Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Synthesis of DIBAC analogues with excellent SPAAC rate constants

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Supporting Information

Experimental Section

General experimental

Unless stated otherwise all chemicals were obtained from commercial sources and used without further purification. The 1M KO^{t}Bu in THF solution was purchased from Sigma-Aldrich and not prepared by solubilizing solid KO^{t}Bu in dry THF. If no further details are given the reaction was performed under ambient atmosphere and temperature. Analytical thin layer chromatography (TLC) was performed on silica gel-coated plates (*Merck* 60 F254) with the indicated solvent mixture, visualization was done using ultraviolet (UV) irradiation (λ = 254 nm) and/or staining with $KMnO_4$. Purification by column chromatography was carried out using *Silicycle* silica gel (0.040-0.063 mm, and ca. 6 nm pore diameter). THF and CH_2Cl_2 were dried over an activated alumina column using an MBraun SPS800 solvent purification system. NEt_3 was distilled under N_2-atmosphere from CaH_2.

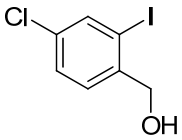
Infrared (IR) Spectroscopy: IR spectra were recorded on an ATI Matson Genesis Series FTIR spectrometer fitted with an ATR cell. The vibrations (v) are given in cm^{-1}.

Nuclear Magnetic Resonance (NMR) Spectroscopy: ^{1}H-NMR spectra were recorded on a *Varian Inova 400* (400 MHz) for room temperature measurements and a *Varian Inova 500* (500 MHz) for low temperature measurements. ^{13}C-NMR spectra were recorded on a *Bruker DMX300* (75 MHz) spectrometer. Unless stated otherwise all spectra were taken at ambient temperature. ^{1}H-NMR chemical shifts (δ) are reported in parts per million (ppm) relative to a residual proton peak of the solvent, δ = 3.31 for CD_3OD and δ = 7.26 for $CDCl_3$. Broad peaks are indicated by the addition of br. Coupling constants are reported as a *J*-value in Hertz (Hz). In case of rotamers the spectrum was taken at lower temperature to freeze the compound in its two rotamer states, causing separate peaks for each rotamer. In these cases shifts, coupling constants and integrals are given of each separate peak. ^{13}C-NMR chemical shifts (δ) are reported in ppm relative to CD_3OD (δ = 49.0) or $CDCl_3$ (δ = 77.0). If rotamers are observed in the spectrum, the minor rotamer peaks are labeled with *.

Mass Spectrometry (MS): High Resolution Mass Analyses were performed using Electrospray Ionization on a JEOL AccuToF.

Synthesis

(4-chloro-2-iodophenyl)methanol (6a)

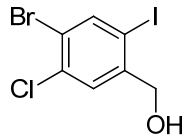


2-amino-4-chlorobenzoic acid (10.0 g, 58.2 mmol) was dissolved in DMSO (100 mL), and 30% H_2SO_4 was added (100 mL). The solution was cooled to 0 ºC, whereupon $NaNO_2$ (8.8 g, 129 mmol) was added. The reaction was stirred for two hours at room temperature, after which a solution of KI (19.3 g, 106 mmol) in H_2O (50 mL) was added. After one hour, an additional portion of KI (9.7 g, 58.2 mmol) in H_2O (25 mL) was added. In addition, DMSO (50 mL) was added to keep the reaction mixture solubilized. After one additional hour, EtOAc (300 mL) was added, and the organic layer was washed with H_2O (3 × 200 mL) and brine (200 mL), and subsequently dried over $MgSO_4$. The solvents were removed in vacuo to obtain crude **9a** as white solid. **9a** was not further purified and used as a crude in the following reaction. ^{1}H-NMR (400 MHz, CD_3OD) δ: 8.01 (d, *J* = 2.1 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.45 (dd, *J* = 8.4, 2.1 Hz, 1H). ^{13}C-

NMR (75 MHz, CD_3OD) δ: 168.9, 141.7, 138.6, 136.0, 132.7, 129.3, 95.0. HRMS (EI+) *m/z* calcd for $C_7H_4O_2ClI$ $[M]^{\bullet+}$ 281.8945, found 281.8936.

4-chloro-2-iodobenzoic acid **9a** (15 g, 53 mmol) was dissolved in dry THF (250 mL) and the solution was cooled to 0 ºC. Hereupon, NEt_3 (11 mL, 80 mmol) and ethyl chloroformate (7.6 mL, 80 mmol) were added. The reaction was stirred for 1.5 hour and subsequently $NaBH_4$ (8.0 g, 210 mmol) was added in four portions. After 1.5 hour, additional $NaBH_4$ (4.0 g, 105 mmol) was added and the reaction was stirred for another hour. Hereupon, the reaction was quenched with H_2O (100 mL) and EtOAc (200 mL) was added. The organic layer was washed with H_2O (3 × 150 mL), brine (100 mL) and subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude product was obtained by gradient column chromatography (EtOAc/*n*-heptane, 1:9 to 1:6). Compound **6a** was obtained as white solid (8.4 g, 75% over 2 steps). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.82 (s, 1H), 7.45–7.33 (m, 2H), 4.65 (d, *J* = 6.2 Hz, 2H), 1.94 (t, *J* = 6.2 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 141.1, 138.3, 133.8, 128.8, 128.6, 96.9, 68.6. HRMS (EI+) *m/z* calcd for C_7H_6OClI $[M]^{\bullet+}$ 267.9152, found 267.9160.

(4-bromo-5-chloro-2-iodophenyl)methanol (6b)

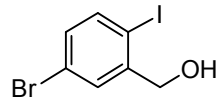


2-amino-4-chlorobenzoic acid (**8a**, 1.1 g, 6.4 mmol) was dissolved in acetic acid (8 mL) and Br_2 (0.33 mL, 6.4 mmol) was added. The mixture was stirred at room temperature for 4 hours and subsequently poured into saturated aqueous $NaHSO_3$ (50 mL). The H_2O-layer was extracted with EtOAc (2 × 50 mL), and the combined organic layers were washed with water (2 × 50 mL), brine (50 mL), and subsequently dried over $MgSO_4$. The solvents were evaporated under reduced pressure to obtain **8b** as a mixture of two products. **8b** was not further purified and used as a crude in the following reaction. ^{1}H-NMR (400 MHz, CD_3OD) δ: 8.00 (s, 1H), 6.92 (s, 1H).

Crude 2-amino-5-bromo-4-chlorobenzoic acid **8b** (6.0 g, 24 mmol) was dissolved in DMSO (100 mL) and 30% H_2SO_4 (100 mL) and the resulting mixture was cooled to 0 ºC. $NaNO_2$ (3.6 g, 53 mmol) was added and the mixture was stirred for 2 hours at room temperature. Hereupon, a solution of KI (8.0 g, 48 mmol) in H_2O (40 mL) was added. After one hour an additional portion of KI (4.0 g, 24 mmol) in H_2O (20 mL) was added. After one more hour, EtOAc (200 mL) was added, and the organic layer was washed with H_2O (2 × 200 mL) and brine (200 mL), and dried over $MgSO_4$. The solvents were removed in vacuo to obtain **9b** as a mixture of two products. **S2** was used as a crude in the following reaction. ^{1}H-NMR (400 MHz, CD_3OD) δ: 8.16 (s, 1H), 8.07 (s, 1H).

Crude 5-bromo-4-chloro-2-iodobenzoic acid (**9b**, 11 g, 30 mmol) was dissolved in dry THF (100 mL) and the solution was cooled to 0 ºC. Next, NEt_3 (6.2 mL, 44 mmol) and ethyl chloroformate (4.3 mL, 44 mmol) were added. The reaction mixture was stirred for 1 hour and subsequently a solution of $NaBH_4$ (2.24 g, 59 mmol) in H_2O (10 mL) was added. The mixture was stirred another hour, prior to quenching with H_2O (100 mL). The H_2O-layer was extracted with EtOAc (2 × 100 mL), and the combined organic layers were washed with H_2O (2 × 150 mL) and brine (150 mL). The organic layer was dried over $MgSO_4$ and the solvents were removed under reduced pressure. The crude product was purified using column chromatography (EtOAc/*n*-heptane, 1:6) to obtain **6b** as a white solid (3.84 g, 38% over 3 steps). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.88 (s, 1H), 7.72 (s, 1H), 4.62 (dd, *J* = 6.0, 0.7 Hz, 2H), 1.96 (t, *J* = 6.1 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 142.8, 139.5, 139.2, 135.7, 132.4, 122.9, 94.3, 68.0, 52.4.

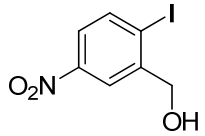
(5-bromo-2-iodophenyl)methanol (6c)



2-amino-5-bromobenzoic acid (2.0 g, 9.2 mmol) was dissolved in DMSO (50 mL) and 30% H_2SO_4 (50 mL) and $NaNO_2$ (0.89 g, 13 mmol) were added. The reaction mixture was stirred for 1 hour at room temperature, whereupon a solution of KI (3.1 g, 19 mmol) in H_2O (20 mL) was added and the reaction mixture was stirred for another hour. Next, another portion of KI (3.1 g, 19 mmol) in H_2O (10 mL) was added and the reaction mixture was stirred for an additional hour. The reaction mixture was quenched with a saturated aqueous Na_2SO_3-solution (75 mL), EtOAc (100 mL) was added and the layers were separated. Hereupon, the H_2O-layer was extracted with EtOAc (100 mL). The combined organic layers were washed with H_2O (2 × 100 mL) and brine (100 mL). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to afford compound **9c** as a yellow solid. **S3** was not further purified further and used as a crude in the following reaction. R_F = 0.05 (EtOAc/*n*-heptane, 1:4). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.13 (d, *J* = 2.4 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.33 (dd, *J* = 8.4, 2.4 Hz, 1H).

5-bromo-2-iodobenzoic acid (**9c**) (750 mg, 2.3 mmol) was dissolved in dry THF (25 mL) and the reaction mixture was cooled to 0 ºC. NEt_3 (0.48 mL, 3.4 mmol) and ethyl chloroformate (0.33 mL, 3.4 mmol) were added and the reaction mixture was stirred for 1 hour. Next a solution of $NaBH_4$ (130 mg, 3.4 mmol) in H_2O (2 mL) was added and the mixture was stirred for 1.5 hour. The reaction was quenched with H_2O (15 mL), whereupon CH_2Cl_2 (20 mL) was added and the layers were separated. Hereupon, the H_2O-layer was extracted with CH_2Cl_2 (20 mL). Subsequently, the combined organic layers were washed with H_2O (25 mL) and brine (25 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by gradient column chromatography (*n*-heptane/EtOAc, 19:1 to 9:1) to obtain compound **6c** as a white solid (410 mg, 54% over 2 steps). Analysis was in accordance with literature.[1] R_F = 0.40 (EtOAc/*n*-heptane, 1:4). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, *J* = 8.3 Hz, 1H), 7.63 (d, *J* = 2.4 Hz, 1H), 7.14 (dd, *J* = 8.3, 2.5 Hz, 1H), 4.64 (d, *J* = 6.1 Hz, 2H), 1.96 (t, *J* = 6.2 Hz, 1H).

(2-iodo-5-nitrophenyl)methanol (6d)

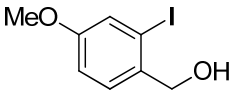


2-amino-5-nitrobenzoic acid (1.82 g, 10 mmol) was dissolved in DMSO (50 mL) and 30% H_2SO_4 (50 mL) was added. The resulting mixture was heated for two hours at 50 ºC. The reaction was cooled to 0 ºC and a solution of $NaNO_2$ (970 mg, 14 mmol) in water (25 mL) was added. The mixture was stirred at 0 ºC for one hour, whereupon a solution of KI (5.0 g, 30 mmol) in H_2O (10 mL) was added and the mixture was stirred for 1 hour at room temperature. Next, another portion of KI (5 g, 30 mmol) in H_2O (10 mL) was added and the mixture was stirred for an additional hour. EtOAc (100 mL) was added and the reaction was quenched with saturated aqueous $NaHSO_3$ (100 mL). The organic layer was washed with water (2 × 100 mL) and brine (100 mL) and subsequently dried over $MgSO_4$. The solvents were evaporated under reduced pressure and the crude product was obtained as yellow solid (12.0 g, 120%). **9d** was not further purified and used as a crude in the following reaction. ^{1}H-NMR (400 MHz, CD_3OD) δ: 8.54 (d, *J* = 2.7 Hz, 1H), 8.29 (d, *J* = 8.6 Hz, 1H), 8.01 (dd, *J* = 8.7, 2.7 Hz, 1H). ^{13}C-NMR (75 MHz, CD_3OD) δ: 168.0, 149.2, 144.1, 139.2, 127.1, 125.8, 103.0, 49.6, 49.3, 49.1, 48.8, 48.5. FT-IR ν_{max} (cm^{-1}): 2932, 1722, 1588, 151, 1342, 1295, 1022, 1234, 728. HRMS (EI+) *m/z* calcd for $C_7H_4NO_4I$ $[M]^{\bullet+}$ 292.9185, found 292.9184.

2-iodo-5-nitrobenzoic acid (**9d**) (3.0 g, 10.2 mmol) was dissolved in dry THF (100 mL) and the reaction was cooled to 0 ºC. NEt_3 (2.1 mL, 15.4 mmol) and ethyl chloroformate

(1.5 mL, 15.4 mmol) were added and the reaction was stirred for 1 hour. Next, a solution of $NaBH_4$ (0.78 g, 20.5 mmol) in H_2O (5 mL) was added and the reaction was stirred for 1.5 hour. Hereupon, an additional portion of $NaBH_4$ (0.78 g, 20.5 mmol) in H_2O (5 mL) was added and the reaction was stirred for an additional 30 minutes. The reaction was then quenched by the addition of H_2O (20 mL). The reaction was diluted with EtOAc (150 mL) and the organic layer was washed with H_2O (2 × 100 mL) and brine (100 mL) and subsequently dried over $MgSO_4$. The solvents were removed *in vacuo* and the crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:9 to 1:3). Compound **6d** was obtained as an orange solid (1.32 g, 55% over 2 steps). Analysis was in accordance with literature.[2] ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.36 (d, *J* = 2.8 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.85 (dd, *J* = 8.6, 2.8 Hz, 1H), 4.75 (d, *J* = 3.4 Hz, 2H), 2.10 (t, *J* = 5.0 Hz, 1H). HRMS (EI+) *m/z* calcd for $C_7H_6NO_3I$ $[M]^{\bullet+}$ 278.9393, found 278.9396.

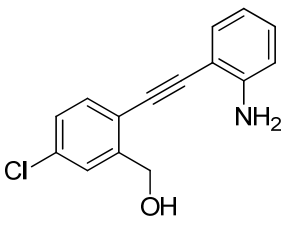
(2-iodo-4-methoxyphenyl)methanol (6e)



2-amino-4-methoxybenzoic acid (2.0 g, 12 mmol) was dissolved in DMSO (75 mL) whereupon 30% H_2SO_4 (75 mL) and $NaNO_2$ (1.156 g, 16.75 mmol) were added. The reaction mixture was stirred for 1 hour at room temperature, before addition of KI (4.0 g, 24 mmol) in H_2O (10 mL) and the reaction mixture was stirred for another hour. Next, another portion of KI (4.0 g, 24 mmol) in H_2O (10 mL) was added and the reaction mixture was stirred for an additional hour. The reaction mixture was quenched with a saturated aqueous Na_2SO_3-solution (50 mL), EtOAc (100 mL) was added, and the layers were separated. Hereupon, the H_2O-layer was extracted with EtOAc (100 mL). The combined organic layers were washed with H_2O (2 × 100 mL) and brine (100 mL). Next, the organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to afford compound **9e** as an orange solid. **9e** was not further purified and used as a crude in the following reaction. R_F = 0.20 (EtOAc/*n*-heptane, 1:1). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.02 (d, *J* = 8.8 Hz, 1H), 7.58 (d, *J* = 2.5 Hz, 1H), 6.94 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.86 (s, 3H).

2-iodo-4-methoxybenzoic acid (**9e**) (3.7 g, 13.4 mmol) was dissolved in dry THF (75 mL) and the reaction mixture was cooled to 0 ºC. NEt_3 (2.8 mL, 20 mmol) and ethyl chloroformate (1.9 mL, 20 mmol) were added and the reaction mixture was stirred for 1 hour. Next, $NaBH_4$ (760 mg, 20 mmol) in H_2O (0.1 mL) was added and the mixture was stirred for 1.5 hour. The reaction was quenched with H_2O (50 mL). CH_2Cl_2 (50 mL) was added, the layers were separated and hereupon the water layer was extracted with CH_2Cl_2 (50 mL). The combined organic layers were washed with H_2O (50 mL) and brine (50 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:9) to obtain compound **6e** as colorless oil (2.3 g, 54% over 2 steps). R_F = 0.40 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38 (d, *J* = 2.6 Hz, 1H), 7.33 (d, *J* = 8.5 Hz, 1H), 6.91 (dd, *J* = 8.5, 2.6 Hz, 1H), 4.64 (d, *J* = 6.3 Hz, 2H), 3.86 (s, 3H), 1.91 (t, *J* = 6.3 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 159.4, 135.0, 129.4, 124.6, 114.2, 98.1, 68.8, 55.3. FT-IR ν_{max} film (cm^{-1}): 3395, 2833, 2362, 2336, 1700, 1593, 1554, 1480, 1282, 1234, 1022, 914, 845, 811, 746, 616. HRMS (EI+) *m/z* calcd for $C_8H_9O_2I$ $[M]^{\bullet+}$ 263.9648, found 263.9650.

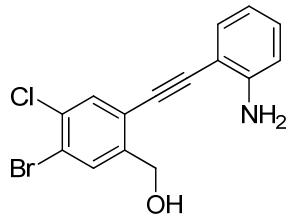
(2-((2-aminophenyl)ethynyl)-5-chlorophenyl)methanol (10a)



Compound **6a** (8.5 g, 29.9 mmol), $Pd(PPh_3)_2Cl_2$ (430 mg, 0.60 mmol), and CuI (57 mg, 0.30 mmol) were added to a flame-dried flask. The flask was evacuated and refilled with an N_2/H_2-mixture

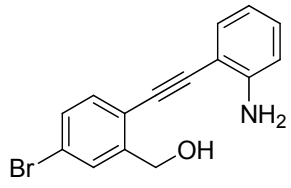
(3:2) three times. THF (150 mL) and NEt_3 (12.4 mL, 89 mmol) were bubbled through with an N_2/H_2-mixture (3/2) for 10 minutes and subsequently added to the reaction mixture. Hereupon, 2-ethynylaniline (3.75 mL, 33 mmol) was added, and the mixture was stirred overnight under N_2/H_2-atmosphere.The reaction mixture was diluted with CH_2Cl_2 (250 mL) and the organic layer was washed with H_2O (3 × 250 mL). The H_2O-layers were combined and back-extracted with CH_2Cl_2 (150 mL). The organic layers were combined and washed with brine (150 mL). The solvents were removed under reduced pressure and the crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 1:1) to obtain **10a** as a yellow solid (7.3 g, 95%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.52 (d, *J* = 1.9 Hz, 1H), 7.35 (t, *J* = 8.7 Hz, 2H), 7.29 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.19-7.14 (m, 1H), 6.74-6.70 (m, 2H), 4.83 (d, *J* = 4.8 Hz, 2H), 4.41 (br s, 2H), 2.06 (t, *J* = 5.6 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 148.34, 140.24, 133.36, 132.08, 131.58, 130.35, 128.92, 128.47, 123.70, 117.92, 114.53, 107.03, 92.26, 90.84, 63.69. HRMS (ESI+) *m/z* calcd for $C_{15}H_{13}ClNO$ $[M+H]^+$ 258.0686, found 258.0677.

(2-((2-aminophenyl)ethynyl)-5-bromo-4-chlorophenyl)methanol (10b)



Compound **6b** (3 g, 8.6 mmol), $Pd(PPh_3)_2Cl_2$ (0.121 g, 0.17 mmol) and CuI (0.016 g, 0.086 mmol) were added to a flame-dried Schlenk flask. The flask was subsequently evacuated and refilled with an N_2/H_2-mixture (3:2) three times. At the same time, dry THF (150 mL) and dry NEt_3 (3.6 mL, 25.9 mmol) were bubbled with a N_2/H_2-mixture for 10 minutes. The bubbled solutions were subsequently added to the Schlenk flask. Next, 2-ethynylaniline (1.08 mL, 9.5 mmol) was added and the mixture was stirred for 4 hours under N_2/H_2-atmosphere. Hereupon, CH_2Cl_2 (150 mL) was added and the organic layer was washed with H_2O (3 × 100 mL). The H_2O-layers were combined and back-extracted with CH_2Cl_2 (150 mL). The organic layers were combined and dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 1:2). Compound **10b** was obtained as a white solid (2.74 g, 94%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.78-7.69 (m, 1H), 7.60 (s, 1H), 7.33 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.18 (ddd, *J* = 8.2, 7.4, 1.6 Hz, 1H), 6.80-6.57 (m, 2H), 4.83 (d, *J* = 5.7 Hz, 2H), 4.37 (br s, 2H), 2.01 (t, *J* = 6.2 Hz, 1H). ^{13}C-NMR (75 MHz, CD_3OD) δ: 150.7, 144.3, 133.7 (2C), 133.2, 133.0, 131.4, 123.7, 122.9, 118.2, 115.7, 107.8, 94.5, 90.5, 62.7. HRMS (ESI+) *m/z* calcd for $C_{15}H_{12}BrClNO$ $[M+H]^+$ 335.9791, found 335.9781.

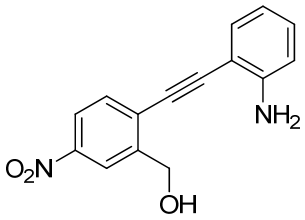
(2-((2-aminophenyl)ethynyl-5-bromophenyl)methanol (10c)



(5-bromo-2-iodophenyl)methanol (**6c**) (106 mg, 0.34 mmol), $Pd(PPh_3)_2Cl_2$ (7.0 mg, 0.01 mmol) and CuI (1.2 mg, 6.3 µmol) were added to a flame-dried Schlenk flask. The flask was evacuated and refilled with an N_2/H_2-mixture (3:2) three times. Dry THF (3 mL) and dry NEt_3 (71 µL, 0.51 mmol) were bubbled through with an N_2/H_2 mixture (3:2) for 10 minutes and subsequently added to the mixture. Hereupon, 2-ethynylaniline (0.060 mL, 0.58 mmol) was added and the mixture was stirred for 16 hours under an N_2/H_2-atmosphere. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and the organic layer was washed with H_2O (5 mL). The water layer was then back-extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layers were washed with H_2O (15 mL) and brine (20 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was

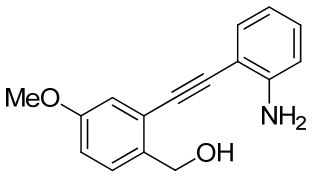
purified by gradient column chromatography (EtOAc/*n*-heptane, 1:6 to 1:2) to obtain **10c** as a yellow solid (102 mg, 100%). R_F = 0.40 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (300 MHz, CD_3OD) δ: 7.68-7,67 (m, 1H), 7.43-7.42 (m, 2H), 7.28 (ddd, *J* = 7.7, 1.5, 0.4 Hz, 1H), 7.12 (ddd, *J* = 7.3, 6.6, 1.6 Hz, 1H) 6.79-6.76 (m, 1H) 6.64 (td, *J* = 7.7, 1.1 Hz, 1H), 4.80 (d, *J* = 0.6 Hz, 2H). ^{13}C-NMR (75 MHz, CD_3OD) δ: 148.6, 144.2, 132.4, 131.0, 129.4, 129.2, 129.1, 121.4, 120.0, 116.5, 113.8, 106.5, 91.6, 89.8, 61.3. FT-IR ν_{max} film (cm^{-1}): 3360, 2923, 2850, 2362, 2202, 1610, 1489, 1450, 815, 750. HRMS (ESI+) *m/z* calcd for $C_{15}H_{13}BrNO$ $[M+H]^+$ 302.0181, found 302.0169.

(2-((2-aminophenyl)ethynyl)-5-nitrophenyl)methanol (10d)



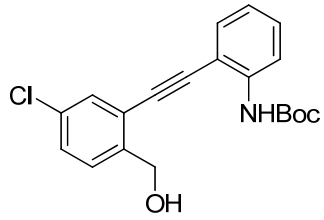
(2-iodo-5-nitrophenyl)methanol (**6d**) (1.32 g, 4.73 mmol), $Pd(PPh_3)_2Cl_2$ (66 mg, 0.095 mmol) and CuI (5 mg, 0.047 mmol) were added to a flame-dried flask. The flask was evacuated and refilled with an N_2/H_2-mixture (3/2). Dry THF (70 mL) and dry NEt_3 (2.0 mL, 14 mmol) were bubbled through with an N_2/H_2 mixture (3:2) for 10 minutes and subsequently added to the mixture. Hereupon, 2-ethynylaniline (0.81 mL, 7.1 mmol) was added, and the mixture was stirred for 3 hours.The reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with H_2O (3 × 100 mL). The H_2O-layers were combined and back-extracted with CH_2Cl_2 (100 mL). The organic layers were combined and dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 2:1). Compound **10d** was obtained as a red solid (1.13 g, 89 % yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.38 (d, *J* = 2.0 Hz, 1H), 8.16 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.50-7.32 (m, 1H), 7.24-7.16 (m, 1H), 6.87-6.53 (m, 2H), 4.98 (d, *J* = 4.0 Hz, 2H), 4.44 (br s, 2H), 2.10 (t, *J* = 6.1 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 177.2, 165.2, 143.4, 132.5, 132.3, 131.1, 128.5, 127.9, 122.6, 122.3, 118.1, 114.7, 96.7, 96.2, 63.4. HRMS (ESI+) *m/z* calcd for $C_{15}H_{13}N_2O_3$ $[M+H]^+$ 269.0926, found 269.0916.

(2-((2-aminophenyl)ethynyl)-4-methoxyphenyl)methanol (10e)



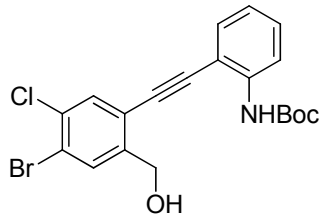
Compound **6e** (100 mg, 0.40 mmol), $Pd(PPh_3)_2Cl_2$ (5.3 mg, 7.6 µmol) and CuI (0,7 mg, 4 µmol) were added to a flame-dried Schlenk flask. The flask was evacuated and refilled with an N_2/H_2 mixture (3:2) three times. Dry THF (7 mL) and dry NEt_3 (84 µL, 0.61 mmol) were bubbled through with an N_2/H_2 mixture (3:2) for 10 minutes and subsequently added to the mixture. Hereupon 2-ethynylaniline (47 µL, 0.42 mmol) was added and the mixture was stirred for 3 hours under an N_2/H_2-atmosphere. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with H_2O (5 mL). The H_2O-layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with H_2O (10 mL) and brine (15 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 1:2) to obtain compound **10e** as a yellow solid (92 mg, 91%). R_F = 0.20 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.36 (d, *J* = 7.7 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 7.16 (d, *J* = 7.4 Hz, 1H), 7.09 (d, *J* = 2.8 Hz, 1H), 6.88 (dd, *J* = 8.4, 2.9 Hz), 6.74 (s, 1H), 6.72 (s, 1H), 4.81 (d, *J* = 6.2 Hz, 2H), 4.47 (s br., 2H), 3.84 (s, 3H), 1.86 (t, *J* = 6.2 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 159.0, 148.4, 134.4, 132.0, 130.1, 129.6, 123.6, 117.8, 116.8, 114.6, 114.4, 107.4, 92.2, 90.8, 64.1, 55.5. FT-IR ν_{max} film (cm^{-1}): 3339, 2924, 2837, 2202, 1601, 1576, 1489, 1450, 1303, 1225, 1087, 1040, 910, 745, 733. HRMS (ESI+) *m/z* calcd for $C_{16}H_{16}NO_2$ $[M+H]^+$ 254.1181, found 254.1183.

***tert*-butyl (2-((5-chloro-2-(hydroxymethyl)phenyl)ethynyl)phenyl)carbamate (11a)**



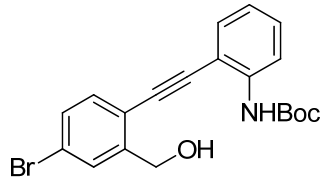
Compound **10a** (7.3 g, 28.4 mmol) was dissolved in THF (34 mL) and Boc_2O (7.4 g, 33.9 mmol) was added. The mixture was heated to 70 ºC and stirred for three days. The mixture was diluted with EtOAc (300 mL) and the organic layer was washed with H_2O (3 × 200 mL), and brine (200 mL) and subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure and the thus obtained crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:7 to 1:4) yielding **11a** as a white solid (8.24 g, 81%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.13 (br d, *J* = 7.0 Hz, 1H), 7.83 (s, 1H), 7.56 (d, *J* = 2.0 Hz, 1H), 7.45 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.39-7.31 (m, 3H), 7.01 (t, *J* = 7.3 Hz, 1H), 4.88 (d, *J* = 4.5 Hz, 2H), 2.38 (br s, 1H), 1.57 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 152.6, 140.2, 139.8, 133.6, 131.8, 131.5, 130.2, 129.5, 128.8, 123.6, 122.3, 118.1, 111.0, 92.6, 90.5, 81.3, 63.7, 28.3 (3C). HRMS (ESI+) *m/z* calcd $[M+Na]^+$ for $C_{20}H_{20}ClNNaO_3$ 380.1029, found 380.1019.

***tert*-butyl (2-((4-bromo-5-chloro-2-(hydroxymethyl)phenyl)ethynyl)phenyl) carbamate (11b)**



Compound **10b** (1.8 g, 5.35 mmol) was dissolved in THF (5.4 mL) and Boc_2O (1.17 g, 5.35 mmol) was added. The mixture was heated to 70 ºC and stirred overnight. The reaction mixture was diluted with EtOAc (100 mL) and the organic layer was washed with H_2O (3 × 100 mL), and brine (100 mL), and was subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:8 to 1:2). Compound **11b** was obtained as a white solid (1.34 g, 57%), also starting material **10b** was re-obtained (540 mg, 30%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.12 (d, *J* = 5.8 Hz, 1H), 7.74 (br s, 1H), 7.72 (s, 1H), 7.63 (s, 1H), 7.44 (ddd, *J* = 7.7, 1.6, 0.5 Hz, 1H), 7.40 – 7.31 (m, 1H), 7.02 (dt, *J* = 7.6, 1.1 Hz, 1H), 4.85 (d, *J* = 4.8 Hz, 2H), 2.43 (br s, 1H), 1.57 (s, 9H). ^{13}C-NMR (75 MHz, CDCl) δ: 151.7, 141.2, 140.2, 133.8, 133.2, 133.1, 131.5, 130.4, 122.9, 122.3, 118.2, 118.0, 110.7, 91.8, 91.3, 81.4, 63.1, 28.3 (3C). HRMS (ESI+) *m/z* calcd $[M+H]^+$ for $C_{20}H_{20}BrClNO_3$ 436.0301, found 436.0315.

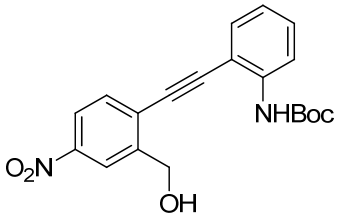
***tert*-butyl 2-((4-bromo-2-hydroxymethyl)phenyl)ethynyl)phenyl)carbamate (11c)**



Compound **10c** (381 mg, 1.26 mmol) was dissolved in THF (1.2 mL) and Boc_2O (275 mg, 1.26 mmol) was added. The reaction was stirred for two days at 70 ºC in a sealed tube. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and the organic layer was washed with H_2O (15 mL). The H_2O-layer was extracted with CH_2Cl_2 (10 mL). The combined organic layers were washed with H_2O (2 × 10 mL) and brine (10 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:4) to obtain compound **11c** as yellow oil (444 mg, 87%). R_F = 0.55 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (300 MHz, CD_3OD) δ: 7.87 (d, *J* = 8.3 Hz, 1H), 7.71 (m, 1H), 7.50-7.48 (m, 1H), 7.46-7.41 (m, 2H), 7.38-7.32 (m, 1H), 7.08 (td, *J* = 8.7, 1.2 Hz, 1H), 4.85 (s, 2H), 1.54 (s, 9H). ^{13}C-NMR (75 MHz, CD_3OD) δ: 154.9, 146.8, 140.8, 134.4, 132.9, 131.3, 131.0, 130.7, 124.4, 124.1, 121.7, 121.0, 115.0, 92.9, 91.9, 81.8, 63.2, 28.7 (3C). FT-IR ν_{max} film (cm^{-1}): 3395, 2976, 2928, 2366, 1735, 1519,

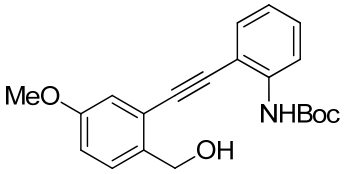
1498, 1455, 1394, 1243, 1161, 1044, 746. HRMS (ESI+) *m/z* calcd for $C_{20}H_{20}BrNNaO_3$ $[M+Na]^+$ 424.0524, found 424.0513.

***tert*-butyl (2-((2-(hydroxymethyl)-4-nitrophenyl)ethynyl)phenyl)carbamate (11d)**



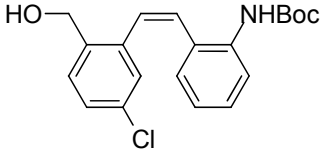
Compound **10d** (100 mg, 0.37 mmol) was dissolved in THF (370 µL) and Boc_2O (81 mg, 0.37 mmol) was added. The reaction was stirred in a sealed tube at 70 ºC overnight. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and the organic layer was washed with H_2O (3 × 10 mL) and brine (10 mL) and subsequently dried over $MgSO_4$. The solvents were removed *in vacuo* and the crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:6 to 1:4). Compound **11d** was obtained as red solid (70 mg, 51%). In addition **10d** was reobtained (40 mg, 40%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.36 (d, *J* = 1.6 Hz, 1H), 8.20 (dd, *J* = 8.5, 2.3 Hz, 1H), 8.15 (br s, 1H), 7.80 (s, 1H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.40 (t, *J* = 7.9 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 5.00 (d, *J* = 4.6 Hz, 2H), 2.59 (br s, 1H), 1.58 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 152.5, 147.1, 142.9, 140.5, 132.7, 131.8, 130.9, 123.1, 122.9, 122.4, 118.3, 114.6, 110.4, 94.6, 92.3, 81.6, 63.5, 28.3 (3C). HRMS (ESI+) *m/z* calcd for $C_{20}H_{20}N_2NaO_5$ $[M+Na]^+$ 391.1270, found 391.1265.

***tert*-butyl 2-((2-(hydroxymethyl)-5-methoxyphenyl)ethynyl)phenylcarbamate (11e)**



Compound **10e** (1.75 g, 6.9 mmol) was dissolved in THF (5 mL) and Boc_2O (1.5 g, 6.9 mmol) was added. The reaction was stirred for two days at 70 ºC in a sealed tube. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and washed with H_2O (15 mL). The H_2O-layer was extracted with CH_2Cl_2 (15 mL). The combined organic layers were washed with H_2O (2 × 15 mL) and brine (20 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:9) to obtain compound **11e** as orange oil (1.94 g, 80%). R_F = 0.50 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.15 (br s, 1H), 7.94 (br s, 1H), 7.46 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.36-7.32 (m, 2H), 7.11 (d, *J* = 2.7 Hz, 1H), 7.00 (td, *J* = 7.6, 1.1 Hz, 1H), 6.90 (dd, *J* = 8.4, 2.7 Hz, 1H), 4.85 (d, *J* = 4.3 Hz, 2H), 3.84 (s, 3H), 1.56 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 159.1, 152.6, 140.2, 133.9, 131.4, 130.0, 129.8, 123.3, 122.2, 118.1, 117.0, 115.0, 111.3, 93.9, 89.1, 81.1, 63.9, 55.5, 28.3 (3C). Ft-IR ν_{max} film (cm^{-1}): 3404, 2980, 2933, 2353, 1727, 1601, 1588, 1519, 1450, 1368, 1303, 1230, 1152, 1053, 1022, 754. HRMS (ESI+) *m/z* calcd for $C_{21}H_{24}NO_4$ $[M+H]^+$ 354.1705, found 354.1715.

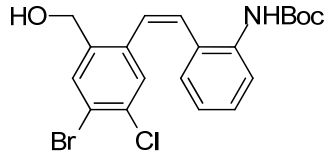
(*Z*)-*tert*-butyl (2-(5-chloro-2-(hydroxymethyl)styryl)phenyl)carbamate (5a)



Compound **11a** (8.24 g, 23.1 mmol) was dissolved in methanol (100 mL). After addition of quinoline (273 µl, 2.31 mmol) and 10% Pd/$BaSO_4$ (492 mg, 0.231 mmol), the reaction was stirred under H_2-atmosphere for 2 hours. The reaction mixture was then filtered over celite and diluted with CH_2Cl_2 (150 mL). The organic layer was washed with 2M aqueous HCl (2 × 100 mL), H_2O (100 mL), and brine (100 mL). The organic layer was dried over $MgSO_4$ and the volatiles were removed under reduced pressure to obtain compound **5a** (7.91 g, 95%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.26-7.18 (m, 2H), 7.14 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.11 (s, 1H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.92 (s, 1H), 6.90 (d, *J* = 12.0 Hz, 1H), 6.69 (d, *J* = 12.0 Hz, 1H), 6.62 (br s,

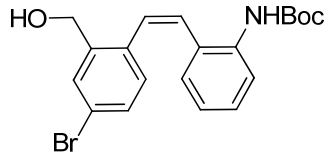
1H), 4.67 (d, *J* = 6.2 Hz, 2H), 1.43 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 150.3, 137.2, 137.0, 134.9, 133.3, 130.0, 129.8, 129.5, 129.3, 128.8, 128.4, 127.8 (2C), 125.8, 123.1, 120.4, 81.0, 63.2, 28.2. HRMS (ESI+) *m/z* calcd for $C_{20}H_{23}ClNO_3$ $[M+H]^+$ 360.1367, found 360.1387.

(*Z*)-*tert*-butyl (2-(4-bromo-5-chloro-2-(hydroxymethyl)styryl)phenyl)carbamate (5b)



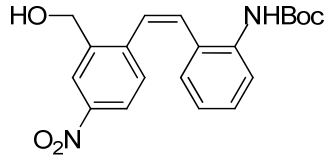
Compound **11b** (470 mg, 1.1 mmol) was dissolved in methanol (20 mL) and 10% Pd/$BaSO_4$ (15 mg, 14 µmol) and quinoline (13 µl, 0.11 mmol) were added. The reaction was stirred under H_2-atmosphere for two hours. Additional 10% Pd/$BaSO_4$ (15 mg, 14 µmol) was added, and after 1 hour again 10% Pd/$BaSO_4$ (15 mg, 14 µmol) was added. After 1 additional hour the reaction was completed and filtered over celite. The celite was washed with CH_2Cl_2 (50 mL), and the thus obtained organic layer was washed with 2M aqueous HCl (2 × 50 mL), H_2O (50 mL), and brine (50 mL) and subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure to obtain **5b** as a single product (470 mg, 100%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.12 (d, *J* = 8.5 Hz, 1H), 7.74 (br s, 1H), 7.72 (m, 1H), 7.63 (s, 1H), 7.44 (ddd, *J* = 7.7, 1.6, 0.5 Hz, 1H), 7.36 (dddd, *J* = 7.5, 1.6, 0.5 Hz, 8.5 Hz, 1H), 7.01 (dt, *J* = 7.5, 1.1 Hz, 1H), 4.85 (d, *J* = 4.8 Hz, 2H), 2.45 (br s, 1H), 1.57 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 152.8, 138.7, 135.9, 134.8, 133.3, 130.3, 129.2, 129.0, 128.6, 128.3 (2C), 125.7, 123.4, 121.4, 120.8, 81.2, 62.5, 28.2 (3C). HRMS (ESI+) *m/z* calcd for $C_{20}H_{22}BrClNO_3$ $[M+H]^+$ 438.0472, found 438.0495.

(*Z*)-*tert*-butyl 2-(4-bromo-2-(hydroxymethyl)styryl)phenylcarbamate (5c)



Compound **11c** (720 mg, 1.8 mmol) was dissolved in methanol (12 mL) and 10% Pd/$BaSO_4$ (35 mg, 33 µmol) and quinoline (21 µL, 0.18 mmol) were added. The reaction mixture was stirred under H_2-atmosphere for 1.5 hour. Next, the mixture was filtered over celite and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:9) to obtain compound **5c** as orange oil (650 mg, 90%). R_F = 0.40 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.48 (s, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.14-7.12 (m, 2H), 6.99 (t, *J* = 7.3 Hz, 1H), 6.88 (d, *J* = 12.1 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 6.64 (d, *J* = 11.9 Hz, 1H), 6.62 (s, 1H), 4.70 (d, *J* = 6.4 Hz, 2H), 1.43 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 152.6, 140.5, 134.8, 134.3, 131.3, 130.7, 130.5, 130.2, 129.4, 128.3, 128.0, 127.3, 123.0, 121.7, 120.2, 81.2, 63.3, 28.2 (3C). FT-IR ν_{max} film (cm^{-1}): 3421, 2976, 2933, 2362, 2327, 1705, 1576, 1519, 1472, 1446, 1398, 1364, 1308, 1230, 1156, 1053, 1022, 767, 763. HRMS (ESI+) *m/z* calcd for $C_{20}H_{23}BrNO_3$ $[M+H]^+$ 404.0861, found 404.0865.

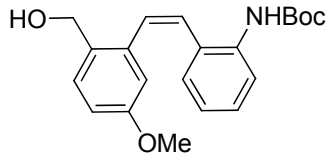
(*Z*)-*tert*-butyl(2-(2-(hydroxymethyl)-4-nitrostyryl)phenyl)carbamate (5d)



Compound **11d** (70 mg, 0.19 mmol) was dissolved in methanol (10 mL) and quinoline (11 µL, 95 µmol) and 10% Pd/$BaSO_4$ (2.66 mg, 2 µmol) were added. The reaction was stirred under H_2- atmosphere for 3 hours after which the mixture was filtered over celite. The celite was washed with CH_2Cl_2 (20 mL) and the organic layer was washed with H_2O (2 × 20 mL) and brine (20 mL) and subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:4) to obtain **5d** as red solid (55 mg, 78%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.24 (d, *J* = 2.4 Hz, 1H), 7.84 (dd,

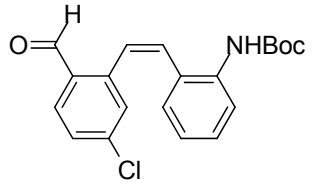
J = 8.5, 2.4 Hz, 1H), 7.73 (br s, 1H), 7.26-7.18 (m, 1H), 7.10 (d, *J* = 8.5 Hz, 1H)), 7.06 (s, 1H), 6.98 (d, *J* = 7.4 Hz, 1H), 6.93 (d, *J* = 12.0 Hz, 1H), 6.81 (d, *J* = 12.0 Hz, 1H), 6.56 (s, 1H), 4.79 (s, 2H), 1.40 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 152.6, 147.0, 142.2, 140.3, 135.0, 129.9, 129.7, 129.3 (2C), 128.8, 125.7, 123.4, 123.1, 122.4, 120.8, 81.3, 62.9, 28.13 (3C). HRMS (ESI+) *m/z* calcd for $C_{20}H_2N_2NaO_5$ $[M+Na]^+$ 393.14264, found 393.14315.

(*Z*)-*tert*-butyl 2-(2-(hydroxymethyl)-5-methoxystyryl)phenylcarbamate (5e)



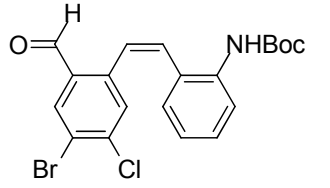
Compound **11e** (1.72 g, 4.87 mmol) was dissolved in methanol (75 mL) and 10% Pd/$BaSO_4$ (84 mg, 79 µmol) and quinoline (2.88 mL, 24.3 mmol) were added. The reaction mixture was stirred under H_2-atmosphere for 1.5 hour. Next, the mixture was filtered over celite and washed with 2M aqueous HCl (50 mL), saturated aqueous $NaHCO_3$-solution (50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:9 to 1:4) to obtain compound **5e** as yellow oil (1.66 g, 96%). R_F = 0.15 (EtOAc/*n*-heptane, 1:4). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.85 (br s, 1H), 7.22-7.18 (m, 3H), 7.03-6.98 (m, 2H), 6.74-6.66 (m, 3H), 6.48 (d, *J* = 2.5 Hz, 1H), 4.68 (d, *J* = 5.2 Hz, 2H), 3.93 (s, 3H), 1.41 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 158.9, 136.7, 135.0, 131.4, 130.9, 130.2, 129.3, 128.0, 126.8, 126.2, 122.8, 119.8, 119.7, 114.6, 113.5, 80.8, 63.5, 54.9, 28.2 (3C). FT-IR ν_{max} film (cm^{-1}): 3417, 2976, 2928, 1722, 1576, 1524, 1442, 1372, 1225, 1152, 1044, 1018, 754, 741, 573. HRMS (ESI+) *m/z* calcd for $C_{21}H_{26}NO_4$ $[M+H]^+$ 356.1862, found 356.1860.

(*Z*)-*tert*-butyl (2-(5-chloro-2-formylstyryl)phenyl)carbamate (12a)



Compound **5a** (7.91 g, 22 mmol) was dissolved in dry CH_2Cl_2 (150 mL) under Ar-atmosphere in a flame-dried flask. Dess-Martin periodinane (11.2 g, 26.4 mmol) and $NaHCO_3$ (5.54 g, 66 mmol) were added and the mixture was stirred for 45 minutes. The reaction was quenched by the addition of saturated aqueous $NaHSO_3$ (100 mL). The layers were separated and the H_2O-layer was extracted with CH_2Cl_2 (100 mL). The organic layers were combined and washed with saturated aqueous $NaHSO_3$ (200 mL), H_2O (2 × 200 mL) and brine (200 mL) and then dried over $MgSO_4$. The organic solvents were evaporated and the crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:9). Compound **12a** was obtained as a yellow solid (7.36 g, 95%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 10.13 (s, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.33 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.25-7.18 (m, 1H), 7.16 (d, *J* = 12.0 Hz, 1H), 7.09 (d, *J* = 2.0 Hz, 1H), 7.00-6.87 (m, 2H), 6.84 (d, *J* = 11.9 Hz, 1H), 6.44 (br s, 1H), 1.46 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 190.6, 152.4, 140.4, 140.0, 135.6, 132.3, 131.7, 130.3, 129.7, 129.5, 129.0, 128.9, 128.3, 125.1, 123.1, 120.3, 80.5, 28.3 (3C). HRMS (ESI+) *m/z* calcd for $C_{20}H_{20}ClNNaO_3$ $[M+Na]^+$ 380.1029, found 380.1032.

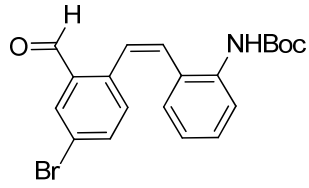
(*Z*)-*tert*-butyl (2-(4-bromo-5-chloro-2-formylstyryl)phenyl)carbamate (12b)



Compound **5b** (1.17 g, 2.67 mmol) was dissolved in dry CH_2Cl_2 (40 mL) under Ar-atmosphere in a flame-dried flask. $NaHCO_3$ (670 mg, 8.0 mmol) and Dess-Martin periodinane (1.47 g, 3.47 mmol) were added and the reaction was stirred for 1 hour. Hereupon, the reaction was quenched with saturated aqueous $NaHSO_3$ and diluted with CH_2Cl_2 (20 mL). The organic layer was

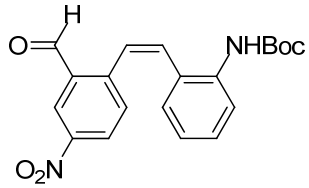
washed with H_2O (3 × 50 mL) and brine (50 mL) and subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:9). Compound **12b** was obtained as a yellow solid (1.02 g, 89%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 10.07 (s, 1H), 8.02 (s, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.26-7.22 (m, 1H), 7.21 (s, 1H), 7.07 (d, *J* = 11.9 Hz, 1H), 6.98-6.90 (m, 2H), 6.87 (d, *J* = 11.9 Hz, 1H), 6.39 (s, 1H), 1.47 (d, *J* = 1.0 Hz, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 189.3, 152.4, 140.1, 138.8, 135.6 (2C), 132.7, 131.9, 130.5, 129.5, 129.1, 127.6, 125.1, 123.4, 122.2, 120.7, 80.7, 28.3 (3C). HRMS (ESI+) *m/z* calcd for $C_{20}H_{19}BrClNNaO_3$ $[M+Na]^+$ 458.0135, found 458.0123.

(*Z*)-*tert*-butyl 2-(4-bromo-2-formylstyryl)phenylcarbamate (12c)



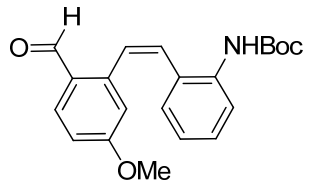
Compound **5c** (651 mg, 1.62 mmol) was dissolved in dry CH_2Cl_2 (15 mL) and placed under an Ar-atmosphere in a flame-dried flask. Subsequently, Dess-Martin periodinane (888 mg, 2.09 mmol) and $NaHCO_3$ (406 mg, 4.83 mmol) were added and the mixture was stirred for 40 minutes. The reaction was quenched with saturated aqueous Na_2SO_3 (15 mL). The mixture was diluted with CH_2Cl_2 (25 mL), washed with saturated aqueous $NaHSO_3$ (15 mL), H_2O (15 mL) and brine (15 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:9) to obtain compound **12c** as a yellow oil which solidified upon storage at -20 ºC (560 mg, 86%). R_F = 0.40 (EtOAc/*n*-heptane, 1:4). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 10.16 (s, 1H), 7.93 (d, *J* = 2.2 Hz, 1H), 7.87 (d, *J* = 7.7 Hz, 1H), 7.43 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.23-7.19 (m, 1H), 7.17 (d, *J* = 12.0 Hz, 1H), 6.99-6.96 (m, 2H), 6.92 (d, *J* = 7.3 Hz, 1H), 6.82 (d, *J* = 11.9 Hz, 1H), 6.42, (br s, 1H), 1.45 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 190.4, 152.4, 137.5, 136.4, 135.5, 134.7, 133.8, 131.9, 129.6, 129.3, 129.2, 128.7, 125.5, 123.1, 122.0, 120.3, 80.6, 28.2 (3C). FT-IR ν_{max} film (cm^{-1}): 2982, 1729, 1695, 1584, 1515, 1445, 1238, 1369, 1148, 1051, 1016, 780, 746. HRMS (ESI+) *m/z* calcd for $C_{20}H_{20}BrNNaO_3$ $[M+Na]^+$ 424.0524, found 424.0516.

(*Z*)-*tert*-butyl (2-(2-formyl-4-nitrostyryl)phenyl)carbamate (12d)



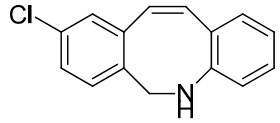
Compound **5d** (170 mg, 0.46 mmol) was dissolved in dry CH_2Cl_2 (5 mL) under Ar-atmosphere in a flame-dried flask. Dess-Martin periodinane (234 mg, 0.55 mmol) and $NaHCO_3$ (116 mg, 1.38 mmol) were added. The reaction was stirred for 30 minutes whereupon saturated aqueous $NaHSO_3$ (10 mL) was added. The mixture was diluted with CH_2Cl_2 (15 mL) and the organic layer was washed with saturated aqueous $NaHSO_3$ (30 mL), water (2 × 30 mL) and brine (30 mL) before drying over $MgSO_4$. The solvents were removed *in vacuo* and the crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:19 to 1:6) to obtain **12d** as a red solid (145 mg, 86%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 10.27 (s, 1H), 8.66 (d, *J* = 2.4 Hz, 1H), 8.14 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 7.32 (d, *J* = 8.6 Hz, 1H), 7.25 (d, *J* = 11.8 Hz, 1H), 7.26-7.21 (m, 1H), 6.97 (d, *J* = 11.9 Hz, 1H), 6.93-6.88 (m, 2H), 6.44-6.35 (br s, 1H), 1.45 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 189.7, 152.4, 144.8, 135.7, 134.1, 133.0, 131.9, 131.6, 129.6, 129.3, 128.4, 127.4, 126.0, 125.4, 123.5, 121.0, 80.8, 28.3 (3C). HRMS (ESI+) *m/z* calcd for $C_{20}H_{20}N_2NaO_5$ $[M+Na]^+$ 391.1270, found 391.1259.

(*Z*)-*tert*-butyl 2-(2-formyl-5-methoxystyryl)phenylcarbamate (12e)



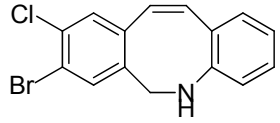
Compound **5e** (1.66 g, 4.67 mmol) was dissolved in dry CH_2Cl_2 (75 mL) and placed under Ar-atmosphere in a flame-dried flask. Subsequently, Dess-Martin periodinane (2.57 g, 6.06 mmol) and $NaHCO_3$ (1.18 g, 14.0 mmol) were added and the mixture was stirred for two hours. The reaction was quenched with a saturated aqueous Na_2SO_3-solution (50 mL). The mixture was diluted with CH_2Cl_2 (50 mL), washed with saturated aqueous $NaHSO_3$ (50 mL), H_2O (50 mL), and brine (50 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:9) to obtain compound **12e** as a yellow oil which solidified upon storage at -20 ºC (1.29 g, 78%). R_F = 0.30 (EtOAc/*n*-heptane, 1:4). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 10.09 (s, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.74 (d, *J* = 8.6 Hz, 1H), 7.33 (d, *J* = 11.9 Hz, 1H), 7.21-7.17 (m, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 6.92 (td, *J* = 7.6, 1.2 Hz, 1H), 6.84 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.78 (d, *J* = 11.9 Hz, 1H), 6.54 (d, *J* = 2.5 Hz, 1H), 6.52 (s, 1H), 3.52 (s, 3H), 1.43 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 190.5, 163.2, 152.4, 140.6, 135.4, 134.0, 130.8, 129.3, 128.3, 128.1, 126.9, 125.8, 122.8, 119.8, 114.4 (2C), 80.1, 55.1, 28.1 (3C). FT-IR ν_{max} film (cm^{-1}): 3356, 2971, 2933, 2855, 1722, 1684, 1588, 1515, 1446, 1234, 1156, 1022, 754. HRMS (ESI+) *m/z* calcd for $C_{21}H_{24}NO_4Na$ $[M+Na]^+$ 354.1705, found 354.1698.

(*Z*)-9-chloro-5,6-dihydrodibenzo[b,f]azocine (4a)



Compound **12a** (7.34 g, 20.6 mmol) was dissolved in 2M HCl in EtOAc (100 ml, 200.00 mmol) and the reaction was stirred for 1 hour. Then, $NaBH_4$ (3.11 g, 82.4 mmol) in H_2O (10 mL) was added and the reaction was stirred overnight. As reduction of the imine was not completed yet, another portion of $NaBH_4$ (2.25 g, 60 mmol) was added and the reaction was stirred for 1.5 hour. Hereupon, the reaction was quenched by the addition of H_2O (50 mL) and the product was extracted with EtOAc (100 mL). The organic layer was washed with H_2O (3 × 100 mL) and brine (100 mL) and subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure to obtain **4a** as a yellow solid (4.7 g, 95%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.18-7.09 (m, 3H), 7.06-6.84 (m, 2H), 6.69-6.60 (m, 1H), 6.58 (d, *J* = 13.2 Hz, 1H), 6.46 (dd, *J* = 8.1, 0.6 Hz, 1H), 6.27 (d, *J* = 13.1 Hz, 1H), 4.55 (s, 2H), 4.22 (br s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 146.8, 141.1, 136.6, 134.7, 134.0, 133.3, 130.3, 129.7, 128.3, 127.3, 126.1, 121.3, 118.0, 117.9, 48.8. HRMS (ESI+) *m/z* calcd for $C_{15}H_{13}ClN$ $[M+H]^+$ 242.0737, found 242.0726.

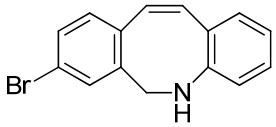
(*Z*)-8-bromo-9-chloro-5,6-dihydrodibenzo[b,f]azocine (4b)



Compound **12b** (920 mg, 2.1 mmol) was dissolved in 2M HCl in EtOAc (40 mL, 80 mmol). After 30 minutes, $NaBH_4$ (240 mg, 6.3 mmol) in H_2O (2 mL) was added. After two hours another portion of $NaBH_4$ (240 mg, 6.3 mmol) in H_2O (2 mL) was added, followed by another portion of $NaBH_4$ (80 mg, 2.1 mmol) in H_2O (1 mL) after 1 hour. After an extra 30 minutes, the reaction was quenched by the addition of H_2O (40 mL). The layers were separated, and the H_2O-layer was extracted with EtOAc (50 mL). The organic layers were combined and washed with H_2O (2 × 100 mL), and brine (100 mL), and subsequently dried over $MgSO_4$. The volatiles were removed under reduced pressure and the crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:6). Compound **4b** was obtained as yellow solid (340 mg, 50%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.44 (s, 1H), 7.24 (s, 1H), 6.99-6.87 (m, 2H), 6.63 (dt, *J* = 7.7, 1.3 Hz, 1H), 6.59 (d, *J* = 13.0 Hz, 1H), 6.47 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.20 (d, *J* = 13.1 Hz, 1H), 4.52 (s), 4.24

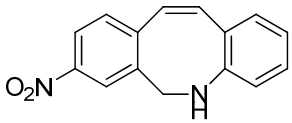
(s). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 146.6, 140.1, 138.4, 134.7, 134.4, 134.0, 133.4, 131.5, 128.5, 125.1, 121.3, 120.1, 118.1, 118.0, 48.6. HRMS (ESI+) *m/z* calcd for $C_{15}H_{12}BrClN$ $[M+H]^+$ 319.9842, found 319.9825.

(*Z*)-8-bromo-5,6-dihydrodibenzo[b,f]azocine (4c)



Compound **12c** (560 mg, 1.4 mmol) was dissolved in 2M HCl in EtOAc (20 mL, 40 mmol) and stirred for 1.5 hour. Next, $NaBH_4$ (196 mg, 5.2 mmol) and a few drops of water were added. The reaction was stirred overnight whereupon an additional portion of $NaBH_4$ (196 mg, 5.2 mmol) was added and, after an additional 90 minutes, the reaction was quenched with H_2O (15 mL). The H_2O-layer was extracted with EtOAc (2 × 15 mL). The organic layers were combined and washed with 2M aqueous NaOH (2 × 20 mL), H_2O (2 × 20 mL) and brine (20 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to obtain compound **4c** as a yellow solid (360 mg, 91%). R_F = 0.55 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.36 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.34 (d, *J* = 2.1 Hz, 1H), 7.02 (d, *J* = 8.1 Hz, 1H), 6.96 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.90 (ddd, *J* = 7.2, 6.5, 1.6 Hz, 1H), 6.62 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 6.55 (d, *J* = 13.1 Hz, 1H), 6.47 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.26 (d, *J* = 13.1 Hz, 1H), 4.54 (s, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 146.3, 139.8, 137.7, 134.3, 132.9, 131.3 (2C), 130.2, 127.7, 126.9, 125.8, 121.1, 119.8, 117.5, 48.7. FT-IR ν_{max} film (cm^{-1}): 3391, 3002, 2924, 2850, 2362, 2098, 1593, 1485, 1325, 1269, 901, 828, 776, 750. HRMS (ESI+) *m/z* calcd for $C_{15}H_{13}BrN$ $[M+H]^+$ 286.02314 found 286.0219.

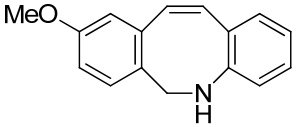
(*Z*)-8-nitro-5,6-dihydrodibenzo[b,f]azocine (4d)



Compound **12d** (200 mg, 0.54 mmol) was dissolved in HCl in EtOAc (10 mL, 20 mmol). After 30 minutes $NaBH_4$ (470 mg, 12.4 mmol) in water (1 mL) was added and after stirring overnight the reaction was quenched with H_2O (10 mL). The H_2O-layer was extracted with EtOAc (20 mL), and the combined organic layers were washed with H_2O (3 × 20 mL), brine (20 mL) and subsequently dried over $MgSO_4$. The solvents were removed *in vacuo* to obtain **4d** as a red solid (140 mg, 100%) ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.11 (dd, *J* = 8.5, 2.4 Hz, 1H), 8.05 (d, *J* = 2.3 Hz, 1H), 7.29 (d, *J* = 8.6 Hz, 1H), 7.01 (d, *J* = 7.7 Hz, 1H), 6.97-6.91 (m, 1H), 6.71-6.62 (m, 2H), 6.51 (d, *J* = 8.1 Hz, 1H), 6.36 (d, *J* = 13.4 Hz, 1H), 4.69 (s, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 147.3, 146.7, 145.9, 139.5, 135.9, 135.4, 131.3, 128.8, 125.0, 124.1, 122.8, 121.2, 118.4, 118.0, 49.6. HRMS (ESI+) *m/z* calcd for $C_{15}H_{13}N_2O_2$ $[M+H]^+$ 253.0977 found 253.0965.

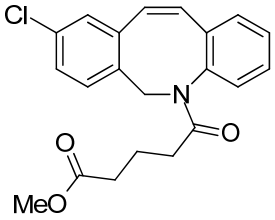
(*Z*)-9-methoxy-5,6-dihydrodibenzo[b,f]azocine (4e)

Compound **12e** (122 mg, 0.35 mmol) was dissolved in 2M HCl in EtOAc (3 mL, 6 mmol) and the solution was stirred for 75 minutes. Next, $NaBH_4$ (39 mg, 1.0 mmol) and a drop of water were added. MeOH (2 mL) was added to keep the reactants in solution. After 75 minutes an additional portion of $NaBH_4$ (39 mg, 1.04 mmol) was added and after another hour, the reaction was quenched with H_2O (10 mL). The H_2O-layer was extracted with EtOAc (2 × 15 mL). The organic layers were combined and washed with 2M aqueous NaOH (2 × 20 mL), H_2O (2 × 20 mL) and brine (20 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to obtain compound **4e** as an orange solid (72 mg, 87%). R_F = 0.55 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.12 (d, *J* = 8.2 Hz, 1H), 6.94 (dd, *J* = 7.8, 1.4 Hz, 1H), 6.88 (td, *J* = 6.6, 1.6 Hz, 1H), 6.73 (dd, *J* = 8.2, 2.7 Hz, 1H), 6.69 (d, *J* = 2.7 Hz, 1H), 6.61-6.59 (m, 1H), 6.55 (d, *J* = 12.8 Hz, 1H), 6.45 (d, *J* =8.1 Hz, 1H), 6.32 (d, *J* = 12.9 Hz, 1H), 4.53 (s, 2H),



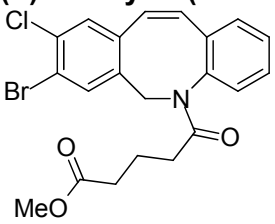
3.78 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 158.9, 146.8, 140.5, 134.4, 133.0, 130.6, 130.0, 127.9, 127.4, 121.3, 117.9, 117.4, 114.3, 113.4, 55.2, 48.5. FT-IR ν_{max} film (cm^{-1}): 3399, 2997, 2924, 2855, 1722, 1601, 1571, 1498, 1455, 1325, 1260, 1217, 1165, 1109, 1035, 862, 746, 573. HRMS (ESI+) *m/z* calcd for $C_{16}H_{16}NO$ $[M+H]^+$ 238.1232, found 238.1229.

(*Z*)-methyl 5- (9-chlorodibenzo [b,f] azocin-5(6*H*)-yl)-5-oxopentanoate (13a)



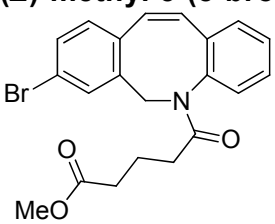
Compound **4a** (3 g, 12.4 mmol) was dissolved in dry CH_2Cl_2 (100 mL) and NEt_3 (3.46 mL, 24.8 mmol) was added. After cooling the mixture to 0 ºC, methyl 5-chloro-5-oxopentanoate (2.13 mL, 15 mmol) was added and the reaction was stirred overnight. Hereupon, the reaction was quenched with H_2O (100 mL) and the layers were separated. The organic layer was washed with 2M aqueous NaOH (2 × 70 mL), water (2 × 70 mL) and brine (70 mL) and subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:2) to obtain **13a** as a yellow solid (2.11 g, 46%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.31-7.27 (m, 3H), 7.23 (d, *J* = 8.8 Hz, 1H), 7.19-7.10 (m, 3H), 6.69 (d, *J* = 13.1 Hz, 1H), 6.62 (d, *J* = 13.1 Hz, 1H), 5.43 (d, *J* = 14.9 Hz, 1H), 4.17 (d, *J* = 14.9 Hz, 1H), 3.59 (s, 3H), 2.25-2.03 (m, 3H), 1.94-1.76 (m, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.5, 171.8, 140.8, 137.6, 135.8, 133.3, 132.7, 131.7, 131.5, 131.4, 131.1, 128.7, 128.5, 128.1, 128.1, 127.3, 53.9, 51.4, 33.5, 33.0, 20.4. HRMS (ESI+) *m/z* calcd for $C_{21}H_{21}ClNO_3$ $[M+H]^+$ 370.1210, found 370.1203.

(*Z*)-methyl 5-(8-bromo-9-chlorodibenzo[b,f]azocin-5(6*H*)-yl)-5-oxopentanoate (13b)



Compound **4b** (200 mg, 0.62 mmol) was dissolved in dry CH_2Cl_2 (15 mL) and the solution was cooled to 0 ºC. Subsequently, NEt_3 (174 µL, 1.25 mmol) and methyl 5-chloro-5-oxopentanoate (133 µl, 0.94 mmol) were added. The reaction was stirred overnight and then quenched with H_2O (10 mL). The layers were separated, and the H_2O-layer was extracted with CH_2Cl_2 (20 mL). The organic layers were combined and washed with H_2O (2 × 30 mL), and brine (30 mL) and dried over $MgSO_4$. The solvents were removed *in vacuo* and the crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:2). Compound **13b** was obtained as yellow solid (230 mg, 82%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.53 (s, 1H), 7.34-7.29 (m, 3H), 7.22 (s, 1H), 7.18 (dd, *J* = 6.4, 2.6 Hz, 1H), 6.64 (d, *J* = 13.3 Hz, 1H), 6.60 (d, *J* = 13.3 Hz, 1H), 5.45 (d, *J* = 15.2 Hz, 1H), 4.12 (d, *J* = 15.2 Hz, 1H), 3.59 (s, 3H), 2.62-2.29 (m, 1H), 2.26-1.96 (m, 2H), 1.93-1.76 (m, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.4, 171.8, 140.5, 136.2, 135.5, 135.0, 134.9, 133.2, 132.7, 131.4, 130.0, 129.0, 128.7, 128.2, 128.1, 120.8, 53.4, 51.3, 33.3, 32.9, 20.3. HRMS (ESI+) *m/z* calcd for $C_{21}H_{20}BrClNO_3$ $[M+H]^+$ 448.0321, found 448.0315.

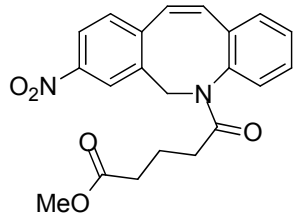
(*Z*)-methyl 5-(8-bromodibenzo[b,f]azocin-5(6*H*)-yl)-5-oxopentano-ate (13c)



Compound **4c** (360 mg, 1.26 mmol) was dissolved in dry CH_2Cl_2 (8 mL) and NEt_3 (351 µL, 2.52 mmol) was added. The mixture was cooled to 0 ºC, whereupon methyl 5-chloro-5-oxopentanoate (221 µL, 1.89 mmol) was added. The reaction was stirred for 90 minutes, after which it was quenched with H_2O (5 mL). The mixture was diluted with CH_2Cl_2 (10 mL) and washed with 2M aqueous NaOH (2 × 10 mL), 2M aqueous HCl (2 × 10 mL), H_2O (2 × 10 mL)

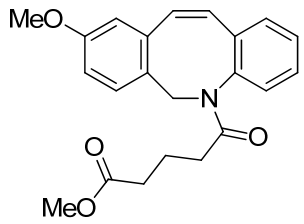
and brine (10 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:2) to obtain compound **13c** as a yellow solid (466 mg, 90%). R_F = 0.30 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.42 (d, *J* = 2.1 Hz, 1H), 7.31-7.27 (m, 4H), 7.19-7.15 (m, 1H), 7.00 (d, *J* = 8.3 Hz, 1H), 6.69 (d, *J* = 13.1 Hz, 1H), 6.59 (d, *J* = 13.1 Hz, 1H), 5.49 (d, *J* = 15.2 Hz, 1H), 4.16 (d, *J* = 15.2 Hz, 1H), 3.59 (s, 3H), 2.22-2.17 (m, 2H), 2.13-2.04 (m, 2H), 1.85-1.79 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.5, 171.8, 140.7, 136.9, 136.1, 134.5, 133.7, 132.9, 131.4, 131.1, 130.1, 128.8, 128.1 (2C), 127.6, 121.2, 54.0, 51.4, 33.3, 33.1, 20.4. FT-IR ν_{max} film (cm^{-1}): 3473, 2947, 2868, 2150, 1874, 1731, 1653, 1498, 1437, 1403, 1195, 1169, 1018, 832, 776. HRMS (ESI+) *m/z* calcd for $C_{21}H_{21}BrNO_3$ $[M+H]^+$ 414.0705, found 414.0699.

(*Z*)-methyl 5-(8-nitrodibenzo[b,f]azocin-5(6*H*)-yl)-5-oxopentanoate (13d)



Compound **4d** (45 mg, 0.18 mmol) was dissolved in dry CH_2Cl_2 (5 ml) and the solution was cooled to 0 ºC. Subsequently, NEt_3 (50 µL, 0.36 mmol) and methyl 5-chloro-5-oxopentanoate (37 µl, 0.27 mmol) were added. The reaction was stirred overnight and quenched by the addition of 0.1 M aqueous NaOH (5 mL). The reaction was diluted with CH_2Cl_2 (10 mL) and the organic layer was washed with 2M aqueous NaOH (2 × 20 mL), H_2O (20 mL) and brine (20 mL), and subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:6 to 2:3). Compound **13d** was obtained as a red solid (25 mg, 37%). Residual 5-chloro-5-oxopentanoate was not completely removed after column chromatography, and the crude product was used without further purification. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.20 (d, *J* = 2.4 Hz, 1H), 8.02 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.32 (dt, *J* = 11.5, 4.1 Hz, 5H), 7.24-7.17 (m, 1H), 6.81 (d, *J* = 13.4 Hz, 1H), 6.73 (d, *J* = 13.3 Hz, 1H), 5.55 (d, *J* = 15.1 Hz, 1H), 4.23 (d, *J* = 15.0 Hz, 1H), 3.58 (s, 3H), 2.25-2.08 (m, 2H), 2.06-1.91 (m, 2H), 1.86-1.66 (m, 2H). HRMS (ESI+) *m/z* calcd for $C_{21}H_{21}N_2O_5$ $[M+H]^+$ 381.1451, found 381.1446.

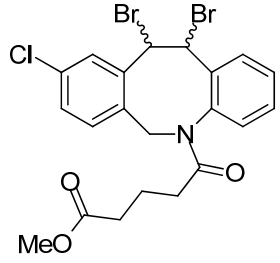
(*Z*)-methyl 5-(9-methoxydibenzo[b,f]azocin-5(6*H*)-yl)-5-oxopentanoate (13e)



Compound **4e** (75 mg, 0.46 mmol) was dissolved in dry CH_2Cl_2 (4 mL) and NEt_3 (85 µL, 0.61 mmol) was added. The mixture was cooled to 0 ºC, whereupon methyl 5-chloro-5-oxopentanoate (53 µL, 0.46 mmol) was added. The reaction was stirred for 90 minutes and another portion of methyl 5-chloro-5-oxopentanoate (23 µL, 0.2 mmol) was added. After 45 minutes the reaction was quenched with H_2O (5 mL). The mixture was diluted with CH_2Cl_2 (10 mL) and washed with 2M aqueous NaOH (2 × 10 mL), 2M aqueous HCl (2 × 10 mL), H_2O (2 × 10 mL) and brine (10 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 1:2) to obtain compound **13e** as a yellow solid (84 mg, 76%). R_F = 0.20 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.25-7.21 (m, 3H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.14-7.11 (m, 1H), 6.74 (d, *J* = 12.9 Hz, 1H), 6.69 (dd, *J* = 8.4, 2.7 Hz, 1H), 6.64-6.58 (m, 1H), 5.38 (d, *J* = 14.7 Hz, 1H), 4.19 (d, *J* = 14.7 Hz, 1H), 3.73 (s, 3H), 3.57 (s, 3H), 2.41 (q, *J* = 7.0 Hz, 2H), 2.17 (q, *J* = 7.4 Hz, 2H), 1.84-1.79 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.5, 171.8, 158.2, 140.7, 137.3, 136.2, 132.5, 131.4, 130.9, 128.3, 128.1, 127.9, 127.7, 126.7, 116.5, 112.7, 55.1, 53.8, 51.3, 33.5, 33.0, 20.4. FT-IR ν_{max} film (cm^{-1}): 2950, 2920, 2850, 1731, 1658, 1606, 1576,

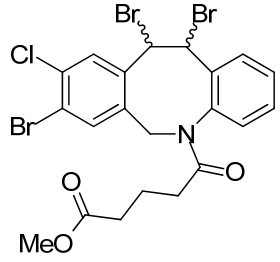
1493, 1442, 1403, 1521, 1204, 1169, 1040, 767. HRMS (ESI+) *m/z* calcd for $C_{22}H_{23}NO_4$ $[M+H]^+$ 366.1705, found 366.1701.

methyl 5-(11,12-dibromo-9-chloro-11,12-dihydrodibenzo[b,f]azocin-5(6*H*)-yl)-5-oxopentanoate (14a)



Compound **13a** (1 g, 2.7 mmol) was dissolved in CH_2Cl_2 (50 mL) and the solution was cooled to 0 ºC. A solution of Br_2 (154 µl, 3 mmol) in CH_2Cl_2 (5 mL) was added dropwise and after 2 hours at 0 ºC additional Br_2 (20 µL, 0.39 mmol) in CH_2Cl_2 (1 mL) was added. After 1 hour the reaction was quenched by addition of saturated aqueous $NaHSO_3$ (50 mL), and layers were separated. The organic layer was washed with saturated aqueous $NaHSO_3$-solution (50 mL), water (2 × 50 mL) and brine (50 mL) and subsequently dried over $MgSO_4$. The volatiles were removed under reduced pressure and the crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 1:2) to obtain compound **14a** (1.02 g, 71%) as mixture of two diastereoisomers (**X** : **Y**, 1:0.8). The isomers could be separated however due to slow isomerization of **X** to **Y**, no full analysis of **14aY** was performed. Analytical data for **14aX**: R_F = 0.30 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.72 (d, *J* = 2.1 Hz, 1H), 7.28-7.15 (m, 2H), 7.12-6.94 (m, 3H), 6.83 (d, *J* = 8.3 Hz, 1H), 5.85 (d, *J* = 9.9 Hz, 1H), 5.77 (d, *J* = 14.8 Hz, 1H), 5.12 (d, *J* = 10.0 Hz, 1H), 4.14 (d, *J* = 14.8 Hz, 1H), 3.61 (s, 3H), 2.97 – 2.27 (m, 3H), 2.27 – 2.13 (m, 1H), 2.08 – 1.92 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.6, 172.7, 138.9, 137.8, 137.0, 134.7, 131.5, 130.9 (2C), 130.7, 130.4, 129.6, 129.0, 128.9, 59.5, 54.5, 51.8, 51.5, 34.8, 33.3, 20.3. HRMS (ESI+) *m/z* calcd for $C_{21}H_{21}Br_2ClNO_3$ $[M+H]^+$ 527.9577, found 527.9564. **49Y**: R_F = 0.35 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (400 MHz, CDCl) δ 7.65 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.25-6.98 (m, 4H), 6.88-6.78 (m, 2H), 5.71 (d, *J* = 9.6 Hz, 1H), 5.14 (d, *J* = 9.6 Hz, 1H), 5.13 (d, *J* = 14.5 Hz, 1H), 4.95 (d, *J* = 14.0 Hz, 1H), 3.63 (s, 3H), 2.48-2.31 (m, 3H), 2.26-2.05 (m, 1H), 2.04-1.80 (m, 2H).

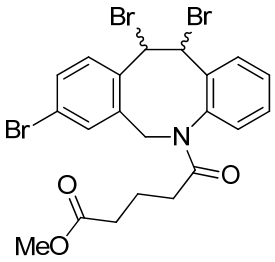
methyl 5-oxo-5-(8,11,12-tribromo-9-chloro-11,12-dihydrodibenzo[b,f]azocin-5(6*H*)-yl)pentanoate (14b)



Compound **13b** (100 mg, 0.22 mmol) was dissolved in CH_2Cl_2 (10 mL) and the solution was cooled to 0 ºC. A solution of Br_2 (11 µl, 0.22 mmol) in CH_2Cl_2 (1 mL) was added dropwise and the reaction was stirred at 0 ºC. After 2 hours, the reaction was quenched with saturated aqueous $NaHSO_3$ (10 mL). The layers were separated and the H_2O-layer was extracted with CH_2Cl_2 (10 mL). The combined organic layers were washed with saturated aqueous $NaHSO_3$ (20 mL), water (2 × 20 mL) and brine (20 mL) and dried over $MgSO_4$. The solvents were removed under reduced pressure to obtain **14b** as white solid (130 mg, 96%). **50** was obtained as a mixture of two diastereoisomers (**14bX** : **14bY**, 0.32:1). For the ^{1}H-NMR signals from **14bX** are designated with ***,** signals from **14bY** with **º**. In the ^{13}C-NMR data, only peaks are given from major isomer **14bX**. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.82***** (s, 0.3H), 7.65**º** (d, *J* = 7.7 Hz, 1H), 7.35**º** (s, 1H), 7.32-7.08***,º** (m, 3.4H), 7.02**º** (s, 1H), 7.00***** (s, 0.3H), 6.90**º** (d, *J* = 7.8 Hz, 1H), 5.80***** (d, *J* = 9.8 Hz, 0.3H), 5.79***** (d, *J* = 15.1 Hz, 0.3H), 5.69**º** (d, *J* = 9.6 Hz, 1H), 5.12***,º** (d, *J* = 9.5 Hz, 1.3H), 5.08**º** (d, *J* = 14.6 Hz, 1H), 4.92**º** (d, *J* = 14.3 Hz, 1H), 4.09***** (d, *J* = 15.3 Hz, 0.3H), 3.63**º** (d, *J* = 0.7 Hz, 3H), 3.62***** (s, 1H), 2.60-2.29***,º** (m, 4H), 2.21-2.02***,º** (m, 1.3H), 2.01-1.83***,º** (m, 2.6H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.6, 172.8, 137.9, 137.7,

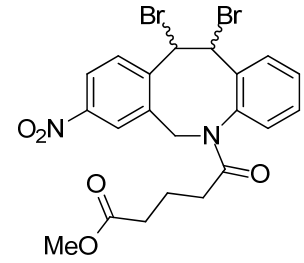
136.8, 134.9, 134.2, 133.2, 131.0 (2C), 130.8, 130.5, 130.0, 122.7, 59.1, 53.9, 51.5, 51.3, 34.7, 33.2, 20.3. HRMS (ESI+) *m/z* calcd for $C_{21}H_{20}Br_3ClNO_3$ $[M+H]^+$ 605.8682, found 605.8686.

methyl 5-oxo-5-(8,11,12-tribromo-11,12-dihydrodibenzo[b,f]azocin-5(6*H*)-yl)pentanoate (14c)



Compound **13c** (100 mg, 0.24 mmol) was dissolved in dry CH_2Cl_2 (5 mL). The solution was cooled to 0 ºC and Br_2 (13 µL, 0.24 mmol) was added. After stirring for 1.5 hour, additional Br_2 (13 µL, 0.24 mmol) was added and the reaction was stirred for an additional hour. Hereupon, the reaction was quenched with saturated aqueous Na_2SO_3 (5 mL). The mixture was diluted with CH_2Cl_2 (10 mL) and washed with saturated aqueous Na_2SO_3 (2 × 10 mL), H_2O (2 × 10 mL) and brine (10 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 1:2) to obtain compound **14c** as a white solid (111 mg, 80%). Compound **14c** was obtained as mixture of diastereoisomers (**14cX** : **14cY**, 1:0.47). The major isomer (**14cX**) could be obtained pure, due to slow isomerization of **14cY** to **14cX**, no spectrum of pure **14cY** was obtained. Analytical data for **14cX**: R_F = 0.25 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.61 (d, *J* = 8.4 Hz, 1H), 7.36 – 7.26 (m, 2H), 7.19 (td, *J* = 7.6, 1.4 Hz, 1H), 7.11 – 7.03 (m, 2H), 7.00 (dd, *J* = 7.8, 1.4 Hz, 1H), 5.84 (d, *J* = 10.0 Hz, 1H), 5.82 (d, *J* = 15.1 Hz, 1H), 5.12 (d, *J* = 10.0 Hz, 1H), 4.09 (d, *J* = 15.2 Hz, 1H), 3.62 (s, 3H), 2.41-2.27 (m, 3H), 2.25 – 2.14 (m, 1H), 2.09 – 1.94 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.6, 172.8, 137.8, 136.8, 136.1, 135.0, 132.2, 131.8, 130.8 (2C), 130.5, 130.4, 129.7, 122.6, 59.4, 54.8, 51.9, 51.5, 34.7, 33.2, 20.3. FT-IR ν_{max} film (cm^{-1}): 3453, 2953, 2367, 1734, 1660, 1593, 1484, 1441, 1398, 1254, 1203, 1179, 1152, 1015, 875, 844, 801, 769. HRMS (ESI+) *m/z* calcd for $C_{21}H_{21}Br_3NO_3$ $[M+H]^+$ 571.9090, found 571.9080. Analytical data for **14cY**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.68-7.61 (m, 1H), 7.38-7.12 (m, 4H), 6.88 (dd, *J* = 7.7, 1.3 Hz, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 5.72 (d, *J* = 9.4 Hz, 1H), 5.19 (d, *J* = 9.6 Hz, 1H), 5.09 (d, *J* = 14.7 Hz, 2H), 4.96 (d, *J* = 14.1 Hz, 1H), 3.63 (s, 3H), 2.45 – 2.30 (m, 3H), 2.24-2.11 (m, 1H), 2.12-1.83 (m, 2H).

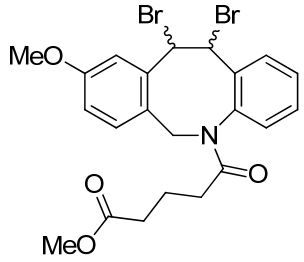
methyl 5-(11,12-dibromo-8-nitro-11,12-dihydrodibenzo[b,f]azocin-5(6*H*)-yl)-5-oxopentanoate (14d)



Crude **13d** (25 mg, 66 µmol) was dissolved in CH_2Cl_2 (2 mL) and the reaction was cooled to 0 ºC. A solution of Br_2 (4.1 µl, 79 µmol) in CH_2Cl_2 (2 mL) was added dropwise. The reaction was stirred at 0 ºC for 1 hour, and subsequently quenched with saturated aqueous $NaHSO_3$ (10 mL) and diluted with CH_2Cl_2 (10 mL). The organic layer was washed with saturated aqueous $NaHSO_3$ (10 mL), water (2 × 10 mL) and brine (10 mL) and dried over $MgSO_4$. The solvents were evaporated under reduced pressure to obtain **14d** as a red solid (30 mg, 84%). **14d** was obtained as a mixture of two diastereoisomers (**14dX** : **14dY**, 0.42:1). For the ^{1}H-NMR signals from **14dX** are designated with ***,** signals from **14dY** with **º**. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.04***** (dd, *J* = 8.6, 2.0 Hz, 0.43H), 7.99-7.90***,º** (m, 2.5H), 7.79***** (d, *J* = 2.0 Hz, 0.4H), 7.66**º** (dd, *J* = 7.8, 1.4 Hz, 1H), 7.34-7.14***,º** (m, 3.1H), 7.12***,º** (d, *J* = 8.4 Hz, 1.2H), 7.09-6.99**º** (m, 1H), 6.91**º** (dd, *J* = 7.8, 1.3 Hz, 1H), 5.93***** (d, *J* = 11.6 Hz, 0.43H), 5.92***** (d, *J* = 13.7 Hz,

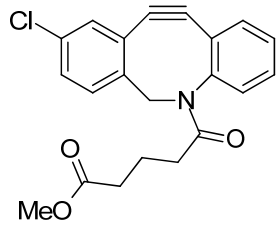
0.43H), 5.75º (d, *J* = 9.5 Hz, 1H), 5.28º (d, *J* = 9.6 Hz, 1H), 5.15* (d, *J* = 9.9 Hz, 0.43H), 5.04º (d, *J* = 14.3 Hz, 1H), 4.28* (d, *J* = 15.3 Hz, 0.43H), 3.63º (s, 3H), 3.62* (s, 1H), 2.48-2.39*,º (m, 1.45H), 2.39-2.32*,º (m, 3H), 2.17-2.05*,º (m, 1.3H), 2.04-1.89*,º (m, 3.4H). HRMS (ESI+) *m/z* calcd for $C_{21}H_{21}Br_2N_2O_5$ $[M+H]^+$ 538.9817, found 538.9822.

methyl 5-(11,12-dibromo-9-methoxy-11,12-dihydrodibenzo[b,f]azocin-5(6*H*)-yl)-5-oxopentanoate (14e)



Compound **13e** (91 mg, 0.25 mmol) was dissolved in dry CH_2Cl_2 (8 mL). The solution was cooled to 0 ºC and a solution of Br_2 (14 µL, 0.27 mmol) in CH_2Cl_2 (1 mL) was added. After stirring for 1.5 hour, another portion of Br_2 (20 µL, 0.39 mmol) in CH_2Cl_2 (1 mL) was added. After stirring for 75 minutes an extra portion of Br_2 (15 µL, 0.29 mmol) in CH_2Cl_2 (1 mL) was added. After stirring for another 75 minutes, the reaction was quenched with a saturated aqueous Na_2SO_3-solution (10 mL). The mixture was diluted with CH_2Cl_2 (25 mL) and washed with H_2O (2 × 15 mL) and brine (15 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product (which was still a mixture of **14eX** and **14eY**, 1:0.2) was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 1:2) to obtain compound **14e** as a white solid (50 mg, 39%). After column chromatography, **14e** was obtained as a single diastereoisomer (**14eX**). R_F = 0.15 (EtOAc/*n*-heptane, 1:2). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: δ 7.30-7.25 (m, 1H), 7.22 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.14 (td, *J* = 7.5, 1.3 Hz, 1H), 7.03 (dd, *J* = 7.7, 1.5 Hz, 1H), 6.96 (dd, *J* = 7.7, 1.3 Hz, 1H), 6.78 (d, *J* = 8.3 Hz, 1H), 6.54 (dd, *J* = 8.4, 2.6 Hz, 1H), 5.85 (d, *J* = 9.9 Hz, 1H), 5.71 (d, *J* = 14.7 Hz, 1H), 5.12 (d, *J* = 9.9 Hz, 1H), 4.12 (d, *J* = 14.8 Hz, 1H), 3.60 (s, 3H), 2.45-2.24 (m, 3H), 2.24-2.11 (m, 1H), 2.07-1.89 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.6, 172.6, 159.8, 138.3, 138.1, 137.3, 130.9, 130.8, 130.5, 130.4, 129.3, 124.8, 114.7, 113.7, 60.1, 55.7, 55.3, 51.8, 51.4, 34.9, 33.3, 20.4. FT-IR ν_{max} film (cm^{-1}): 2920, 2855, 1735, 1658, 1610, 1580, 1502, 1463, 1385, 1286, 1251, 1200, 1096, 1040, 824, 772, 715, 672, 612. HRMS (ESI+) *m/z* calcd for $C_{22}H_{24}Br_2NO_4$ $[M+H]^+$ 524.0072, found 524.0096.

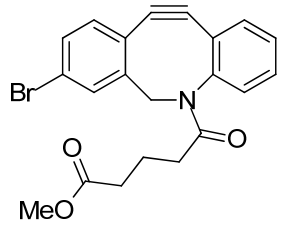
methyl 5-(9-chlorodidehydrodibenzo[b,f]azocin-5(6*H*)-yl)-5-oxopentanoate (3a)



Compound **14aX** (90 mg, 0.17 mmol) was dissolved in dry THF (3 mL) under Ar-atmosphere in a flame-dried flask. The solution was cooled to -40 ºC and a KO*t*Bu-solution in THF (1M, 340 µL, 0.34 mmol) was added dropwise. After stirring at -40 ºC for 1.5 hour, additional KO*t*Bu-solution in THF (1M, 50 µL, 0.05 mmol) was added. After 30 minutes, the reaction was quenched with H_2O (5 mL) and diluted with CH_2Cl_2 (10 mL). The layers were separated and the organic layer was washed with H_2O (3 × 15 mL) and brine (15 mL) and subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by column chromatography (EtOAc/*n*-heptane, 1:3). Compound **3a** was obtained as a white solid (23 mg, 37%), with a 5% contamination of compound **13a**. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.60 (d, *J* = 8.2 Hz, 1H), 7.48-7.35 (m, 3H), 7.34-7.27 (m, 2H), 7.21 (d, *J* = 2.2 Hz, 1H), 5.11 (d, *J* = 13.8 Hz. 1H), 3.59 (d, *J* = 13.9 Hz, 1H), 3.55 (s, 3H), 2.43-2.21 (m, 1H), 2.20-1.98 (m, 2H), 1.98-1.82 (m, 1H), 1.82-1.64 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.4, 172.5, 151.7, 146.2, 133.5, 133.3, 129.0, 128.7, 128.2, 128.1, 127.2, 125.4, 124.6, 122.0, 113.3, 109.2, 54.7, 51.4,

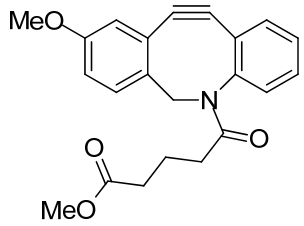
33.6, 32.8, 20.5. HRMS (ESI+) *m/z* calcd for $C_{21}H_{19}ClNO_3$ $[M+H]^+$ 368.1054, found 368.1043.

methyl 5-(8-bromodidehydrodibenzo[b,f]azocin-5(6*H*)-yl)-5-oxopentanoate (3c)



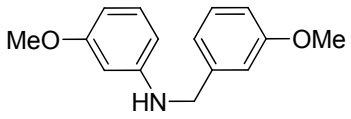
Compound **14cX** (75 mg, 0.13 mmol) was dissolved in dry THF in a flame-dried flask under Ar-atmosphere, and the solution was cooled to -40 ºC. Next, a solution of KO*t*Bu in THF (1M, 260 µL, 0.26 mmol) was added dropwise. After 2 hours, only one bromide was eliminated, whereupon additional KO*t*Bu (130 µL, 0.13 mmol) was added. After each subsequent hour an additional amount of KO*t*Bu (30 µL, 0.03 mmol) was added, while maintaining the reaction at -40 ºC. After 5.5 hours the reaction was completed and quenched by the addition of H_2O (5 mL). The H_2O-layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with H_2O (20 mL), and brine (20 mL) and subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 1:2) to obtain compound **3c** as a brown oil (20 mg, 37%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.84 (d, *J* = 2.0 Hz, 1H), 7.44 (ddd, *J* = 8.1, 2.0, 0.4 Hz, 1H), 7.42-7.36 (m, 3H), 7.35-7.30 (m, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 5.08 (d, *J* = 13.9 Hz, 1H), 3.61 (d, *J* = 13.9 Hz, 1H), 3.56 (s, 3H), 2.36-2.24 (m, 1H), 2.21-2.05 (m, 2H), 1.97-1.85 (m, 1H), 1.83-1.69 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.4, 172.5, 151.5, 149.6, 135.3, 131.0, 129.0, 128.6, 128.2, 127.1, 126.5, 122.5, 122.3, 122.0, 113.9, 108.8, 54.8, 51.4, 33.6, 32.8, 20.5. HRMS (ESI+) *m/z* calcd for $C_{21}H_{18}BrNNaO_3$ $[M+Na]^+$ 434.0368, found 434.0366.

methyl 5-(9-methoxydidehydrodibenzo[b,f]azocin-5(6*H*)-yl)-5-oxopentanoate (3e)



Compound **14eX** (42 mg, 0.08 mmol) was dissolved in dry THF in a flame-dried flask under Ar-atmosphere, and the solution was cooled to -40 ºC. Next, a solution of KO*t*Bu in THF (1M, 160 µL, 0.16 mmol) was added dropwise. After 2 hours, only one bromide was eliminated, whereupon additional KO*t*Bu (80 µL, 0.08 mmol) was added. After each subsequent hour an additional amount of KO*t*Bu (40 µL, 0.04 mmol) was added, while maintaining the reaction at -40 ºC. After 5.5 hours the reaction was completed and quenched by the addition of H_2O (5 mL). The H_2O-layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with H_2O (20 mL), and brine (20 mL) and subsequently dried over $MgSO_4$. The solvents were removed under reduced pressure and the crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 1:2) to obtain compound **3e** as a brown oil (10 mg, 34%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, *J* = 8.5 Hz, 1H), 7.45 – 7.33 (m, 3H), 7.32 – 7.28 (m, 1H), 6.90 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.78 (d, *J* = 2.7 Hz, 1H), 5.11 (d, *J* = 13.9 Hz, 1H), 3.81 (s, 3H), 3.59 (d, *J* = 13.9 Hz, 1H), 3.56 (s, 3H), 2.34 – 2.26 (m, 1H), 2.19 – 2.07 (m, 2H), 1.96 – 1.86 (m, 1H), 1.82 – 1.72 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 173.1, 172.0, 158.5, 151.4, 140.0, 132.7, 128.5, 128.0, 127.5, 126.7, 123.5, 122.0, 114.2, 113.5, 110.5, 107.5, 55.0, 54.3, 50.9, 33.3, 32.4, 20.6. HRMS (ESI+) *m/z* calcd for $C_{22}H_{21}NNaO_4$ $[M+Na]^+$ 386.1368, found 368.1372.

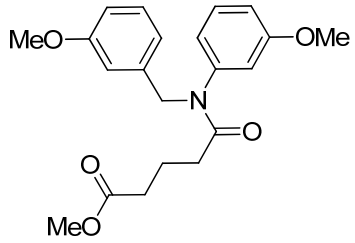
3-methoxy-*N*-(3-methoxybenzyl)aniline (15)



To a solution of 3-methoxyaniline (615 µL, 5.5 mmol) in dry MeOH (50 mL), 3-methoxybenzaldehyde (608 µL, 5.0 mmol)

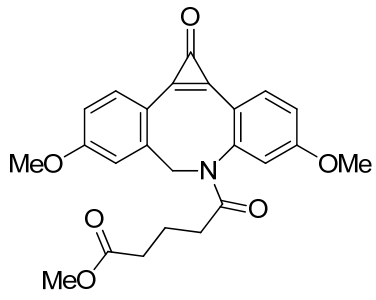
was added and the mixture was stirred for 1.5 hour. Next, $NaBH_4$ (567 mg, 15.0 mmol) was added. After stirring for 30 minutes, the reaction was quenched with H_2O (25 mL). The H_2O-layer was extracted with EtOAc (2 × 75 mL) and the organic layers were combined and washed with 2M aqueous NaOH (50 mL), H_2O (2 × 50 mL) and brine (50 mL). Next, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography (EtOAc/*n*-heptane 1:9) to obtain compound **15** as yellow oil (1.19 g, 98%). R_F = 0.30 (EtOAc/*n*-heptane, 1:4). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.25 (t, *J* = 7.9 Hz, 1H), 7.07 (t, *J* = 8.1 Hz, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.92 (m, 1H), 6.81 (dd, *J* = 8.2, 2.6 Hz, 1H), 6.30-6.24 (m, 2H), 6.19 (t, *J* = 2.3 Hz, 1H), 4.29 (s, 2H), 3.79 (s, 3H), 3.75 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 160.7, 159.8, 149.5, 141.0, 129.9, 129.5, 119.6, 112.9, 112.5, 105.9, 102.6, 98.8, 55.1, 54.9, 48.2. FT-IR ν_{max} film (cm^{-1}): 3412, 3002, 2933, 2829, 1597, 1489, 1463, 1429, 1256, 1217, 1165, 1044, 983, 828, 759, 685, 556, 452. HRMS (ESI+) *m/z* calcd for $C_{15}H_{18}NO_2$ $[M+H]^+$ 244.1338, found 244.1341.

Methyl 5-((3-methoxybenzyl)(3-methoxyphenyl)amino)-5-oxopentanoate (16)



Compound **15** (652 mg, 2.7 mmol) was dissolved in CH_2Cl_2 (20 mL). Then, NEt_3 (750 µL, 5.4 mmol) was added. Subsequently, the mixture was cooled to 0 ºC and then methyl 5-chloro-5-oxopentanoate (354 µL, 2.56 mmol) was added. The reaction was stirred for 1.5 hour whereupon it was quenched with water (10 mL), diluted with CH_2Cl_2 (10 mL) and washed with 2M NaOH (2 × 20 mL), 2M HCl (2 × 20 mL), water (2 × 20 mL) and brine (20 mL). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 1:2). The product was obtained as a brown oil (510 mg, 54%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.22 (t, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 7.9 Hz, 1H), 6.85-6.82 (m, 1H), 6.80-6.76 (m, 3H), 6.57 (d, *J* = 7.8 Hz, 1H), 6.50 (s br., 1H), 4.83 (s, 2H), 3.75 (s, 3H), 3.72 (s, 3H), 3.60 (s, 3H), 2.32 (t, *J* = 7.3 Hz, 2H), 2.16 (t, *J* = 7.2 Hz, 2H), 1.97-1.90 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.5, 171.9, 160.3, 159.6, 143.4, 139.1, 130.1, 129.3, 121.1, 120.5, 114.1 (2C), 113.5, 113.0, 55.3, 55.2, 52.8, 51.4, 33.2 (2C), 20.7. FT-IR ν_{max} film (cm^{-1}): 2946, 2842, 1735, 1653, 1597, 1489, 1433, 1394, 1260, 1191, 1152, 1044, 862, 785, 703, 577, 556. HRMS (ESI+) *m/z* calcd for $C_{21}H_{26}NO_5$ $[M+H]^+$ 372.1811, found 372.1804.

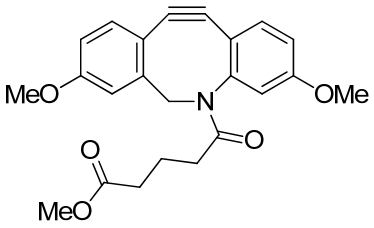
Methyl 5-(4,9-dimethoxy-1-oxo-1H-dibenzo[b,f]cyclopropa[d]azocin-6(7*H*)-yl)-5-oxopentanoate (17)



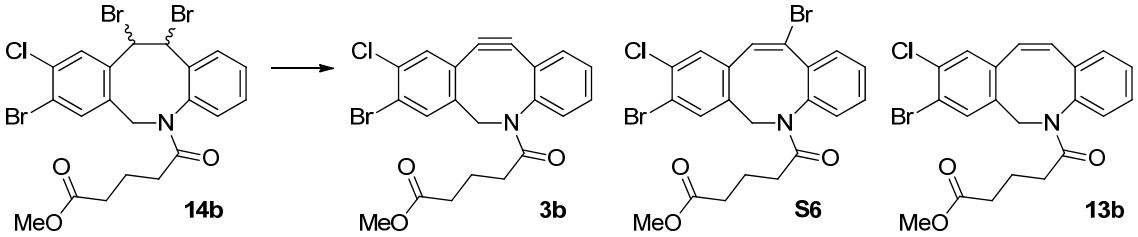
A flame-dried flask under Ar-atmosphere was charged with aluminium chloride (144 mg, 1.08 mmol) in dry CH_2Cl_2 (3 mL) at -78 ºC. Perchlorocycloprop-1-ene (53 µL, 0.43 mmol) was added dropwise and stirred for one hour. A solution of **16** (100 mg, 0.269 mmol) in dry CH_2Cl_2 (0.6 ml) was added dropwise at -78 ºC. The mixture was stirred for 2.5 hours at -78 ºC and then slowly warmed to room temperature and stirred for 16 hours. Subsequently, the reaction was quenched by the addition of 1M aqueous HCl (5 mL). After stirring for 5 minutes, H_2O (5 mL) was added and the layers were separated. The H_2O-layer was extracted with CH_2Cl_2 (2 × 10 mL) and the organic layers were combined and washed with brine (20 mL). Next, the organic layer was dried over

$MgSO_4$ and concentrated *in vacuo*. The crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:3 to 1:0) to obtain compound **17** as a green oil (34 mg, 81 µmol, 30%). R_F = 0.35 (EtOAc). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.25 (d, *J* = 2.5 Hz, 1H), 7.05 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.95 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.89 (d, *J* = 2.5 Hz, 1H), 5.18 (d, *J* = 14.3 Hz, 1H), 4.09 (d, *J* = 14.3 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.56 (s, 3H), 2.37-2.29 (m, 1H), 2.18-2.10 (m, 1H), 2.04-1.89 (m, 2H), 1.82-1.66 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.1, 172.5, 162.9, 162.6, 152.4, 145.8, 143.1, 141.4, 138.9, 135.6, 135.1, 118.1, 115.4, 115.2, 114.9, 113.7, 113.6, 56.0, 55.8, 55.5, 51.4, 33.4, 32.5, 20.5. FT-IR ν_{max} film (cm^{-1}): 3447, 2941, 2837, 1848, 1740, 1662, 1601, 1558, 1429, 1364, 1286, 1256, 1022, 828, 733. HRMS (ESI+) *m/z* calcd for $C_{24}H_{23}NO_6Na$ $[M+Na]^+$ 444.1423, found 444.1435.

methyl 5-(3,8-dimethoxydidehydrodibenzo[b,f]azocin-5(6*H*)-yl)-5-oxopentanoate (3f)



Compound **17** (100 mg, 0.237 mmol) was dissolved in acetonitrile (5 mL) and irradiated with UV-light using a *Bluespot 2 Easycure* for 65 minutes. After completion of the reaction, the solvent was removed under reduced pressure. The crude product was purified by gradient column chromatography (EtOAc/*n*-heptane, 1:4 to 1:2) to obtain compound **3f** as an orange oil (33 mg, 0.084 mmol, 35%). R_F = 0.30 (EtOAc/*n*-heptane, 1:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.27 (d, *J* = 8.3 Hz, 1H), 7.23 (d, *J* = 2.6 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.91-6.87 (m, 2H), 6.81 (dd, *J* = 8.5, 2.6 Hz, 1H), 5.06 (d, *J* = 13.8 Hz, 1H), 3.85 (s, 6H), 3.69 (d, *J* = 13.7 Hz, 1H), 3.57 (s, 3H), 2.22-1.92 (m, 4H), 1.81-1.71 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.5, 172.6, 159.3 (2C), 152.4, 149.6, 127.2, 126.1, 118.3, 115.8, 115.1, 114.9, 113.9, 113.3, 113.1, 106.5, 55.6 (2C), 55.3, 51.3, 33.6, 32.8, 20.6. FT-IR ν_{max} film (cm^{-1}): 2928, 2850, 2163, 1727, 1658, 1601, 1563, 1489, 1433, 1390, 1286, 1264, 1230, 1195, 1174, 1035, 819, 750, 590, 504. HRMS (ESI+) *m/z* calcd for $C_{23}H_{24}NO_5$ $[M+H]^+$ 394.16545, found 394.16571.



Scheme S1. Treatment of dibromide **14b** with base.

Table S1. Results of elimination attempts on dibromide **14b**.

Entry	*Base*	*Equivalents*	*Temperature*	*Product*
1	KO^{t}Bu	2	-40 ºC	**13b** + **S6**
2	NaH	5	r.t. to 70 ºC	**S6**
3	KH	10	0 ºC to r.t.	**S6**
4	NaHMDS	2	-78 ºC	**13b** + **3b**
5	DBU	10	r.t.	**S6**

6	2.2	r.t.	**13b**

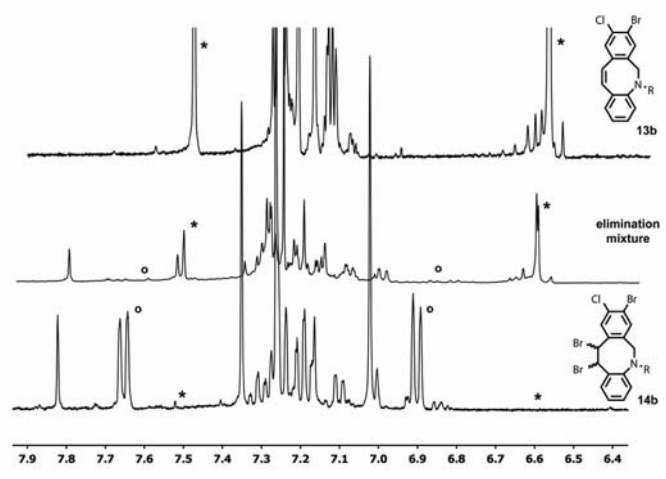


Figure S1. Spectrum of alkene **13b**, dibromide **14b**, and the mixture obtained after elimination. Peaks specific for **13b** are assigned with *****, peaks specific for **14b** are labelled with **º**.

Spectrum of Bluepoint 2 easycure

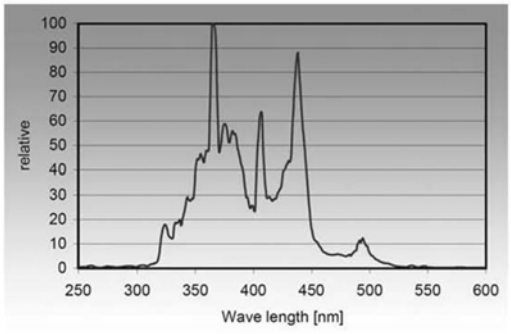


Figure S2. Emission Spectrum of Bluepoint 2 easycure.

Kinetic experiments

Kinetic experiments for **1**, **3a**, **3c**, **3e**, and **3f** were performed similar as described previously. Due to increased reaction kinetics, 2.25 µmol alkyne was mixed with 2.25 µmol benzylazide in 0.5 mL CD_3OD. The exact ratio between benzyl azide and alkyne was determined by comparison of the integrals of the aromatic signals and the benzylic protons of the alkyne. As some of the alkynes could not be obtained pure, the concentration of the benzyl azide was assumed to be accurate, and the alkyne concentration was adjusted using the ratio as determined in the NMR-spectrum. For **1**, **3a**, **3c**, **3e**, and **3f**, the rate constant was determined by comparing the signal from the methyl-ester of the starting material (δ: 3.52 ppm), to the signal from the methyl-ester of

the product (δ: 3.60 ppm). Product formation was confirmed by mass spectrometry. For **3a**: HRMS (ESI+) *m/z* calcd for $C_{28}H_{26}ClN_4O_3$ $[M+H]^+$ 501.1693, found 501.1693. For **3c**: HRMS (ESI+) *m/z* calcd for $C_{28}H_{26}BrN_4O_3$ $[M+H]^+$ 545.1188, found 545.1189. For **3e**: HRMS (ESI+) *m/z* calcd for $C_{29}H_{29}N_4O_4$ $[M+H]^+$ 497.2189, found 497.2177. For **3f**: HRMS (ESI+) *m/z* calcd for $C_{30}H_{31}N_4O_5$ $[M+H]^+$ 527.2294, found 527.2280.

Table S2. Rate constants of DIBAC and analogues.

Entry	*Rate constant* $(M^{-1}s^{-1})$
DIBAC (1)	0.4 ± 0.1
Cl-DIBAC (3a)	0.9 ± 0.1
Br-DIBAC (3c)	0.80 ± 0.05
MeO-DIBAC (3e)	0.45 ± 0.06
$(MeO)_2$-DIBAC (3f)	0.62 ± 0.05

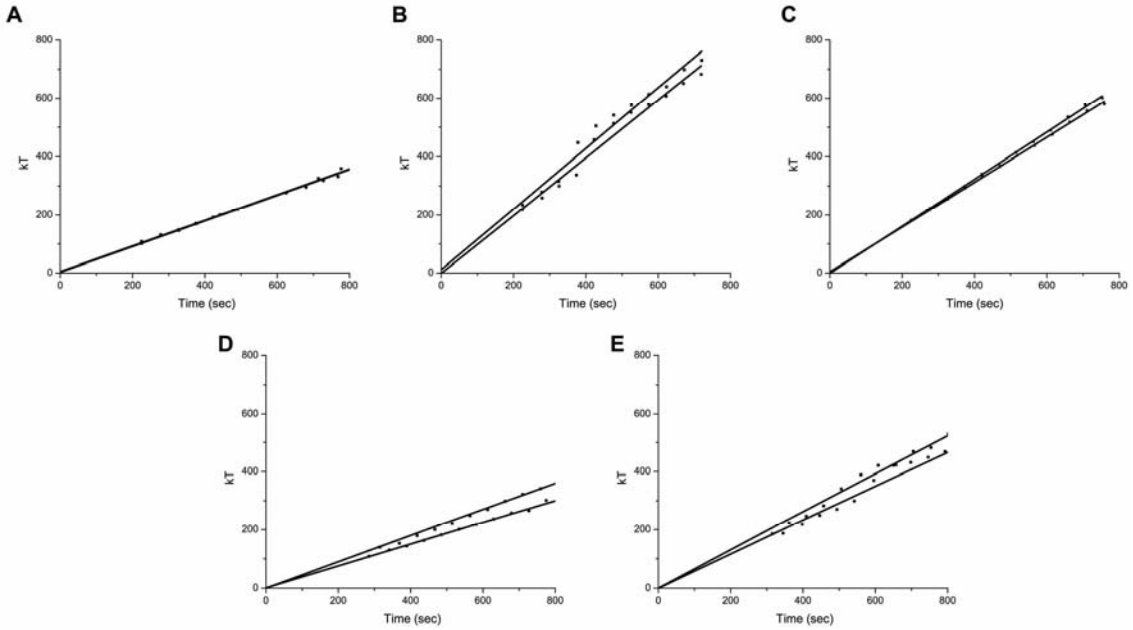


Figure S3. Logarithmic plots of (A) DIBAC (**1**); (B) Cl-DIBAC (**3a**), (C) Br-DIBAC (**3c**); (D) MeO-DIBAC (**3e**); (E) $(MeO)_2$-DIBAC (**3f**).

Modeling results

Energy minimizations were performed using ChemBio3D Ultra version 13.0 using MOPAC interface version 13.0.

Cis-1 (Figure 4)

Mopac Job: AUX PM6 CHARGE=0 EF GNORM=0.100 SHIFT=80
Finished @ RMS Gradient = 0.06190 (< 0.10000) Heat of Formation = -89.31756 Kcal/Mol
Chem3D Core 13.0.203081416183D

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    0.8383    1.0212    4.2115 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.9695    0.5658    2.8998 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.9316    1.4730    1.8280 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.7632    2.8648    2.0637 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.6350    3.2891    3.3926 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.0482    0.9498    0.4812 N   0  0  0  0  0  0  0  0  0  0  0  0
    2.1254    1.5214   -0.3674 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.6050    2.2577   -1.5827 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.5493    3.1855   -1.5231 C   0  0  0  0  0  0  0  0  0  0  0  0
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    0.7713    3.8369    0.9163 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.2369    2.0075   -2.8124 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.8239    2.6598   -3.9739 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.7632    3.5701   -3.9201 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.1323    3.8281   -2.7041 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.3585   -0.2355    0.0927 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.5093   -0.6641   -1.3522 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.3431   -0.8198    0.8948 O   0  0  0  0  0  0  0  0  0  0  0  0
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   -0.2683   -2.3337   -3.0802 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.7692   -3.7362   -3.2880 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.7776   -3.6983   -4.2291 O   0  0  0  0  0  0  0  0  0  0  0  0
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   -2.4054   -4.9613   -4.5737 C   0  0  0  0  0  0  0  0  0  0  0  0
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   -1.4813    2.0968    0.1367 Br  0  0  0  0  0  0  0  0  0  0  0  0
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    0.4902    4.3443    3.6352 H   0  0  0  0  0  0  0  0  0  0  0  0
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    2.7577    2.2174    0.2386 H   0  0  0  0  0  0  0  0  0  0  0  0
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   -1.2066   -1.9870   -1.1388 H   0  0  0  0  0  0  0  0  0  0  0  0
   -0.9245   -1.6050   -3.6063 H   0  0  0  0  0  0  0  0  0  0  0  0
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   -2.9702   -4.7138   -5.4781 H   0  0  0  0  0  0  0  0  0  0  0  0
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Cis-2 (Figure 4)

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Finished @ RMS Gradient = 0.09107 (< 0.10000) Heat of Formation = -90.60139 Kcal/Mol

Chem3D Core 13.0.203081416183D

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  0.0756   3.1377   -1.6589 C   0 0 0 0 0 0 0 0 0 0 0 0
  0.1003   4.0355   -0.4524 C   0 0 0 0 0 0 0 0 0 0 0 0
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  0.3037   3.0760   -4.0911 C   0 0 0 0 0 0 0 0 0 0 0 0
  0.2995   3.7846   -2.8927 C   0 0 0 0 0 0 0 0 0 0 0 0
  1.7803   -0.0271   0.4210 C   0 0 0 0 0 0 0 0 0 0 0 0
  1.8238   -0.9733   -0.7607 C   0 0 0 0 0 0 0 0 0 0 0 0
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  1.5510   -2.4013   -0.2711 C   0 0 0 0 0 0 0 0 0 0 0 0
  1.1853   -3.3463   -1.4190 C   0 0 0 0 0 0 0 0 0 0 0 0
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Trans-1 (Figure 4)

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Finished @ RMS Gradient = 0.09647 (< 0.10000) Heat of Formation = -146.83383 Kcal/Mol

Chem3D Core 13.0.203081416173D

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   1.6614   -1.3145    3.4037 C   0  0  0  0  0  0  0  0  0  0  0  0
   1.1133   -0.2851    2.6215 C   0  0  0  0  0  0  0  0  0  0  0  0
   0.4271    0.7951    3.2113 C   0  0  0  0  0  0  0  0  0  0  0  0
   0.3953    0.8712    4.6144 C   0  0  0  0  0  0  0  0  0  0  0  0
   1.3003   -0.2798    1.1873 N   0  0  0  0  0  0  0  0  0  0  0  0
   2.2763    0.7542    0.7363 C   0  0  0  0  0  0  0  0  0  0  0  0
   1.7149    1.8460   -0.1323 C   0  0  0  0  0  0  0  0  0  0  0  0
   0.8759    2.8632    0.3835 C   0  0  0  0  0  0  0  0  0  0  0  0
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   0.9982    3.9914   -1.8004 C   0  0  0  0  0  0  0  0  0  0  0  0
   0.5542    3.9459   -0.4845 C   0  0  0  0  0  0  0  0  0  0  0  0
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   0.8719   -1.0719   -1.1254 C   0  0  0  0  0  0  0  0  0  0  0  0
   0.2464   -2.2807    0.8631 O   0  0  0  0  0  0  0  0  0  0  0  0
   0.2569   -2.2466   -1.8880 C   0  0  0  0  0  0  0  0  0  0  0  0
   0.0684   -1.8931   -3.3694 C   0  0  0  0  0  0  0  0  0  0  0  0
  -0.3362   -3.1006   -4.1593 C   0  0  0  0  0  0  0  0  0  0  0  0
  -1.5529   -2.8388   -4.7663 O   0  0  0  0  0  0  0  0  0  0  0  0
   0.2275   -4.1559   -4.3289 O   0  0  0  0  0  0  0  0  0  0  0  0
  -2.1214   -3.8942   -5.5802 C   0  0  0  0  0  0  0  0  0  0  0  0
  -1.4173    0.6910    1.0318 Br  0  0  0  0  0  0  0  0  0  0  0  0
   2.0379    3.5105    3.1033 Br  0  0  0  0  0  0  0  0  0  0  0  0
   0.9484   -0.0468    6.4814 H   0  0  0  0  0  0  0  0  0  0  0  0
   2.0046   -2.0260    5.4061 H   0  0  0  0  0  0  0  0  0  0  0  0
   2.1252   -2.1708    2.9191 H   0  0  0  0  0  0  0  0  0  0  0  0
  -0.0722    1.7324    5.0921 H   0  0  0  0  0  0  0  0  0  0  0  0
   3.1223    0.2373    0.2300 H   0  0  0  0  0  0  0  0  0  0  0  0
   2.7184    1.2477    1.6498 H   0  0  0  0  0  0  0  0  0  0  0  0
  -0.2582    3.8650    1.8853 H   0  0  0  0  0  0  0  0  0  0  0  0
  -1.1722    2.2032    3.0606 H   0  0  0  0  0  0  0  0  0  0  0  0
   2.8080    1.1206   -1.8485 H   0  0  0  0  0  0  0  0  0  0  0  0
   2.1449    2.9843   -3.3323 H   0  0  0  0  0  0  0  0  0  0  0  0
   0.7272    4.8277   -2.4383 H   0  0  0  0  0  0  0  0  0  0  0  0
  -0.0581    4.7584   -0.0978 H   0  0  0  0  0  0  0  0  0  0  0  0
   1.9239   -0.9140   -1.4282 H   0  0  0  0  0  0  0  0  0  0  0  0
   0.3403   -0.1196   -1.3695 H   0  0  0  0  0  0  0  0  0  0  0  0
  -0.7187   -2.5177   -1.4264 H   0  0  0  0  0  0  0  0  0  0  0  0
   0.8939   -3.1478   -1.7778 H   0  0  0  0  0  0  0  0  0  0  0  0
   1.0107   -1.4870   -3.7960 H   0  0  0  0  0  0  0  0  0  0  0  0
  -0.6880   -1.0817   -3.4726 H   0  0  0  0  0  0  0  0  0  0  0  0
  -3.1223   -3.5143   -5.8066 H   0  0  0  0  0  0  0  0  0  0  0  0
  -2.1588   -4.8277   -5.0088 H   0  0  0  0  0  0  0  0  0  0  0  0
  -1.5146   -4.0185   -6.4814 H   0  0  0  0  0  0  0  0  0  0  0  0
 1  2  2  0
 6  1  1  0
 1 28  1  0
```

```
 2  3  1  0
 2 29  1  0
 3  4  2  0
 3 30  1  0
 4  5  1  0
 7  4  1  0
 5  6  2  0
 5 12  1  0
 6 31  1  0
 8  7  1  0
 7 17  1  0
 8  9  1  0
 8 32  1  0
 8 33  1  0
 9 10  2  0
 9 13  1  0
11 10  1  0
16 10  1  0
12 11  1  0
11 27  1  0
11 34  1  0
12 26  1  0
12 35  1  0
13 14  2  0
13 36  1  0
14 15  1  0
14 37  1  0
15 16  2  0
15 38  1  0
16 39  1  0
17 18  1  0
17 19  2  0
18 20  1  0
18 40  1  0
18 41  1  0
20 21  1  0
20 42  1  0
20 43  1  0
21 22  1  0
21 44  1  0
21 45  1  0
22 23  1  0
22 24  2  0
23 25  1  0
25 46  1  0
25 47  1  0
25 48  1  0
M  CHG  1  13  -1
M  END
```

[1] D. W. Thompson, L. Wang, Y. Zhao, N. Zhou, *Org. Lett.*,2008, **10**, 3001-3004.
[2] Y. C. Fan, O. Kwon, *Org. Lett.*, 2012, **14**, 3264-3267.