Supporting Information

Supramolecular Subphthalocyanine Complexes –

Cellular Uptake and Phototoxicity

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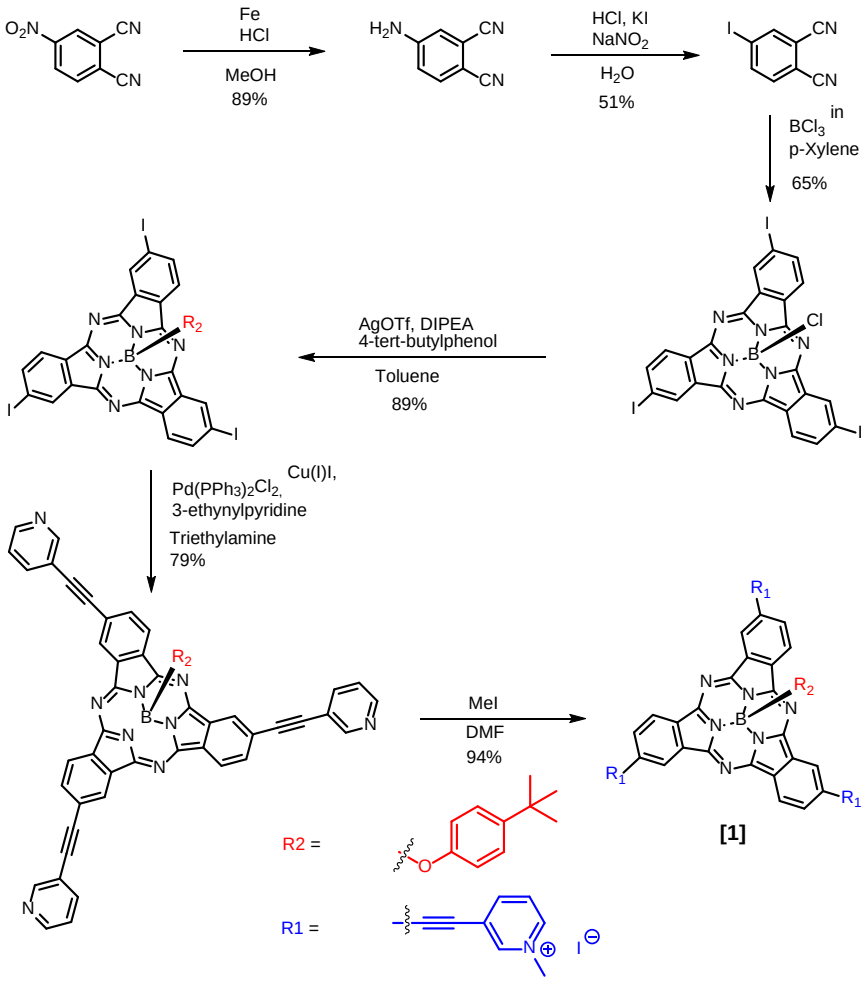
Content

1. General information

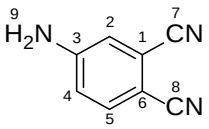
Chemicals were purchased from Sigma Aldrich, Alfa Aesar, PanReac AppliChem, Deutero, Fluka, Fluorochem, GE Healthcare, Carl Roth, Merck Millipore or from TCI Chemicals and used without further purification. Reactions were monitored by thin-layer chromatography (TLC), which was performed on 0.2 mm Macherey-Nagel Polygram Sil G/UV254 precoated silica gel sheets. Spots were visualized by treatment with basic $KMnO_4$ solution (2.0 g $KMnO_4$, 13.3 g K_2CO_3, 3.33 mL NaOH 5 % aq. solution, 200 mL distilled water) or by an UV-handlamp (254 nm and 365 nm). Dimethylformamide was distilled and dried with molecular sieves (0.4 nm). Triethylamine and methyl iodide have been freshly distilled before use. For the column chromatography, silica gel with a particle size of 0.04 – 0.063 mm from Macherey-Nagel was used. Freeze-drying of the products was carried out by first dissolving the sample in distilled water and sonification in an ultrasonic bath over a period of 30 min. The sample was then frozen in liquid nitrogen followed by connecting it to the lyophilizer Alpha 1-4 LD plus. The NMR spectra were recorded on a Bruker DMX 300 spectrometer [^{1}H: 300.16 MHz, ^{13}C: 75.47 MHz] or DMX 600 [^{1}H: 600.16 MHz, ^{13}C: 151.47 MHz, ^{11}B: 192.55 MHz]. All measurements were performed at room temperature, using d_1-chloroform, d_6-DMSO or D_2O as solvents. The chemical shifts are referenced relative to the residual proton signals of the solvents in the ^{1}H-NMR spectrum ($CDCl_3$: δ = 7.24 ppm (*s*), d_6-DMSO: δ = 2.50 ppm (*quin*), D_2O: 4.79 ppm (*s*)) or relative to the solvent signal in the ^{13}C-NMR spectrum ($CDCl_3$: δ = 77.16 ppm (*t*), d_6-DMSO: δ = 39.51 ppm (*sept*)). Coupling constants (*J*) are reported in Hertz (Hz). High resolution mass spectrum of the phthalonitriles were measured on a Bruker amaZon SL with flow-injection and electrospray ionization and of the subpththalocyanines on a LTQ Orbitap LTQ XL (Thermo-Fisher Scientific, Bremen). The infrared spectra were measured as solid matter with an IRTracer-100 spectrometer with ATR unit included.

2. Synthetic procedures



Scheme S1: Synthetic procedure to compound [**1**].

4-Aminophthalonitrile (**A-Pn**)[1]

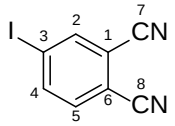


The synthesis was carried out according to a modified literature procedure. 4-Nitrophthalonitrile (4.00 g, 23.10 mmol, 1.0 eq.) was added to a mixture of methanol (80 mL) and concentrated hydrochloric acid (21.40 g, 586.84 mol, 18.0 mL, 25.4 eq.). The mixture was heated to boiling. Iron powder (4.13 g, 73.79 mmol, 3.2 eq.) was added in small portions and the resulting suspension was heated under reflux for 1 h. After the hydrogen formation stopped the solution was poured carefully into an ice-water mixture (200 mL) and the resulting suspension filtered off. The solid was washed with a little amount of cold water followed by solving in acetone (50 mL) and filtrating. The solvent was evaporated and the remaining solid was suspended in water and freeze-dried.

Molecular formula: $C_8H_5N_3$ (brown solid). **Yield:** 89 % (2.93 g, 20.47 mmol). **^{1}H-NMR (300 MHz, DMSO-d_6):** δ (ppm) = 7.62 (*d*, ^3J = 8.0 Hz, 1H, 5-H), 7.00 (*s*, 1H, 2-H), 6.86 (*d*, ^3J = 8.0 Hz, 1H, 4-H), 6.68 (*s*, 1H, 9-H). **^{13}C-NMR (75 MHz, DMSO-d_6):** δ (ppm) = 153.01, 134.85, 117.46, 117.21, 116.91, 116.38, 115.45, 97.74. **IR:** ν (cm^{-1}) = 3483, 3378, 3210, 2234, 2214,

1622, 1597, 1553, 1508, 1449, 1354, 1331, 1261, 1211, 1175, 1067, 864, 841, 710, 625. **ESI-HRMS (m/z):** 144.0569 (calcd. 144.0556 for $[M+H]^+$).

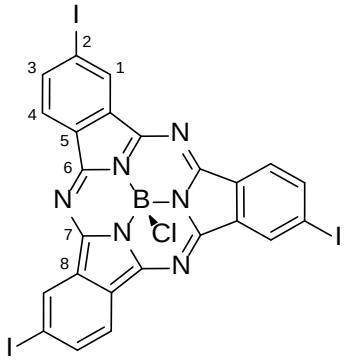
4-Iodophthalonitrile (**I-Pn**)[2]



The synthesis was carried out according to a modified literature procedure. Concentrated hydrochloric acid (59.76 g, 1.64 mol, 50.2 mL, 90.2 eq.) and ice were placed together in a 250 mL three-neck round-bottom flask. 4-Aminophthalonitrile (2.60 g, 18.16 mmol, 1.0 eq.) was added and the mixture was further cooled down with an ice bath. Afterwards a solution of sodium nitrite (1.97 g, 28.52 mmol, 1.6 eq.) in distilled water (17 mL) was added dropwise carefully to the mixture and the resulting suspension was stirred for 1.5 h. During the whole process the temperature should not rise above 5 °C. The suspension was filtered off and washed with ice-cold distilled water, the permeate was still cooled down to 5 °C. During the meantime, potassium iodide (4.55 g, 27.43 mmol, 1.5 eq.) was placed into another 250 mL three-neck round-bottom flask and solved in distilled water (42 mL). The reaction mixture was cooled to 0 °C and the permeate was slowly added to the reaction solution via addition funnel so that the temperature did not rise above 5 °C. After the addition was completed, the ice bath was removed, and the reaction mixture was stirred for 30 min at room temperature. The aqueous solution was then extracted with toluene (6 x 65 mL), the organic phases were combined and successively washed with distilled water (50 mL), saturated NaHCO3 solution (50 mL), distilled water (50 mL), saturated Na2S2O3 solution (50 mL) and distilled water (50 mL). Afterwards the organic phase was dried via MgSO4, the desiccant was filtered off and the solvent was removed in vacuo. The purification of the raw product was performed by column chromatography on silica gel (toluene).

Molecular formula: $C_8H_3IN_2$ (white solid). **Yield:** 51 % (2.36 g, 9.29 mmol). **^{1}H-NMR (300 MHz, $CDCl_3$):** δ (ppm) = 8.16 (*d*, ^3J = 1.6 Hz, 1H, 2-H), 8.10 (*dd*, $^{3,4}J$ = 8.3 Hz, 1.8 Hz, 1H, 4-H), 7.51 (*d*, ^3J = 8.3 Hz, 1H, 5-H). **^{13}C-NMR (75 MHz, $CDCl_3$):** δ (ppm) = 142.59, 142.18, 134.07, 117.16, 115.20, 115.03, 113.95, 99.78. **IR:** ν (cm^{-1}) = 3092, 3061, 3017, 2232, 1813, 1682, 1574, 1545, 1470, 1391, 1373, 1277, 1267, 1206, 1180, 1113, 1074, 976, 955, 907, 837, 721, 714. **ESI-HRMS (m/z):** 254.9421 (calcd. 254.9414 for $[M+H]^+$).

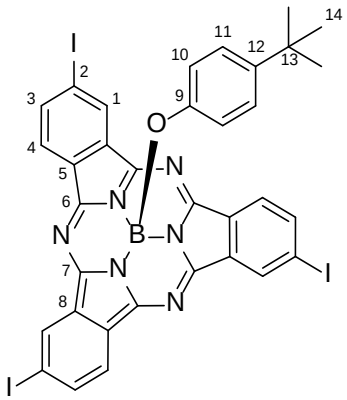
Chloro-[2,9,16-tris-iodo]subphthalocyaninatoboron (III) (**I-SubPC-Cl**)[3]



The synthesis was carried out according to a modified literature procedure. 4-Iodophthalonitrile (0.50 g, 1.98 mmol, 1.0 eq.) was placed in a 25 mL schlenk flask and stirred under argon for 30 minutes. A 1 M solution of borontrichloride in *p*-xylene (3.96 g, 4.35 mmol, 4.40 mL, 2.2 eq.) was added to the flask with the help of a syringe. The reaction mixture was refluxed under argon at 155 °C for 2 h. The reaction was monitored by TLC (cyclohexane : DCM = 30 : 70). After cooling down to room temperature the excess BCl_3 and solvent were gently removed under reduced pressure at 40 °C. The compound was easily purified by a silica plug (cyclohexane : DCM = 30 : 70) to give a dark purple solid.

Molecular formula: $C_{24}H_9BClI_3N_6$ (metallic purple solid). **Yield:** 65 % (283.10 mg, 0.35 mmol). **^{1}H-NMR (300 MHz, $CDCl_3$):** δ (ppm) = 9.20 (*s*, 3H, 1-H), 8.54 (*d*, ^3J = 6.6 Hz, 3H, 3-H), 7.91 (*d*, ^3J = 8.6 Hz, 3H, 4-H). **^{13}C-NMR (75 MHz, $CDCl_3$):** δ (ppm) = 150.49, 149.34, 139.65, 132.87, 133.87, 130.44, 124.16, 97.25. **IR:** *v* (cm^{-1}) = 3188, 3076, 2918, 2324, 2116, 1996, 1771, 1709, 1599, 1545, 1460, 1435, 1354, 1289, 1261, 1225, 1180, 1142, 1094, 1040, 959, 918, 882, 862, 816, 777, 756, 735, 700, 638. **APCI-HRMS (m/z):** 807.7794 (calcd. 807.7803 for $[M]^+$), 808.7847 (calcd. 808.7881 for $[M+H]^+$), 772.8105 (calcd. 772.8115 for $[M-Cl]^+$).

4-*tert*-butylphenoxy-[2,9,16-tris-iodo]subphthalocyaninatoboron (III) (**I-SubPC-Ph**)[4]

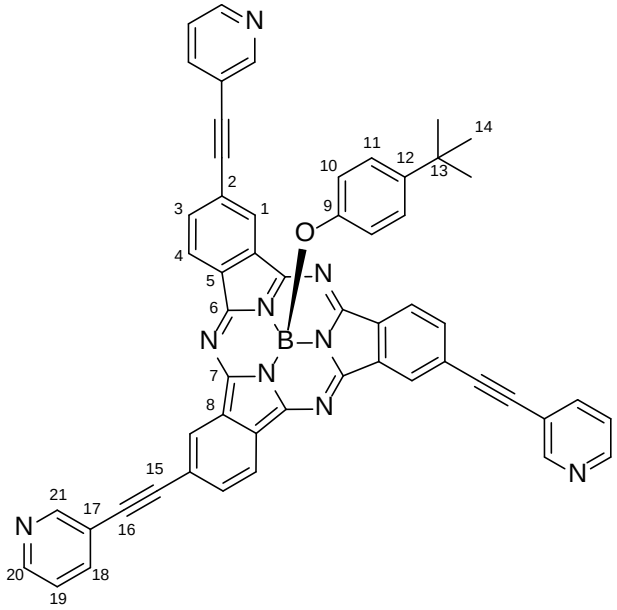


The synthesis was carried out according in analogy to a literature procedure. Chloro-[2,9,16-tris-iodo]subphthalocyaninatoboron (III) (0.30 g, 0.37 mmol, 1.0 eq.) and silver triflate (0.12 g, 0.46 mmol, 1.25 eq.) were placed in a 25 mL schlenk flask and solved in dry toluene (7 mL). The mixture was allowed to stir at room temperature under argon atmosphere for 2 h and monitored by TLC (toluene). Once the SubPCBOTf reagent is completely generated, 4-*tert*-butylphenol (0.11 g, 0.74 mmol, 2.0 eq.) and *N*,*N*-diisopropylethylamine (60.0 mg, 0.46 mmol,

79.0 µL, 1.25 eq.) were added and the mixture was stirred at room temperature for 3 d. The reaction was again monitored by TLC (toluene). The solvent was removed by evaporation under reduced pressure and the compound was directly purified by silica gel (toluene) to obtain a purple solid.

Molecular formula: $C_{34}H_{22}BI_3N_6O$ (metallic purple solid). **Yield:** 89 % (303.30 mg, 0.33 mmol). **^{1}H-NMR (300 MHz, $CDCl_3$):** *δ* (ppm) = 9.18 (*s*, 3H, 1-H), 8.52 (*m*, 3H, 3-H), 8.18 (*m*, 3H, 4-H), 6.76 (*m*, 2H, 11-H), 5.27 (*m*, 2H, 10-H), 1.10 (*s*, 9H, 14-H). **^{13}C-NMR (75 MHz, $CDCl_3$):** *δ* (ppm) = 152.00, 150.87, 144.79, 139.24, 138.45, 132.85, 132.03, 130.51, 126.37, 124.08, 118.35, 96.53, 34.40, 31.80. **IR:** *ν* (cm^{-1}) = 3086, 2239, 1721, 1620, 1549, 1491, 1478, 1427, 1325, 1256, 1192, 1148, 1130, 1113, 1092, 947, 895, 858, 808, 781, 729, 718, 683, 615. **APCI-HRMS (m/z):** 921.9113 (calcd. 921.8083 for $[M]^+$), 922.9137 (calcd. 922.9161 for $[M+H]^+$).

4-*tert*-Butylphenoxy-[2,9,16-tris-(2-(3-pyridinyl)ethynyl)]subphthalocyaninatoboron (III) (**Pyr-SubPC-Ph**)[5]

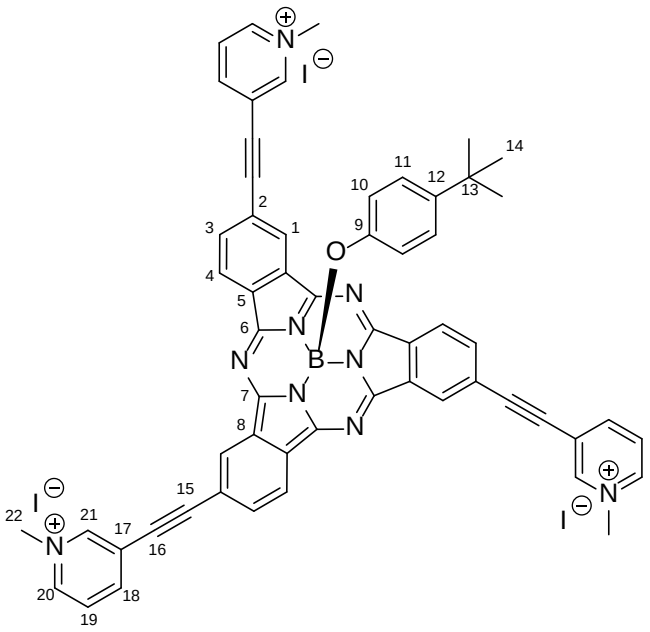


The synthesis was carried out according in analogy to a literature procedure. 4-*tert*-butylphenoxy-[2,9,16-tris-iodo]subphthalocyaninatoboron (III) (0.20 g, 0.22 mmol, 1.0 eq.), bis(triphenylphosphine)palladium chloride (10.67 mg, 15.20 µmol, 0.07 eq.), copper(I) iodide (33.0 mg, 0.17 mmol, 0.8 eq.) and 3-ethynylpyridine (0.27 g, 2.60 mmol, 12.0 eq.) were placed in a 15 mL schlenk tube. Freshly distilled and degassed TEA (4 mL) was added to the mixture. All reactants were protected from light and allowed to stir under argon atmosphere at room temperature. The reaction was monitored by TLC (acetone : DCM = 50 : 50) ; after 20 h the starting material reacted. The solvent was removed under reduced pressure and the compound was directly purified on silica gel (acetone : DCM = 30 : 70) to obtain a dark purple solid as the desired product. Afterwards the residue was dissolved in chloroform (60 mL) and successively extracted with distilled water (2 x 20 mL), saturated $NaHCO_3$ solution (25 mL) and saturated NaCl solution (2 x 20 mL). The organic phase was dried over Na_2SO_4, the desiccant was filtered off and the solvent was removed in vacuo.

Molecular formula: $C_{55}H_{34}BN_9O$ (metallic darkpurple solid). **Yield:** 79 % (147.40 mg, 0.19 mmol). **^{1}H-NMR (300 MHz, $CDCl_3$):** *δ* (ppm) = 8.93 (*d*, ^3J = 11.2 Hz, 3H, 20-H), 8.80 (*br s*,

3H, 21-H), 8.67 (*dd*, $^{3,4}J$ = 10.5 Hz, 81. Hz, 3H, 18-H), 8.52 (*d*, ^{4}J = 4.4 Hz, 3H, 1-H), 7.91 (*dd*, $^{3,4}J$ = 8.0 Hz, 1.2 Hz, 3H, 3-H), 7.86-7.80 (*m*, 3H, 4-H), 7.26 (*m*, 3H, 19-H), 6.85 (*d*, ^{3}J = 8.9 Hz, 2H, 11-H), 5.47 (*d*, ^{3}J = 8.9 Hz, 2H, 10-H), 1.10 (*s*, 9H, 14-H). **^{13}C-NMR (75 MHz, $CDCl_3$):** *δ* (ppm) = 152.35, 152.29, 150.04, 149.02, 144.10, 138.63, 132.74, 130.98, 130.14, 125.92, 124.39, 124.36, 123.19, 122.34, 122.27, 120.03, 118.04, 92.62, 88.74, 33.95, 21.38. **IR:** *v* (cm^{-1}) = 3032, 2959, 2313, 2114, 1929, 1723, 1613, 1559, 1510, 1479, 1433, 1404, 1289, 1258, 1179, 1150, 1115, 1080, 1053, 1020, 951, 891, 829, 800, 760, 702, 627. **APCI-HRMS (m/z):** 847.3064 (calcd. 847.2994 for $[M]^+$), 848.3037 (calcd. 848.3072 for $[M+H]^+$).

4-*tert*-Butylphenoxy-[2,9,16-tris-(2-(3-(*N*-methyl)pyridinyl)ethynyl)]subphthalocyaninatoboron (III) [**1**][3]



The synthesis was carried out according in analogy to a literature procedure. To a solution of 4-*tert*-butylphenoxy-[2,9,16-tris-(2-(3-pyridinyl)ethynyl)]subphthalocyaninatoboron (III) (60.0 mg, 0.07 mmol, 1.0 eq.) in dry DMF was added an excess of methyl iodide (13.20 g, 93.00 mmol, 6.0 mL, 1329.0 eq.). At first, the mixture was stirred for 4 h at 50 °C and afterwards for 12 h at room temperature under argon atmosphere. The methyl iodine was evaporated, and the reaction product was precipitated in diethyl ether. The precipitate was centrifuged and washed with diethyl ether multiple times. Finally, the compound was dissolved in water and freeze-dried to obtain a dark purple solid.

Molecular formula: $C_{58}H_{43}BI_3N_9O$ (purple solid). **Yield:** 94 % (84.60 mg, 66.43 µmol). **^{1}H-NMR (300 MHz, DMSO-d_6):** *δ* (ppm) = 9.37 (*s*, 3H, 21-H), 9.13 (*d*, ^{3}J = 6.9 Hz, 3H, 20-H), 8.94 (*m*, 6H, 1,18-H), 8.80 (*d*, ^{3}J = 7.6 Hz, 3H, 3-H), 8.24 (*d*, ^{3}J = 8.2 Hz, 3H, 4-H), 8.16 (*t*, ^{3}J = 6.3 Hz, 3H, 19-H), 6.77 (*d*, ^{3}J = 8.9 Hz, 3H, 11-H), 5.29 (*d*, ^{3}J = 9.4 Hz, 3H, 10-H), 4.38 (*s*, 9H, 22-H), 1.00 (*s*, 9H, 14-H). **^{11}B-NMR (193 MHz, DMSO-d_6):** *δ* (ppm) = -14.33. **^{13}C-NMR (151 MHz, DMSO-d_6):** *δ* (ppm) = 151.62, 149.56, 148.02, 146.53, 144.20, 143.61, 132.99, 132.88, 130.27, 127.81, 125.85, 125.69, 123 65, 122.88, 122.37, 121.95, 177.79, 95.57, 85.10, 48.31, 33.59, 31.08. **IR:** *v* (cm^{-1}) = 3412, 3025, 2947, 2212, 2112, 1996, 1773, 1713, 1613,

1578, 1503, 1454, 1433, 1290, 1248, 1188, 1121, 1053, 893, 808, 758, 743, 731, 710, 667, 621. **ESI-HRMS (m/z):** 1146.1794 (calcd. 1146.1777 for $[M-I]^+$), 509.6361 (calcd. 509.6363 for $[M-2I]^{2+}$), 297.4556 (calcd. 297.4559 for $[M-3I]^{3+}$).

3. NMR spectra

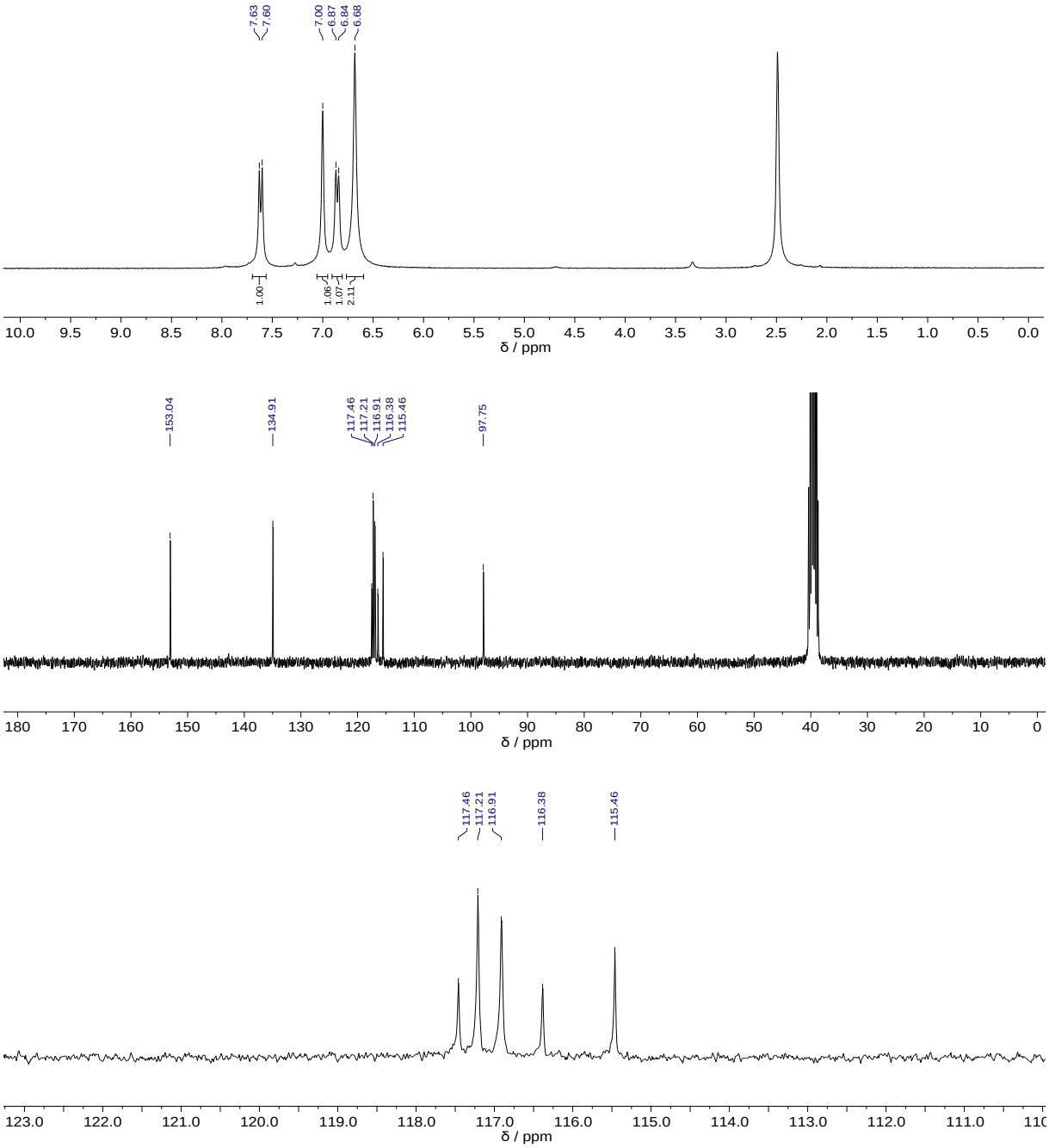


Fig. S1: ^{1}H-NMR and ^{13}C-NMR spectra of **A-Pn** in DMSO-d_6.

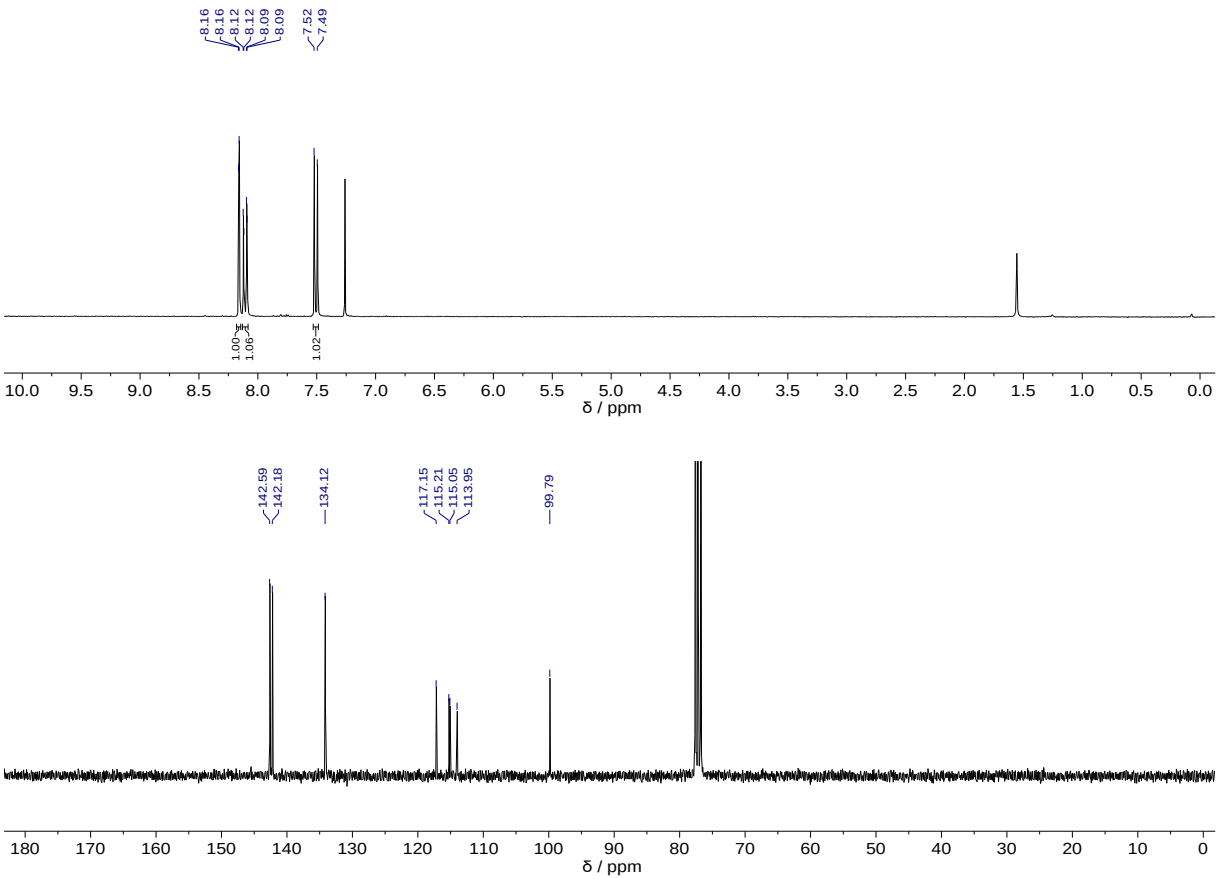


Fig. S2: ^{1}H-NMR and ^{13}C-NMR spectra of **I-Pn** in $CDCl_3$.

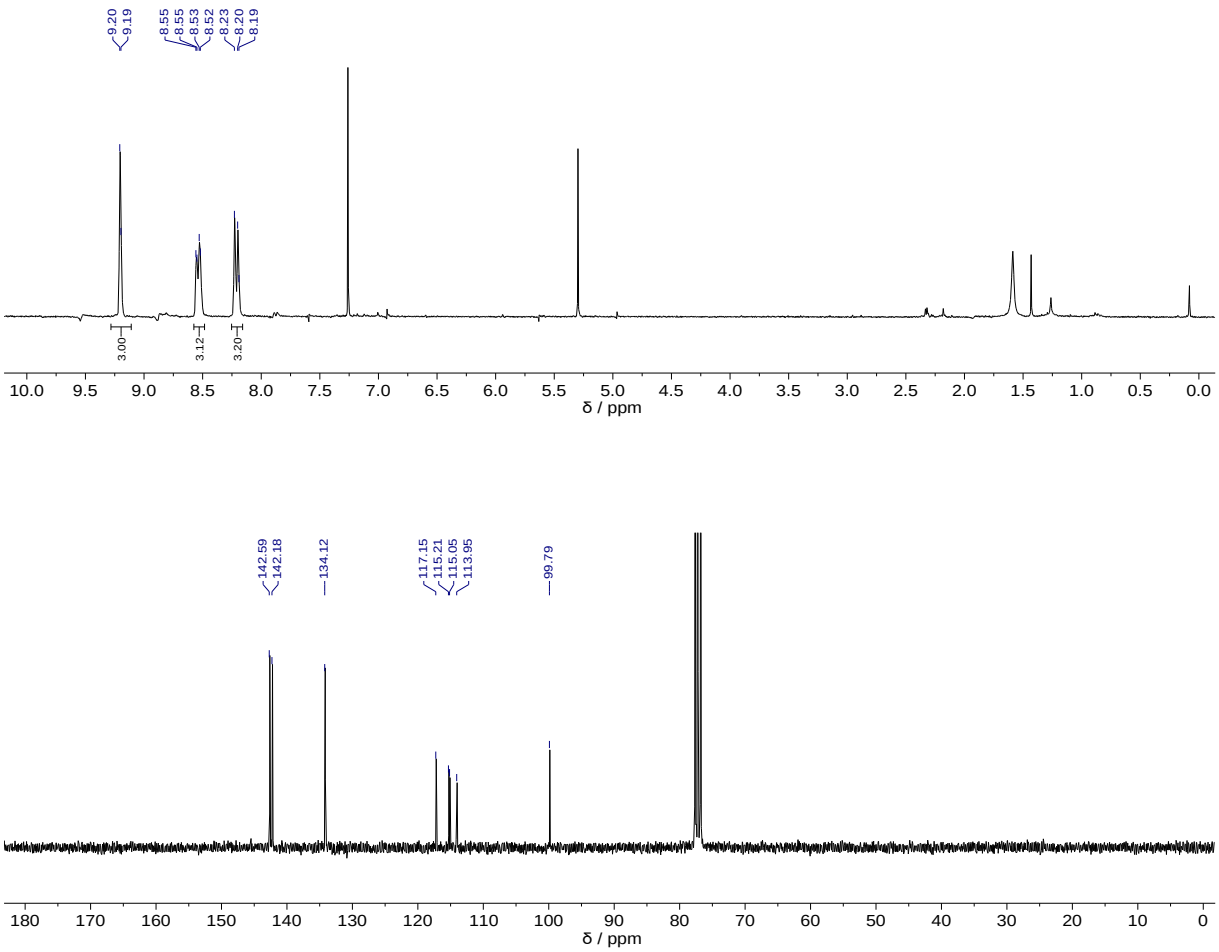


Fig. S3: ^{1}H-NMR and ^{13}C-NMR spectra of **I-SubPC-Cl** in $CDCl_3$.

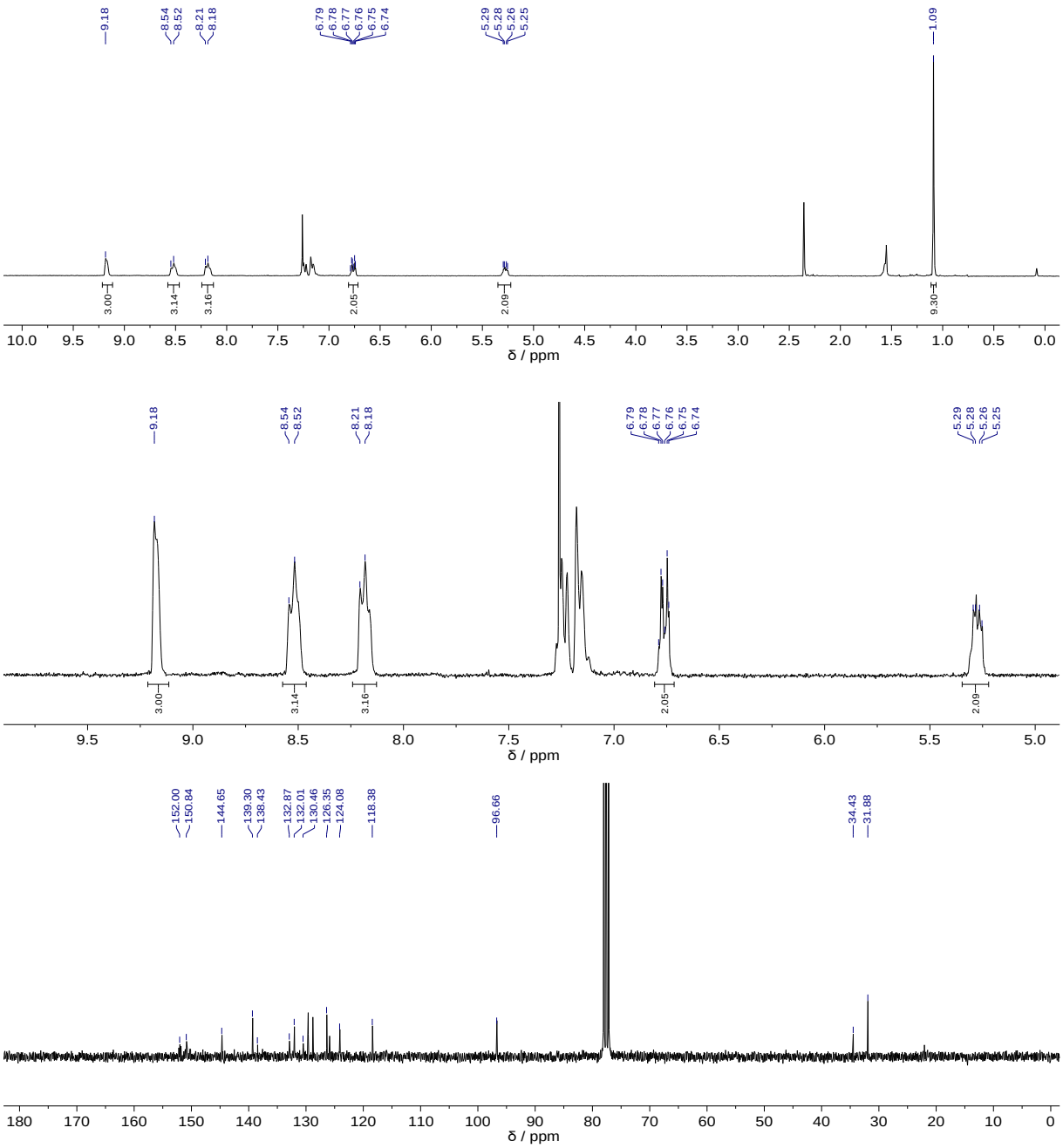


Fig. S4: ^{1}H-NMR and ^{13}C-NMR spectra of **I-SubPC-Ph** in $CDCl_3$.

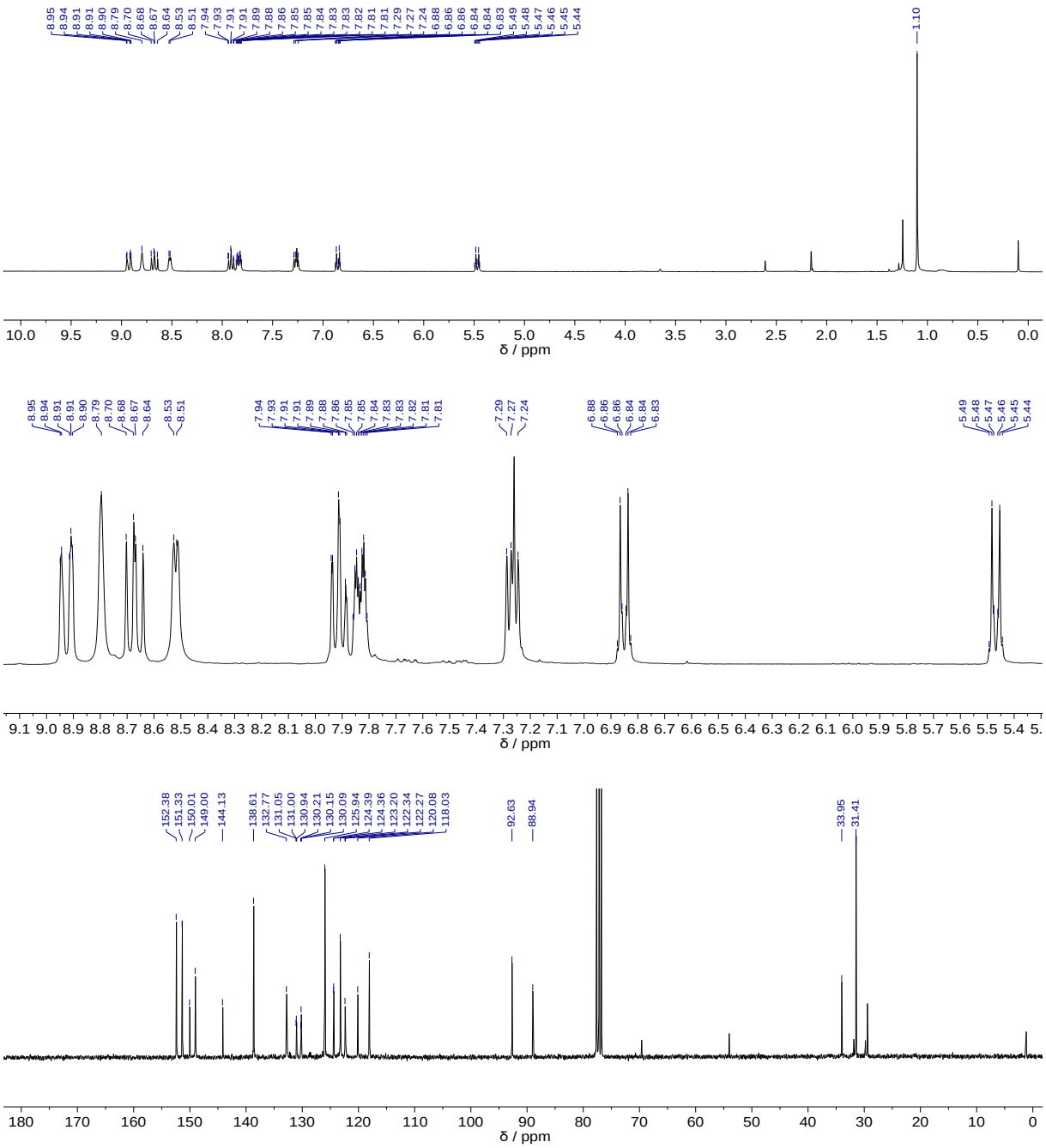


Fig. S5: ^{1}H-NMR and ^{13}C-NMR spectra of **Pyr-SubPC-Ph** in $CDCl_3$.

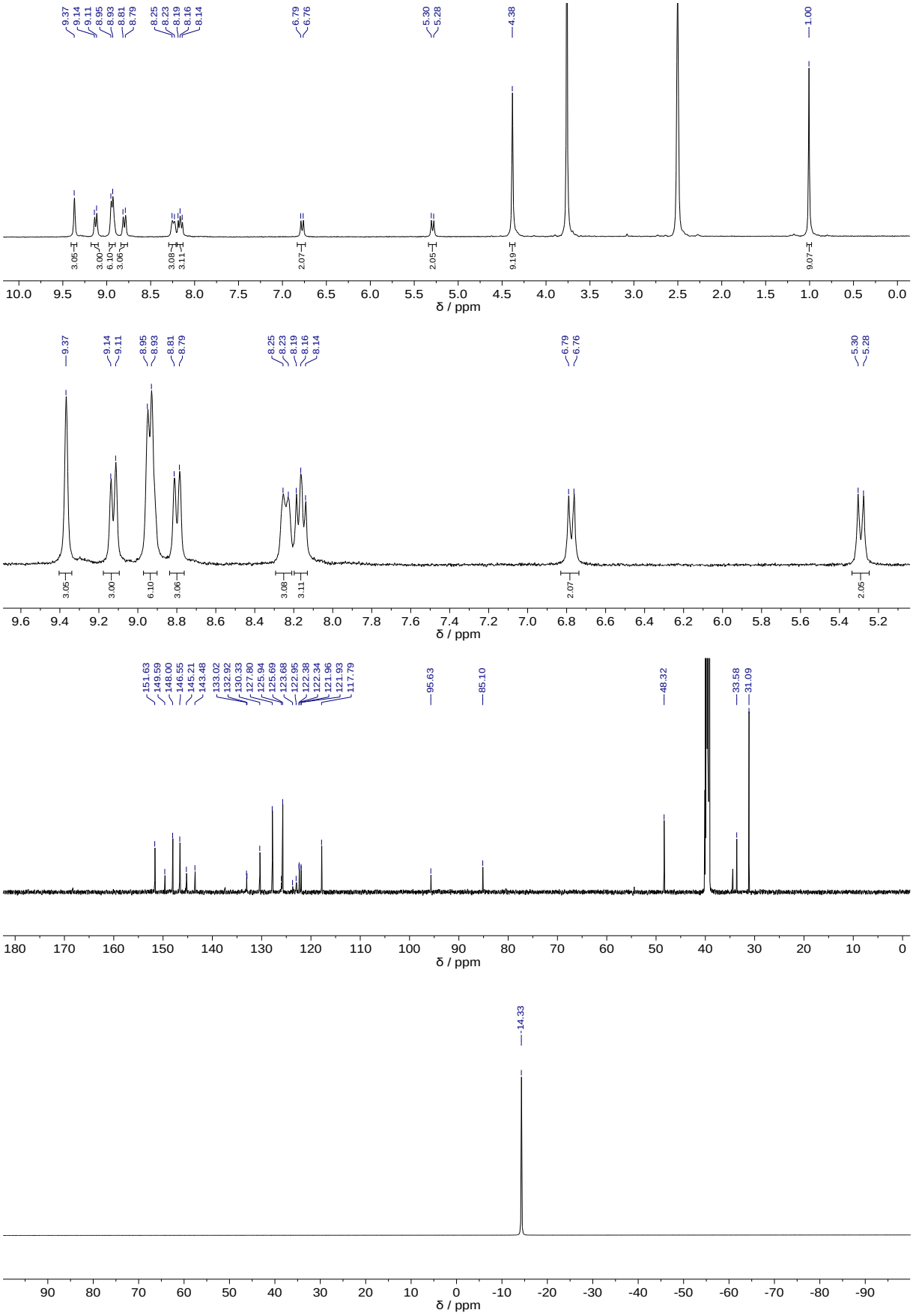


Fig. S6: ^{1}H-NMR, ^{13}C-NMR and ^{11}B-NMR spectra of [**1**] in DMSO-d_6

4. Mass spectra

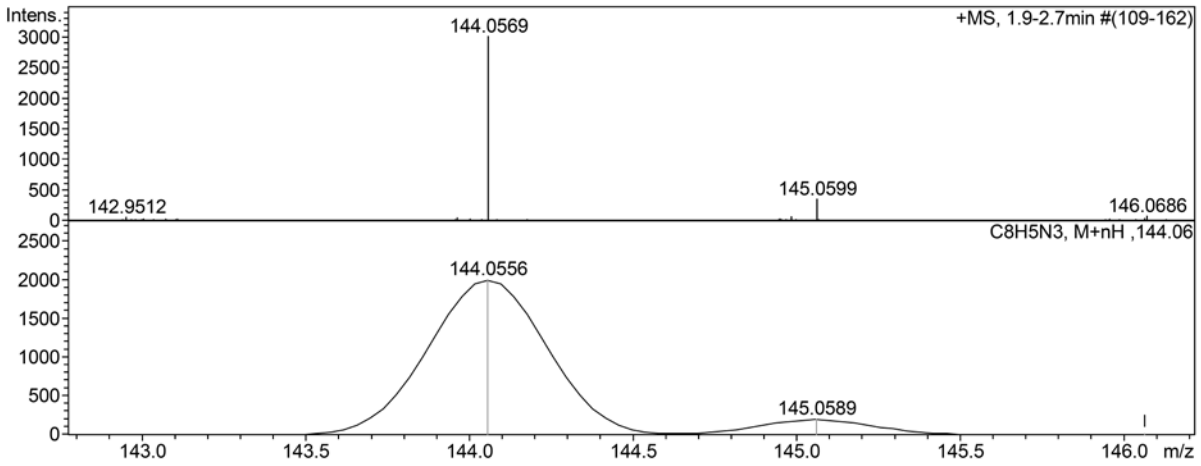


Fig. S7: HR-ESI-MS spectrum of compound **A-Pn**.

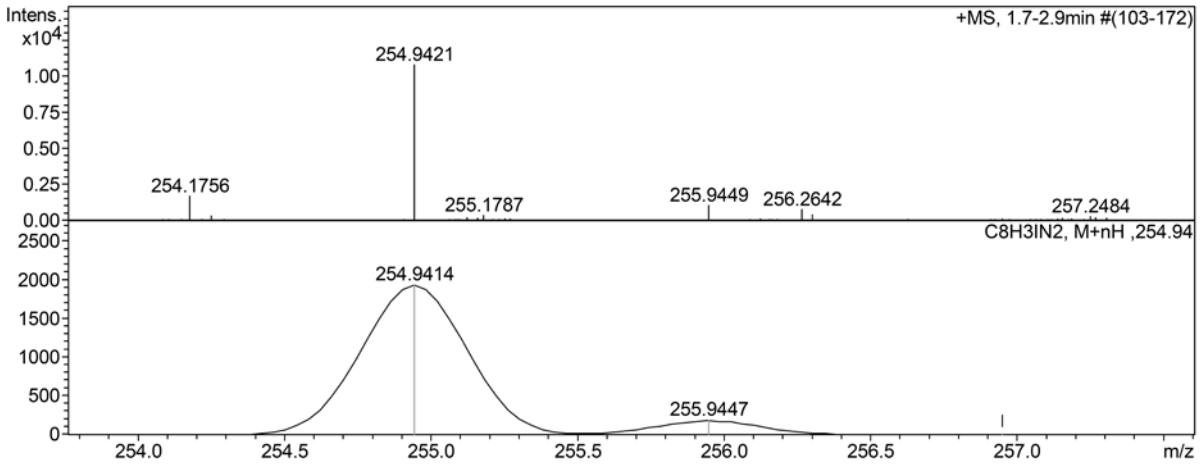


Fig. S8: HR-ESI-MS spectrum of compound **I-Pn**.

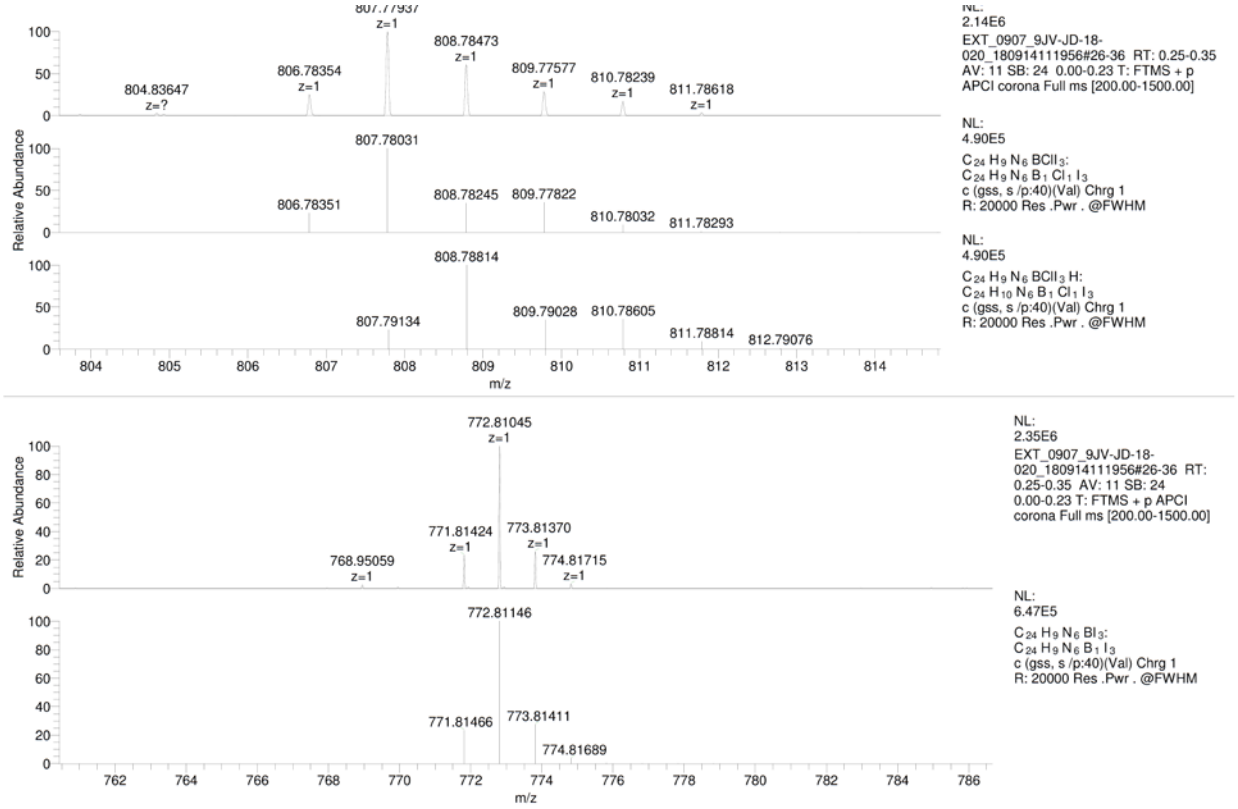


Fig. S9: HR-APCI-MS spectrum of compound **I-SubPC-Cl**.

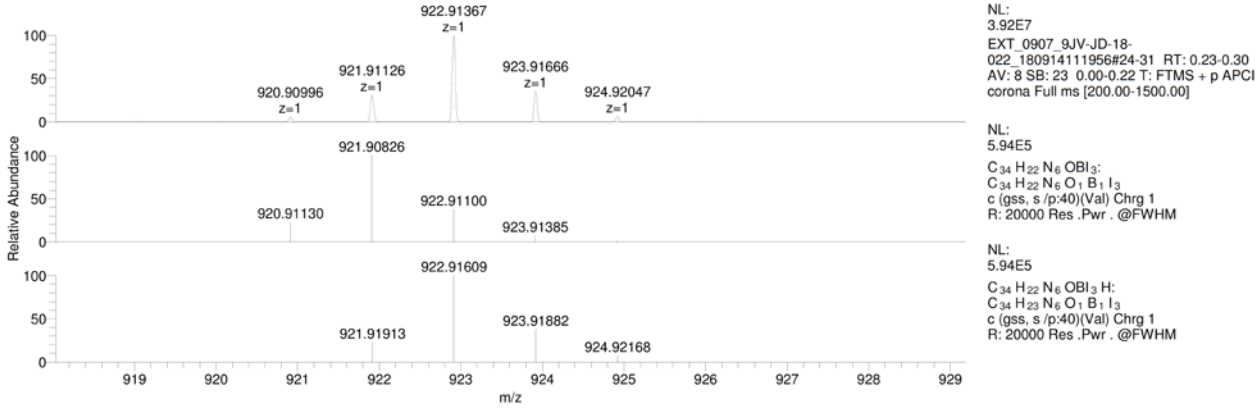


Fig. S10: HR-APCI-MS spectrum of compound **I-SubPC-Ph**.

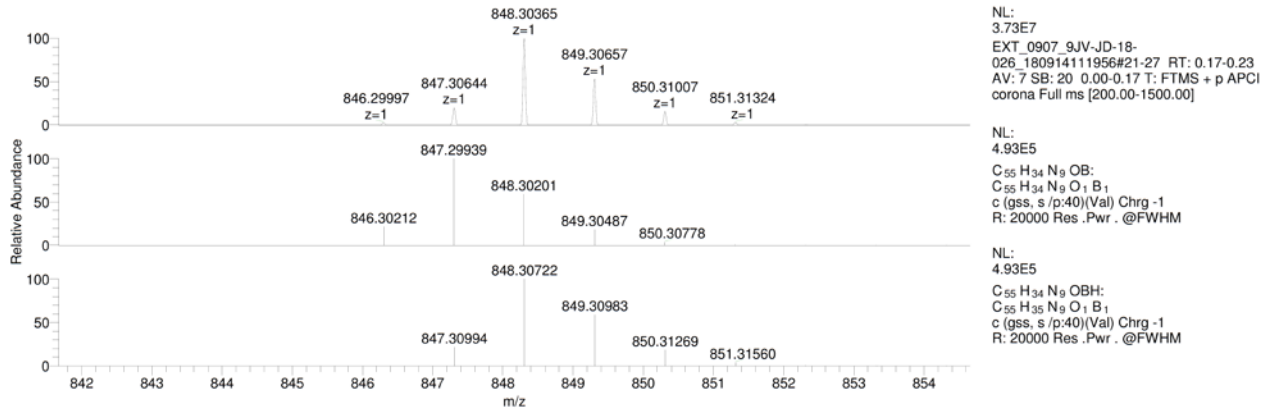


Fig. S11: HR-APCI-MS spectrum of compound **Pyr-SubPC-Ph**.

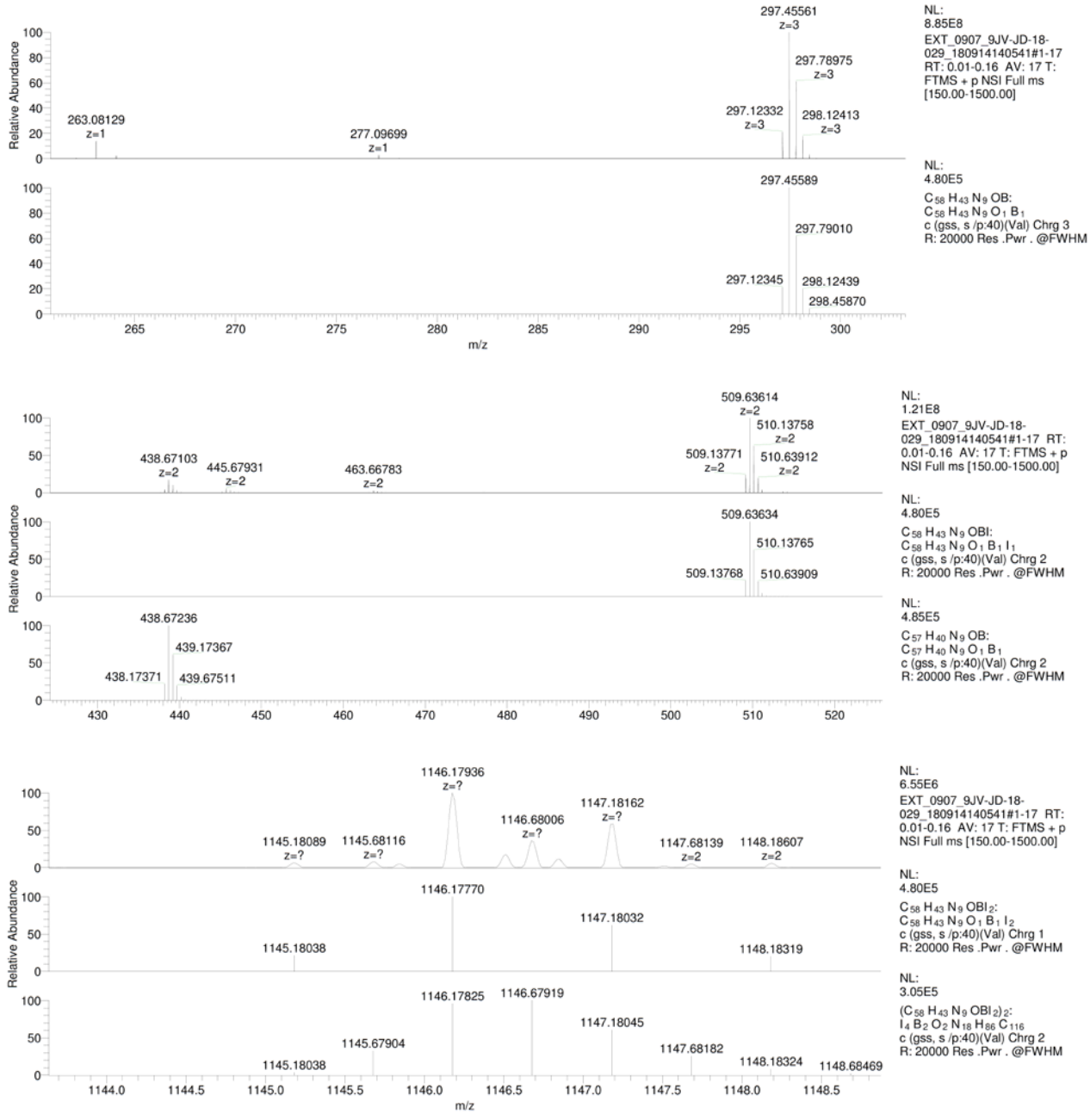


Fig. S12: HR-ESI-MS spectrum of compound [**1**].

5. NMR experiments

General information

The NMR spectra for the Job's method and NMR titration were recorded on a Bruker DMX 600. All measurements were performed at room temperature, using D_2O as solvent. The chemical shifts are referenced relative to the residual proton signals of the solvents in the ^{1}H-NMR spectrum (D_2O: 4.79 ppm (*s*)). Equimolar solutions of the guest and receptor molecule were prepared for the Job's method measurements. For this purpose, a concentration of $3.93 \cdot 10^{-3}$ mol·L^{-1} and a volume of 3 mL were selected for the individual solutions. The guest and receptor solutions were then mixed in different ratios so that the resulting total volume was always 0.6 mL. A total of seven different mixtures with mole fractions of 0.00, 0.17, 0.33, 0.50, 0.66, 0.83 and 1.00 were prepared and transferred to NMR tubes. For the NMR titration experiments a 10 mM stock solution of β-cyclodextrin and a 6 mM stock solution of [**1**] were prepared. A total of twelve samples with the following different equivalents of [**1**] : β-cyclodextrin were prepared and transferred to NMR tubes: 1:0, 1:0.2, 1:0.4, 1:0.6, 1:0.8, 1:1, 1:1.4, 1:1.8, 1:2.5, 1:5, 1:10, 0:1. The total volume of the individual solutions was 0.7 mL each. The resulting binding constant was then calculated using the free analysis tool on the website http://supramolecular.org/, which also created the included fit function.

Job's Method

Tab. S1: Summary of the chemical shifts of the β-cyclodextrin signal and the difference between successive signals depending on the mole fraction of [**1**].

Mole fraction x_{SubPC}	δ / ppm	$\Delta\delta$ / ppm	$x_{SubPC} \cdot \Delta\delta$ / ppm
0.00	5.0802	0.0000	0.0000
0.17	5.0729	0.0073	0.0061
0.33	5.0632	0.0097	0.0065
0.50	5.0460	0.0172	0.0086
0.67	5.0308	0.0152	0.0050
0.83	5.0231	0.0077	0.0013
1.00	-	0.0000	0.0000

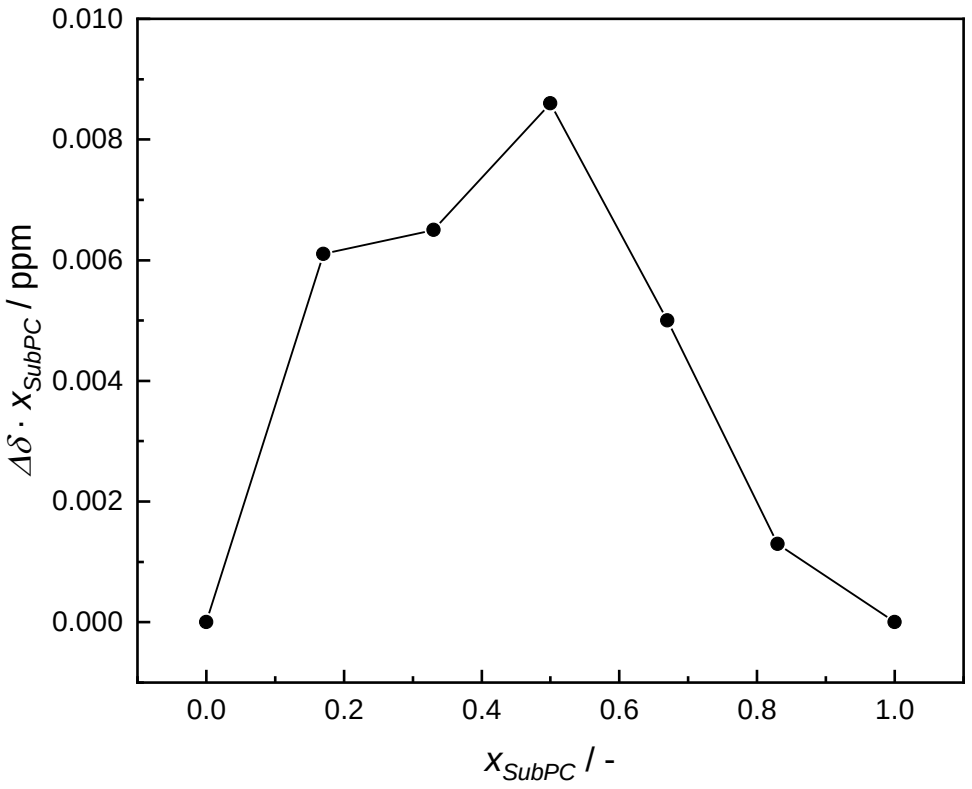


Fig. S13: Job plot of the formation of the host-guest system between [**1**] and β-cyclodextrin based on the cyclodextrin signal.

Tab. S2: Summary of the chemical shifts of the SubPC [**1**] signal and the difference between successive signals depending on the mole fraction of β-cyclodextrin.

Mole fraction $x_{\beta\text{-CD}}$	δ / ppm	$\Delta\delta$ / ppm	$x_{\text{SubPC}} \cdot \Delta\delta$ / ppm
0.00	8.6703	0.0000	0.0000
0.17	8.6706	0.0004	0.0003
0.33	8.6786	0.0079	0.0053
0.50	8.7120	0.0334	0.0167
0.67	8.7480	0.0361	0.0119
0.83	8.7646	0.0166	0.0028
1.00	-	0.0000	0.0000

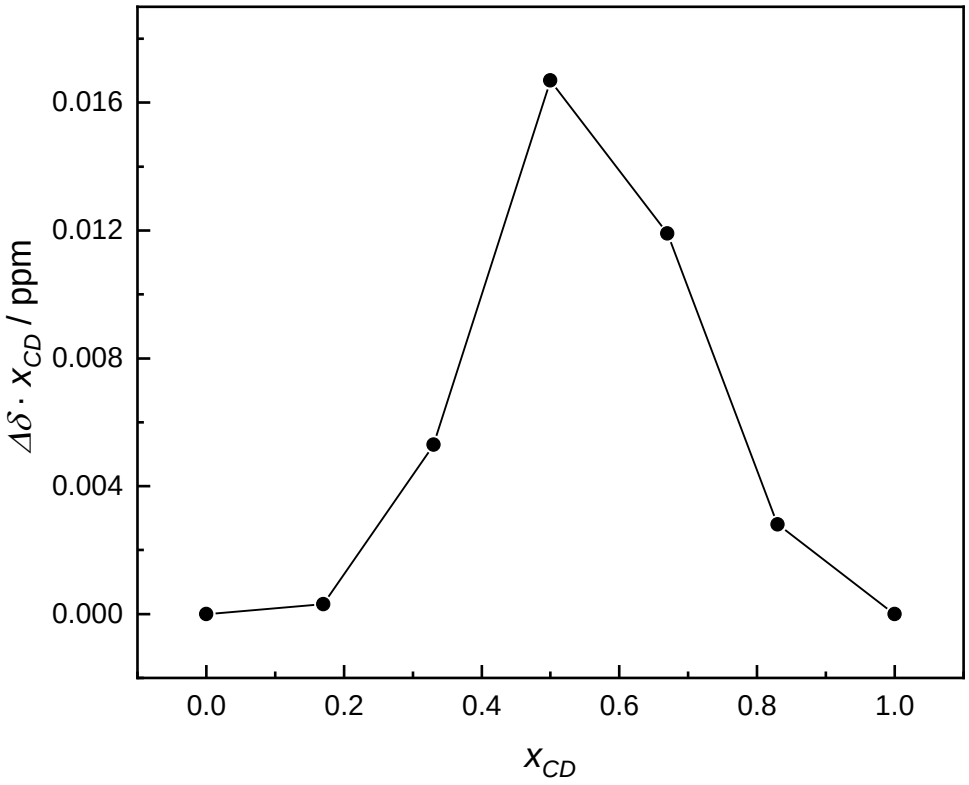


Fig. S14: Job plot of the formation of the host-guest system between [**1**] and β-cyclodextrin based on the SubPC signal.

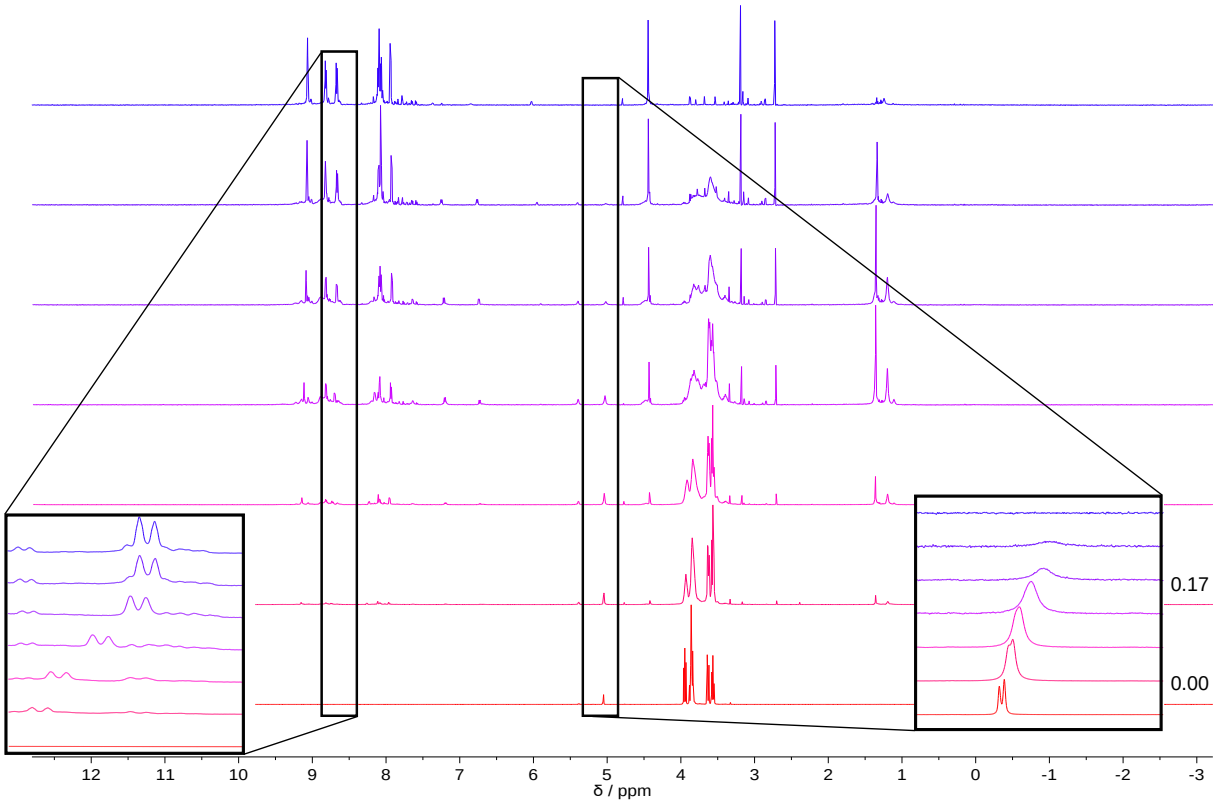


Fig. S15: Staggered ^{1}H-NMR spectra (D_2O, 600 MHz, 298 K) of [**1**] with varying amounts of β-cyclodextrin and the sections of the signals used between 5.0231 to 5.0802 ppm and 8.6703 to 8.7646 ppm.

NMR titration

Tab. S3: Summary of the shifts as well as the differences of the signals of the anomeric proton of the β-cyclodextrin as well from two protons of [**1**] depending on the mixing ratio of β-cyclodextrin to [**1**].

[β-CD]:[SubPC] / -	H_{CD}: δ / ppm	H_{Ar}: δ / ppm	H_{Ar2}: δ / ppm
10 : 1.0	5.07161	7.99235	8.79213
5.0 : 1.0	5.06699	7.98584	8.77764
1.8 : 1.0	5.05792	7.97008	8.74676
1.4 : 1.0	5.05818	7.96341	8.73591
1.0 : 1.0	5.04869	7.95579	8.71064
0.8 : 1.0	5.03228	7.94423	8.68678
0.6 : 1.0	5.03241	7.94604	8.68458
0.4 : 1.0	5.02200	7.94395	8.67445

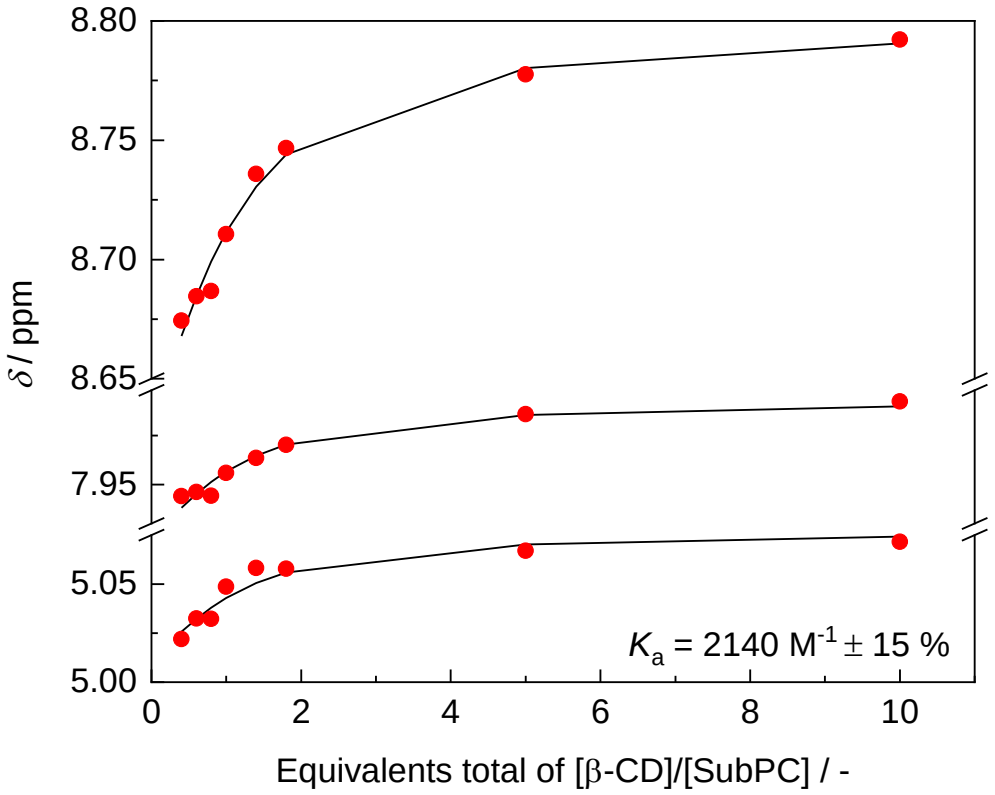


Fig. S16: Obtained titration curves of the observed β-cyclodextrin and aromatic subphthalocyanine signals with fit according to Nelder-Mead (www.supramolecular.org).[6-8]

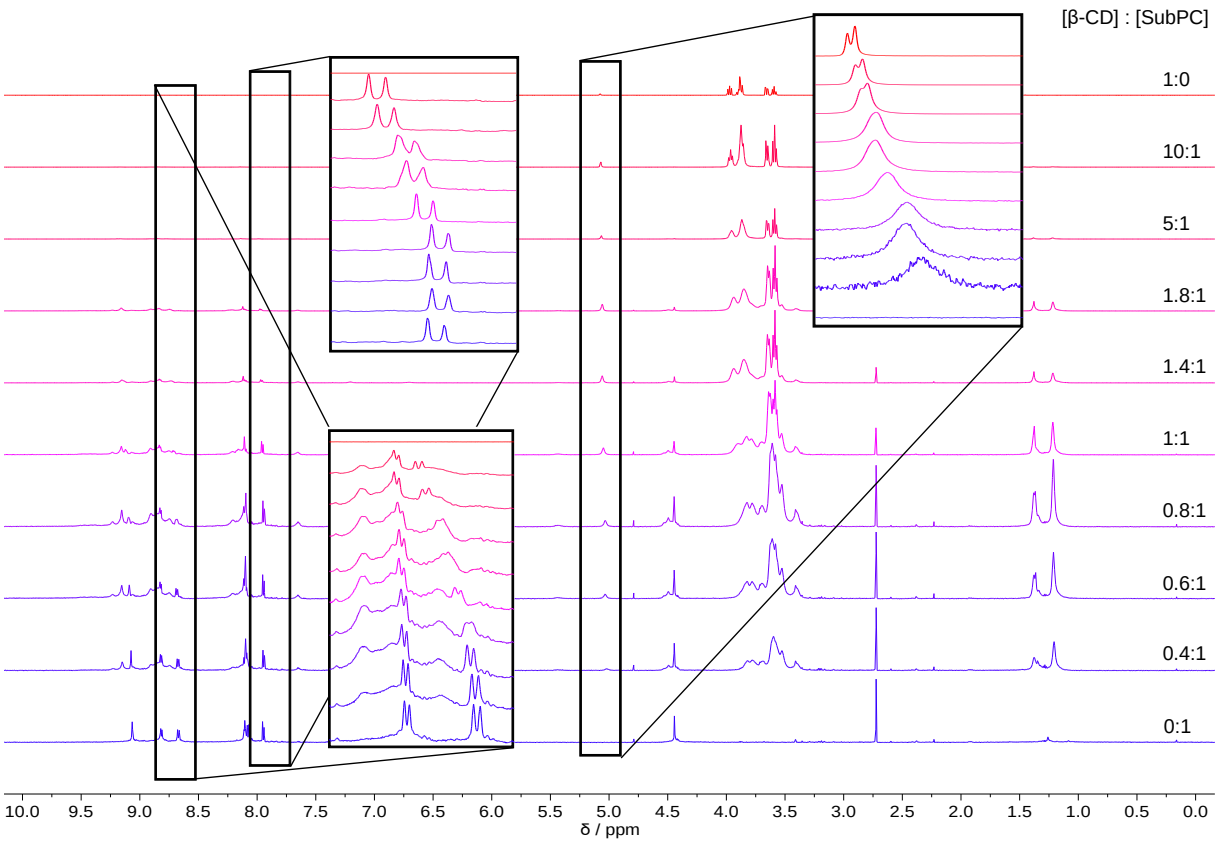


Fig. S17: Staggered ^{1}H-NMR spectra (D_2O, 600 MHz, 298 K) of [**1**] with β-cyclodextrin in varying mixing ratios and the sections of the signals used between 5.02200 to 5.07161 ppm, 7.94395 to 7.99235 ppm and 8.67445 to 8.79213 ppm.

6. Photophysical characterization

General information

UV/VIS absorption spectra were measured on a Jasco V-550 and excitation and emission spectra were recorded on a Shimdazu RF-6000 spectrofluorometer. All measurements were performed at room temperature, using H_2O as solvent. Emission and excitation spectra were corrected for source intensity (lamp and grating) and detection response (detector and grating) by standard correction curves. A concentration of 30 µM was chosen for the absorption, emission and excitation spectrum of the pure compound.

For the determination of the singlet oxygen and luminescence quantum yield a final concentration of 50 µM for the subphthalocyanine [**1**] (SubPC), 500 µM for 9,10-anthracenediyl-bis(methylene)dimalonic acid (ADMADM), 50 µM for the β-cyclodextrin (β-CD) and 200 µM (based on the single cyclodextrin content in the polymer (Mw = 2k-300k g/mol, an average of 151k g/mol was used for the calculations) for the β-cyclodextrin polymer (β-CD-polymer) was chosen, so that the host to guest ratio was 1:1 (for β-CD) and 4:1 (based on the single cyclodextrin content in the polymer) respectively. Luminescence quantum yields were measured with a Shimdazu RF-6000 spectrofluorometer and an Ulbricht-sphere from hamatsu photonocs. A Visilight Cl-150 halogen lamp from VWR with a light intensity of 10 mW/cm^2 served as the irradiation source. All solvents used were of spectroscopic grade.

All measurements were performed in quartz cuvettes (from Hellma Analytics, Germany) with a final solution volume of 1 mL.

Excitation and emission spectra

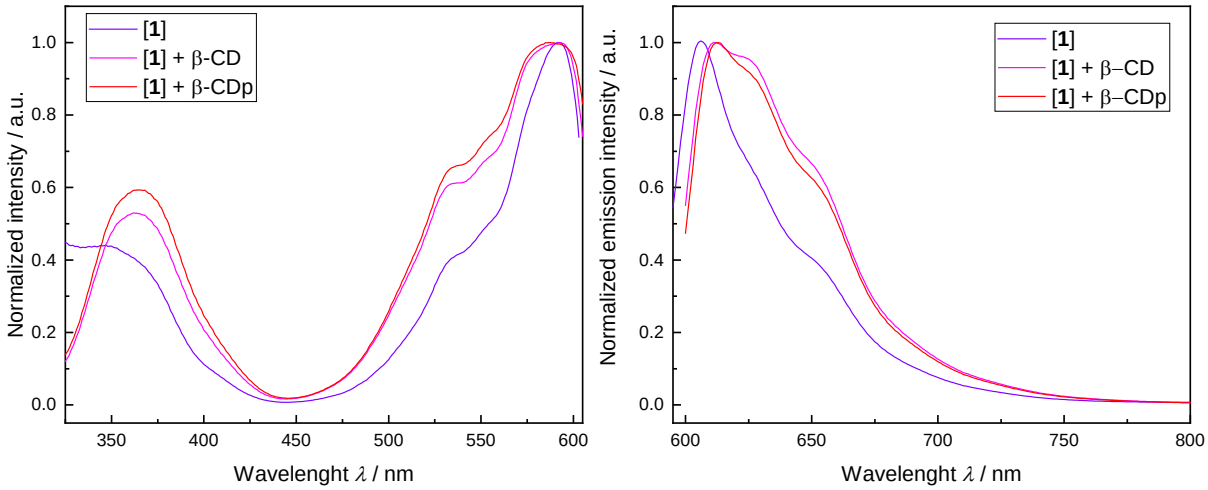


Fig. S18: Left: excitation spectra of [**1**], [**1**] + β-CD and [**1**] + β-CD polymer between 340 to 605 nm in distilled water. Right: emission spectra of [**1**], [**1**] + β-CD and [**1**] + β-CD polymer between 595 to 800 nm in distilled water. c[**1**] = 30 µM, c[β-CD] = 30 µM, c[β-CD polymer] = 120 µM.

Determination of singlet molecular oxygen quantum yields

Singlet molecular oxygen photo generation rates were derived using photochemical monitor bleaching rates. Polychromatic irradiation by a halogen lamp was applied to perform the experiments. Calculation of the singlet oxygen quantum yield for the subphthalocyanines were done according to eqn. S1, where *r* is the singlet oxygen photo generation rate (measured as slope of the monitor's bleaching over time), λ_1 - λ_2 is the irradiation wavelength interval, $I_0(\lambda)$ the incident spectral photon flow,*A(λ) t*he absorbance, and the subscripts R and S stand for reference (methylene blue (MB)) and sample ([**1**], [**1**] + β-CD or [**1**] + β-CDp), respectively.

$$\phi_{\Delta}^{S} = \phi_{\Delta}^{R} \frac{r_S}{r_R} \frac{\int_{\lambda_1}^{\lambda_2} I_0(\lambda) \left(1\text{-}10^{-A_R(\lambda)}\right) d\lambda}{\int_{\lambda_1}^{\lambda_2} I_0(\lambda) \left(1\text{-}10^{-A_S(\lambda)}\right) d\lambda} \qquad \text{(eqn. S1)}$$

The incident intensity $I_0(\lambda)$ can be approximated by a constant value, drawn out of the integral and therefore cancelled. The measured data is depicted in the following figures.

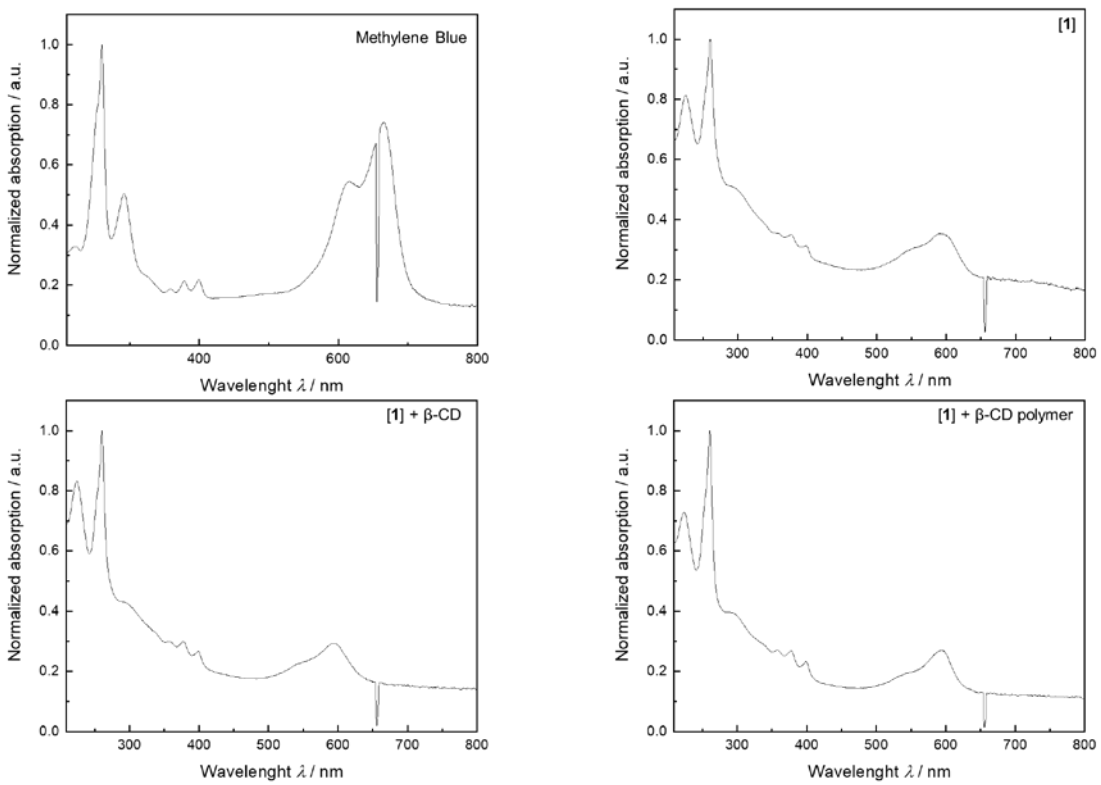


Fig. S19: UV/VIS absorption spectra of MB and [**1**], [**1**] + β-CD and [**1**] + β-CD-polymer between 210 to 800 nm. The negative signal at 653 nm was attributed to a lamp signal during the measurement. c[**1**] = 30 µM, c[β-CD] = 30 µM, c[β-CD-polymer] = 120 µM.

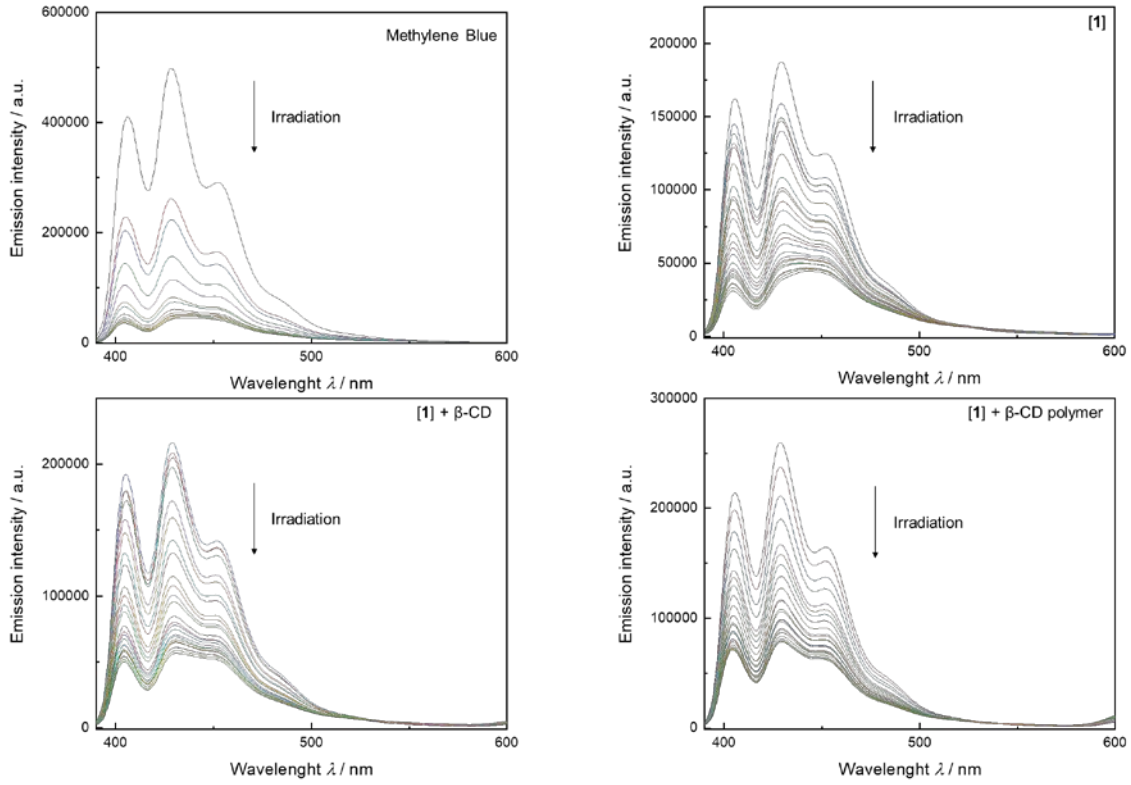


Fig. S20: Decrease of emission intensity of ADMADM between 390 to 600 nm after different irradiation times: 0 to 60 s for MB and from 0 to 120 s with an increment of 5 s for [**1**], [**1**] with β-CD and [**1**] with β-CD polymer. c[**1**] = 50 µM, c[ADMADM] = 500 µM, c[β-CD] = 50 µM, c[β-CD-polymer] = 200 µM.

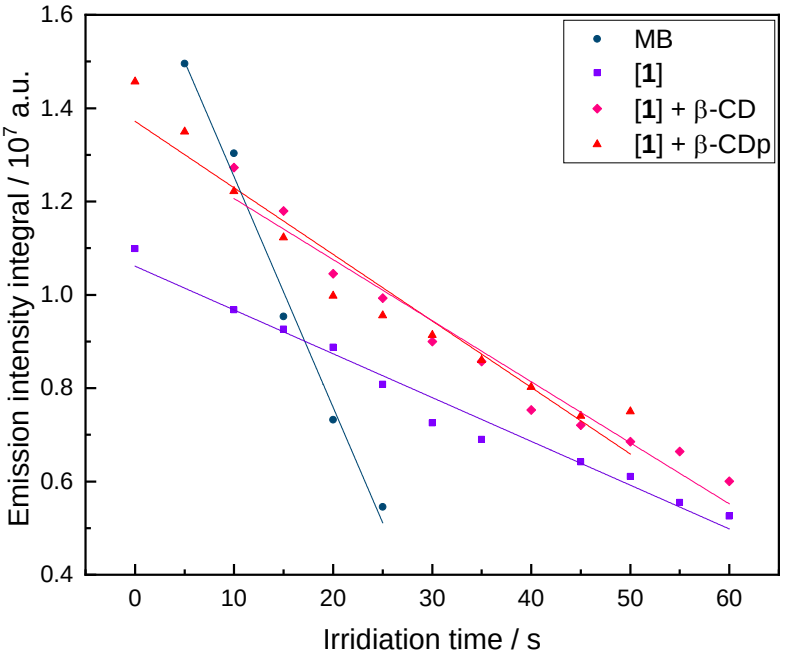


Fig. S21: Slopes of ADMADM decay for MB (blue), [**1**] (purple), [**1**] with β-CD (pink) and [**1**] with β-CD-polymer (red).

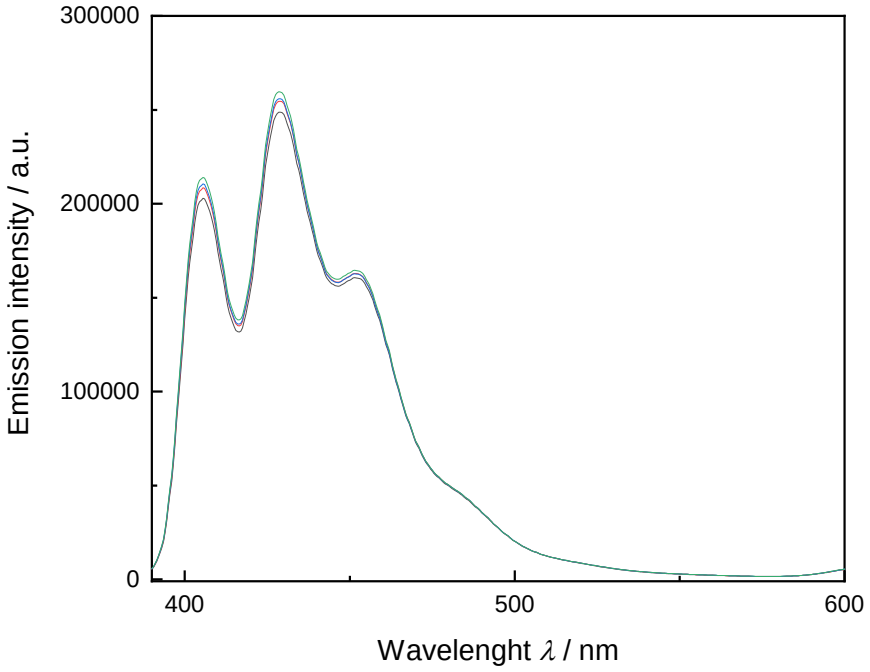


Fig. S22: Stacked emission spectra of ADMADM with [**1**] between 390 to 600 nm without irradiation after 0 to 20 s with an increment of 5 s.

	[**1**]	[**1**] + β-CD	[**1**] + β-CD-polymer
λ_{max} / nm (Soret-band)	289	291	291
λ_{max} / nm (Q-band)	589	592	592
λ_{max} / nm (Emission)	610	611	613
ΦF (±0.02)	0.11	0.14	0.13
ΦΔ (±0.02)	0.17	0.25	0.28

Tab. S4: Photophysical parameters of [**1**] in pure solution and present in host-guest complexes with β-CD or β-CD-polymer in distilled water.

7. Biological Assays and Bioimaging

Phototoxicity assay

1 x 10^4 HeLa cells were cultured in Corning 96 Well microplates (SigmaAldrich) in 100 µl Dulbecco's modified eagle medium (DMEM) (Thermo Fisher Scientific) supplied with 10 % (v/v) fetal calf serum (FCS) (Life Technologies GmbH), Antibiotic-Antimycotic (Life Technologies GmbH) and incubated at 37 °C and 5 % CO_2 over night. Then, medium was exchanged for fresh medium containing 100 µM of the compound dissolved in DMSO. After 1 h incubation at 37 °C and 5 % CO_2, the compound was removed by washing the cells with 100 µl PBS to remove extracellular compound. To avoid a filter effect by the DMEM ingredients during the light exposure, the medium was exchanged for 100 µl of Fluorobrite DMEM (Thermo Fisher Scientific) that is especially designed for fluorophore-based assays. A Visilight Cl-150 halogen lamp (VWR) with a light intensity of 10 W served as the irradiation source. The cells were then exposed to light by a Visilight Cl-150 halogen lamp (full intensity, 20 cm, 1.4 mW/cm^2) equipped with a filter to block UV-radiation under 450 nm, that would be harmful to the tumor cells. The exposure took place at room temperature under a laminar flow cabinet to provide a sterile environment, since the lid of the 96 well plate had to be removed during light exposure to avoid filter effects.

To make sure that the change in temperature and environment for the time of the exposure affects all cells equally, we kept all the samples outside of the incubator for the same time and simply covered the wells until the desired exposure time was reached.

To subsequently analyze the induction of apoptosis, we incubated the cells for 24 h at 37 °C and 5 % CO_2. After that, we checked the cell viability using the CellTiter-Fluor Cell Viability Assay (Promega) kit as specified by the manufacturer with a Promega Glow Max (Promega). Data was normalized against controls for toxicity caused by photo treatment alone, against controls for dark toxicity of the compound and are the mean ± standard error of the mean from three replicates.

Microscopy

2 x 10^4 HeLa cells were cultured in µ-Slide 8 Wells (Ibidi) in 200 µl DMEM supplemented supplied with 10 % (v/v) FCS (Life Technologies GmbH), Antibiotic-Antimycotic (Life Technologies GmbH) and incubated over night at 37 °C and 5 % CO_2. Then, cells were stained with 200 ng/µL Hoechst 33342 nuclear dye (Thermo Fisher Scientific) for 15 min at 37 °C and 5 % CO_2. The medium was exchanged for DMEM containing the compounds, and the cells incubated for 1 h at 37 °C and 5 % CO_2. Then, the compound was removed by replacing the DMEM medium. Live cell microscopy was performed on a Leica TCS SP8X Falcon (Leica) at 37 °C and 5 % CO_2. The 3D-images were created by stacking multiple images using the software LAS X (Leica).

Co-Localization of SubPC and the nucleoli

2 x 10^4 HeLa cells were cultured in µ-Slide 8 Wells (Ibidi) in 200 µl DMEM supplemented supplied with 10 % (v/v) FCS (Life Technologies GmbH), Antibiotic-Antimycotic (Life Technologies GmbH) and incubated over night at 37 °C and 5 % CO_2. For co-localization experiments, we used the plasmid pc3-NPM-GFP encoding for human Nucleophosmin (NPM), a nucleolar protein, fused to a green fluorescent protein (GFP). For each well, 30 µL Opti-MEM (Thermo Fisher Scientific) and 0.4 µL Lipofectamin 2000 (Thermo Fisher Scientific) were mixed, vortexed and incubated for 5 min at room temperature. Also, for each well, 30 µL Opti-Mem and 0.1 ng of the plasmid pc3-NPM-GFP were mixed, vortexed and incubated for 5 min at room temperature. Lipofectamin and plasmid were then mixed, vortexed and again incubated at room temperature for 5 min. After that, the mixture was added slowly to the HeLa cells. After 24 h, we continued with Hoechst staining, compound incubation and microscopy as described in the Microscopy section.

Co-localization of SubPC + ß-CD-polymer and the Golgi apparatus

2 x 10^4 HeLa cells were cultured in µ-Slide 8 Wells (Ibidi) in 200 µl DMEM supplemented supplied with 10 % (v/v) FCS (Life Technologies GmbH,), Antibiotic-Antimycotic (Life Technologies GmbH) and incubated over night at 37 °C and 5 % CO_2. For the co-localization experiments, we used the plasmid pEYFP-Golgi (Clontech) that encodes for a fusion protein consisting of enhanced yellow fluorescent protein (YFP) and the first 81 amino acids of the 1,4-Galactosyltransferase, that is located at the golgi-apparatus and contains a membrane-anchoring signal. For each well, 30 µL Opti-MEM (Thermo Fisher Scientific) and 0.4 µL Lipofectamin 2000 (Thermo Fisher Scientific) were mixed, vortexed and incubated for 5 min at room temperature. Also, for each well, 30 µL Opti-MEM and 0.1 ng of the plasmid pEYFP-Golgi were mixed, vortexed and incubated for 5 min at room temperature. Lipofectamin and plasmid were then mixed, vortexed and again incubated at room temperature for 5 min. After that, the mixture was added slowly to the HeLa cells. After 24 h, we continued with Hoechst staining, compound incubation and microscopy as described in the Microscopy section.

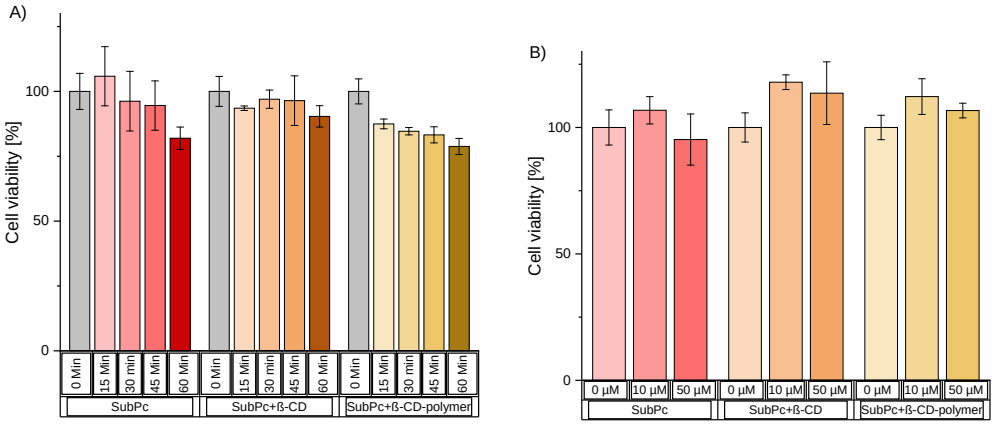


Fig. S23: A) Viability control of HeLa cells for exposure to 1.4 mW/cm^2 light. Data was normalized against non-irradiated controls and are the mean ± standard error of the mean from three replicates. B) Control for dark toxicity of the compound. HeLa cells have been treated with the respective compound concentrations and not exposed to light, but kept in the dark for 60 min. Data was normalized against untreated controls, and columns represent the mean ± standard error of the mean from three replicates. Cell viability was assessed using the CellTiter-Fluor Cell Viability Assay.

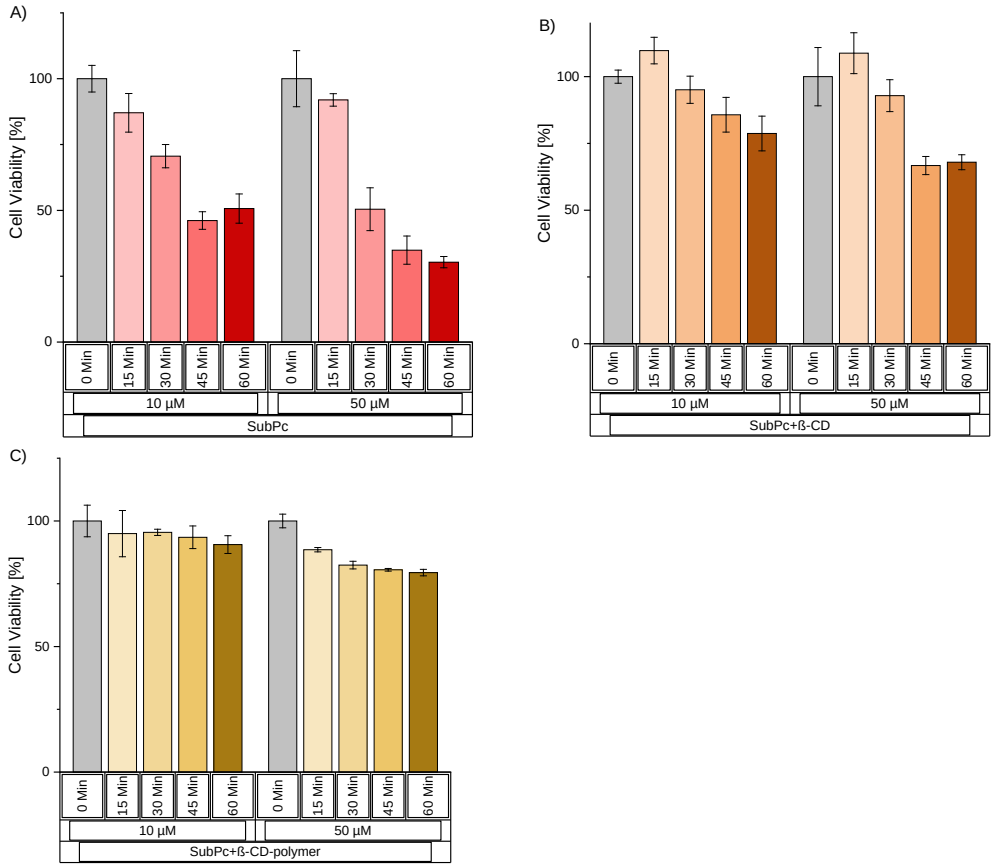


Fig. S24: Viability of of HeLa cells after photodynamic therapy with SubPC (A), SubPC-C (B) and SubPC-CP (C). Data was normalized against non-irradiated controls and columns represent the mean ± standard error of the mean from three replicates. Cell viability was assessed using the CellTiter-Fluor Cell Viability Assay.

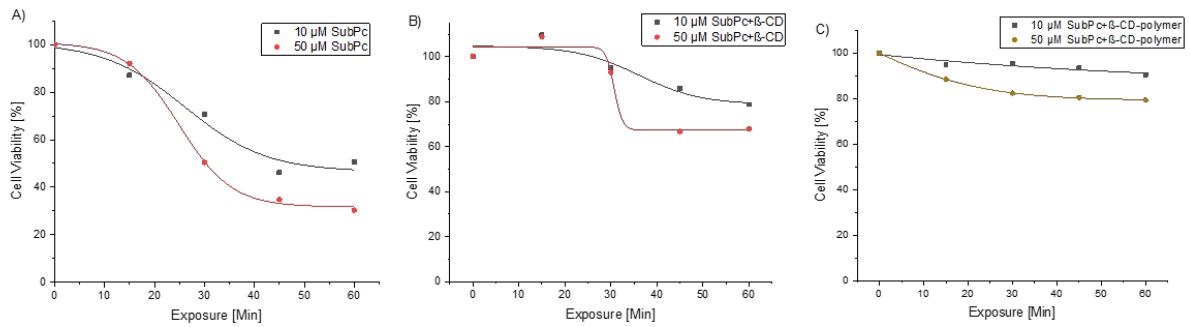


Fig. S25: Dose-response curve of the exposure time for the photodynamic treatment of HeLa cells with different concentrations of SubPC (A), SubPC-C (B) and SubPC-CP (C). Data was normalized against non-irradiated controls and are the mean from three replicates. Data fitting was performed by using the Dose-Response analysis from Origin 2019 (OriginLab). Cell viability was assessed using the CellTiter-Fluor Cell Viability Assay.

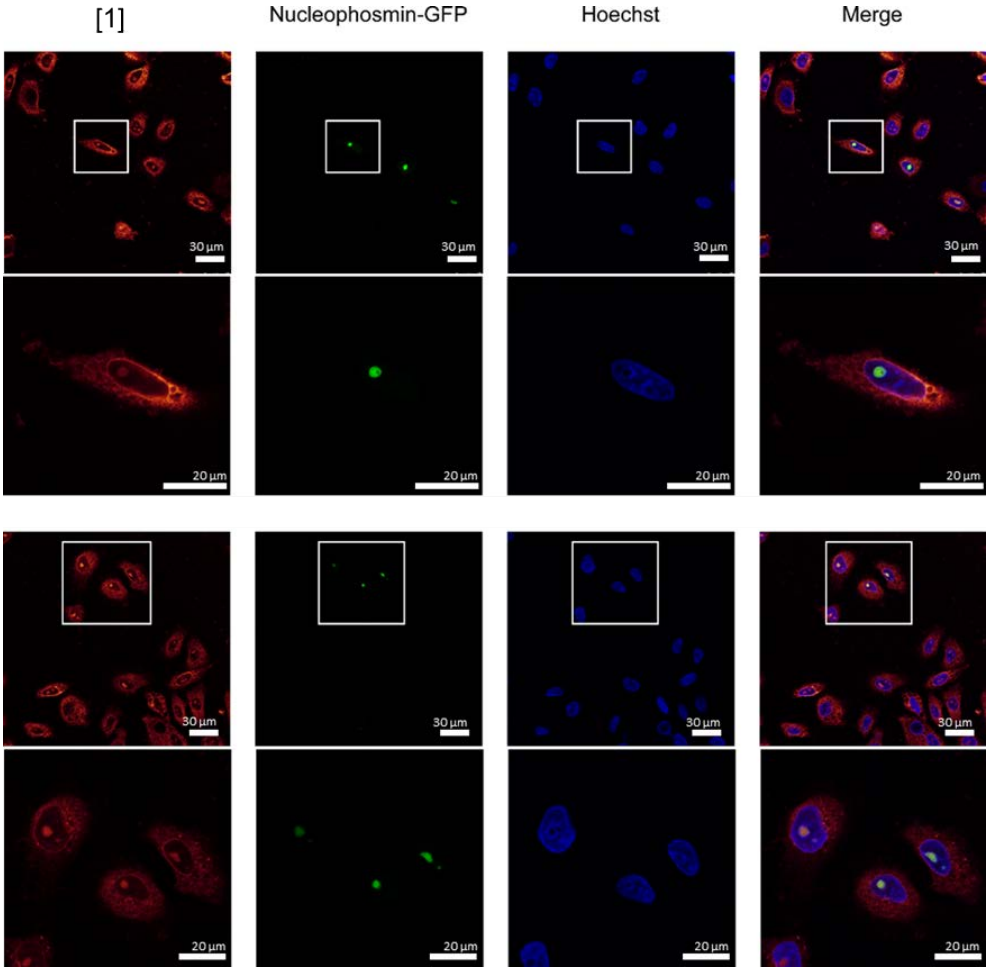


Fig. S26: Co-localization of [**1**] (red) with the nucleoli. HeLa cells were transfected with a plasmid encoding the nucleolar protein nucleophosmin fused to a green fluorescent protein (GFP, green), and nuclei were stained with Hoechst 33342 (blue). Magnifications are indicated by a frame, scale bars, 30 µm and 20 µm, respectively. Concentration of [**1**] was 100 µM.

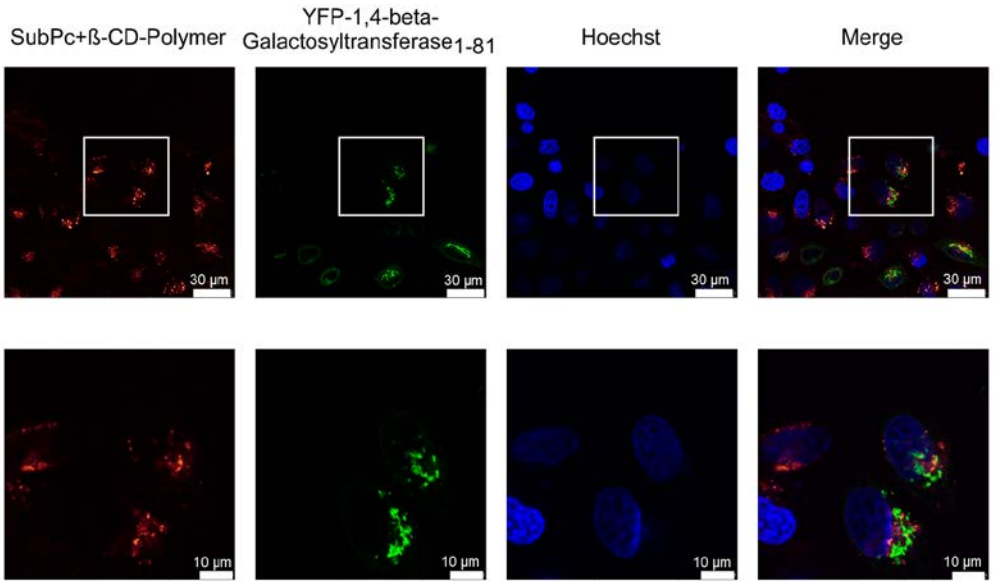


Fig. S27: Co-localization of [**1**] + β-CD-polymer (red) with the golgi apparatus. HeLa cells were transfected with the golgi marker 1,4-beta-Galactosyltransferase$_{1-81}$ fused to a yellow fluorescent protein (YFP, green), and nuclei were stained with Hoechst 33342 (blue). Magnifications are indicated by a frame, scale bars, 30 µm and 10 µm, respectively. Concentration of [**1**] + β-CD-polymer was 100 µM.

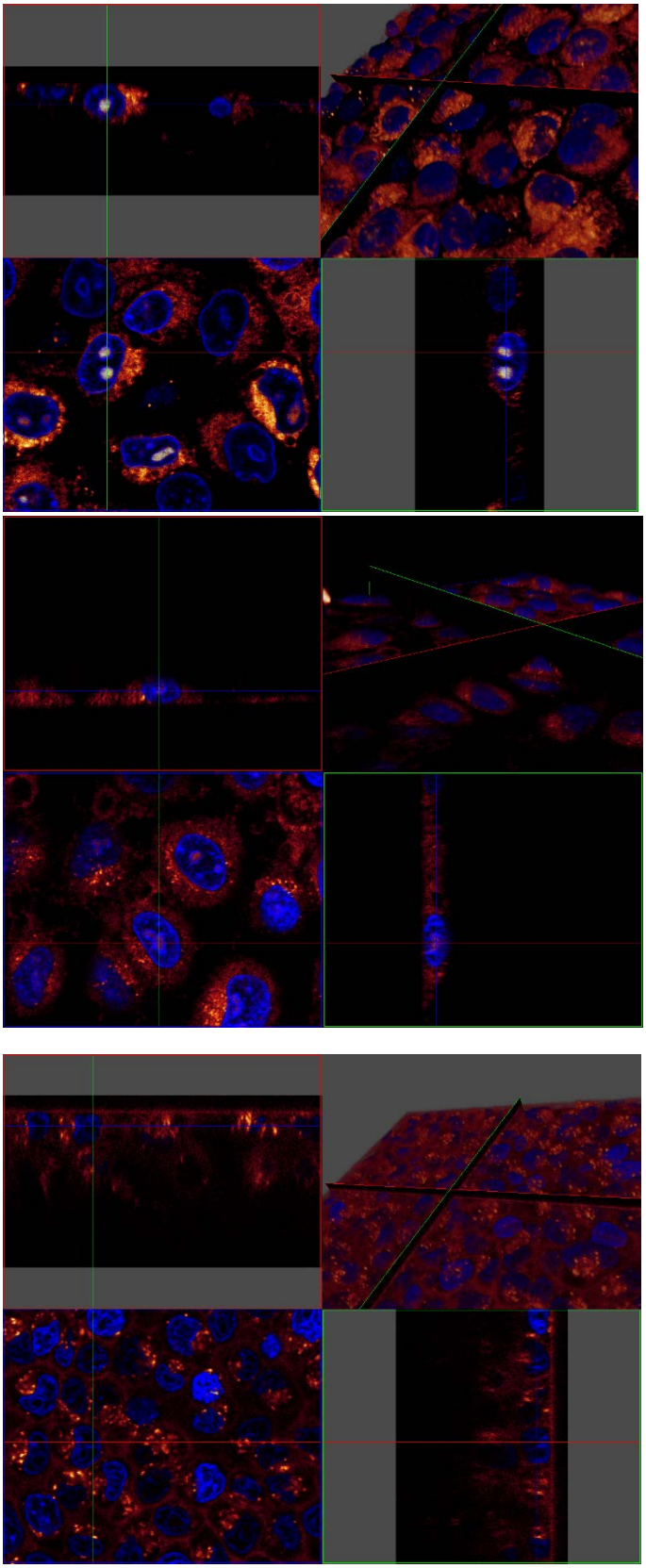


Fig. S28: Fig. S28: 3D-image of HeLa cells treated with Top) [1], Middle) [1] + β-CD, Bottom) [1] + β-CD-polymer. Nuclei were and stained with Hoechst 33342 (blue). The pictures were generated by stacking multiple microscopic images. The lines indicate sections through the same spot (Blue: x-axis, Green: y-axis, Red: z-axis).

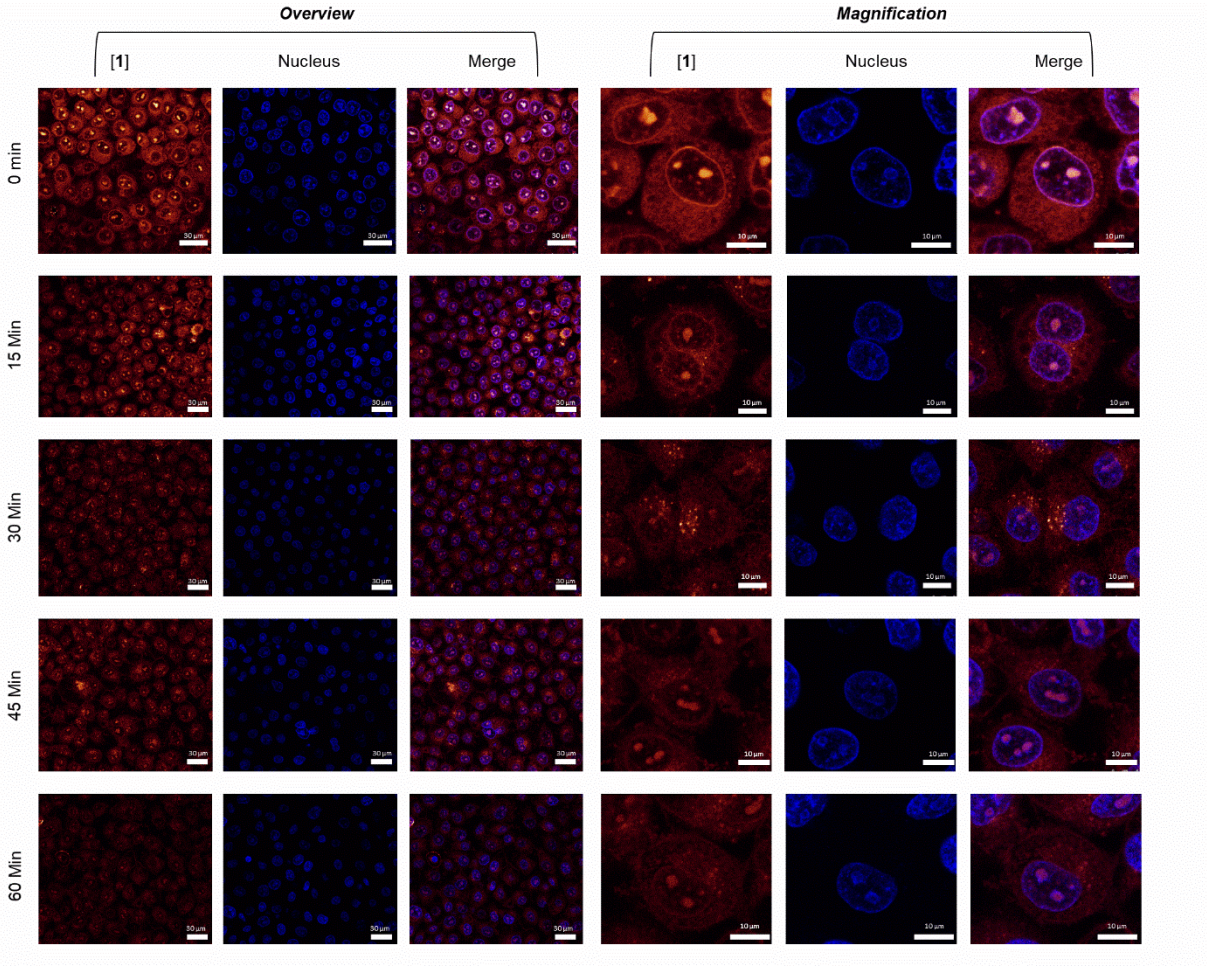


Fig. S29: Intracellular distribution of [**1**] monitored over time. Nuclei were stained with Hoechst 33342 (blue). Scale bars, 30 *µm* and 10 *µm*, respectively. Concentration of [**1**] was 100 µM.

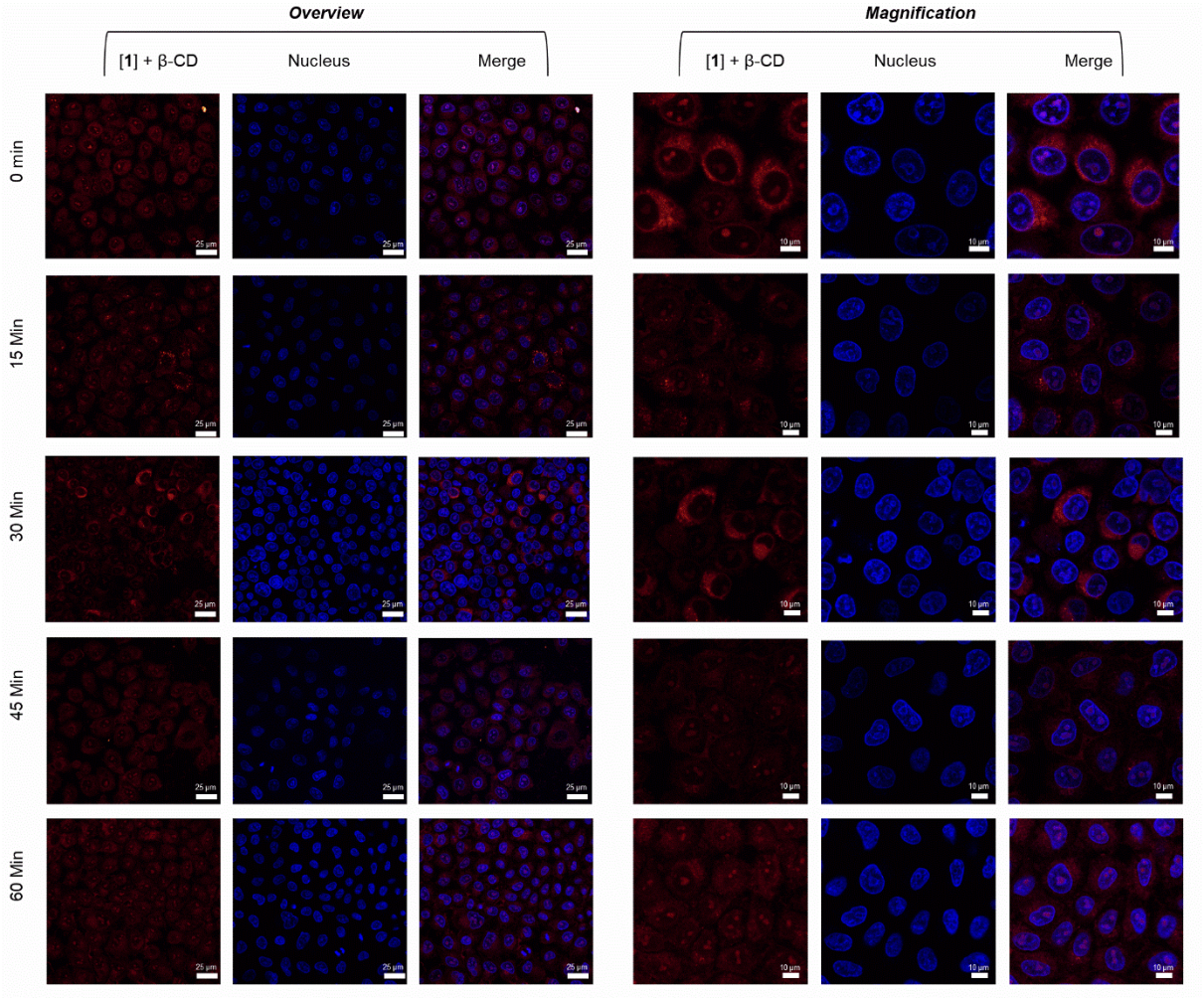


Fig. S30: Intracellular distribution of [**1**] + β-CD monitored over time. Nuclei were stained with Hoechst 33342 (blue). Scale bars, 30 *µm* and 10 *µm*, respectively. Concentration of [**1**] + β-CD was 100 µM.

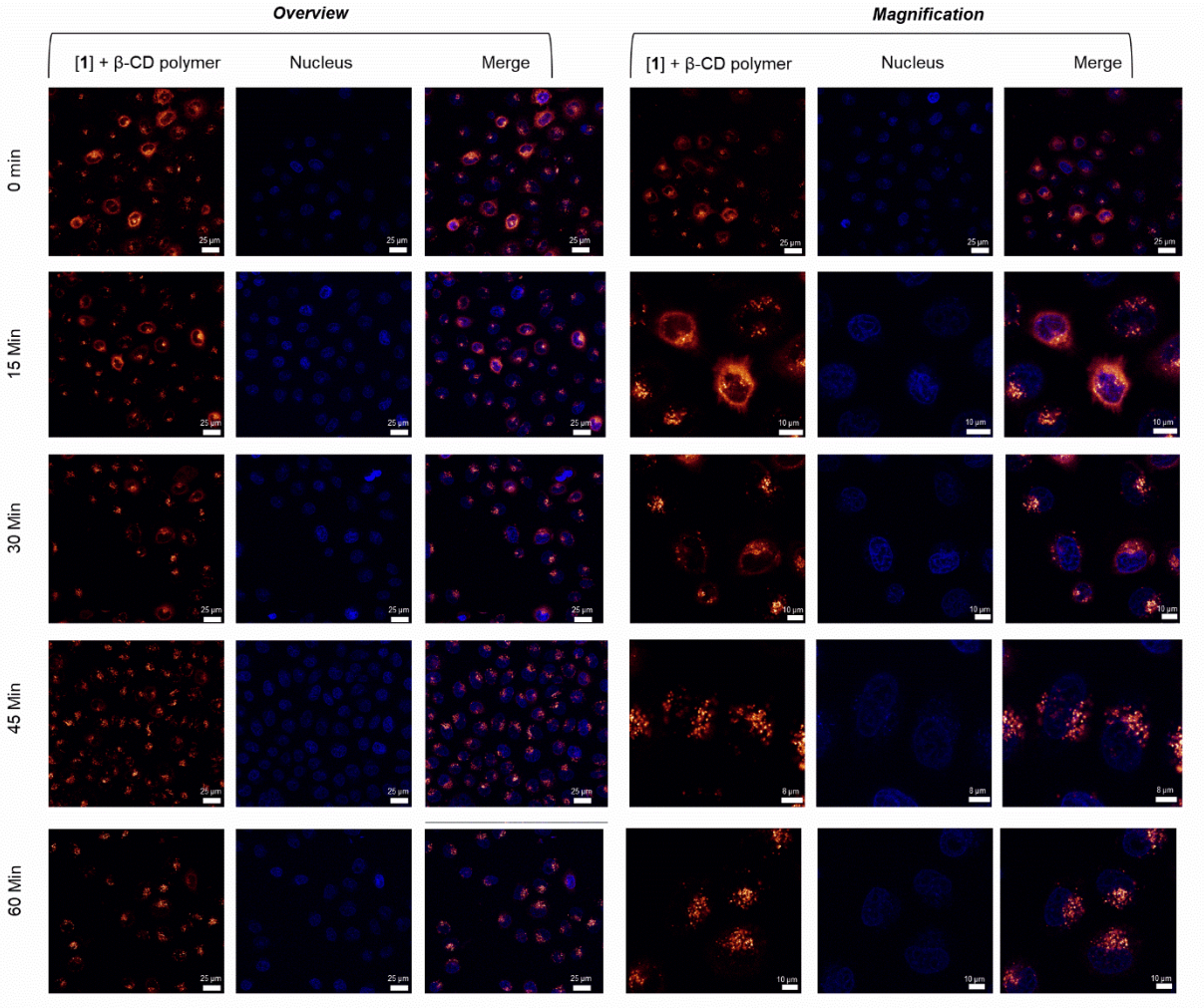


Fig. S31: Intracellular distribution of [**1**] + β-CD-polymer monitored over time. Scale bars, 30 µm and 10 µm, respectively. Concentration of [**1**] + β-CD polymer was 100 µM.

8. Literature

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