmol, 1.1 equiv) of Br$_2$ were added dropwise and the reaction was allowed to proceed for 30 minutes at 0-10 ^{o}C. Aqueous Na$_2$S$_2$O$_3$ (sat) was then added to quench the reaction and the mixture was transferred to a separatory funnel and extracted twice with ethyl ether. The two organic phases were combined and washed once with aqueous NaCl (sat) and once with H$_2$O. After drying the ether phase over MgSO$_4$, the solvent was removed under vacuum. The crude residue was redissolved in CH$_2$Cl$_2$, applied to a silica column and eluted with CH$_2$Cl$_2$. Purification afforded 2.89 g (9.7 mmol, 65%) of **3** as a white solid. **^{1}H-NMR (CDCl$_3$, 7.26 ppm)-δ (ppm):** 5.49 (1H, singlet), 6.79 (1H, doublet, *J*=8.4 Hz), 7.49 (1H, doublet, *J*=8.4 Hz), 7.76 (1H, singlet). **MS (ESI)-*m/z*:** (M-H)$^-$-found: 296.87, (M-H)$^-$-calculated: 296.84.



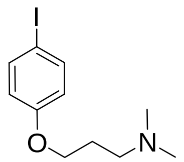
4

<u>4:</u> Procedure: A round-bottom flask was charged with 5.50 g (25 mmol) of 4-iodophenol (**1**). 90 mL of toluene, followed by 0.035 mL (0.026 g, 0.2 mmol, 0.008 equiv) of di-*iso*-butylamine were added under argon, and the solution was warmed up to 70 ^{o}C. 6.1 mL (10.1 g, 75 mmol, 3 equiv) of SO$_2$Cl$_2$ were slowly syringed in (gas escapes to balloon!) and the mixture was stirred at 70 ^{o}C for 1 h. It was then cooled, diluted with ethyl ether and washed once with aqueous $NaHCO_3$ (sat), once with aqueous NaCl (sat) and once with H_2O. After drying the organic phase over $MgSO_4$, the solvent was removed under vacuum. The crude product was redissolved in 5:1 (v/v) hexane-ethyl ether, applied to a silica column and eluted using the same solvent. Purification afforded 6.43 g (22.25 mmol, 89%) of **4** as a white solid. **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 5.85 (1H, singlet), 7.57 (2H, singlet). **MS (ESI)-*m/z*:** $(M-H)^-$-found: 286.82, $(M-H)^-$-calculated: 286.85.



5

<u>5:</u> **Procedure:** A round-bottom flask was charged with 5.94 g (27 mmol) of 4-iodophenol (**1**). 150 mL of toluene, followed by 0.0375 mL (0.028 g, 0.216 mmol, 0.008 equiv) of di-*iso*-butylamine were added under argon, and the solution was warmed up to 70 °C. 2.2 mL (3.66 g, 27 mmol, 1 equiv) of SO_2Cl_2 were slowly syringed in (gas escapes to balloon!) and the mixture was stirred at 70 °C for 1 h. It was then cooled, diluted with ethyl ether and washed once with aqueous $NaHCO_3$ (sat), once with aqueous NaCl (sat) and once with H_2O. After drying the organic phase over $MgSO_4$, the solvent was removed under vacuum. The crude product was redissolved in 4:1 (v/v) hexane-ethyl ether, applied to a silica column and eluted using the same solvent. Purification afforded 7.02 g (24.3 mmol, 90%) of **5** as a white solid. **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 5.54 (1H, singlet), 6.79 (1H, doublet, *J*=8.4 Hz), 7.46 (1H, doublet, *J*=8.4 Hz), 7.62 (1H, singlet). **MS (ESI)-*m/z*:** $(M-H)^-$-found: 252.92, $(M-H)^-$-calculated: 252.89.



6a

<u>6a:</u> Procedure: A round-bottom flask was charged with 1.10 g (5 mmol) of **1**, 1.03 g (6.5 mmol, 1.3 equiv) of 1-chloro-3-dimethylamino-propane hydrochloride, 4.07 g (12.5 mmol, 2.5 equiv) of Cs_2CO_3 and 0.19 g (1.25 mmol, 0.25 equiv) of NaI. 50 mL of CH_3CN were added and the mixture was stirred at 65 ^{o}C under argon for 12 h. It was then cooled and filtered to remove inorganic solids. The solvent was evaporated under vacuum and the crude product was redissolved in CH_2Cl_2, applied to a silica column and eluted with 9:1 (v/v) CH_2Cl_2-CH_3OH. Purification afforded 1.01 g (3.3 mmol, 66%) of **6a** as a white solid. **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.94 (2H, apparent quintet, apparent *J*=6.8 Hz), 2.25 (6H, singlet), 2.43 (2H, triplet, *J*=7.2 Hz), 3.97 (2H, triplet, *J*=6.4 Hz), 6.69 (2H, doublet, *J*=8.9 Hz), 7.54 (2H, doublet, *J*=8.9 Hz). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 306.02, $(M+H)^+$-calculated: 306.04.

This method is general and was used for preparing iodides **6a-10a** from phenols **1-5** respectively.

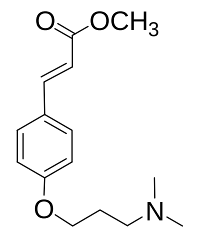
<u>7a:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 2.12 (2H, apparent quintet, apparent *J*=6.8 Hz), 2.39 (6H, singlet), 2.68 (2H, triplet, *J*=8.1 Hz), 4.05 (2H, triplet, *J*=5.5 Hz), 7.81 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 461.89, $(M+H)^+$-calculated: 461.86.

<u>8a:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 2.02 (2H, apparent quintet, apparent *J*=6.7 Hz), 2.28 (6H, singlet), 2.53 (2H, triplet, *J*=7.2 Hz), 4.05 (2H, triplet, *J*=6.2 Hz), 6.65

(1H, doublet, *J*=8.6 Hz), 7.50 (1H, doublet, *J*=8.6 Hz), 7.81 (1H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 383.98, $(M+H)^+$-calculated: 383.95.

<u>9a:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 2.02 (2H, apparent quintet, apparent *J*=6.9 Hz), 2.28 (6H, singlet), 2.56 (2H, triplet, *J*=7.4 Hz), 4.05 (2H, triplet, *J*=6.4 Hz), 7.60 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 373.93, $(M+H)^+$-calculated: 373.96.

<u>10a:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 2.01 (2H, apparent quintet, apparent *J*=6.7 Hz), 2.28 (6H, singlet), 2.51 (2H, triplet, *J*=7.1 Hz), 4.06 (2H, triplet, *J*=6.3 Hz), 6.69 (1H, doublet, *J*=8.6 Hz), 7.47 (1H, doublet, *J*=8.6 Hz), 7.64 (1H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 340.03, $(M+H)^+$-calculated: 340.00.



6b

<u>6b:</u> Procedure: A round-bottom flask was charged with 1.01 g (3.3 mmol) of **6a**, 0.185 g (0.825 mmol, 0.25 equiv) of $Pd(OAc)_2$, 1.06 g (3.3 mmol, 1 equiv) of Bu_4NBr, 0.97 g (9.9 mmol, 3 equiv) of KOAc and a few 4 Å molecular sieves. 25 mL of DMF were added to dissolve the solids, followed by 1.49 mL (16.5 mmol, 5 equiv) of methyl acrylate. The mixture was vigorously agitated on a lab shaker at room temperature for 8 h under argon. It was then diluted with ethyl ether and washed once with aqueous $NaHCO_3$ (sat), once with aqueous NaCl (sat) and once with H_2O. After drying the organic phase over $MgSO_4$, the solvent was removed under vacuum. The residue was redissolved in CH_2Cl_2, applied to a silica column and eluted with 9:1 (v/v) CH_2Cl_2-CH_3OH. Purification afforded 0.61 g (2.3 mmol, 70%) of **6b** as a white wax. **^{1}H-**

NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 1.98 (2H, apparent quintet, apparent *J*=6.7 Hz), 2.31 (6H, singlet), 2.51 (2H, triplet, *J*=7.0 Hz), 3.82 (3H, singlet), 4.05 (2H, triplet, *J*=6.4 Hz), 6.32 (1H, doublet, *J*=16.0 Hz), 6.89 (2H, doublet, *J*=8.7 Hz), 7.46 (2H, doublet, *J*=8.7 Hz), 7.66 (1H, doublet, *J*=16.0 Hz). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 264.15, $(M+H)^+$-calculated: 264.16.

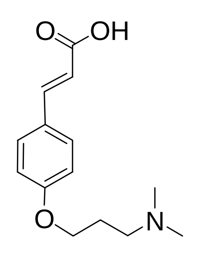
This method is general and was used for preparing methyl esters **6b-10b** from iodides **6a-10a** respectively.

<u>7b:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 2.06 (2H, apparent quintet, apparent *J*=6.8 Hz), 2.29 (6H, singlet), 2.58 (2H, triplet, *J*=7.5 Hz), 3.79 (3H, singlet), 4.07 (2H, triplet, *J*=6.1 Hz), 6.34 (1H, doublet, *J*=16.0 Hz), 7.48 (1H, doublet, *J*=16.0 Hz), 7.64 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 420.00, $(M+H)^+$-calculated: 419.98.

<u>8b:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 2.03 (2H, apparent quintet, apparent *J*=6.7 Hz), 2.29 (6H, singlet), 2.53 (2H, triplet, *J*=7.2 Hz), 3.79 (3H, singlet), 4.05 (2H, triplet, *J*=6.2 Hz), 6.30 (1H, doublet, *J*=16.0 Hz), 6.89 (1H, doublet, *J*=8.6 Hz), 7.40 (1H, doublet, *J*=8.6 Hz), 7.57 (1H, doublet, *J*=16.0 Hz), 7.72 (1H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 342.04, $(M+H)^+$-calculated: 342.07.

<u>9b:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 2.04 (2H, apparent quintet, apparent *J*=6.9 Hz), 2.29 (6H, singlet), 2.57 (2H, triplet, *J*=7.4 Hz), 3.81 (3H, singlet), 4.11 (2H, triplet, *J*=6.4 Hz), 6.35 (1H, doublet, *J*=15.9 Hz), 7.44 (2H, singlet), 7.51 (1H, doublet, *J*=15.9 Hz). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 332.05, $(M+H)^+$-calculated: 332.08.

<u>10b:</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 2.02 (2H, apparent quintet, apparent *J*=6.8 Hz), 2.27 (6H, singlet), 2.50 (2H, triplet, *J*=7.2 Hz), 3.79 (3H, singlet), 4.06 (2H, triplet, *J*=6.4 Hz), 6.31 (1H, doublet, *J*=16.0 Hz), 6.92 (1H, doublet, *J*=8.6 Hz), 7.35 (1H, doublet, *J*=8.6 Hz), 7.57 (1H, singlet), 7.61 (1H, doublet, *J*=16.0 Hz). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 298.13, $(M+H)^+$-calculated: 298.12 .



6c

<u>6c:</u> **Procedure:** A flask was charged with 0.61 g (2.3 mmol) of **6b** and 0.64 g (11.5 mmol, 5 equiv) of KOH as a fine powder. 10 mL of CH_3OH and 0.207 mL (11.5 mmol, 5 equiv) of H_2O were added and the solution was vigorously stirred at room temperature for 12 h. The reaction mixture was then concentrated under vacuum, applied directly to a silica column and eluted using a CH_2Cl_2-CH_3OH gradient, starting with a 9-1 (v/v) mixture and finishing with a 7-3 (v/v) mixture, modifying each mixture with 0.5% triethylamine. Purification afforded 0.545 g (2.19 mmol, 95%) of **6c** as a white solid. **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.18 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.81 (6H, singlet), 3.19 (2H, triplet, *J*=7.5 Hz), 4.11 (2H, triplet, *J*=5.7 Hz), 6.26 (1H, doublet, *J*=15.9 Hz), 6.90 (2H, doublet, *J*=8.6 Hz), 7.30 (1H, doublet, *J*=15.9 Hz), 7.40 (2H, doublet, *J*=8.6 Hz). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 250.12, $(M+H)^+$-calculated: 250.15.

This method is general and was used for preparing acids **6c-10c** from methyl esters **6b-10b** respectively.

<u>7c:</u> ^{1}H-NMR (CD$_3$OD, 3.31 ppm)-δ (ppm): 2.21 (2H, apparent quintet, apparent *J*=6.8 Hz), 2.76 (6H, singlet), 3.23 (2H, triplet, *J*=7.8 Hz), 4.08 (2H, triplet, *J*=5.8 Hz), 6.44 (1H, doublet, *J*=15.9 Hz), 7.21 (1H, doublet, *J*=15.9 Hz), 7.71 (2H, singlet). **MS (ESI)-*m/z*:** (M+H)$^+$-found: 405.95, (M+H)$^+$-calculated: 405.97.

<u>8c:</u> ^{1}H-NMR (CD$_3$OD, 3.31 ppm)-δ (ppm): 2.22 (2H, apparent quintet, apparent *J*=6.5 Hz), 2.81 (6H, singlet), 3.22 (2H, triplet, *J*=7.2 Hz), 4.19 (2H, triplet, *J*=5.8 Hz), 6.21 (1H, doublet, *J*=15.9 Hz), 6.99 (1H, doublet, *J*=8.5 Hz), 7.12 (1H, doublet, *J*=15.9 Hz), 7.36 (1H, doublet, *J*=8.5 Hz), 7.65 (1H, singlet). **MS (ESI)-*m/z*:** (M+H)$^+$-found: 328.07, (M+H)$^+$-calculated: 328.06.

<u>9c:</u> ^{1}H-NMR (CD$_3$OD, 3.31 ppm)-δ (ppm): 2.20 (2H, apparent quintet, apparent *J*=6.9 Hz), 2.76 (6H, singlet), 3.22 (2H, triplet, *J*=7.9 Hz), 4.12 (2H, triplet, *J*=5.9 Hz), 6.44 (1H, doublet, *J*=16.0 Hz), 7.21 (1H, doublet, *J*=15.9 Hz), 7.55 (2H, singlet). **MS (ESI)-*m/z*:** (M+H)$^+$-found: 318.06, (M+H)$^+$-calculated: 318.07.

<u>10c:</u> ^{1}H-NMR (CD$_3$OD, 3.31 ppm)-δ (ppm): 2.24 (2H, apparent quintet, apparent *J*=6.4 Hz), 2.84 (6H, singlet), 3.25 (2H, triplet, *J*=7.1 Hz), 4.20 (2H, triplet, *J*=5.7 Hz), 6.16 (1H, doublet, *J*=16.0 Hz), 7.00 (1H, doublet, *J*=8.5 Hz), 7.08 (1H, doublet, *J*=16.0 Hz), 7.29 (1H, doublet, *J*=8.5 Hz), 7.46 (1H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 284.09, $(M+H)^+$-calculated: 284.11.

__**11a-18a:**__ Iodides **11a-18a** were prepared using the same procedure as for **6a**, from phenol **2** and chlorides **11-18** respectively.

__**11a:**__ **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 2.39 (6H, singlet), 2.82 (2H, triplet, *J*=5.7 Hz), 4.09 (2H, triplet, *J*=5.7 Hz), 7.81 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 447.87, $(M+H)^+$-calculated: 447.84.

__**12a:**__ **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.08 (6H, triplet, *J*=7.0 Hz), 2.68 (4H, quartet, *J*=7.0 Hz), 2.99 (2H, triplet, *J*=6.5 Hz), 4.06 (2H, triplet, *J*=6.5 Hz), 7.81 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 475.84, $(M+H)^+$-calculated: 475.87.

__**13a:**__ **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.02 (12H, doublet, *J*=6.4 Hz), 2.90 (2H, triplet, *J*=7.8 Hz), 3.02 (2H, septet, *J*=6.4 Hz), 3.87 (2H, triplet, *J*=7.8 Hz), 7.79 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 503.90, $(M+H)^+$-calculated: 503.91.

__**14a:**__ **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.83 (4H, broad singlet), 2.67 (4H, broad singlet), 2.99 (2H, triplet, *J*=6.0 Hz), 4.12 (2H, triplet, *J*=6.0 Hz), 7.80 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 473.84, $(M+H)^+$-calculated: 473.86.

<u>15a:</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.45 (2H, broad singlet), 1.63 (4H, broad singlet), 2.56 (4H, broad singlet), 2.87 (2H, triplet, *J*=5.7 Hz), 4.13 (2H, triplet, *J*=5.7 Hz), 7.80 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 487.87, $(M+H)^+$-calculated: 487.87.

<u>16a:</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 2.62 (4H, broad singlet), 2.88 (2H, triplet, *J*=5.7 Hz), 3.76 (4H, broad singlet), 4.13 (2H, triplet, *J*=5.7 Hz), 7.81 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 489.88, $(M+H)^+$-calculated: 489.85.

<u>17a:</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.44 (2H, broad singlet), 1.60 (4H, broad singlet), 2.06 (2H, apparent quintet, apparent *J*=6.9 Hz), 2.43 (4H, broad singlet), 2.57 (2H, triplet, *J*=7.4 Hz), 4.03 (2H, triplet, *J*=6.4 Hz), 7.80 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 501.90, $(M+H)^+$-calculated: 501.89.

<u>18a:</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.65 (1H, multiplet), 1.78 (1H, multiplet), 1.88 (2H, multiplet), 2.17 (1H, multiplet), 2.27 (1H, multiplet), 2.36 (1H, multiplet), 2.45 (3H, singlet), 2.56 (1H, multiplet), 3.22 (1H, multiplet), 4.03 (2H, multiplet), 7.80 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 487.89, $(M+H)^+$-calculated: 487.87.

<u>11b-18b:</u> Methyl esters **11b**-**18b** were prepared using the same procedure as for **6b**, from iodides **11a**-**18a** respectively.

<u>11b:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 2.42 (6H, singlet), 2.84 (2H, triplet, *J*=6.4 Hz), 3.80 (3H, singlet), 4.15 (2H, triplet, *J*=6.4 Hz), 6.35 (1H, doublet, *J*=16.0 Hz), 7.50 (1H, doublet, *J*=16.0 Hz), 7.65 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 405.97, $(M+H)^+$-calculated: 405.97.

<u>12b:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 1.09 (6H, triplet, *J*=7.0 Hz), 2.69 (4H, quartet, *J*=7.0 Hz), 3.01 (2H, triplet, *J*=6.5 Hz), 3.80 (3H, singlet), 4.13 (2H, triplet, *J*=6.5 Hz), 6.36 (1H, doublet, *J*=15.9 Hz), 7.50 (1H, doublet, *J*=15.9 Hz), 7.65 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 434.03, $(M+H)^+$-calculated: 434.00.

<u>13b:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 1.04 (12H, doublet, *J*=6.5 Hz), 2.94 (2H, triplet, *J*=7.6 Hz), 3.04 (2H, septet, *J*=6.5 Hz), 3.80 (3H, singlet), 3.92 (2H, triplet, *J*=7.6 Hz), 6.34 (1H, doublet, *J*=16.0 Hz), 7.49 (1H, doublet, *J*=16.0 Hz), 7.65 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 462.01, $(M+H)^+$-calculated: 462.03.

<u>14b:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 1.85 (4H, broad singlet), 2.72 (4H, broad singlet), 3.03 (2H, triplet, *J*=5.7 Hz), 3.80 (3H, singlet), 4.18 (2H, triplet, *J*=5.7 Hz), 6.35 (1H, doublet, *J*=16.0 Hz), 7.50 (1H, doublet, *J*=16.0 Hz), 7.65 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 431.96, $(M+H)^+$-calculated: 431.98.

<u>15b:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 1.47 (2H, broad singlet), 1.65 (4H, broad singlet), 2.58 (4H, broad singlet), 2.90 (2H, triplet, *J*=5.7 Hz), 3.80 (3H, singlet), 4.18

(2H, triplet, *J*=5.7 Hz), 6.35 (1H, doublet, *J*=15.9 Hz), 7.50 (1H, doublet, *J*=15.9 Hz), 7.65 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 446.03, $(M+H)^+$-calculated: 446.00.

<u>**16b:**</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 2.64 (4H, broad singlet), 2.91 (2H, triplet, *J*=5.7 Hz), 3.77 (4H, broad singlet), 3.81 (3H, singlet), 4.19 (2H, triplet, *J*=5.7 Hz), 6.36 (1H, doublet, *J*=16.0 Hz), 7.51 (1H, doublet, *J*=16.0 Hz), 7.65 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 447.99, $(M+H)^+$-calculated: 447.98.

<u>**17b:**</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.45 (2H, broad singlet), 1.62 (4H, broad singlet), 2.08 (2H, apparent quintet, apparent *J*=6.8 Hz), 2.46 (4H, broad singlet), 2.59 (2H, triplet, *J*=7.2 Hz), 3.80 (3H, singlet), 4.07 (2H, triplet, *J*=6.4 Hz), 6.34 (1H, doublet, *J*=16.0 Hz), 7.50 (1H, doublet, *J*=16.0 Hz), 7.64 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 460.00, $(M+H)^+$-calculated: 460.01.

<u>**18b:**</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.60 (1H, multiplet), 1.75 (1H, multiplet), 1.83 (2H, multiplet), 2.13 (1H, multiplet), 2.23 (1H, multiplet), 2.35 (1H, multiplet), 2.43 (4H, broad singlet-two overlapping peaks), 3.15 (1H, multiplet), 3.80 (3H, singlet), 4.07 (2H, multiplet), 6.35 (1H, doublet, *J*=16.0 Hz), 7.50 (1H, doublet, *J*=16.0 Hz), 7.65 (2H, singlet)**. MS (ESI)-*m/z*:** $(M+H)^+$-found: 445.98, $(M+H)^+$-calculated: 446.00.

<u>**11c-18c:**</u> Acids **11c-18c** were prepared using the same procedure as for **6c**, from methyl esters **11b-18b** respectively.

<u>11c:</u> ^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm): 2.88 (6H, singlet), 3.43 (2H, triplet, *J*=5.1 Hz), 4.28 (2H, triplet, *J*=5.1 Hz), 6.47 (1H, doublet, *J*=16.0 Hz), 7.25 (1H, doublet, *J*=16.0 Hz), 7.76 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 391.94, $(M+H)^+$-calculated: 391.95.

<u>12c:</u> ^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm): 1.27 (6H, triplet, *J*=7.3 Hz), 3.12 (4H, quartet, *J*=7.3 Hz), 3.38 (2H, triplet, *J*=5.7 Hz), 4.25 (2H, triplet, *J*=5.7 Hz), 6.48 (1H, doublet, *J*=15.9 Hz), 7.23 (1H, doublet, *J*=15.9 Hz), 7.77 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 420.00, $(M+H)^+$-calculated: 419.98.

<u>13c:</u> ^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm): 1.21 (12H, doublet, *J*=6.6 Hz), 3.19 (2H, triplet, *J*=7.2 Hz), 3.35 (2H, septet, *J*=6.6 Hz), 4.10 (2H, triplet, *J*=7.2 Hz), 6.46 (1H, doublet, *J*=15.9 Hz), 7.24 (1H, doublet, *J*=15.9 Hz), 7.77 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 447.98, $(M+H)^+$-calculated: 448.01.

<u>14c:</u> ^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm): 2.05 (4H, broad singlet), 3.26 (4H, broad singlet), 3.45 (2H, triplet, *J*=5.2 Hz), 4.26 (2H, triplet, *J*=5.2 Hz), 6.45 (1H, doublet, *J*=15.9 Hz), 7.20 (1H, doublet, *J*=15.9 Hz), 7.75 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 418.00, $(M+H)^+$-calculated: 417.97.

<u>15c:</u> ^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm): 1.62 (2H, broad singlet), 1.81 (4H, broad singlet), 3.07 (4H, broad singlet), 3.29 (2H, triplet, *J*=5.4 Hz), 4.27 (2H, triplet, *J*=5.4

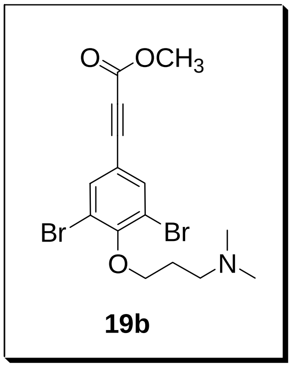
Hz), 6.45 (1H, doublet, *J*=16.0 Hz), 7.21 (1H, doublet, *J*=16.0 Hz), 7.76 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 432.00, $(M+H)^+$-calculated: 431.98.

16c: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.70 (4H, broad singlet), 2.95 (2H, triplet, *J*=5.6 Hz), 3.73 (4H, broad singlet), 4.19 (2H, triplet, *J*=5.6 Hz), 6.47 (1H, doublet, *J*=16.0 Hz), 7.30 (1H, doublet, *J*=16.0 Hz), 7.80 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 433.99, $(M+H)^+$-calculated: 433.96.

17c: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.62 (2H, broad singlet), 1.79 (4H, broad singlet), 2.21 (2H, apparent quintet, apparent *J*=6.5 Hz), 2.98 (4H, broad singlet), 3.12 (2H, triplet, *J*=7.3 Hz), 4.07 (2H, triplet, *J*=5.7 Hz), 6.45 (1H, doublet, *J*=15.9 Hz), 7.22 (1H, doublet, *J*=15.9 Hz), 7.72 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 445.98, $(M+H)^+$-calculated: 446.00.

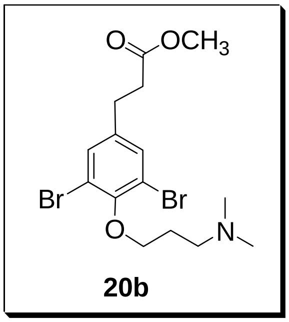
18c: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.81 (1H, multiplet), 2.01 (1H, multiplet), 2.14 (3H, multiplet), 2.31 (2H, multiplet), 2.50 (1H, multiplet), 2.79 (3H, singlet), 3.48 (1H, multiplet), 4.12 (1H, multiplet), 4.74 (1H, multiplet), 6.46 (1H, doublet, *J*=15.9 Hz), 7.22 (1H, doublet, *J*=15.9 Hz), 7.77 (2H, singlet)**.** **MS (ESI)-*m/z*:** $(M+H)^+$-found: 431.95, $(M+H)^+$-calculated: 431.98.

19b: **Procedure:** A round-bottom flask was charged with 0.65 g (1.4 mmol) of **7a**, 0.081 g (0.7 mmol, 0.05 equiv) of $Pd(PPh_3)_4$ and 0.38 g (1.68 mmol, 1.2 equiv) of $ZnBr_2$. 5 mL of THF were added, followed by 0.94 mL (0.68 g, 6.7 mmol, 4.8 equiv) of TEA and 0.16



19b

mL (0.16 g, 1.9 mmol, 1.4 equiv) of methyl propiolate. The mixture was stirred vigorously under argon in the dark for 8 h. It was then diluted with ethyl ether and washed once with aqueous $NaHCO_3$ (sat), once with aqueous NaCl (sat) and once with H_2O. After drying the organic phase over $MgSO_4$, the solvent was removed under vacuum. The residue was redissolved in CH_2Cl_2, applied to a silica column and eluted with 9:1 (v/v) CH_2Cl_2-CH_3OH. Purification afforded 0.42 g (1.0 mmol, 71%) of **19b** as a yellowish oil. **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 2.06 (2H, apparent quintet, apparent J=6.6 Hz), 2.30 (6H, singlet), 2.58 (2H, triplet, J=6.8 Hz), 3.83 (3H, singlet), 4.04 (2H, triplet, J=6.4 Hz), 7.64 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 418.00, $(M+H)^+$-calculated: 417.97.



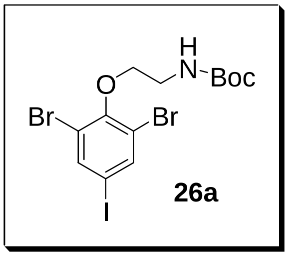
20b

20b: Procedure: 0.21 g (0.5 mmol) of **7b** were transferred to a 5 mL microwave vial, in which we had pre-mixed 2.5 mL of DMSO, 0.115 mL (0.14 g, 3.0 mmol, 6 equiv) of formic acid and 0.35 mL (0.25 g, 2.5 mmol, 5 equiv) of TEA. The mixture was agitated until it became a transparent solution. 0.014 g (0.015 mmol, 0.03 equiv) of $RhCl(PPh_3)_3$ were then added to the solution and the vial was sealed. It was inserted in the microwave synthesizer cavity and after 60 sec pre-stirring, it was submitted to microwave irradiation at 150 ^oC for 30 sec (fixed time). It was then cooled numerous times before opening the cavity, and once the cavity was open remaining pressure was carefully released by piercing the top septum of the vial with a long needle (CAUTION: Pressure is still high after cooling!). The mixture was diluted with ethyl ether and washed once with aqueous $NaHCO_3$ (sat), once with aqueous NaCl (sat) and once with H_2O. After drying the organic phase over $MgSO_4$, the solvent was removed under vacuum. The residue was redissolved in CH_2Cl_2, applied to a silica column and eluted with 9:1 (v/v) CH_2Cl_2-CH_3OH. Purification afforded 0.17 g (0.4 mmol, 80%) of **20b** as a viscous colorless oil. **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 2.08 (2H, apparent quintet, apparent *J*=7.0 Hz), 2.33 (6H, singlet), 2.58 (2H, triplet, *J*=7.6 Hz), 2.63 (2H, triplet, *J*=7.6 Hz), 2.85 (2H, triplet, *J*=7.6 Hz), 3.67 (3H, singlet), 4.02 (2H, triplet, *J*=6.4 Hz), 7.33 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 422.03, $(M+H)^+$-calculated: 422.00.

19c-20c: Acids **19c** and **20c** were prepared using the same procedure as for **6c**, from methyl esters **19b** and **20b** respectively.

19c: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.24 (2H, apparent quintet, apparent *J*=6.3 Hz), 2.80 (6H, singlet), 3.28 (2H, triplet, *J*=6.8 Hz), 4.13 (2H, triplet, *J*=5.8 Hz), 7.75 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 403.92, $(M+H)^+$-calculated: 403.95.

20c: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.16 (2H, apparent quintet, apparent *J*=6.8 Hz), 2.45 (2H, triplet, *J*=7.4 Hz), 2.80 (6H, singlet), 2.83 (2H, triplet, *J*=7.4 Hz), 3.29 (2H, triplet, *J*=7.8 Hz), 4.02 (2H, triplet, *J*=5.8 Hz), 7.47 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 407.96, $(M+H)^+$-calculated: 407.98.



26a

<u>26a:</u> Procedure: A round-bottom flask was charged with 1.13 g (3 mmol) of **2**, 0.87 g (3.9 mmol, 1.3 equiv) of *N*-Boc-2-bromoethylamine, 1.47 g (4.5 mmol, 1.5 equiv) of Cs_2CO_3 and 0.11 g (0.75 mmol, 0.25 equiv) of NaI. 20 mL of CH_3CN were added and the mixture was stirred at 65 ^{o}C for 8 h under argon. It was then cooled and filtered to remove inorganic solids. The solvent was evaporated under vacuum and the crude product was redissolved in a small amount of ethyl ether, applied to a silica column and eluted with 4:1 (v/v) hexane-ethyl ether. Purification afforded 1.18 g (2.28 mmol, 76%) of **26a** as a white solid. **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.45 (9H, singlet), 3.57 (2H, apparent quartet, apparent *J*=4.0 Hz), 4.08 (2H, triplet, *J*=4.0 Hz), 5.18 (1H, broad singlet), 7.82 (2H, singlet). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 419.84, (M-Boc+2H)$^+$-calculated: 419.81.

This method is general and was used for preparing (apart from **26a**) iodides **21a-25a** from phenols **1-5** respectively.

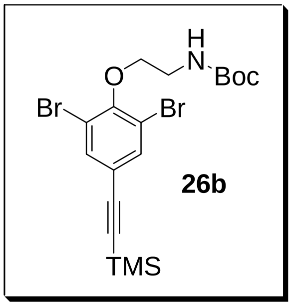
<u>21a:</u> ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 1.43 (9H, singlet), 1.96 (2H, apparent quintet, apparent *J*=6.0 Hz), 3.30 (2H, apparent quartet, apparent *J*=6.0 Hz), 3.96 (2H, triplet, *J*=6.0 Hz), 4.75 (1H, broad singlet), 6.66 (2H, doublet, *J*=8.9 Hz), 7.53 (2H, doublet, *J*=8.9 Hz). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 278.04, (M-Boc+2H)$^+$-calculated: 278.01.

22a: **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.45 (9H, singlet), 2.04 (2H, apparent quintet, apparent *J*=5.9 Hz), 3.43 (2H, apparent quartet, apparent *J*=5.9 Hz), 4.04 (2H, triplet, *J*=5.9 Hz), 4.88 (1H, broad singlet), 7.81 (2H, singlet). **MS (ESI)-*m/z*:** $(M\text{-}Boc+2H)^+$-found: 433.86, $(M\text{-}Boc+2H)^+$-calculated: 433.83.

23a: **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.43 (9H, singlet), 2.04 (2H, apparent quintet, apparent *J*=5.9 Hz), 3.42 (2H, apparent quartet, apparent *J*=5.9 Hz), 4.05 (2H, triplet, *J*=5.9 Hz), 5.14 (1H, broad singlet), 6.64 (1H, doublet, *J*=8.6 Hz), 7.53 (1H, doublet, *J*=8.6 Hz), 7.82 (1H, singlet). **MS (ESI)-*m/z*:** $(M\text{-}Boc+2H)^+$-found: 355.93, $(M\text{-}Boc+2H)^+$-calculated: 355.92.

24a: **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.45 (9H, singlet), 2.02 (2H, apparent quintet, apparent *J*=6.0 Hz), 3.41 (2H, apparent quartet, apparent *J*=6.0 Hz), 4.05 (2H, triplet, *J*=6.0 Hz), 4.87 (1H, broad singlet), 7.62 (2H, singlet). **MS (ESI)-*m/z*:** $(M\text{-}Boc+2H)^+$-found: 345.92, $(M\text{-}Boc+2H)^+$-calculated: 345.93.

25a: **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.43 (9H, singlet), 2.03 (2H, apparent quintet, apparent *J*=5.8 Hz), 3.40 (2H, apparent quartet, apparent *J*=5.8 Hz), 4.07 (2H, triplet, *J*=5.8 Hz), 5.09 (1H, broad singlet), 6.66 (1H, doublet, *J*=8.7 Hz), 7.49 (1H, doublet, *J*=8.7 Hz), 7.65 (1H, singlet). **MS (ESI)-*m/z*:** $(M\text{-}Boc+2H)^+$-found: 311.97, $(M\text{-}Boc+2H)^+$-calculated: 311.97.



26b

<u>26b:</u> Procedure: A round-bottom flask was charged with 1.04 g (2 mmol) of **26a**, 0.092 g (0.08 mmol, 0.04 equiv) of $Pd(PPh_3)_4$ and 0.030 g (0.16 mmol, 0.08 equiv) of CuI. 30 mL of TEA were added to dissolve the solids, followed by 0.40 mL (2.8 mmol, 1.4 equiv) of ethynyltrimethylsilane. The reaction mixture was vigorously stirred under argon in the dark for 4 h at room temperature. Most of the solvent was then removed under vacuum and the solid residue was redissolved in ethyl ether and washed once with aqueous $CuSO_4$ (sat), once with aqueous NaCl (sat) and once with H_2O. After drying over $MgSO_4$, the organic phase was concentrated under vacuum and applied to a silica column. A 4:1 (v/v) hexane-ethyl ether mixture was used for elution. Purification yielded 0.81 g (1.65 mmol, 83%) of **26b** as a viscous colorless oil. **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 0.23 (9H, singlet), 1.45 (9H, singlet), 3.56 (2H, apparent quartet, apparent *J*=4.8 Hz), 4.09 (2H, triplet, *J*=4.8 Hz), 5.19 (1H, broad singlet), 7.60 (2H, singlet). **MS (ESI)-*m/z*:** $(M\text{-}Boc+2H)^+$-found: 389.98, $(M\text{-}Boc+2H)^+$-calculated: 389.95.

This method is general and was used for preparing (apart from **26b**) TMS-alkynes **21b-25b** from iodides **21a-25a** respectively.

<u>21b</u>: **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 0.23 (9H, singlet), 1.44 (9H, singlet), 1.98 (2H, apparent quintet, apparent *J*=6.1 Hz), 3.31 (2H, apparent quartet, apparent *J*=6.1 Hz), 4.00 (2H, triplet, *J*=6.1 Hz), 4.74 (1H, broad singlet), 6.80 (2H, doublet, *J*=8.7 Hz), 7.39 (2H, doublet, *J*=8.7 Hz). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 248.15, (M-Boc+2H)$^+$-calculated: 248.15.

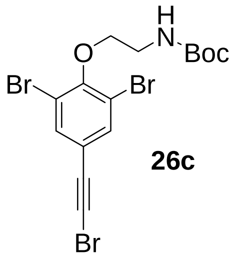
<u>**22b**:</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 0.23 (9H, singlet), 1.45 (9H, singlet), 2.04 (2H, apparent quintet, apparent *J*=6.1 Hz), 3.43 (2H, apparent quartet, apparent *J*=6.1 Hz), 4.04 (2H, triplet, *J*=6.1 Hz), 4.91 (1H, broad singlet), 7.62 (2H, singlet). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 404.00, (M-Boc+2H)$^+$-calculated: 403.97.

<u>**23b:**</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 0.23 (9H, singlet), 1.44 (9H, singlet), 2.04 (2H, apparent quintet, apparent *J*=5.8 Hz), 3.38 (2H, apparent quartet, apparent *J*=5.8 Hz), 4.10 (2H, triplet, *J*=5.8 Hz), 5.17 (1H, broad singlet), 6.79 (1H, doublet, *J*=8.5 Hz), 7.37 (1H, doublet, *J*=8.5 Hz), 7.66 (1H, singlet). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 326.03, (M-Boc+2H)$^+$-calculated: 326.06.

<u>**24b:**</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 0.23 (9H, singlet), 1.45 (9H, singlet), 2.02 (2H, apparent quintet, apparent *J*=5.9 Hz), 3.42 (2H, apparent quartet, apparent *J*=5.9 Hz), 4.06 (2H, triplet, *J*=5.9 Hz), 4.87 (1H, broad singlet), 7.39 (2H, singlet). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 316.04, (M-Boc+2H)$^+$-calculated: 316.07.

<u>**25b:**</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 0.23 (9H, singlet), 1.44 (9H, singlet), 2.04 (2H, apparent quintet, apparent *J*=5.8 Hz), 3.39 (2H, apparent quartet, apparent *J*=5.8 Hz), 4.10 (2H, triplet, *J*=5.8 Hz), 5.18 (1H, broad singlet), 6.81 (1H, doublet, *J*=8.6 Hz),

7.37 (1H, doublet, *J*=8.6 Hz), 7.50 (1H, singlet). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 282.08, (M-Boc+2H)$^+$-calculated: 282.11.


26c

<u>26c:</u> Procedure: A round-bottom flask was charged with 0.81 g (1.65 mmol) of **26b** and 0.085 g (0.5 mmol, 0.3 equiv) of $AgNO_3$. 8 ml of acetone were added and the mixture was cooled at 0 ^{o}C. 0.41 g (2.3 mmol, 1.4 equiv) of NBS in 8 ml of acetone were added dropwise at a very slow rate under argon. The reaction was then allowed to warm up to room temperature and stirring continued for 1.5 h. The mixture was concentrated under vacuum and directly applied to a silica column. It was eluted with 3:1 hexane-ethyl acetate. Purification afforded 0.76 g (1.53 mmol, 93%) of **26c** as a brownish oil. **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.45 (9H, singlet), 3.57 (2H, apparent quartet, apparent *J*=4.8 Hz), 4.08 (2H, triplet, *J*=4.8 Hz), 5.19 (1H, broad singlet), 7.59 (2H, singlet). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 395.86, (M-Boc+2H)$^+$-calculated: 395.83.

This method is general and was used for preparing (apart from **26c**) bromoacetylides **21c-25c** from TMS-alkynes **21b-25b** respectively.

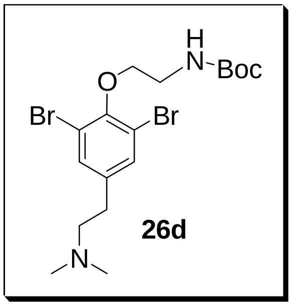
<u>21c</u>: ^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm): 1.43 (9H, singlet), 1.97 (2H, apparent quintet, apparent *J*=6.1 Hz), 3.31 (2H, apparent quartet, apparent *J*=6.1 Hz), 4.00 (2H, triplet, *J*=6.1 Hz), 4.75 (1H, broad singlet), 6.80 (2H, doublet, *J*=8.8 Hz), 7.37 (2H, doublet, *J*=8.8 Hz). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 253.99, (M-Boc+2H)$^+$-calculated: 254.02.

<u>22c</u>: **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-*δ* (ppm):** 1.44 (9H, singlet), 2.04 (2H, apparent quintet, apparent *J*=6.0 Hz), 3.44 (2H, apparent quartet, apparent *J*=6.0 Hz), 4.05 (2H, triplet, *J*=6.0 Hz), 4.88 (1H, broad singlet), 7.59 (2H, singlet). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 409.82, (M-Boc+2H)$^+$-calculated: 409.84.

<u>23c:</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-*δ* (ppm):** 1.43 (9H, singlet), 2.04 (2H, apparent quintet, apparent *J*=5.7 Hz), 3.37 (2H, apparent quartet, apparent *J*=5.7 Hz), 4.10 (2H, triplet, *J*=5.7 Hz), 5.15 (1H, broad singlet), 6.79 (1H, doublet, *J*=8.5 Hz), 7.35 (1H, doublet, *J*=8.5 Hz), 7.64 (1H, singlet). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 331.96, (M-Boc+2H)$^+$-calculated: 331.93.

<u>24c:</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-*δ* (ppm):** 1.45 (9H, singlet), 2.02 (2H, apparent quintet, apparent *J*=5.9 Hz), 3.42 (2H, apparent quartet, apparent *J*=5.9 Hz), 4.07 (2H, triplet, *J*=5.9 Hz), 4.86 (1H, broad singlet), 7.38 (2H, singlet). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 321.95, (M-Boc+2H)$^+$-calculated: 321.94.

<u>25c:</u> **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-*δ* (ppm):** 1.43 (9H, singlet), 2.04 (2H, apparent quintet, apparent *J*=5.7 Hz), 3.37 (2H, apparent quartet, apparent *J*=5.8 Hz), 4.10 (2H, triplet, *J*=5.8 Hz), 5.15 (1H, broad singlet), 6.79 (1H, doublet, *J*=8.6 Hz), 7.35 (1H, doublet, *J*=8.6 Hz), 7.45 (1H, singlet). **MS (ESI)-*m/z*:** (M-Boc+2H)$^+$-found: 287.95, (M-Boc+2H)$^+$-calculated: 287.98.


26d

<u>26d:</u> Procedure: A cylindrical flask was charged with 0.76 g (1.53 mmol) of **26c**. The residue was dissolved in 7.65 mL of a 2M dimethylamine solution in THF (15.3 mmol, 10 equiv) and 1.40 mL of acetonitrile. The reaction mixture was vigorously agitated under argon for 3 h at room temperature on a lab shaker. When LC-MS showed complete consumption of **26c**, the mixture was cooled to 0 ^{o}C and 0.29 g (7.65 mmol, 5 equiv) of $NaBH_4$, dissolved in 7.5 mL of ice-cold CH_3OH, was syringed in. The reaction was allowed to stir at 0 ^{o}C for 30 min. The solvent was subsequently removed under vacuum and the residue was redissolved in a small amount of CH_3OH, applied to a silica column and eluted with 9:1 CH_2Cl_2-CH_3OH. Purification afforded 0.56 g (1.21 mmol, 79%) of **26d** as a white solid. **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.45 (9H, singlet), 2.53 (6H, singlet), 2.84 (4H, broad singlet/two overlapping triplets), 3.48 (2H, triplet, *J*=5.4 Hz), 4.02 (2H, triplet, *J*=5.4 Hz), 7.52 (2H, singlet). **MS (ESI)-*m/z*:** (M+H)$^+$-found: 465.05, (M+H)$^+$-calculated: 465.04.

This method is general and was used for preparing (apart from **26d**) Boc-amines **21d-25d** from bromoacetylides **21c-25c** respectively.

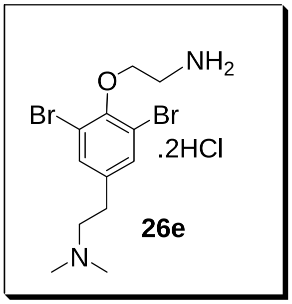
<u>21d</u>: ^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm): 1.44 (9H, singlet), 1.93 (2H, apparent quintet, apparent *J*=6.4 Hz), 2.45 (6H, singlet), 2.72 (2H, triplet, *J*=7.7 Hz), 2.79 (2H, triplet, *J*=7.7 Hz), 3.23 (2H, triplet, *J*=6.7 Hz), 3.99 (2H, triplet, *J*=6.1 Hz), 6.86 (2H, doublet, *J*=8.5 Hz), 7.15 (2H, doublet, *J*=8.5 Hz). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 323.23, $(M+H)^+$-calculated: 323.24.

__22d__: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.44 (9H, singlet), 2.01 (2H, apparent quintet, apparent *J*=6.4 Hz), 2.35 (6H, singlet), 2.61 (2H, triplet, *J*=7.8 Hz), 2.76 (2H, triplet, *J*=7.8 Hz), 3.27 (2H, triplet, *J*=6.7 Hz), 4.02 (2H, triplet, *J*=6.1 Hz), 7.47 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 479.03, $(M+H)^+$-calculated: 479.06.

__23d__: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.43 (9H, singlet), 1.97 (2H, apparent quintet, apparent *J*=6.3 Hz), 2.69 (6H, singlet), 2.89 (2H, triplet, *J*=8.3 Hz), 3.03 (2H, triplet, *J*=8.3 Hz), 3.28 (2H, triplet, *J*=6.6 Hz), 4.07 (2H, triplet, *J*=6.0 Hz), 6.99 (1H, doublet, *J*=8.4 Hz), 7.21 (1H, doublet, *J*=8.4 Hz), 7.48 (1H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 401.16, $(M+H)^+$-calculated: 401.15.

__24d__: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.44 (9H, singlet), 1.99 (2H, apparent quintet, apparent *J*=6.4 Hz), 2.42 (6H, singlet), 2.71 (2H, triplet, *J*=7.8 Hz), 2.80 (2H, triplet, *J*=7.8 Hz), 3.27 (2H, triplet, *J*=6.7 Hz), 4.03 (2H, triplet, *J*=6.1 Hz), 7.28 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 391.16, $(M+H)^+$-calculated: 391.16.

__25d__: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.43 (9H, singlet), 1.97 (2H, apparent quintet, apparent *J*=6.2 Hz), 2.80 (6H, singlet), 2.93 (2H, triplet, *J*=8.1 Hz), 3.18 (2H, triplet, *J*=8.1 Hz), 3.27 (2H, triplet, *J*=6.4 Hz), 4.08 (2H, triplet, *J*=6.0 Hz), 7.02 (1H, doublet, *J*=8.4 Hz), 7.17 (1H, doublet, *J*=8.4 Hz), 7.34 (1H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 357.17, $(M+H)^+$-calculated: 357.20.



<u>26e:</u> Procedure: A cylindrical flask was charged with 0.28 g of **26d (**0.6 mmol). 12 mL of a 4M HCl solution in dioxane (48 mmol, 80 equiv) were added and the mixture was stirred first at 0 °C for 10 min and then at room temperature for 20 min. The solvent was subsequently removed under vacuum and the residue was extensively dried on a lyophilizer. 0.26 g (0.6 mmol, 100%) of **26e** were obtained as a white solid and shown to be pure by LC-MS and NMR. **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.95 (6H, singlet), 3.06 (2H, triplet, *J*=8.3 Hz), 3.38 (2H, triplet, *J*=8.3 Hz), 3.44 (2H, triplet, *J*=5.0 Hz), 4.26 (2H, triplet, *J*=5.0 Hz), 7.66 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 365.01, $(M+H)^+$-calculated: 364.99.

This method is general and was used for preparing (apart from **26e**) amines **21e-25e** from Boc-amines **21d-25d** respectively.

<u>21e</u>: ^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm): 2.14 (2H, apparent quintet, apparent *J*=6.5 Hz), 2.94 (6H, singlet), 3.00 (2H, triplet, *J*=8.1 Hz), 3.16 (2H, triplet, *J*=7.2 Hz), 3.34 (2H, triplet, *J*=8.1 Hz), 4.11 (2H, triplet, *J*=5.8 Hz), 6.96 (2H, doublet, *J*=8.6 Hz), 7.24 (2H, doublet, *J*=8.6 Hz). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 223.16, $(M+H)^+$-calculated: 223.18.

<u>22e</u>: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.22 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.94 (6H, singlet), 3.05 (2H, triplet, *J*=8.3 Hz), 3.30 (2H, triplet, *J*=7.5 Hz), 3.37 (2H, triplet, *J*=8.3 Hz), 4.12 (2H, triplet, *J*=5.7 Hz), 7.63 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 378.97, $(M+H)^+$-calculated: 379.00.

<u>23e</u>: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.10 (2H, apparent quintet, apparent *J*=5.9 Hz), 2.84 (6H, singlet), 2.92 (2H, triplet, *J*=8.3 Hz), 3.13 (2H, triplet, *J*=6.1 Hz), 3.25 (2H, triplet, *J*=8.3 Hz), 4.09 (2H, triplet, *J*=5.7 Hz), 6.96 (1H, doublet, *J*=8.4 Hz), 7.21 (1H, doublet, *J*=8.4 Hz), 7.47 (1H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 301.08, $(M+H)^+$-calculated: 301.09.

<u>24e</u>: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.10 (2H, apparent quintet, apparent *J*=6.5 Hz), 2.85 (6H, singlet), 2.95 (2H, triplet, *J*=8.3 Hz), 3.19 (2H, triplet, *J*=7.3 Hz), 3.27 (2H, triplet, *J*=8.3 Hz), 4.04 (2H, triplet, *J*=5.7 Hz), 7.34 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 291.10, $(M+H)^+$-calculated: 291.11.

<u>25e</u>: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.20 (2H, apparent quintet, apparent *J*=6.4 Hz), 2.94 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.21 (2H, triplet, *J*=7.1 Hz), 3.36 (2H, triplet, *J*=8.3 Hz), 4.20 (2H, triplet, *J*=5.7 Hz), 7.09 (1H, doublet, *J*=8.4 Hz), 7.24 (1H, doublet, *J*=8.4 Hz), 7.40 (1H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 257.13, $(M+H)^+$-calculated: 257.14.

27d-30d: Boc-amines **27d-30d** were prepared using variations of the procedure for **26d**, from **22c** and amines **27-30** respectively (see Scheme 5 in paper).

27d: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.05 (6H, triplet, *J*=7.2 Hz), 1.43 (9H, singlet), 2.01 (2H, apparent quintet, apparent *J*=6.0 Hz), 2.58 (4H, quartet, *J*=7.2 Hz), 2.65 (2H, triplet, *J*=7.8 Hz), 3.41 (2H, triplet, *J*=6.2 Hz), 3.45 (2H, triplet, *J*=7.8 Hz), 4.01 (2H, triplet, *J*=5.8 Hz), 7.31 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 507.12, $(M+H)^+$-calculated: 507.09.

28d: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.18 (3H, triplet, *J*=7.2 Hz), 1.44 (9H, singlet), 2.01 (2H, apparent quintet, *J*=6.6 Hz), 2.50 (3H, singlet), 2.77 (2H, quartet, *J*=7.2 Hz), 2.84 (2H, triplet, *J*=7.0 Hz), 3.27 (2H, triplet, *J*=7.1 Hz), 3.32 (2H, triplet, *J*=7.0 Hz), 4.02 (2H, triplet, *J*=6.1 Hz), 7.50 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 493.10, $(M+H)^+$-calculated: 493.07.

29d: **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.44 (9H, singlet), 2.01 (2H, apparent quintet, apparent *J*=6.1 Hz), 2.51 (2H, broad singlet), 2.97 (2H, triplet, *J*=7.6 Hz), 3.21 (2H, triplet, *J*=7.6 Hz), 3.43 (2H, apparent quartet, apparent *J*=6.4 Hz), 3.95 (4H, broad singlet), 4.03 (2H, triplet, *J*=5.8 Hz), 4.91 (1H, broad singlet), 7.42 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 491.04, $(M+H)^+$-calculated: 491.06.

30d: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.44 (9H, singlet), 2.02 (2H, apparent quintet, apparent *J*=6.5 Hz), 2.72 (3H, singlet), 2.95 (2H, triplet, *J*=7.7 Hz), 3.25 (2H, triplet, *J*=7.7 Hz), 3.34 (2H, triplet, *J*=7.0 Hz), 4.03 (2H, triplet, *J*=6.0 Hz), 7.58 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 465.01, $(M+H)^+$-calculated: 465.04.

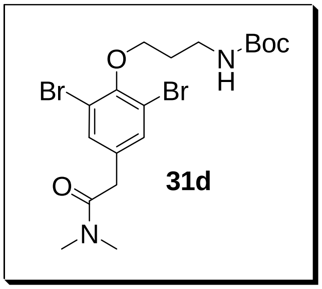
<u>27e-30e</u>: Amines **27e-30e** were prepared using the same procedure as for **26e**, from Boc-amines **27d-30d** respectively.

<u>27e</u>: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.37 (6H, triplet, *J*=7.3 Hz), 2.23 (2H, apparent quintet, apparent *J*=6.3 Hz), 3.06 (2H, triplet, *J*=8.5 Hz), 3.32 (8H, multiplet-three peaks overlapping), 4.14 (2H, triplet, *J*=5.7 Hz), 7.66 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 407.07, $(M+H)^+$-calculated: 407.04.

<u>28e</u>: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 1.38 (3H, triplet, *J*=7.3 Hz), 2.21 (2H, apparent quintet, apparent *J*=6.1 Hz), 2.91 (3H, singlet), 3.06 (4H, multiplet-two peaks overlapping), 3.20 (2H, triplet, *J*=8.3 Hz), 3.38 (2H, triplet, *J*=6.5 Hz), 4.15 (2H, triplet, *J*=5.7 Hz), 7.62 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 393.00, $(M+H)^+$-calculated: 393.02.

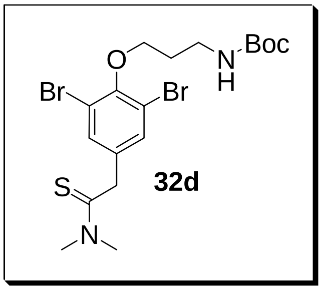
<u>29e</u>: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.21 (2H, apparent quintet, apparent *J*=6.3 Hz), 2.42 (1H, multiplet), 2.57 (1H, multiplet), 2.86 (2H, triplet, *J*=7.8 Hz), 3.29 (2H, triplet, *J*=6.8 Hz), 3.44 (2H, triplet, *J*=7.8 Hz), 4.12 (4H, multiplet-two peaks overlapping), 4.21 (2H, multiplet), 7.61 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 391.00, $(M+H)^+$-calculated: 391.00.

<u>30e</u>: ^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm): 2.22 (2H, apparent quintet, apparent *J*=6.9 Hz), 2.73 (3H, singlet), 2.98 (2H, triplet, *J*=7.8 Hz), 3.25 (2H, triplet, *J*=8.0 Hz), 3.33 (2H, triplet, *J*=7.8 Hz), 4.14 (2H, triplet, *J*=5.8 Hz), 7.61 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 365.00, $(M+H)^+$-calculated: 364.99.

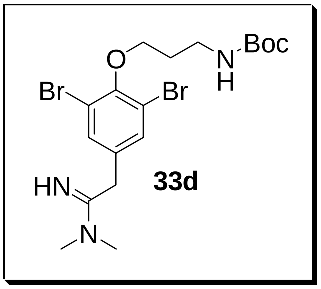


<u>31d:</u> Procedure: A cylindrical flask was charged with 0.51 g (1 mmol) of **22c**. The residue was dissolved in 5 mL of a 2M dimethylamine solution in THF (10 mmol, 10 equiv), 0.18 mL (0.18 g, 10 mmol, 10 equiv) of H_2O and 1 mL of acetonitrile. The reaction mixture was vigorously agitated under argon for 3 h at room temperature on a lab shaker. The solvent was subsequently removed under vacuum and the residue was redissolved in CH_2Cl_2, applied to a silica column and eluted using a CH_2Cl_2-CH_3OH gradient, starting with 100% CH_2Cl_2 and finishing with 95-5% CH_2Cl_2-CH_3OH. Purification afforded 0.37 g (0.75 mmol, 75%) of **31d** as a viscous colorless oil. **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.44 (9H, singlet), 2.02 (2H, apparent quintet, apparent *J*=5.9 Hz), 2.97 (3H, singlet), 3.03 (3H, singlet), 3.44 (2H, apparent quartet, apparent *J*=6.0 Hz), 3.60 (2H, singlet), 4.03 (2H, triplet, *J*=5.8 Hz), 4.96 (1H, broad singlet), 7.41 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 493.01, $(M+H)^+$-calculated: 493.04.

<u>32d:</u> Procedure: A cylindrical flask was charged with 0.33 g (0.67 mmol) of **22c**. 15 mL of toluene were added to dissolve the residue, followed by 0.40 g (1 mmol, 1.5 equiv) of Lawesson's reagent. The mixture was heated at 80 ^oC under argon for 1 h. The solvent



was subsequently removed under vacuum and the residue was redissolved in CH_2Cl_2, applied to a silica column and eluted using a CH_2Cl_2-CH_3OH gradient, starting with 100% CH_2Cl_2 and finishing with 95-5% CH_2Cl_2-CH_3OH. Purification afforded 0.29 g (0.57 mmol, 85%) of **32d** as a viscous colorless oil. **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.45 (9H, singlet), 2.03 (2H, apparent quintet, apparent *J*=6.1 Hz), 3.22 (3H, singlet), 3.44 (2H, apparent quartet, *J*=6.4 Hz), 3.52 (3H, singlet), 4.05 (2H, triplet, *J*=5.8 Hz), 4.19 (2H, singlet), 4.95 (1H, broad singlet), 7.48 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 509.00, $(M+H)^+$-calculated: 509.01.



33d: Procedure: A cylindrical flask was charged with 0.51 g (1 mmol) of **22c**. The residue was dissolved in 5 mL of a 2M dimethylamine solution in THF (10 mmol, 10 equiv), 5 mL of a 2M NH_3 solution in EtOH (10 mmol, 10 equiv) and 1 mL of acetonitrile. The reaction mixture was vigorously agitated under argon for 12 h at room temperature on a lab shaker. The solvent was subsequently removed under vacuum and the residue was redissolved in a 7:3 (v/v) CH_2Cl_2-CH_3OH mixture, applied to a silica column and eluted with the same solvent. Purification afforded 0.33 g (0.68 mmol, 68%) of **33d** as a brownish solid. **^{1}H-NMR of protonated tautomer of 33d ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.45 (9H, singlet), 2.05 (2H, apparent quintet, apparent *J*=6.0 Hz), 3.15 (3H, singlet), 3.42 (2H, apparent quartet, apparent *J*=6.8 Hz), 3.44 (3H, singlet), 4.06 (2H, triplet, *J*=5.8 Hz), 4.23 (2H, singlet), 4.93 (1H, broad singlet), 7.49 (2H, singlet), 9.31 (1H, doublet, *J*=14.0 Hz), 9.82 (1H, doublet, *J*=14.0 Hz). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 492.02, $(M+H)^+$-calculated: 492.05.

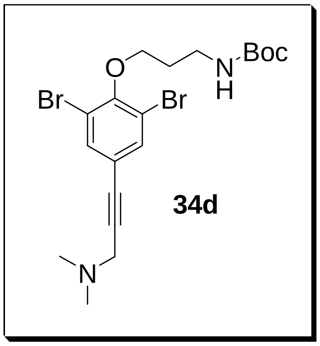
31e-33e: Amines **31e-33e** were prepared using the same procedure as for **26e**, from Boc-amines **31d-33d** respectively.

31e: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.21 (2H, apparent quintet, apparent *J*=5.8 Hz), 2.97 (3H, singlet), 3.11 (3H, singlet), 3.28 (2H, triplet, *J*=5.8 Hz), 3.75 (2H, singlet), 4.15 (2H, triplet, *J*=5.8 Hz), 7.51 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 393.00, $(M+H)^+$-calculated: 392.98.

32e: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.22 (2H, apparent quintet, apparent *J*=6.1 Hz), 3.28 (3H, singlet), 3.32 (2H, triplet, *J*=6.5 Hz), 3.46 (3H, singlet), 4.14 (2H, triplet, *J*=5.7 Hz), 4.20 (2H, singlet), 7.60 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 408.97, $(M+H)^+$-calculated: 408.96.

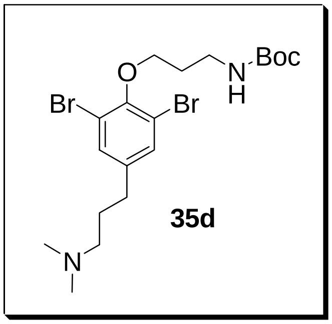
33e: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.23 (2H, apparent quintet, apparent *J*=5.8 Hz), 3.19 (3H, singlet), 3.22 (3H, singlet), 3.35 (2H, triplet, *J*=5.8 Hz), 4.03 (2H, singlet), 4.16 (2H, triplet, *J*=5.8 Hz), 7.62 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 392.00, $(M+H)^+$-calculated: 392.00.

34d: Procedure: A round-bottom flask was charged with 1.02 g (1.9 mmol) of **22a**, 0.088 g (0.076 mmol, 0.04 equiv) of $Pd(PPh_3)_4$ and 0.029 g (0.15 mmol, 0.08 equiv) of



34d

CuI. 25 mL of TEA were added to dissolve the solids, followed by 0.28 mL (0.22 g, 2.66 mmol, 1.4 equiv) of *N,N*-dimethyl-propargylamine. The reaction mixture was vigorously stirred under argon in the dark for 4 h at room temperature. The solvent was then removed under vacuum. The solid residue was redissolved in a 9:1 (v/v) CH_2Cl_2-CH_3OH mixture, applied to a silica column and eluted with the same solvent. Purification yielded 0.66 g (1.35 mmol, 71%) of **34d** as a viscous yellowish oil. **^{1}H-NMR (CDCl$_3$, 7.26 ppm)-δ (ppm):** 1.44 (9H, singlet), 2.03 (2H, apparent quintet, apparent *J*=6.0 Hz), 2.38 (6H, singlet), 3.45 (2H, triplet, *J*=6.2 Hz), 3.50 (2H, singlet), 4.05 (2H, triplet, *J*=5.8 Hz), 4.92 (1H, broad singlet), 7.58 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 489.01, $(M+H)^+$-calculated: 489.04.



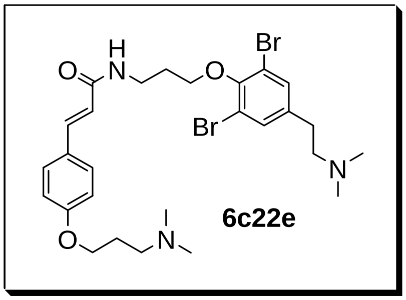
35d

<u>35d:</u> Procedure: 0.20 g (0.41 mmol) of **34d** dissolved in 1 mL of DMSO were added to a 5 mL microwave vial, in which we had pre-mixed 1.5 mL of DMSO, 0.17 mL (0.21 g, 4.51 mmol, 11 equiv) of formic acid and 0.57 mL (0.415 g, 4.1 mmol, 10 equiv) of TEA. The mixture was agitated briefly before adding 0.011 g (0.012 mmol, 0.03 equiv) of $RhCl(PPh_3)_3$ and sealing the vial. The vial was inserted in the microwave synthesizer cavity and after 60 sec pre-stirring, it was submitted to microwave irradiation at 150 ^{o}C for 60 sec (fixed time). It was then cooled numerous times before opening the cavity, and once the cavity was open remaining pressure was carefully released by piercing the top septum of the vial with a long needle (CAUTION: pressure is still high after cooling!). The mixture was concentrated under vacuum, resuspended in CH_2Cl_2 and washed once with aqueous NaCl (sat) and once with H_2O. After drying the organic phase over $MgSO_4$, the solvent was removed under vacuum. The residue was redissolved in 8:2 (v/v) CH_2Cl_2-CH_3OH, applied to a silica column and eluted with the same solvent. Purification afforded 0.11 g (0.23 mmol, 56%) of **35d** as a viscous colorless oil. **^{1}H-NMR ($CDCl_3$, 7.26 ppm)-δ (ppm):** 1.44 (9H, singlet), 1.76 (2H, apparent quintet, apparent *J*=7.2 Hz), 2.02 (2H, apparent quintet, apparent *J*=6.0 Hz), 2.26 (6H, singlet), 2.31 (2H, triplet, *J*=6.6 Hz), 2.56 (2H, triplet, *J*=7.8 Hz), 3.44 (2H, triplet, *J*=6.2 Hz), 4.03 (2H, triplet, *J*=5.8 Hz), 4.98 (1H, broad singlet), 7.32 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 493.06, $(M+H)^+$-calculated: 493.07.

34e-35e: Amines **34e** and **35e** were prepared using the same procedure as for **26e**, from Boc-amines **34d** and **35d** respectively.

34e: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.23 (2H, apparent quintet, apparent *J*=5.9 Hz), 3.01 (6H, singlet), 3.30 (2H, triplet, *J*=6.1 Hz), 4.17 (2H, triplet, *J*=5.7 Hz), 4.33 (2H, singlet), 7.82 (2H, singlet). **MS (ESI)-*m/z*:** $(M+H)^+$-found: 389.00, $(M+H)^+$-calculated: 388.99.

35e: **^{1}H-NMR (CD_3OD, 3.31 ppm)-δ (ppm):** 2.02 (2H, apparent quintet, apparent *J*=8.0 Hz), 2.22 (2H, apparent quintet, apparent *J*=6.0 Hz), 2.67 (2H, triplet, *J*=7.8 Hz), 2.89 (6H, singlet), 3.14 (2H, triplet, *J*=8.2 Hz), 3.31 (2H, triplet, *J*=6.3 Hz), 4.12 (2H, triplet, *J*=5.7 Hz), 7.56 (2H, singlet). **MS (ESI)-*m/z*:** (M+H)$^+$-found: 393.00, (M+H)$^+$-calculated: 393.02.



6c22e

<u>6c22e:</u> Procedure: A flask was charged with 0.037 g (0.15 mmol) of **6c**. 2 mL of THF were added, followed by 0.105 mL (0.076 g, 0.75 mmol, 5 equiv) of triethylamine. After 5 mins of stirring at room temperature, 0.027 mL (0.029 g, 0.18 mmol, 1.2 equiv) of DEPC dissolved in 1 mL THF were added and the mixture was stirred for 5 more minutes. Finally, 0.068 g (0.15 mmol, 1 equiv) of **22e** were added in solid form and the reaction was allowed to proceed for 2 h, after which LC-MS revealed 89% (0.081 g, 0.133 mmol) of product in the crude mixture. The solvent was then removed under vacuum. The residue was redissolved in 9:1 (v/v) CH_2Cl_2-CH_3OH, applied to a silica column and eluted with the same solvent, to afford **6c22e** as a colorless semi-solid. This was further purified by HPLC (C18 reversed-phase column, H_2O-CH_3CN gradient modified with 0.1% TFA) to give a colorless solid. **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-δ (ppm):** 2.12 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.24 (2H, multiplet), 2.93 (6H, singlet), 2.94 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.35 (4H, multiplet-two peaks overlapping), 3.59 (2H, triplet, *J*=7.1 Hz), 4.08 (2H, triplet, *J*=6.1 Hz), 4.14 (2H, triplet, *J*=5.7 Hz), 6.50 (1H, doublet, *J*=15.7 Hz), 6.97 (2H, doublet, *J*=8.8 Hz), 7.48 (1H, doublet, *J*=15.7 Hz), 7.51 (2H, doublet, *J*=8.8 Hz), 7.58 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-δ (ppm):** 25.69, 30.32, 30.92, 37.93, 43.56, 43.63, 56.68, 59.13, 66.02, 72.20, 115.92, 119.48, 119.64, 129.37, 130.50, 134.42, 136.59, 141.31, 153.66, 161.25, 169.13. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 610.15, $(M+H)^+$-calculated: 610.13.

This method is general and was used for preparing all final psammaplysene-like compounds from the corresponding acid and amine building blocks (see Table on pages S-50/51). All final amides were purified on silica prior to HPLC purification, except 7c30e which was too polar and 7c33e which was unstable on silica. Both were HPLC-purified directly. No TFA was used in the HPLC purification of 7c29e.

8c22e: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-δ (ppm):** 2.13 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.30 (2H, multiplet), 2.93 (6H, singlet), 2.98 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.36 (2H, triplet, *J*=8.3 Hz), 3.41 (2H, triplet, *J*=7.6 Hz), 3.59 (2H, triplet, *J*=7.1 Hz), 4.08 (2H, triplet, *J*=6.1 Hz), 4.23 (2H, triplet, *J*=5.7 Hz), 6.54 (1H, doublet, *J*=15.7 Hz), 7.10 (1H, doublet, *J*=8.6 Hz), 7.44 (1H, doublet, *J*=15.7 Hz), 7.54 (1H, doublet, *J*=8.6 Hz), 7.58 (2H, singlet), 7.81 (1H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-δ (ppm):** 25.52, 30.32, 30.90, 37.98, 43.57, 43.78, 56.89, 59.14, 67.45, 72.19, 113.33, 114.53, 119.49, 121.19, 129.91, 130.96, 133.30, 134.43, 136.60, 139.80, 153.66, 157.17, 168.63. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 688.07, $(M+H)^+$-calculated: 688.04.

9c22e: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-δ (ppm):** 2.13 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.30 (2H, multiplet), 2.93 (6H, singlet), 2.97 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.36 (2H, triplet, *J*=8.3 Hz), 3.51 (2H, triplet, *J*=8.0

Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 4.08 (2H, triplet, *J*=6.1 Hz), 4.18 (2H, triplet, *J*=5.6 Hz), 6.62 (1H, doublet, *J*=15.7 Hz), 7.41 (1H, doublet, *J*=15.7 Hz), 7.59 (2H, singlet), 7.64 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 26.48, 30.32, 30.94, 38.08, 43.61, 43.71, 56.88, 59.19, 71.67, 72.25, 119.53, 124.37, 129.33, 130.89, 134.46, 134.86, 136.59, 138.29, 152.70, 153.78, 167.91. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 678.02, $(M+H)^+$-calculated: 678.05.

<u>10c22e</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.12 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.31 (2H, multiplet), 2.93 (6H, singlet), 2.97 (6H, singlet), 3.00 (2H, triplet, *J*=8.3 Hz), 3.35 (2H, triplet, *J*=8.3 Hz), 3.40 (2H, triplet, *J*=7.6 Hz), 3.59 (2H, triplet, *J*=7.1 Hz), 4.08 (2H, triplet, *J*=6.1 Hz), 4.24 (2H, triplet, *J*=5.7 Hz), 6.54 (1H, doublet, *J*=15.7 Hz), 7.12 (1H, doublet, *J*=8.6 Hz), 7.43 (1H, doublet, *J*=15.7 Hz), 7.49 (1H, doublet, *J*=8.6 Hz), 7.58 (2H, singlet), 7.64 (1H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 25.59, 30.32, 30.97, 38.00, 43.59, 43.76, 56.92, 59.17, 67.49, 72.26, 114.80, 119.50, 121.35, 124.30, 129.22, 130.14, 130.60, 134.45, 136.61, 139.89, 153.74, 156.30, 168.62. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 644.09, $(M+H)^+$-calculated: 644.09.

<u>11c22e</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.13 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.93 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.10 (6H, singlet), 3.36 (2H, triplet, *J*=8.3 Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 3.71 (2H, triplet, *J*=4.9 Hz), 4.08 (2H, triplet, *J*=6.1 Hz), 4.38 (2H, triplet, *J*=4.9 Hz), 6.63 (1H, doublet, *J*=15.7 Hz), 7.41 (1H, doublet, *J*=15.7 Hz), 7.58 (2H, singlet), 7.86 (2H, singlet). **^{13}C-**

NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-δ (ppm): 30.32, 30.93, 38.09, 43.60, 44.10, 58.18, 59.18, 67.79, 72.24, 119.39, 119.51, 124.80, 133.16, 134.46, 136.55, 136.61, 137.83, 153.75, 153.83, 167.79. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 751.97, $(M+H)^+$-calculated: 751.94.

<u>12c22e</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-δ (ppm):** 1.40 (6H, triplet, *J*=7.3 Hz), 2.11 (2H, apparent quintet, apparent *J*=6.5 Hz), 2.88 (6H, singlet), 2.97 (2H, triplet, *J*=8.4 Hz), 3.26 (2H, triplet, *J*=8.4 Hz), 3.44 (4H, broad singlet), 3.60 (2H, triplet, *J*=7.0 Hz), 3.65 (2H, triplet, *J*=4.8 Hz), 4.06 (2H, triplet, *J*=6.0 Hz), 4.35 (2H, triplet, *J*=4.8 Hz), 6.51 (1H, doublet, *J*=15.7 Hz), 7.36 (1H, doublet, *J*=15.7 Hz), 7.46 (2H, singlet), 7.72 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-δ (ppm):** 9.10, 30.32, 30.92, 38.09, 43.58, 49.07, 52.32, 59.16, 67.85, 72.23, 119.38, 119.49, 124.81, 133.14, 134.45, 136.52, 136.64, 137.80, 153.71, 153.92, 167.77. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 780.00, $(M+H)^+$-calculated: 779.97.

<u>13c22e</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-δ (ppm):** 1.49 (12H, doublet, *J*=6.4 Hz), 2.13 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.93 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.36 (2H, triplet, *J*=8.3 Hz), 3.60 (2H, triplet, *J*=7.2 Hz), 3.75 (2H, triplet, *J*=5.7 Hz), 4.00 (2H, septet, *J*=6.4 Hz), 4.08 (2H, triplet, *J*=6.1 Hz), 4.40 (2H, triplet, *J*=5.7 Hz), 6.63 (1H, doublet, *J*=15.7 Hz), 7.41 (1H, doublet, *J*=15.7 Hz), 7.59 (2H, singlet), 7.87 (2H, singlet). **^{13}C-NMR shifts of HPLC-purified product from HMQC/HMBC (CD_3OD, 49.05 ppm)-δ (ppm):** 18.03, 30.01, 30.66, 37.81, 43.32, 47.54, 56.79, 58.90, 69.22, 71.96, 119.09, 119.26, 124.53, 132.94, 133.08,

134.17, 134.22, 137.63, 153.48, 153.92, 167.50. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 807.97, $(M+H)^+$-calculated: 808.00.

__14c22e__: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.11 (4H, multiplet), 2.23 (2H, broad singlet), 2.93 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.29 (2H, broad singlet), 3.35 (2H, triplet, *J*=8.3 Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 3.76 (2H, triplet, *J*=4.9 Hz), 3.90 (2H, broad singlet), 4.08 (2H, triplet, *J*=6.1 Hz), 4.36 (2H, triplet, *J*=4.9 Hz), 6.64 (1H, doublet, *J*=15.8 Hz), 7.41 (1H, doublet, *J*=15.8 Hz), 7.58 (2H, singlet), 7.86 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 24.05, 30.32, 30.93, 38.09, 43.60, 55.55, 55.87, 59.18, 68.84, 72.24, 119.44, 119.51, 124.77, 133.16, 134.46, 136.51, 136.62, 137.85, 153.75, 153.85, 167.80. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 777.98, $(M+H)^+$-calculated: 777.95.

__15c22e__: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 1.59 (1H, multiplet), 1.88 (3H, multiplet), 2.01 (2H, multiplet), 2.13 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.93 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.15 (2H, multiplet), 3.36 (2H, triplet, *J*=8.3 Hz), 3.60 (2H, triplet, *J*=7.2 Hz), 3.67 (2H, triplet, *J*=4.9 Hz), 3.83 (2H, multiplet), 4.08 (2H, triplet, *J*=6.1 Hz), 4.40 (2H, triplet, *J*=4.9 Hz), 6.63 (1H, doublet, *J*=15.7 Hz), 7.41 (1H, doublet, *J*=15.7 Hz), 7.59 (2H, singlet), 7.87 (2H, singlet). **^{13}C-NMR shifts of HPLC-purified product from HMQC/HMBC (CD_3OD, 49.05 ppm)-*δ* (ppm):** 23.65, 23.83, 30.07, 30.71, 37.86, 43.36, 54.62, 57.23, 58.94, 67.27, 72.00, 119.15, 119.26, 124.54, 132.96, 133.01, 134.20, 134.24, 137.60, 153.54, 153.61, 167.55. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 791.97, $(M+H)^+$-calculated: 791.97.

16c22e: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.13 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.93 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.36 (2H, triplet, *J*=8.3 Hz), 3.43 (4H, broad singlet), 3.60 (2H, triplet, *J*=7.1 Hz), 3.76 (2H, triplet, *J*=4.9 Hz), 4.01 (4H, broad singlet), 4.08 (2H, triplet, *J*=6.1 Hz), 4.43 (2H, triplet, *J*=4.9 Hz), 6.63 (1H, doublet, *J*=15.7 Hz), 7.40 (1H, doublet, *J*=15.7 Hz), 7.58 (2H, singlet), 7.86 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 30.32, 30.84, 38.07, 43.57, 53.67, 57.78, 59.14, 64.87, 67.35, 72.16, 119.38, 119.48, 124.67, 133.13, 134.43, 136.45, 136.62, 137.86, 153.65, 153.80, 167.80. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 793.97, $(M+H)^+$-calculated: 793.95.

17c22e: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 1.55 (1H, multiplet), 1.80 (2H, multiplet), 1.86 (1H, multiplet), 1.98 (2H, multiplet), 2.13 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.32 (2H, multiplet), 2.93 (6H, singlet), 3.01 (4H, multiplet), 3.36 (2H, triplet, *J*=8.3 Hz), 3.48 (2H, triplet, *J*=8.3 Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 3.62 (2H, multiplet), 4.08 (2H, triplet, *J*=6.1 Hz), 4.15 (2H, triplet, *J*=5.6 Hz), 6.60 (1H, doublet, *J*=15.7 Hz), 7.40 (1H, doublet, *J*=15.7 Hz), 7.59 (2H, singlet), 7.84 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 22.72, 24.41, 26.05, 30.32, 30.93, 38.08, 43.60, 54.53, 55.94, 59.18, 71.27, 72.24, 119.51, 119.57, 124.38, 133.10, 134.46, 135.89, 136.61, 138.02, 153.75, 154.64, 167.88. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 806.00, $(M+H)^+$-calculated: 805.98.

18c22e: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 1.98 (1H, multiplet), 2.13 (3H, multiplet), 2.20 (2H, multiplet), 2.58 (1H, multiplet), 2.64 (1H, multiplet), 2.93 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.03 (3H, singlet), 3.22 (1H, multiplet), 3.36 (2H, triplet, *J*=8.3 Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 3.73 (2H, multiplet), 4.08 (2H, triplet, *J*=6.1 Hz), 4.16 (1H, multiplet), 4.23 (1H, multiplet), 6.61 (1H, doublet, *J*=15.7 Hz), 7.39 (1H, doublet, *J*=15.7 Hz), 7.59 (2H, singlet), 7.83 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-δ (ppm):** 22.60, 30.32, 30.95, 30.99, 32.07, 38.08, 40.10, 43.61, 57.42, 59.19, 68.57, 71.07, 72.25, 119.53, 119.59, 124.42, 133.12, 134.46, 135.98, 136.59, 138.01, 153.79, 154.68, 167.88. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 792.00, $(M+H)^+$-calculated: 791.97.

<u>19c22e</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-δ (ppm):** 2.11 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.32 (2H, multiplet), 2.93 (6H, singlet), 2.97 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.36 (2H, triplet, *J*=8.3 Hz), 3.52 (2H, triplet, *J*=8.0 Hz), 3.57 (2H, triplet, *J*=7.1 Hz), 4.07 (2H, triplet, *J*=6.0 Hz), 4.18 (2H, triplet, *J*=5.6 Hz), 7.59 (2H, singlet), 7.84 (2H, singlet). **^{13}C-NMR shifts of HPLC-purified product from HMQC/HMBC (CD_3OD, 49.05 ppm)-δ (ppm):** 26.12, 30.01, 30.30, 37.98, 43.31, 43.41, 56.58, 58.88, 71.26, 71.73, 81.66, 119.07, 119.19, 134.16, 134.17, 137.42, 137.45, 153.42, 154.76, 155.40, 1 shift undetermined. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 763.91, $(M+H)^+$-calculated: 763.94.

<u>20c22e</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-δ (ppm):** 1.98 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.28 (2H, multiplet), 2.48 (2H, triplet, *J*=7.4 Hz), 2.88 (2H, triplet, *J*=7.4 Hz), 2.93 (6H, singlet), 2.96 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.35 (2H, triplet, *J*=8.3 Hz), 3.42 (2H, triplet, *J*=7.1 Hz), 3.51 (2H, triplet, *J*=7.9

Hz), 3.98 (2H, triplet, *J*=6.1 Hz), 4.09 (2H, triplet, *J*=5.6 Hz), 7.47 (2H, singlet), 7.58 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 26.40, 30.32, 30.94, 31.49, 37.78, 38.26, 43.59, 43.70, 57.07, 59.18, 71.13, 72.17, 118.79, 119.51, 134.09, 134.46, 136.62, 142.09, 152.11, 153.71, 174.47. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 767.99, $(M+H)^+$-calculated: 767.97

<u>7c21e</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.03 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.31 (2H, multiplet), 2.92 (6H, singlet), 2.97 (8H, multiplet-2 peaks overlapping), 3.32 (2H, triplet, *J*=8.1 Hz), 3.49 (2H, triplet, *J*=6.9 Hz), 3.52 (2H, triplet, *J*=8.0 Hz), 4.03 (2H, triplet, *J*=6.1 Hz), 4.16 (2H, triplet, *J*=5.6 Hz), 6.58 (1H, doublet, *J*=15.7 Hz), 6.91 (2H, doublet, *J*=8.7 Hz), 7.20 (2H, doublet, *J*=8.7 Hz), 7.37 (1H, doublet, *J*=15.7 Hz), 7.80 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 26.38, 30.23, 30.97, 37.79, 43.55, 43.66, 56.86, 60.04, 66.59, 71.35, 116.06, 119.57, 124.24, 129.20, 130.90, 133.07, 135.84, 138.01, 154.52, 159.62, 167.88. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 610.15, $(M+H)^+$-calculated: 610.13.

<u>7c23e</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.08 (2H, apparent quintet, apparent *J*=6.5 Hz), 2.31 (2H, multiplet), 2.93 (6H, singlet), 2.98 (6H, singlet), 3.34 (2H, triplet, *J*=8.2 Hz), 3.39 (2H, triplet, *J*=6.8 Hz), 3.52 (2H, triplet, *J*=8.2 Hz), 3.55 (2H, triplet, *J*=7.0 Hz), 4.12 (2H, triplet, *J*=6.0 Hz), 4.17 (2H, triplet, *J*=5.6 Hz), 6.58 (1H, doublet, *J*=15.7 Hz), 7.01 (1H, doublet, *J*=8.4 Hz), 7.24 (1H, doublet, *J*=8.4 Hz), 7.39 (1H, doublet, *J*=15.7 Hz), 7.53 (1H, singlet), 7.83 (2H, singlet). **^{13}C-**

NMR shifts of HPLC-purified product from HMQC/HMBC (CD_3OD, 49.05 ppm)-*δ* (ppm): 26.16, 29.77, 30.29, 37.75, 43.36, 43.48, 56.78, 59.50, 67.84, 71.08, 113.11, 114.60, 119.31, 124.16, 129.95, 129.99, 132.85, 132.90, 134.35, 137.78, 154.29, 155.79, 167.60. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 688.01, $(M+H)^+$-calculated: 688.04.

<u>7c24e</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.10 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.32 (2H, multiplet), 2.93 (6H, singlet), 2.98 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.36 (2H, triplet, *J*=8.3 Hz), 3.52 (2H, triplet, *J*=8.0 Hz), 3.58 (2H, triplet, *J*=7.1 Hz), 4.09 (2H, triplet, *J*=6.1 Hz), 4.17 (2H, triplet, *J*=5.6 Hz), 6.60 (1H, doublet, *J*=15.8 Hz), 7.38 (2H, singlet), 7.40 (1H, doublet, *J*=15.7 Hz), 7.83 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 26.42, 30.55, 31.00, 37.98, 43.61, 43.71, 56.98, 59.12, 71.41, 72.47, 119.58, 124.38, 130.67, 130.78, 133.10, 135.48, 135.96, 138.00, 151.87, 154.56, 167.88. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 678.02, $(M+H)^+$-calculated: 678.05.

<u>7c25e</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.08 (2H, apparent quintet, apparent *J*=6.5 Hz), 2.31 (2H, multiplet), 2.93 (6H, singlet), 2.97 (8H, multiplet-2 peaks overlapping), 3.34 (2H, triplet, *J*=8.3 Hz), 3.52 (2H, triplet, *J*=8.0 Hz), 3.54 (2H, triplet, *J*=6.9 Hz), 4.12 (2H, triplet, *J*=6.0 Hz), 4.16 (2H, triplet, *J*=5.6 Hz), 6.58 (1H, doublet, *J*=15.7 Hz), 7.05 (1H, doublet, *J*=8.5 Hz), 7.19 (1H, doublet, *J*=8.5 Hz), 7.35 (1H, singlet), 7.37 (1H, doublet, *J*=15.7 Hz), 7.80 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 26.39, 30.11, 30.63, 37.94, 43.56, 43.67, 56.88, 59.66, 67.97, 71.35, 115.00, 119.57, 124.07, 124.29, 129.51, 130.54, 131.47, 133.05, 135.84, 137.97, 154.51, 154.96, 167.88. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 644.07, $(M+H)^+$-calculated: 644.09.

<u>**7c26e**</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.31 (2H, multiplet), 2.93 (6H, singlet), 2.98 (6H, singlet), 3.01 (2H, triplet, *J*=8.3 Hz), 3.35 (2H, triplet, *J*=8.3 Hz), 3.53 (2H, triplet, *J*=8.0 Hz), 3.76 (2H, triplet, *J*=5.4 Hz), 4.12 (2H, triplet, *J*=5.4 Hz), 4.17 (2H, triplet, *J*=5.6 Hz), 6.67 (1H, doublet, *J*=15.7 Hz), 7.44 (2H, doublet, *J*=15.7 Hz), 7.59 (2H, singlet), 7.84 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 26.43, 30.32, 40.88, 43.61, 43.72, 57.00, 59.16, 71.42, 72.69, 119.48, 119.61, 124.30, 133.16, 134.51, 135.93, 136.80, 138.33, 153.47, 154.61, 168.08. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 751.93, $(M+H)^+$-calculated: 751.94.

<u>**7c27e**</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 1.33 (6H, triplet, *J*=7.3 Hz), 2.13 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.31 (2H, multiplet), 2.98 (6H, singlet), 3.00 (2H, triplet, *J*=8.4 Hz), 3.29 (4H, quartet, *J*=7.3 Hz), 3.35 (2H, triplet, *J*=8.4 Hz), 3.53 (2H, triplet, *J*=8.0 Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 4.08 (2H, triplet, *J*=6.1 Hz), 4.17 (2H, triplet, *J*=5.6 Hz), 6.61 (1H, doublet, *J*=15.7 Hz), 7.41 (1H, doublet, *J*=15.7 Hz), 7.60 (2H, singlet), 7.83 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 9.17, 26.43, 29.79, 30.95, 38.08, 43.72, 48.60, 53.66, 57.01, 71.41, 72.25, 119.52, 119.59, 124.41, 133.11, 134.47, 135.99, 136.78, 138.02, 153.78, 154.56, 167.88. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 794.00, $(M+H)^+$-calculated: 793.98.

7c28e: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 1.35 (3H, triplet, *J*=7.3 Hz), 2.13 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.31 (2H, multiplet), 2.90 (3H, singlet), 2.98 (6H, singlet), 3.02 (2H, triplet, *J*=8.4 Hz), 3.27 (2H, quartet, *J*=7.3 Hz), 3.38 (2H, triplet, *J*=8.4 Hz), 3.52 (2H, triplet, *J*=8.0 Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 4.08 (2H, triplet, *J*=6.1 Hz), 4.17 (2H, triplet, *J*=5.6 Hz), 6.61 (1H, doublet, *J*=15.7 Hz), 7.40 (1H, doublet, *J*=15.7 Hz), 7.59 (2H, singlet), 7.82 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 9.54, 26.42, 30.03, 30.94, 38.07, 39.87, 43.71, 52.65, 56.97, 57.11, 71.40, 72.24, 119.50, 119.59, 124.41, 133.10, 134.47, 135.94, 136.74, 138.00, 153.74, 154.56, 167.87. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 779.94, $(M+H)^+$-calculated: 779.97.

7c29e: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.13 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.31 (2H, multiplet), 2.43 (1H, multiplet), 2.60 (1H, multiplet), 2.84 (2H, triplet, *J*=7.7 Hz), 2.98 (6H, singlet), 3.44 (2H, triplet, *J*=7.7 Hz), 3.53 (2H, triplet, *J*=8.0 Hz), 3.60 (2H, triplet, *J*=7.2 Hz), 4.08 (2H, triplet, *J*=6.1 Hz), 4.10 (4H, broad singlet), 4.17 (2H, triplet, *J*=5.6 Hz), 6.61 (1H, doublet, *J*=15.7 Hz), 7.40 (1H, doublet, *J*=15.7 Hz), 7.56 (2H, singlet), 7.84 (2H, singlet). **^{13}C-NMR shifts of HPLC-purified product from HMQC/HMBC (CD_3OD, 49.05 ppm)-*δ* (ppm):** 26.14, 30.12, 30.71, 31.98, 37.84, 43.45, 56.30, 56.78, 56.81, 71.12, 71.96, 119.27, 119.29, 124.11, 132.83, 132.88, 134.11, 134.14, 137.79, 153.48, 154.26, 167.60. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 777.98, $(M+H)^+$-calculated: 777.95.

7c30e: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.13 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.31 (2H, multiplet), 2.73 (3H, singlet), 2.95 (2H, triplet, *J*=7.9 Hz), 2.97 (6H, singlet), 3.33 (2H, triplet, *J*=7.9 Hz), 3.48 (2H, triplet, *J*=7.9 Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 4.08 (2H, triplet, *J*=6.1 Hz), 4.16 (2H, triplet, *J*=5.7 Hz), 6.61 (1H, doublet, *J*=15.7 Hz), 7.40 (1H, doublet, *J*=15.7 Hz), 7.57 (2H, singlet), 7.82 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 27.75, 30.32, 30.93, 33.82, 38.07, 43.55, 48.39, 59.18, 71.74, 72.25, 119.52, 119.60, 124.40, 133.10, 134.46, 135.93, 136.60, 138.02, 153.76, 154.60, 167.88. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 751.97, $(M+H)^+$-calculated: 751.94.

7c31e: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.12 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.31 (2H, multiplet), 2.95 (3H, singlet), 2.98 (6H, singlet), 3.09 (3H, singlet), 3.53 (2H, triplet, *J*=8.0 Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 3.72 (2H, singlet), 4.08 (2H, triplet, *J*=6.1 Hz), 4.17 (2H, triplet, *J*=5.6 Hz), 6.59 (1H, doublet, *J*=15.7 Hz), 7.38 (1H, doublet, *J*=15.7 Hz), 7.47 (2H, singlet), 7.82 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-*δ* (ppm):** 26.43, 30.90, 36.08, 38.05, 39.44, 43.74, 57.04, 71.41, 72.21, 118.96, 119.58, 124.46, 133.12, 134.86, 135.98, 136.02, 137.98, 153.25, 154.52, 167.86, 172.66. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 779.96, $(M+H)^+$-calculated: 779.93.

7c32e: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-*δ* (ppm):** 2.12 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.31 (2H, multiplet), 2.95 (3H, singlet), 2.98 (6H, singlet), 3.09 (3H, singlet), 3.53 (2H, triplet, *J*=7.9 Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 3.72

(2H, singlet), 4.08 (2H, triplet, *J*=6.1 Hz), 4.17 (2H, triplet, *J*=5.6 Hz), 6.61 (1H, doublet, *J*=15.7 Hz), 7.39 (1H, doublet, *J*=15.7 Hz), 7.48 (2H, singlet), 7.84 (2H, singlet). **^{13}C-NMR shifts of HPLC-purified product from HMQC/HMBC (CD$_3$OD, 49.05 ppm)-*δ* (ppm):** 26.14, 30.52, 35.82, 37.78, 37.84, 39.16, 43.47, 56.79, 71.13, 71.91, 118.70, 119.32, 123.98, 132.88, 132.90, 134.60, 134.65, 137.77, 153.01, 154.26, 167.58, 172.40. **MS (ESI)-*m/z*:** (M+H)$^+$-found: 795.93, (M+H)$^+$-calculated: 795.91.

<u>7c33e</u>: **^{1}H-NMR of HPLC-purified product (CD$_3$OD, 3.31 ppm)-*δ* (ppm):** 2.14 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.32 (2H, multiplet), 2.98 (6H, singlet), 3.18 (3H, singlet), 3.20 (3H, singlet), 3.53 (2H, triplet, *J*=8.0 Hz), 3.60 (2H, triplet, *J*=7.2 Hz), 3.97 (2H, singlet), 4.11 (2H, triplet, *J*=6.1 Hz), 4.17 (2H, triplet, *J*=5.6 Hz), 6.61 (1H, doublet, *J*=15.7 Hz), 7.40 (1H, doublet, *J*=15.7 Hz), 7.57 (2H, singlet), 7.84 (2H, singlet). **^{13}C-NMR shifts of HPLC-purified product from HMQC/HMBC (CD$_3$OD, 49.05 ppm)-*δ* (ppm):** 26.16, 30.72, 36.47, 37.80, 39.66, 40.75, 43.48, 56.77, 71.14, 72.07, 119.32, 119.79, 124.11, 132.27, 132.86, 132.92, 133.88, 137.87, 154.28, 154.31, 166.40, 167.64. **MS (ESI)-*m/z*:** (M+H)$^+$-found: 778.97, (M+H)$^+$-calculated: 778.95.

<u>7c34e</u>: **^{1}H-NMR of HPLC-purified product (CD$_3$OD, 3.31 ppm)-*δ* (ppm):** 2.14 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.32 (2H, multiplet), 2.98 (6H, singlet), 3.00 (6H, singlet), 3.53 (2H, triplet, *J*=8.0 Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 4.13 (2H, triplet, *J*=6.0 Hz), 4.17 (2H, triplet, *J*=5.6 Hz), 4.31 (2H, singlet), 6.60 (1H, doublet, *J*=15.7 Hz), 7.40 (1H, doublet, *J*=15.7 Hz), 7.79 (2H, singlet), 7.83 (2H, singlet). **^{13}C-NMR shifts of HPLC-purified product from HMQC/HMBC (CD$_3$OD, 49.05 ppm)-*δ* (ppm):** 26.16,

30.70, 37.77, 42.77, 43.48, 48.08, 56.79, 71.15, 72.36, 80.06, 87.25, 119.22, 119.34, 124.11, 132.88, 132.92, 136.98, 137.07, 137.84, 154.30, 155.80, 167.56. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 775.95, $(M+H)^+$-calculated: 775.94.

<u>7c35e</u>: **^{1}H-NMR of HPLC-purified product (CD_3OD, 3.31 ppm)-δ (ppm):** 2.00 (2H, apparent quintet, apparent *J*=7.7 Hz), 2.12 (2H, apparent quintet, apparent *J*=6.6 Hz), 2.32 (2H, multiplet), 2.65 (2H, triplet, *J*=7.7 Hz), 2.88 (6H, singlet), 2.98 (6H, singlet), 3.12 (2H, triplet, *J*=8.3 Hz), 3.52 (2H, triplet, *J*=8.0 Hz), 3.60 (2H, triplet, *J*=7.1 Hz), 4.07 (2H, triplet, *J*=6.1 Hz), 4.17 (2H, triplet, *J*=5.6 Hz), 6.61 (1H, doublet, *J*=15.7 Hz), 7.40 (1H, doublet, *J*=15.7 Hz), 7.50 (2H, singlet), 7.82 (2H, singlet). **^{13}C-NMR of HPLC-purified product (CD_3OD, 49.05 ppm)-δ (ppm):** 26.42, 27.16, 30.92, 32.06, 38.09, 43.48, 43.68, 56.96, 58.28, 71.38, 72.13, 119.24, 119.60, 124.36, 133.10, 133.92, 135.94, 138.01, 140.90, 153.00, 154.54, 167.86. **MS (ESI)-*m/z*:** $(M+H)^+$-found: 780.00, $(M+H)^+$-calculated: 779.97.