

Supporting Information

Photophysical characterization and fluorescence cell imaging applications of 4-N-substituted benzothiadiazoles

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Contents

I. General Information	3
II. Synthesis of the Benzothiadiazole Derivatives 2-15	7
4-(Methylamino)-2,1,3-benzothiadiazole (2).....	7
4-(Dimethylamino)-2,1,3-benzothiadiazole (3)	7
4-(Acetamido)-2,1,3-benzothiadiazole (4).....	7
4-(Butyramido)-2,1,3-benzothiadiazole (5)	8
General procedure for the synthesis of compounds 6-12	8
4-(1-Piperidinyl)-2,1,3-benzothiadiazole (6).....	8
4-(4-Morpholinyl)-2,1,3-benzothiadiazole (7)	9
4-(4-Thiomorpholinyl)-2,1,3-benzothiadiazole (8)	9
4-(4-Methylpiperazinyl)-2,1,3-benzothiadiazole (9).....	9
4-(1-Pyrrolidinyl)-2,1,3-benzothiadiazole (10).....	9
4-(Cyclohexylamino)-2,1,3-benzothiadiazole (11)	10
4-(Phenylamino)-2,1,3-benzothiadiazole (12)	10
4-(Diphenylamino)-2,1,3-benzothiadiazole (13).....	10
4-(L-Phenylalanino)-2,1,3-benzothiadiazole (14).....	11
4-(L-Valino)-2,1,3-benzothiadiazole (15)	11
III. Photophysical Data	12
IV. Lipophilicity (logP) Data	36
V. Computational Results.....	36
VI. Fluorescence Cell Imaging Pictures	39
VII. NMR Spectra.....	50
VIII. Optimized structures from computations	65
IX. References and Notes.....	89

I. General Information

Compounds **2**,^[1] **3**,^[2] **4**,^[3] **5**^[4] and **10**^[5] have previously been reported in the literature.

Materials. All reagents were purchased from Sigma-Aldrich (Merck) or Fluorochem and used without further purification unless otherwise stated. Solvents used for synthesis or photophysical characterization were obtained from Sigma-Aldrich (Merck) or VWR Chemicals and used without further purification unless otherwise indicated. Toluene was distilled prior to use. Aqueous solutions for spectroscopic measurements were prepared with 5% DMSO in distilled water to enhance compound solubility. 4-Amino-2,1,3-benzothiadiazole (**BTD-NH₂**, **1**) was purchased from Sigma-Aldrich (Merck) and purified by sublimation before photophysical characterization and cell studies.

Chromatography. Thin-layer chromatography (TLC) was carried out using aluminum plates coated with silica gel (60F₂₅₄, Merck) and visualized through exposure to UV light ($\lambda = 254$ nm and 365 nm). Purification by column chromatography was performed using silica gel (particle size 40–63 μm , VWR Chemicals).

Chemical characterization. NMR spectra were recorded at 298 K using an Agilent MR400-DD2 instrument at 400 MHz (¹H) and 101 MHz (¹³C). Chemical shifts (δ) are reported in ppm using the residual solvent peak in CDCl₃ ($\delta_{\text{H}} = 7.26$ and $\delta_{\text{C}} = 77.16$ ppm) as internal reference.^[6] Coupling constants (J) are given in Hz and the apparent resonance multiplicity is reported as s (singlet), d (doublet), t (triplet), sext (sextet) or m (multiplet). High-resolution mass spectrometry (HRMS) data (ESI-TOF and APCI) was determined at the Division of Mass Spectrometry, Department of Chemistry, Imperial College London, UK.

Photophysical characterization. UV-vis absorption spectra were acquired on a UV-1650PC Shimadzu instrument at room temperature using quartz cuvettes (10 mm). Absorption maxima (λ_{Amax}) are reported in nm and the molar extinction coefficient (ϵ) in M⁻¹ cm⁻¹ with a margin of error of up to 3%. For each compound three data points with known different concentrations were acquired and the measured absorbances (≤ 1.0) were plotted against the concentrations. The molar extinction coefficients were then determined according to the Beer-Lambert law as the slope of the linear fit. Fluorescence measurements were carried out using a Spex Fluorolog 1680 0.22m Double Spectrometer instrument (experiments shown in Figures S21-24 were performed using a Shimadzu RF-6000 spectrofluorophotometer). Fluorescence quantum yields (Φ_{F}) were determined relative to fluorescein in 20 mM aq. NaOH ($\Phi_{\text{F}} = 0.93$)^[7] or quinine sulfate in 0.1 M aq. H₂SO₄ ($\Phi_{\text{F}} = 0.55$)^[8]. Three fluorescence spectra were recorded per compound per solvent, and integrated peak areas were plotted against the absorbances at the excitation wavelength. The quantum yields were then calculated from the slope of the linear fit *via* the comparative method, with a margin of error of up to 10%. Refractive indices of solvents were adjusted for quantum yield calculations based on the excitation wavelength used.^[9-11] The excitation wavelength (360 or 430 nm) and concentrations for the quantum yield measurements were selected so that the absorbance was below 0.1 to prevent self-absorption effects. Obtained raw data was processed using OriginPro 8 software. Absorption and emission spectra illustrated herein were normalized to the peak maximum of interest. Additionally, emission spectra were smoothed using an FFT filter function with 5 point window. Spectra with weak emission and low signal-to-noise ratio ($\Phi_{\text{F}} < 0.03$) were smoothed using an FFT filter function with 30 point window.

Photostability measurements. Photostability experiments (spectra and time course) were performed on a Shimadzu RF-6000 spectrofluorophotometer. The compound (**11**, **12**, or **13**) was dissolved in toluene and the concentration was adjusted to correspond to an absorbance value at 0.10 ($\lambda_{\text{abs}} = 445$ nm). The solution (2.50 mL) was transferred to a fluorescence cuvette (10x10x35 mm) and a fluorescence spectrum was measured ($\lambda_{\text{ex}} = 445$ nm, ex./em. bandwidth = 5/5 nm). The sample was then irradiated in the fluorometer for 6×5 min periods (*i.e.*, total irradiation time = 30 min). Between these periods the cuvette was briefly shaken to ensure that the measured intensity values represent a homogenous sample solution. The initial intensity of each irradiation period was plotted against the corresponding accumulated irradiation time. Fluorometer settings: $\lambda_{\text{ex}} = 445$ nm; $\lambda_{\text{em}} = 554$ (**11**), 544 (**12**) or 573 nm (**13**); ex./em. bandwidth = 20/1 nm, accumulation time = 50 ms. A new fluorescence spectrum was measured after the total irradiation time (30 min).

Determination of lipophilicity. The octanol/water partition coefficient (logP) of most compounds (**1-5**, **7**, **9**, **14**, **15**) was determined using the shake-flask method. The compound was dissolved in octanol/water 1:1 (4.0 mL) followed by vigorous shaking. After phase separation, a 0.5 mL sample was taken from the octanol phase and 1.0 mL from the water phase. Octanol (0.5 mL), water (1.0 mL) and methanol (3.0 mL) were added to the octanol sample, while octanol (1.0 mL) and methanol (3.0 mL) were added to the water sample. Thus, the final solvent mixture of octanol/water/methanol was 1:1:3 for both samples. Subsequently, the absorption spectra of both samples were recorded and the logP value was determined as

$$\log P = \log \left(\frac{2 \text{Abs}_{\text{octanol}}}{\text{Abs}_{\text{water}}} \right).$$

Reported experimental logP values represent the average of triplicates. LogP values for **6**, **8** and **10-13** were calculated instead due to poor water solubility. The Molinspiration Cheminformatics web service was used to calculate logP values.^[12] Nevertheless, comparison of calculated and experimental logP values indicated that the calculated values are reasonably good approximations (deviations ≤ 0.6).

Computational details. All density functional theory (DFT) calculations were performed using Gaussian 09^[13] software and CAM-B3LYP/6-31G** level of theory. DFT was applied to ground states and time-dependent density functional theory (TDDFT) was applied to excited states. To cover a wide range of solvent polarity, calculations of **1-4** were carried out for solutions in hexane, THF and water. The polarizable continuum model (PCM) was used to account for implicit solvation effects. Explicit solvent effects in terms of hydrogen bonding were allowed for by defining one explicit solvent molecule of THF or water. For **1** and **2** two explicit water molecules were considered; one as hydrogen bond donor, the other as hydrogen bond acceptor (see Figure S25). Vertical transitions (ten excited states) were generally calculated with state-specific solvation. Optimized ground-state geometries were used for absorption and optimized excited-state geometries were used for emission. Optimized geometries were confirmed as energetic minimum by vibrational frequency calculations. Natural transition orbitals of **1-4** were calculated in hexane. To compare the pyramidalization of the amine nitrogen in compounds **6** and **10**, geometry optimizations were performed in hexane using the described method. Hydrogen bond energies were calculated at the same level of theory but without implicit solvation using one explicit water molecule either as hydrogen bond donor (for tertiary amines) or as hydrogen bond acceptor (secondary amines). For primary amine **1**, two explicit water molecules were computed (both as hydrogen bond acceptors) and the resulting energy was divided by two to obtain the averaged hydrogen bond energy per water molecule. The basis set superposition

error was corrected by applying the counterpoise method. Computed structures and orbitals were visualized using Avogadro 1.2.0.^[14-15]

Cell cultures. SK-MEL-28 and MDA-MB-231 were grown in Dulbecco's Modified Eagle Medium (DMEM), high glucose, GlutaMAX™ (Thermo Fisher Scientific, Cat#61965026) supplemented with 10% heat inactivated Fetal Bovine Serum (Thermo Fisher Scientific, Cat#10270106) and Penicillin-Streptomycin (Sigma-Aldrich, Cat#P0781) using 100mm TC treated dishes (VWR, Cat#734-0006) and a humidified incubator at 37 °C with 5% CO₂. Cells were passaged using Trypsin – EDTA Solution (Sigma-Aldrich, Cat#T3924) after washing with Dulbecco's Phosphate-Buffered Saline (DPBS) (Thermo Fisher Scientific, Cat#14190094).

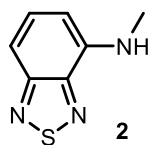
Cell viability assay. Cells were counted using a Countess II Automated Cell Counter (Thermo Fisher Scientific, Cat#AMQAX1000) and seeded in 96 well plates, 10 000 live cells/well, the day before treatment. Compounds were dissolved in dimethyl sulfoxide (DMSO) (Sigma-Aldrich, Cat#317275) and further diluted in extra cell culture medium before cell treatment. Cells were incubated with compounds for 24 hours at a final concentration of 10 μM or 30 μM (*i.e.*, 0.2 vol% or 0.6 vol% DMSO) with DMSO treated cells as control. Cell viability was analyzed after 2.5 hours incubation with Resazurin Reagent (1:10) (Sigma-Aldrich, Cat#R7017) using a Synergy™ HTX Multi-Mode Reader (BioTek), and the fluorescence was detected by excitation at 530 nm and emission at 590 nm. Experiments were run in sextuplets and repeated three to six times.

Cell staining and fluorescence microscopy. SK-MEL-28 and MDA-MB-231 cells were counted (as mentioned above) and seeded in chamber slides (Sarstedt, Cat#94.6140.802) the day before treatment at 80 000 live cells/well. Stock solutions of the compounds in DMSO were prepared at 5.0 mM concentration, which was diluted with cell medium to the indicated final compound concentration used. Live cells were incubated with compounds at a final concentration of 10 μM or 30 μM for 24 hours with DMSO treated cells as control (*i.e.*, 0.2 vol% or 0.6 vol% DMSO). Subsequent fixation was performed using a 4% Buffered Formaldehyde Solution (Histolab Cat#02176) for 15 minutes at room temperature, followed by incubation with DAPI (1:1000) (Sigma-Aldrich, Cat#D9564) diluted in Tris-Buffered Saline (VWR, Cat# 97062-370) with 1% TWEEN® 20 (Sigma-Aldrich, Cat#P1379) (TBST) for 15 minutes at room temperature. Cells not stained with DAPI were incubated with TBST alone. Slides were then washed in TBST and mounted using Fluoromount (Sigma-Aldrich, Cat#F4680). For the staining of fixated cells, cells were first fixated (as described above) two days after seeding, permeabilized using 0.2% Triton X/ PBS for 5 min at 4 °C,^[16] washed with PBS (×2), and then incubated with the compounds in PBS (10 μM; *i.e.*, 0.2 vol% DMSO) for 1 h at 37 °C, followed by washing with PBS and incubation with DAPI (1:1000) diluted in TBST for 15 min at room temperature, washing in TBST and mounting. For lipid supplementation experiments, a stock solution of oleic acid in DMSO was prepared at 50 mM concentration and either added to live cells (100 μM final concentration) and incubated for 24 h together with the compounds (10 μM; *i.e.*, 0.4 vol% DMSO in total) or added to live cells, incubated for 24 h (*i.e.*, 0.2 vol% final DMSO concentration) and then following the procedure for cell fixation and staining of fixated cells. Staining was performed at least twice for each compound to ensure reproducibility. Fluorescence cell imaging pictures were taken using a Leica DMI8 microscope.^[17] The acquired raw data was processed using ImageJ (Fiji distribution).^[18-19] Background subtraction, brightness and contrast adjustments were made to improve visibility.

Colocalization experiments. Organelle localization was investigated using the Organelle Localization IF Antibody Sampler Kit from Cell Signaling (Cat#8653T) and Anti-ADFP antibody [EPR3713] from Abcam (ab108323).^[20] Anti-rabbit IgG Fab2 Alexa Fluor® 647 from Cell Signaling (Cat#4414S) was used as secondary antibody. The procedure for staining living cells (as mentioned above) was followed (10 μ M or 30 μ M final compound concentration). After fixation, cells were permeabilized with 0.2% Triton X/ PBS for 5 min at 4 °C, washed with PBS ($\times 2$), and blocked with 0.5% BSA/ PBS for 30 min at room temperature. The cells were then incubated with the primary antibody diluted in 0.5% BSA/ PBS (200 μ L; 1:1000) for 2 h at room temperature, washed with PBS (3 \times 5 min), followed by incubation with secondary antibody (1:1000) together with DAPI (1:1000) diluted in 0.5% BSA/ PBS (200 μ L) for 1 h at room temperature, washing with PBS (3 \times 5 min) and mounting. Fluorescence microscopy and data processing was performed as described above.

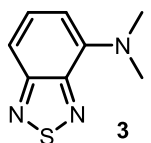
II. Synthesis of the Benzothiadiazole Derivatives 2-15

4-(Methylamino)-2,1,3-benzothiadiazole (2)



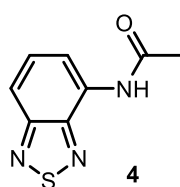
The procedure was adapted from reported literature^[21] as follows: methyl iodide (0.11 mL, 1.77 mmol, 2.7 equiv) was added to a solution of 4-amino-2,1,3-benzothiadiazole (99 mg, 0.66 mmol, 1.0 equiv) and K₂CO₃ (380 mg, 2.75 mmol, 4.2 equiv) in dimethylformamide (2.0 mL). The reaction mixture was stirred at 50 °C for 20.5 h. After cooling down to rt, saturated aq. NaHCO₃ solution (25 mL) was added and the aqueous layer was extracted with EtOAc (4 × 15 mL). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄ and concentrated under reduced pressure. To remove dimethylformamide residues, the crude material was dissolved again in EtOAc (20 mL) and washed thoroughly with brine (4 × 25 mL). The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. Purification by column chromatography (hexane/EtOAc 96:4 to 9:1, R_f = 0.42) gave **2** as an orange solid (39 mg, 36%). ¹H NMR (400 MHz, CDCl₃) δ 7.46 (dd, *J* = 8.8, 7.4 Hz, 1H), 7.24 (dd, *J* = 8.8, 0.8 Hz, 1H), 6.33 (d, *J* = 7.4 Hz, 1H), 5.26 (s_{br}, 1H), 3.04 (d, *J* = 4.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 155.9, 148.0, 141.5, 132.0, 108.3, 101.0, 30.2. HRMS (ESI-TOF) calcd for [C₇H₇N₃S + H]⁺ 166.0439; found 166.0443.

4-(Dimethylamino)-2,1,3-benzothiadiazole (3)



The procedure was adapted from reported literature^[22] as follows: 4-amino-2,1,3-benzothiadiazole (97 mg, 0.64 mmol, 1.0 equiv) was dissolved in glacial acetic acid (12 mL) under nitrogen atmosphere. Paraformaldehyde (366 mg, 12.2 mmol, 19 equiv) was added followed by NaBH₃CN (457 mg, 7.27 mmol, 11 equiv). The reaction mixture was stirred at rt for 26 h. The mixture was carefully basified with 3 M aq. NaOH solution (75 mL) and then extracted with CH₂Cl₂ (4 × 20 mL). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. Purification by column chromatography (hexane/EtOAc 96:4, R_f = 0.29; then pentane/Et₂O 95:5, R_f = 0.35) gave **3** as an orange-red oil (49 mg, 42%). ¹H NMR (400 MHz, CDCl₃) δ 7.47 – 7.41 (m, 2H), 6.56 (d_{br}, *J* = 6.7 Hz, 1H), 3.27 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 157.0, 149.4, 144.5, 130.9, 111.3, 109.1, 42.7. HRMS (ESI-TOF) calcd for [C₈H₉N₃S + H]⁺ 180.0595; found 180.0598.

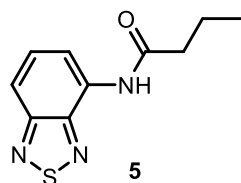
4-(Acetamido)-2,1,3-benzothiadiazole (4)



The procedure was adapted from reported literature^[23] as follows: pyridine (0.10 mL, 1.24 mmol, 2.0 equiv) was added to a solution of 4-amino-2,1,3-benzothiadiazole (94 mg, 0.62 mmol, 1.0 equiv) in dry CH₂Cl₂ (1.0 mL) under nitrogen atmosphere. The mixture was cooled down to 0 °C before acetyl chloride (52 μL, 0.73 mmol, 1.2 equiv) was added dropwise. The reaction mixture was then allowed to reach rt and further stirred for 3.5 h. CH₂Cl₂ (1 mL) was added and the mixture was washed with aqueous HCl solution (1 M, 1.5 mL), water (1.5 mL) and brine (1.5 mL). The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. Purification by column chromatography (hexane/EtOAc 7:3, R_f = 0.28) gave **4** as a colorless, crystalline solid (111 mg, 92%). ¹H NMR (400 MHz, CDCl₃) δ 8.47 (d_{br}, *J* = 7.3 Hz, 2H), 7.67 (dd, *J* = 8.9, 1.0 Hz, 1H), 7.59 (dd, *J* = 8.9, 7.3 Hz, 1H), 2.34 (s,

3H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.8, 154.9, 147.8, 131.3, 130.1, 115.9, 115.1, 25.0. HRMS (ESI-TOF) calcd for $[\text{C}_8\text{H}_7\text{N}_3\text{OS} + \text{H}]^+$ 194.0388; found 194.0395.

4-(Butyramido)-2,1,3-benzothiadiazole (5)

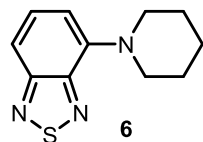


The procedure was adapted from reported literature^[23] as follows: pyridine (0.11 mL, 1.37 mmol, 2.1 equiv) was added to a solution of 4-amino-2,1,3-benzothiadiazole (99 mg, 0.66 mmol, 1.0 equiv) in dry CH_2Cl_2 (1.0 mL) under nitrogen atmosphere. The mixture was cooled down to 0 °C before butyryl chloride (90 μL , 0.87 mmol, 1.3 equiv) was added dropwise. The reaction mixture was allowed to reach rt and was then further stirred for 2.5 h. CH_2Cl_2 (5 mL) was added and the mixture was washed with aqueous HCl solution (1 M, 5 mL), water (5 mL) and brine (5 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography (hexane/ CH_2Cl_2 1:3 to 0:1, R_f (CH_2Cl_2) = 0.38) gave **5** as a yellowish solid (94 mg, 65%). ^1H NMR (400 MHz, CDCl_3) δ 8.48 (d, J = 7.3 Hz, 1H), 8.45 (s_{br} , 1H), 7.65 (dd, J = 8.9, 1.1 Hz, 1H), 7.57 (dd, J = 8.9, 7.3 Hz, 1H), 2.51 (t, J = 7.4 Hz, 2H), 1.83 (sext, J = 7.4 Hz, 2H), 1.05 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.8, 154.9, 147.8, 131.3, 130.1, 115.7, 115.0, 39.9, 19.1, 13.9. HRMS (ESI-TOF) calcd for $[\text{C}_{10}\text{H}_{11}\text{N}_3\text{OS} + \text{H}]^+$ 222.0701; found 222.0701.

General procedure for the synthesis of compounds 6-12

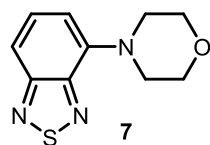
The procedure was adapted from reported literature^[24] as follows: 4-bromo-2,1,3-benzothiadiazole (100 mg, 0.47 mmol, 1.0 equiv) and the relevant amine (0.51 mmol, 1.1 equiv) were added to a suspension of *t*-BuOK (63 mg, 0.56 mmol, 1.2 equiv) and PEPPSI-IPr (7 mg, 0.01 mmol, 2 mol%) in dry toluene (1.6 mL). The reaction mixture was stirred at 120 °C for 3.5 h under nitrogen atmosphere, unless otherwise specified. The mixture was allowed to cool down to rt, followed by filtration through Celite. The solvent was removed under reduced pressure and the crude product was purified by column chromatography.

4-(1-Piperidinyl)-2,1,3-benzothiadiazole (6)



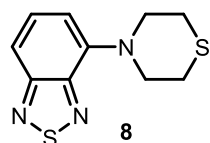
The compound was synthesized according to the general procedure described above using piperidine (51 μL , 0.51 mmol, 1.1 equiv). Purification by column chromatography (hexane/EtOAc 96:4, R_f = 0.28; then hexane/ CH_2Cl_2 4:1 to 1:1) gave **6** as an orange-brown solid (86 mg, 85%). ^1H NMR (400 MHz, CDCl_3) δ 7.50 (dd, J = 8.7, 1.1 Hz, 1H), 7.44 (dd, J = 8.7, 7.2 Hz, 1H), 6.72 (dd, J = 7.2, 1.1 Hz, 1H), 3.49 – 3.46 (m, 4H), 1.87 – 1.82 (m, 4H), 1.71 – 1.65 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 156.8, 150.1, 145.5, 130.7, 113.1, 111.5, 51.8, 26.1, 24.7. HRMS (ESI-TOF) calcd for $[\text{C}_{11}\text{H}_{13}\text{N}_3\text{S} + \text{H}]^+$ 220.0906; found 220.0908.

4-(4-Morpholinyl)-2,1,3-benzothiadiazole (7)



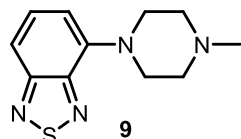
The compound was synthesized according to the general procedure, on half the scale described above, using morpholine (22 μ L, 0.25 mmol, 1.1 equiv). Purification by column chromatography (hexane/EtOAc 9:1, R_f = 0.21) gave **7** as a yellow-orange solid (37 mg, 73%). ^1H NMR (400 MHz, CDCl_3) δ 7.57 (dd, J = 8.8, 0.9 Hz, 1H), 7.48 (dd, J = 8.8, 7.3 Hz, 1H), 6.75 (d, J = 7.3 Hz, 1H), 4.01 – 3.98 (m, 4H), 3.56 – 3.53 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 156.8, 149.7, 144.1, 130.5, 114.2, 111.5, 67.0, 50.7. HRMS (ESI-TOF) calcd for $[\text{C}_{10}\text{H}_{11}\text{N}_3\text{OS} + \text{H}]^+$ 222.0701; found 222.0707.

4-(4-Thiomorpholinyl)-2,1,3-benzothiadiazole (8)



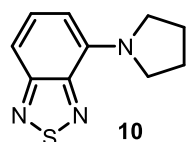
The compound was synthesized according to the general procedure described above using thiomorpholine (52 μ L, 0.51 mmol, 1.1 equiv). Purification by column chromatography (hexane/EtOAc 96:4, R_f = 0.23) gave **8** as a yellow-orange solid (64 mg, 59%). ^1H NMR (400 MHz, CDCl_3) δ 7.55 (dd, J = 8.7, 1.0 Hz, 1H), 7.46 (dd, J = 8.7, 7.3 Hz, 1H), 6.77 (d, J = 7.3 Hz, 1H), 3.83 – 3.81 (m, 4H), 2.92 – 2.90 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 156.8, 149.9, 144.5, 130.5, 114.0, 112.4, 53.0, 27.6. HRMS (ESI-TOF) calcd for $[\text{C}_{10}\text{H}_{11}\text{N}_3\text{S}_2 + \text{H}]^+$ 238.0473; found 238.0474.

4-(4-Methylpiperazinyl)-2,1,3-benzothiadiazole (9)



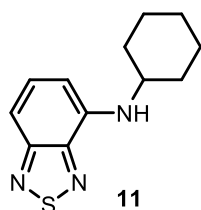
The compound was synthesized according to the general procedure described above using 1-methylpiperazine (57 μ L, 0.51 mmol, 1.1 equiv). Purification by column chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$ 95:5, R_f = 0.18) gave **9** as a dark yellow solid (59 mg, 54%). ^1H NMR (400 MHz, CDCl_3) δ 7.54 (dd, J = 8.7, 1.0 Hz, 1H), 7.46 (dd, J = 8.7, 7.3 Hz, 1H), 6.73 (dd, J = 7.3, 1.0 Hz, 1H), 3.58 (t, J = 5.0 Hz, 4H), 2.72 (t, J = 5.0 Hz, 4H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 156.8, 149.8, 144.3, 130.6, 113.7, 111.6, 55.2, 50.2, 46.3. HRMS (ESI-TOF) calcd for $[\text{C}_{11}\text{H}_{14}\text{N}_4\text{S} + \text{H}]^+$ 235.1017; found 235.1011.

4-(1-Pyrrolidinyl)-2,1,3-benzothiadiazole (10)



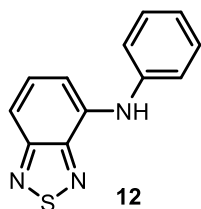
The compound was synthesized according to the general procedure described above using pyrrolidine (43 μ L, 0.51 mmol, 1.1 equiv). Purification by column chromatography (hexane/EtOAc 96:4, R_f = 0.41) gave **10** as an orange solid (68 mg, 71%). ^1H NMR (400 MHz, CDCl_3) δ 7.40 (dd, J = 8.6, 7.6 Hz, 1H), 7.20 (d, J = 8.6 Hz, 1H), 6.23 (d, J = 7.6 Hz, 1H), 3.84 – 3.81 (m, 4H), 2.08 – 2.02 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 157.2, 148.5, 141.3, 131.6, 107.3, 104.0, 50.4, 25.7. HRMS (ESI-TOF) calcd for $[\text{C}_{10}\text{H}_{11}\text{N}_3\text{S} + \text{H}]^+$ 206.0752; found 206.0750.

4-(Cyclohexylamino)-2,1,3-benzothiadiazole (11)



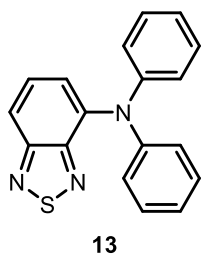
The compound was synthesized according to the general procedure described above using cyclohexylamine (60 μ L, 0.52 mmol, 1.1 equiv) and stirring the reaction mixture at 120 $^{\circ}$ C for 4.5 h. Purification by column chromatography (hexane/EtOAc 96:4, R_f = 0.23) gave **11** as an orange-brown oil (76 mg, 70%). ^1H NMR (400 MHz, CDCl_3) δ 7.41 (dd, J = 8.7, 7.5 Hz, 1H), 7.18 (d, J = 8.7 Hz, 1H), 6.34 (d, J = 7.5 Hz, 1H), 5.18 (d, J = 6.3 Hz, 1H), 3.49 – 3.41 (m, 1H), 2.17 – 2.13 (m, 2H), 1.86 – 1.80 (m, 2H), 1.71 – 1.65 (m, 1H), 1.49 – 1.24 (m, 5H). ^{13}C NMR (101 MHz, CDCl_3) δ 156.0, 148.1, 139.4, 132.1, 107.5, 101.3, 51.6, 32.9, 26.0, 25.0. HRMS (ESI-TOF) calcd for $[\text{C}_{12}\text{H}_{15}\text{N}_3\text{S} + \text{H}]^+$ 234.1065; found 234.1072.

4-(Phenylamino)-2,1,3-benzothiadiazole (12)



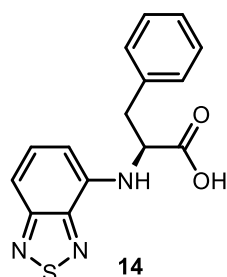
The compound was synthesized according to the general procedure described above using aniline (47 μ L, 0.52 mmol, 1.1 equiv). The reaction mixture was stirred at 120 $^{\circ}$ C for 4 h, then allowed to cool down to rt and further stirred overnight. Purification by column chromatography (hexane/ CH_2Cl_2 2:1, R_f = 0.20) gave **12** as an orange solid (80 mg, 76%). ^1H NMR (400 MHz, CDCl_3) δ 7.45 (dd, J = 8.8, 7.2 Hz, 1H), 7.42 – 7.38 (m, 3H), 7.36 – 7.33 (m, 2H), 7.15 (dd, J = 7.2, 1.1 Hz, 1H), 7.13 – 7.08 (m, 1H); integrals indicate N-H signal at around 7.15 ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 155.9, 148.4, 140.7, 136.2, 131.4, 129.7, 123.3, 120.6, 110.9, 104.8. HRMS (ESI-TOF) calcd for $[\text{C}_{12}\text{H}_9\text{N}_3\text{S} + \text{H}]^+$ 228.0595; found 228.0603.

4-(Diphenylamino)-2,1,3-benzothiadiazole (13)



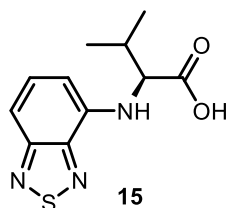
The procedure was adapted from reported literature^[25] as follows: $\text{Pd}_2(\text{dba})_3$ (23 mg, 0.03 mmol, 11 mol%), RuPhos (27 mg, 0.06 mmol, 12 mol%) and Cs_2CO_3 (316 mg, 0.97 mmol, 2.1 equiv) were added to a solution of freshly recrystallized diphenylamine (127 mg, 0.75 mmol, 1.6 equiv) and 4-bromo-2,1,3-benzothiadiazole (100 mg, 0.47 mmol, 1.0 equiv) in dry toluene (6.0 mL). The reaction mixture was stirred at 120 $^{\circ}$ C for 24 h under nitrogen atmosphere. After cooling down to rt, the mixture was poured into water (40 mL) and extracted with CH_2Cl_2 (4 \times 20 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography (hexane/ CH_2Cl_2 1:1, R_f = 0.37) gave **13** as an orange solid (49 mg, 35%). ^1H NMR (400 MHz, CDCl_3) δ 7.73 (dd, J = 8.8, 0.9 Hz, 1H), 7.48 (dd, J = 8.8, 7.4 Hz, 1H), 7.29 – 7.24 (m, 4H), 7.16 (dd, J = 7.4, 0.9 Hz, 1H), 7.09 – 7.04 (m, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 156.8, 151.3, 147.9, 140.3, 130.1, 129.4, 124.3, 123.5, 123.3, 116.7. HRMS (ESI-TOF) calcd for $[\text{C}_{18}\text{H}_{13}\text{N}_3\text{S} + \text{H}]^+$ 304.0908; found 304.0906.

4-(*L*-Phenylalano)-2,1,3-benzothiadiazole (**14**)



The procedure was adapted from reported literature^[26] as follows: CuI (9 mg, 0.047 mmol, 10 mol%) was added to a solution of *L*-phenylalanine (76 mg, 0.46 mmol, 1.0 equiv), 4-bromo-2,1,3-benzothiadiazole (100 mg, 0.46 mmol, 1.0 equiv) and K₂CO₃ (99 mg, 0.71 mmol, 1.5 equiv) in dimethylacetamide (1.6 mL). The reaction mixture was stirred at 90 °C for 5 d. After cooling down to rt, the mixture was diluted with EtOAc (5 mL) and water (2.5 mL). While cooling to ca 10 °C, concentrated HCl solution was added dropwise until pH 2 was reached. The organic layer was separated and the aqueous layer was extracted with EtOAc (5 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried over Na₂SO₄. The solvent was concentrated under reduced pressure and residual dimethylacetamide was partially removed by co-evaporation with toluene. Recrystallization from CH₂Cl₂/hexane (2:1) gave **14** as orange-red crystals (36 mg, 26%). ¹H NMR (400 MHz, CDCl₃) δ 7.40 (dd, *J* = 8.9, 7.3 Hz, 1H), 7.32 – 7.24 (m, 4H), 6.34 (d, *J* = 7.3 Hz, 1H), 5.68 (s_{br}, 1H), 4.55 (dd, *J* = 6.9, 5.7 Hz, 1H), 3.39 (dd, *J* = 13.9, 5.7 Hz, 1H), 3.26 (dd, *J* = 13.9, 6.9 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 176.9, 155.7, 147.8, 138.5, 135.7, 131.5, 129.4, 128.9, 127.5, 110.2, 102.9, 57.2, 38.3. HRMS (APCI) calcd for [C₁₅H₁₃N₃O₂S + H]⁺ 300.0801; found 300.0806.

4-(*L*-Valino)-2,1,3-benzothiadiazole (**15**)



The procedure was adapted from reported literature^[26] as follows: CuI (11 mg, 0.058 mmol, 12 mol%) was added to a solution of *L*-valine (54 mg, 0.46 mmol, 1.0 equiv), 4-bromo-2,1,3-benzothiadiazole (101 mg, 0.47 mmol, 1.0 equiv) and K₂CO₃ (104 mg, 0.75 mmol, 1.6 equiv) in dimethylacetamide (1.6 mL). The reaction mixture was stirred at 90 °C for 6 d. After cooling down to rt, the mixture was diluted with EtOAc (7 mL) and water (5 mL). While cooling to ca 10 °C, concentrated HCl solution was added dropwise until pH 2 was reached. The organic layer was separated and the aqueous layer was extracted with EtOAc (4 × 10 mL). The combined organic layers were washed with brine (2 × 20 mL) and dried over Na₂SO₄. The solvent was concentrated under reduced pressure and residual dimethylacetamide was partially removed by co-evaporation with toluene. Purification by column chromatography (CH₂Cl₂/MeOH 10:0 to 9:1, *R*_f = 0.48; then CH₂Cl₂/acetone/MeOH 100:20:5, *R*_f = 0.26) gave **15** as a dark orange solid (43 mg, 36%). ¹H NMR (400 MHz, CDCl₃) δ 7.40 (dd, *J* = 8.8, 7.3 Hz, 1H), 7.29 (dd, *J* = 8.8, 0.8 Hz, 1H), 6.36 (d, *J* = 7.3 Hz, 1H), 5.62 (s_{br}, 1H), 4.08 (d, *J* = 5.6 Hz, 1H), 2.42 – 2.30 (m, 1H), 1.15 (dd, *J* = 13.2, 6.8 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 177.8, 155.8, 147.9, 139.3, 131.6, 109.7, 102.6, 61.8, 31.4, 19.4, 18.6. HRMS (ESI-TOF) calcd for [C₁₁H₁₃N₃O₂S + H]⁺ 252.0807; found 252.0810.

III. Photophysical Data

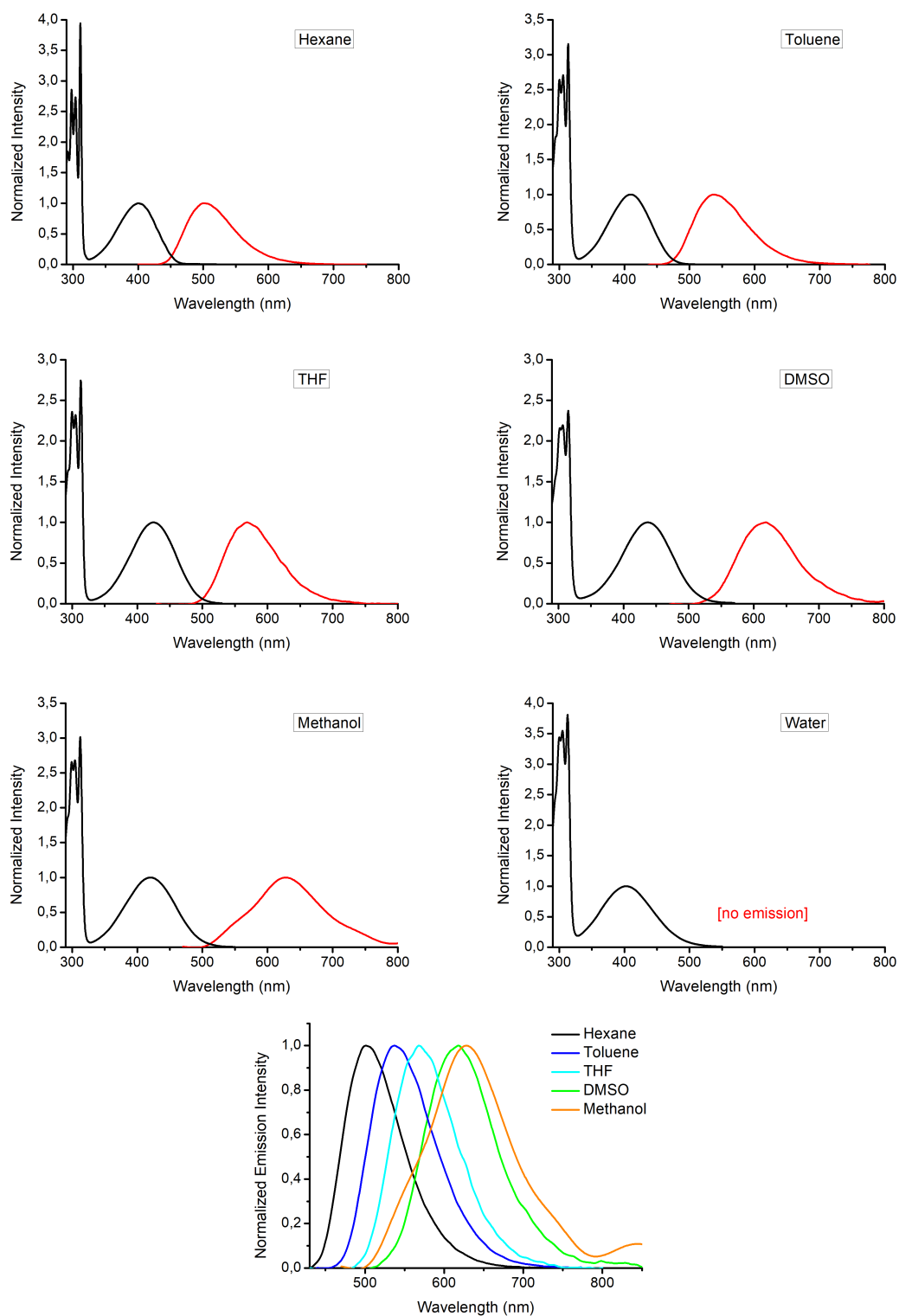
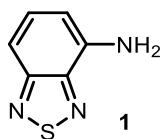


Figure S1. Normalized UV-vis absorption (black) and emission spectra (red) of **1** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

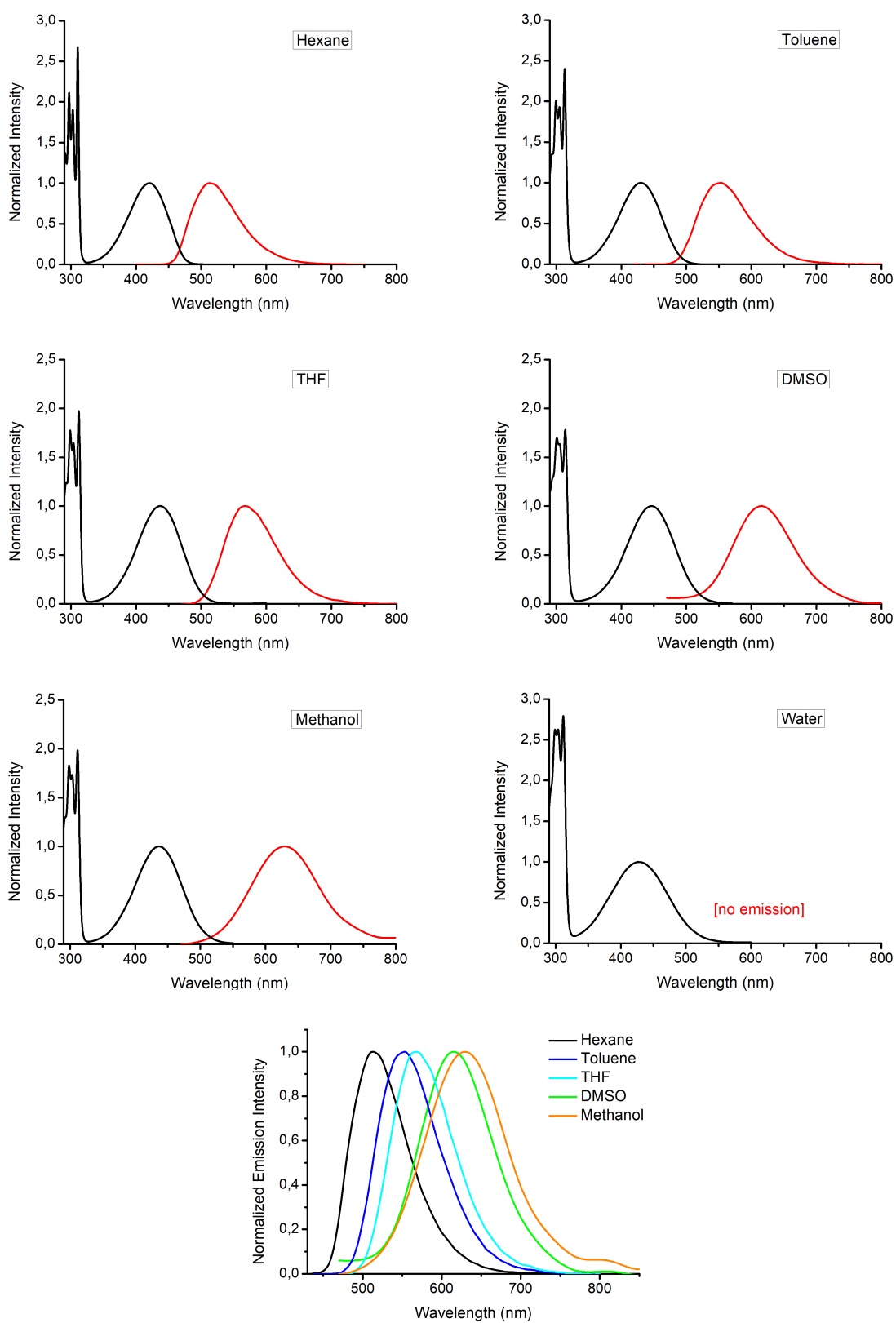
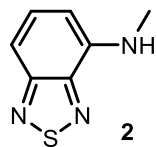


Figure S2. Normalized UV-vis absorption (black) and emission spectra (red) of **2** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

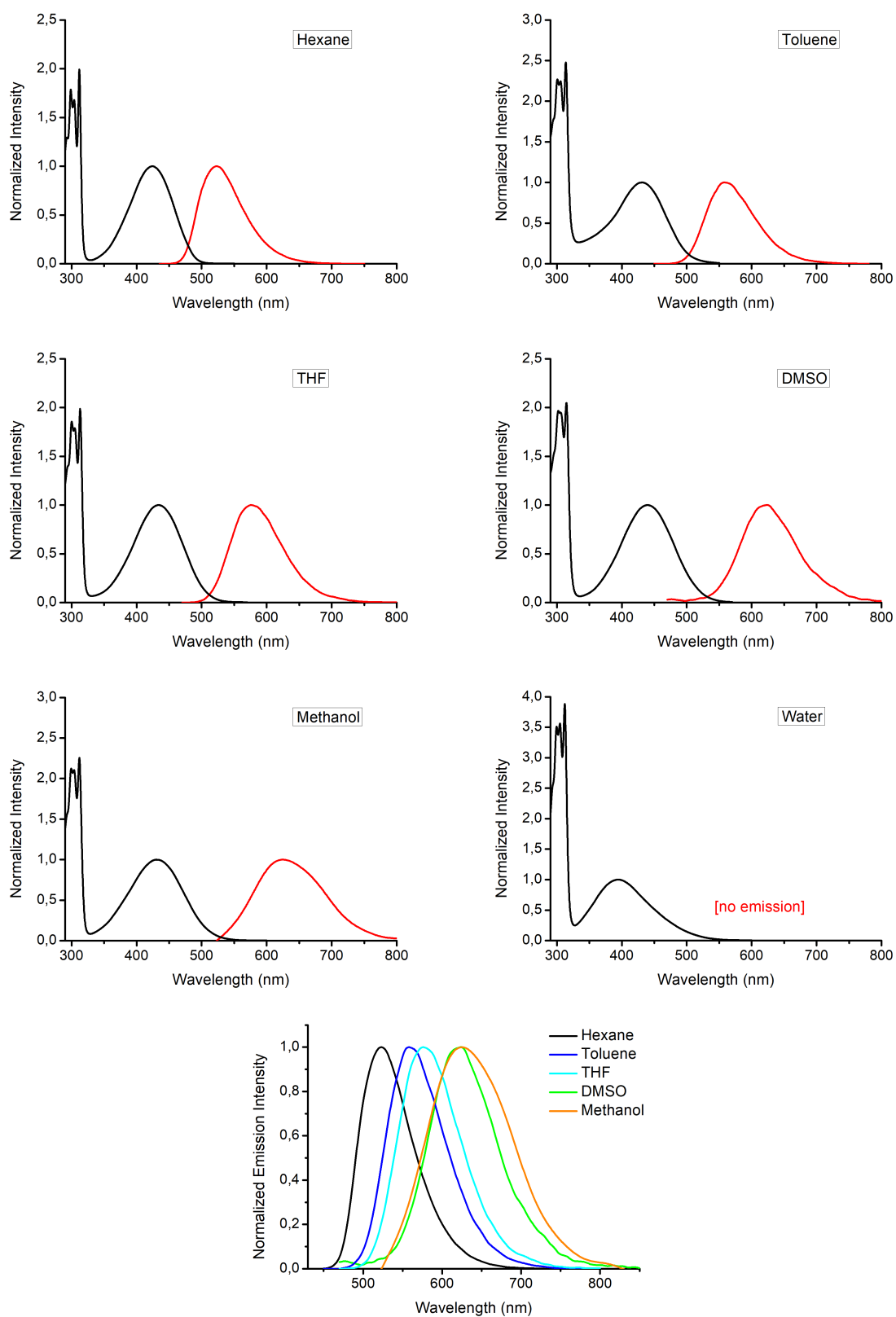
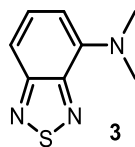


Figure S3. Normalized UV-vis absorption (black) and emission spectra (red) of **3** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

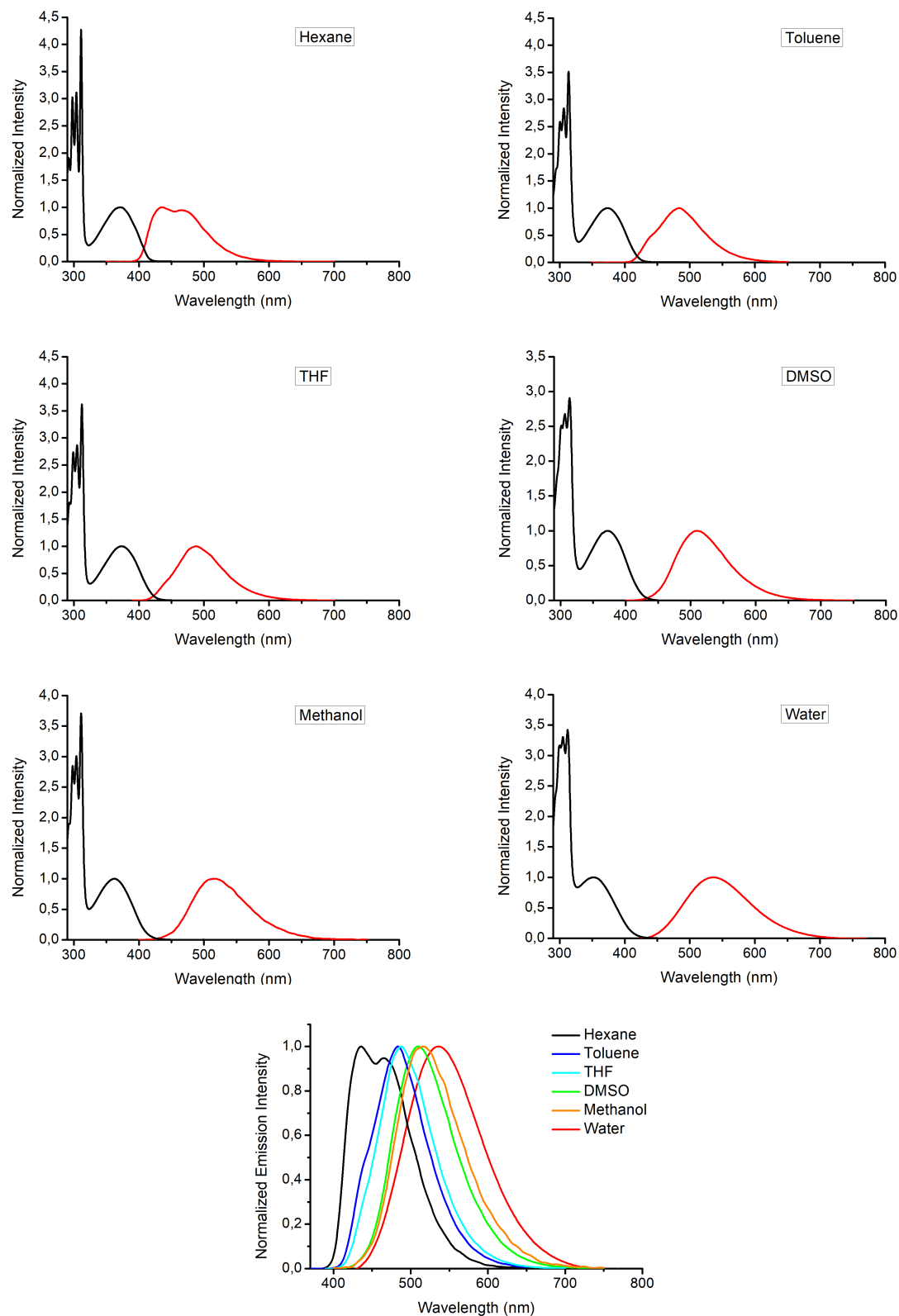
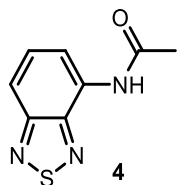


Figure S4. Normalized UV-vis absorption (black) and emission spectra (red) of **4** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

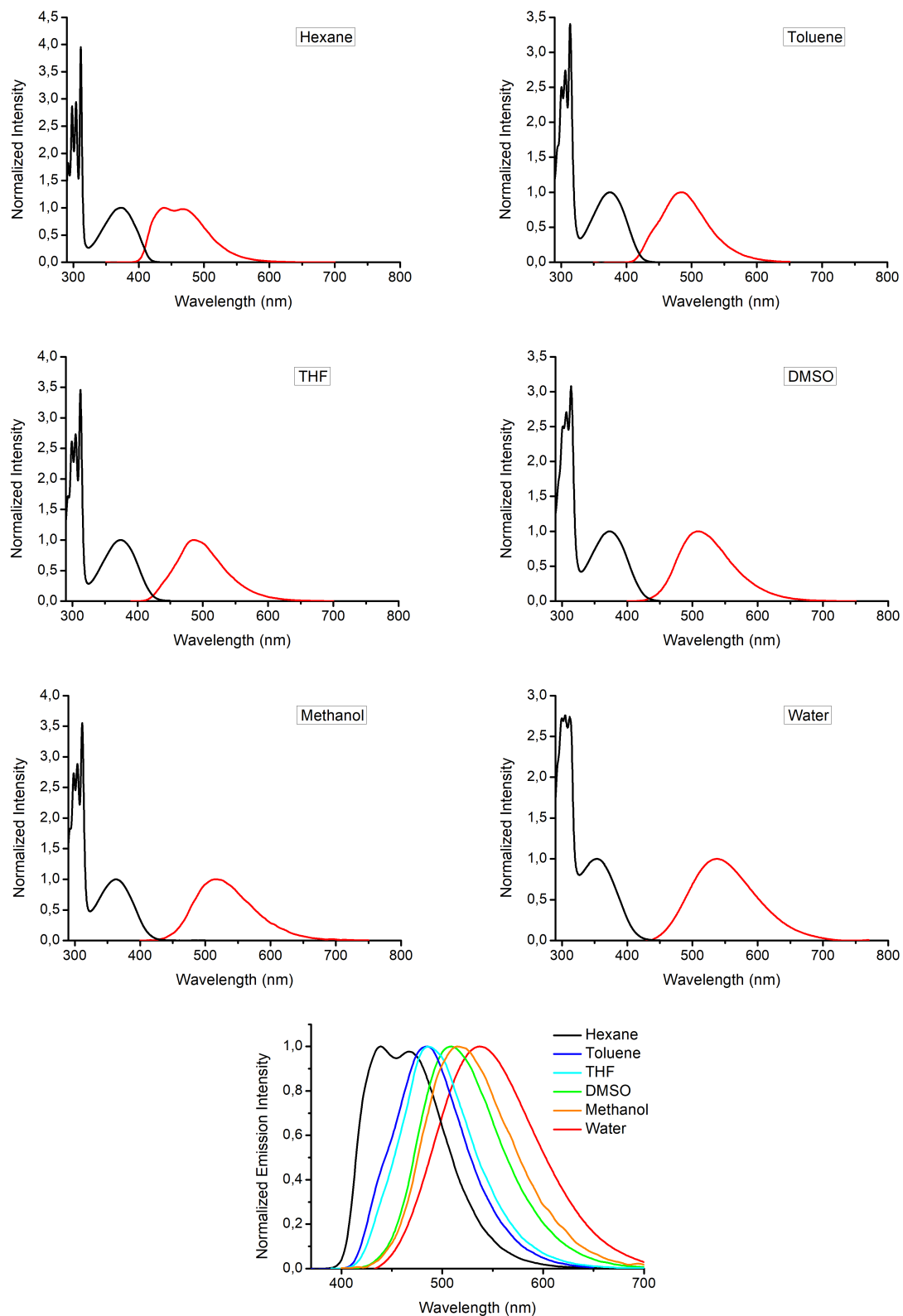
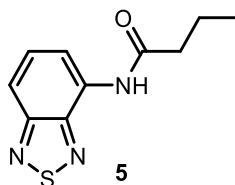


Figure S5. Normalized UV-vis absorption (black) and emission spectra (red) of **5** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

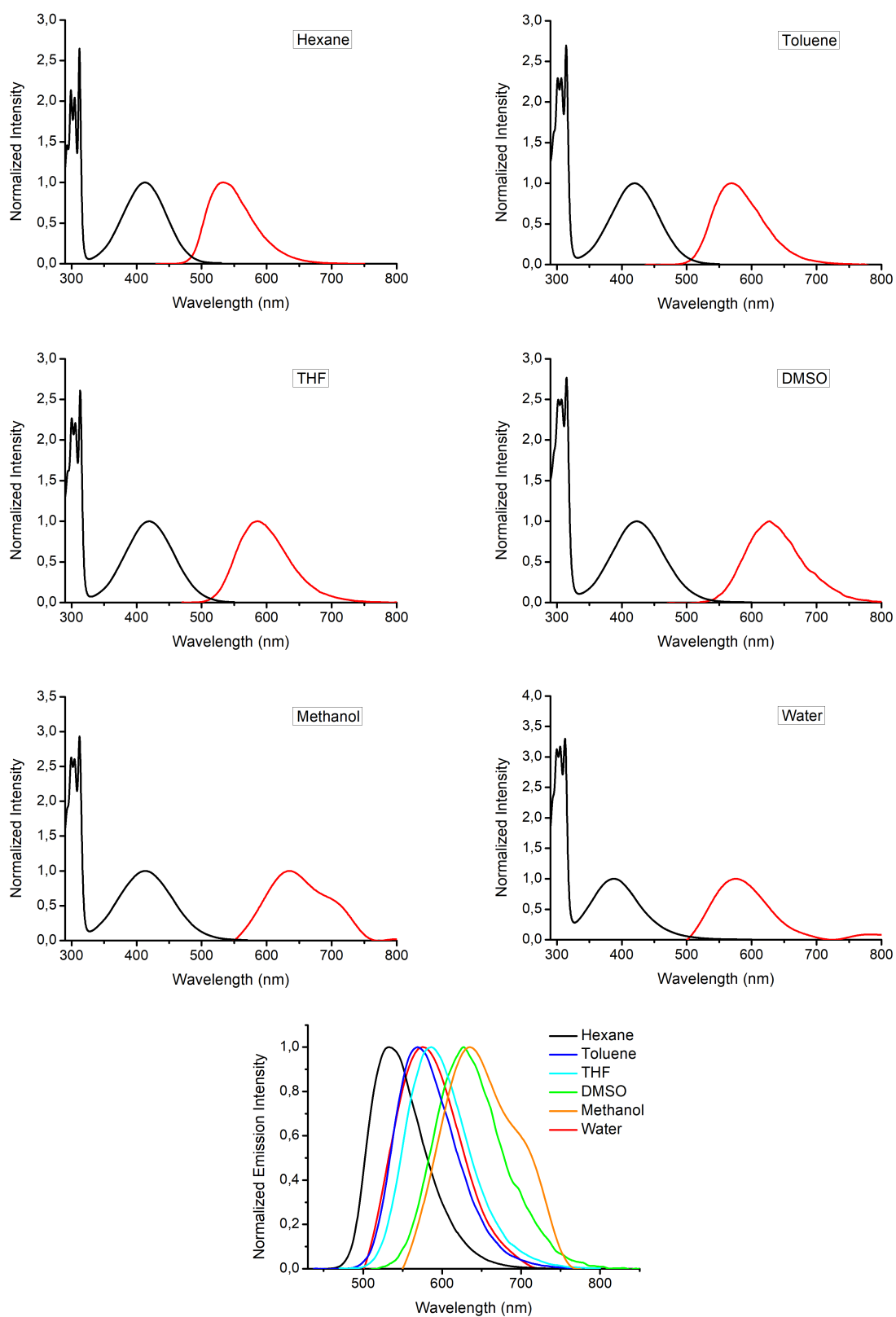
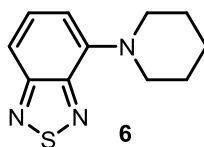


Figure S6. Normalized UV-vis absorption (black) and emission spectra (red) of **6** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission. The observed emission in water likely originated from aggregates.

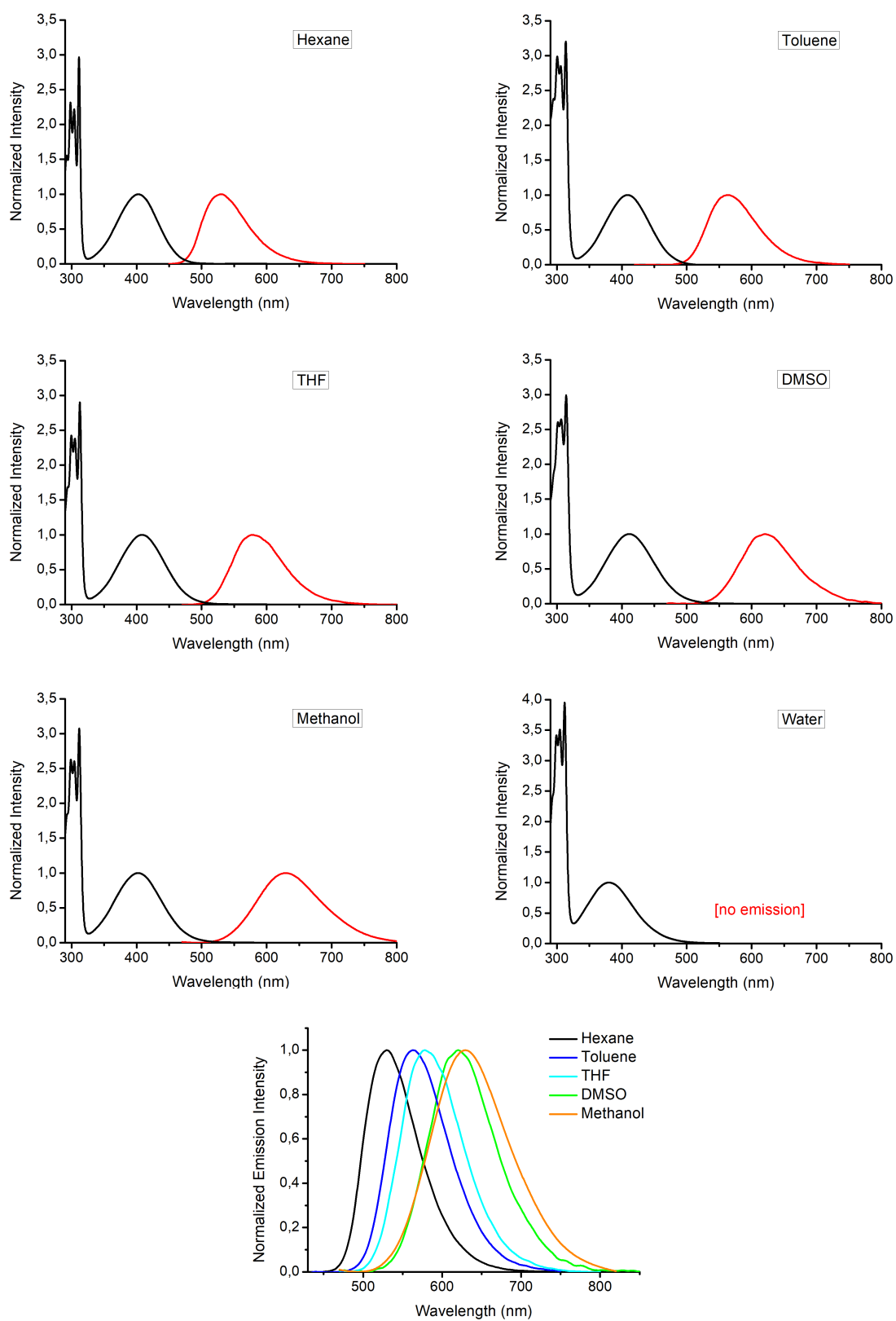
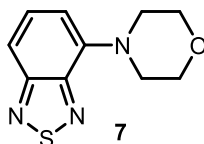


Figure S7. Normalized UV-vis absorption (black) and emission spectra (red) of **7** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

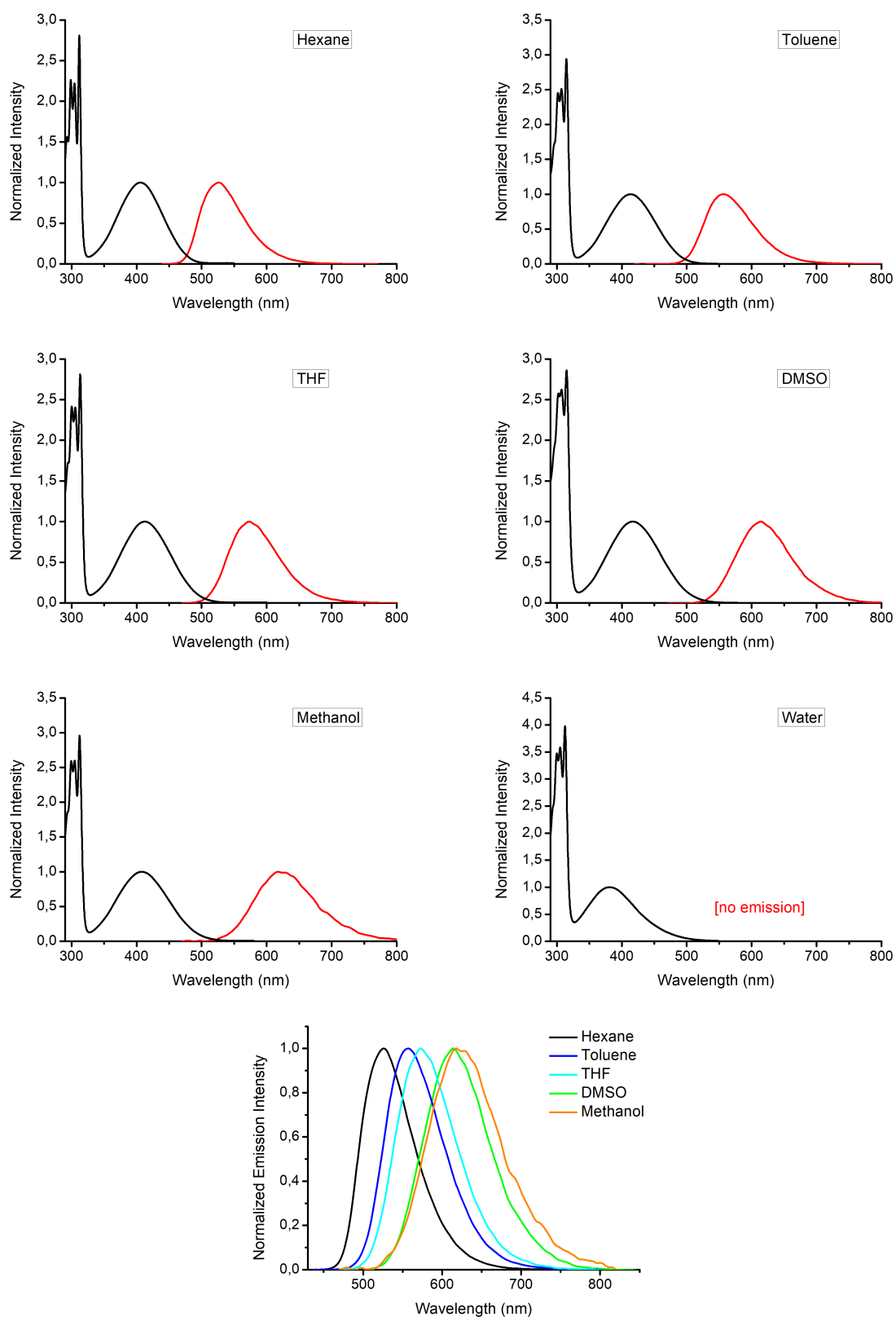
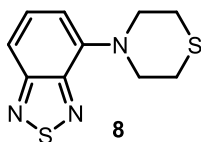


Figure S8. Normalized UV-vis absorption (black) and emission spectra (red) of **8** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

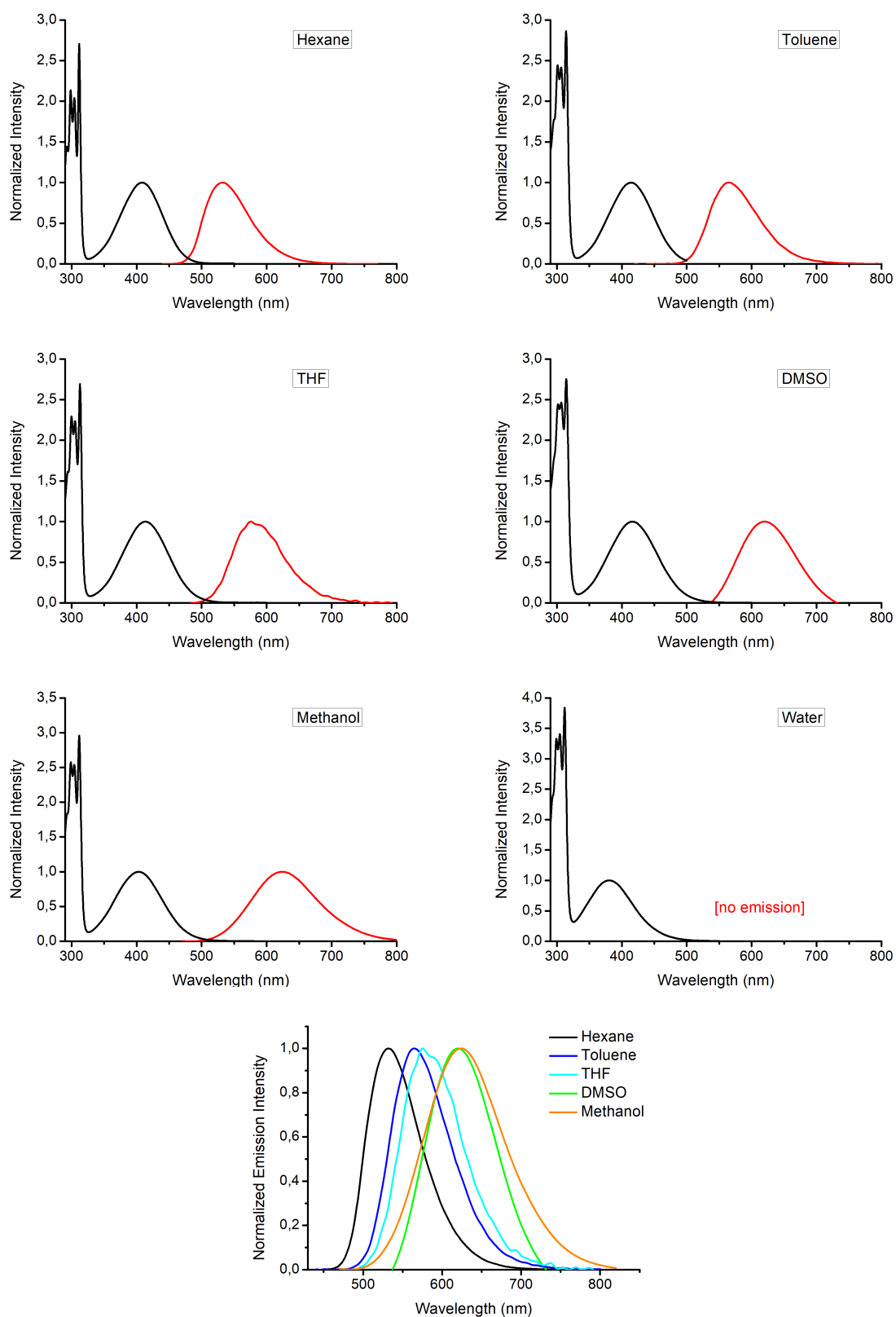
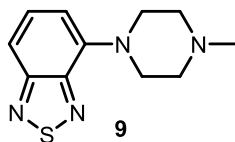


Figure S9. Normalized UV-vis absorption (black) and emission spectra (red) of **9** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

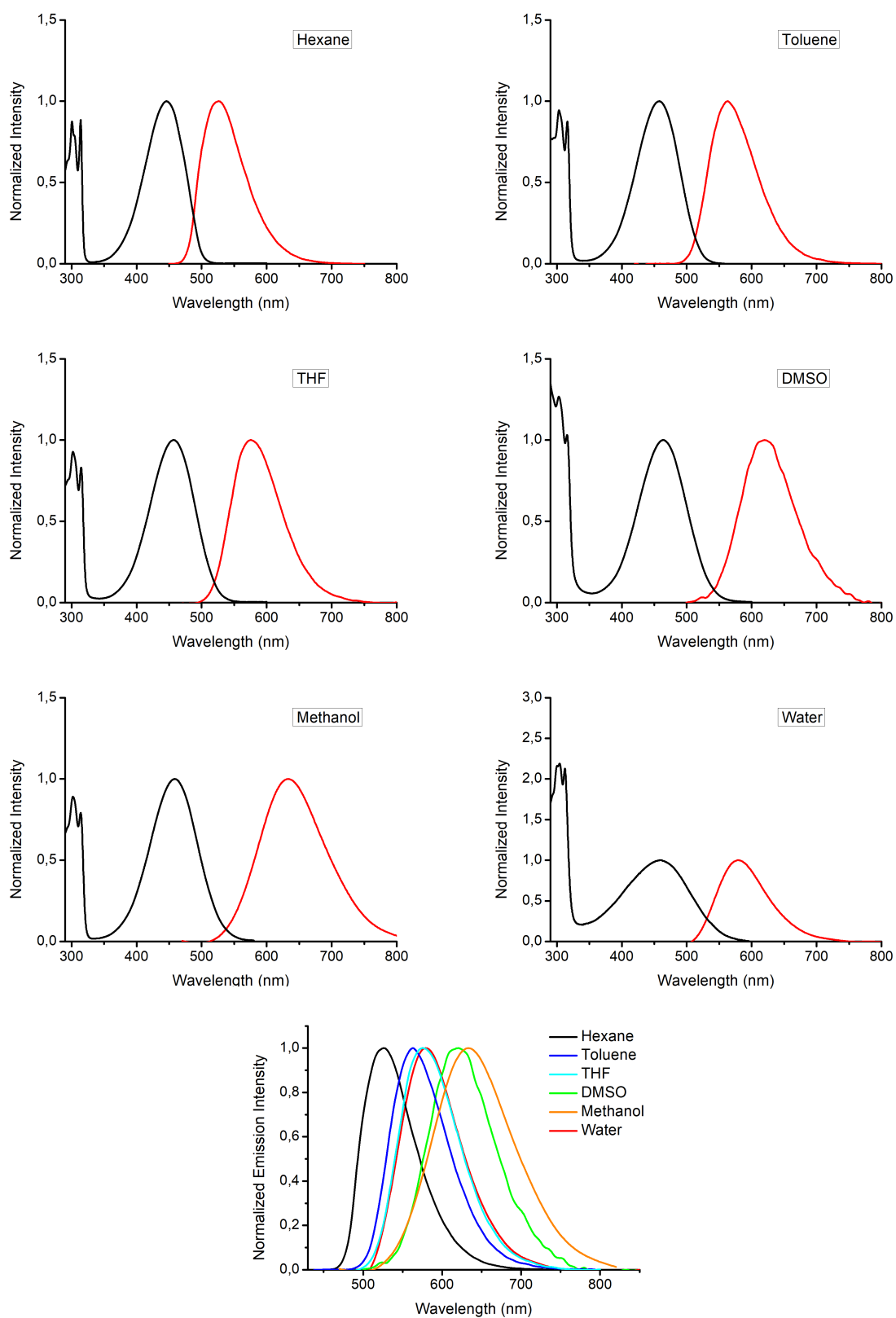
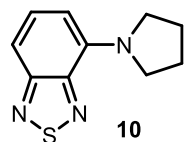


Figure S10. Normalized UV-vis absorption (black) and emission spectra (red) of **10** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission. The observed emission in water likely originated from aggregates.

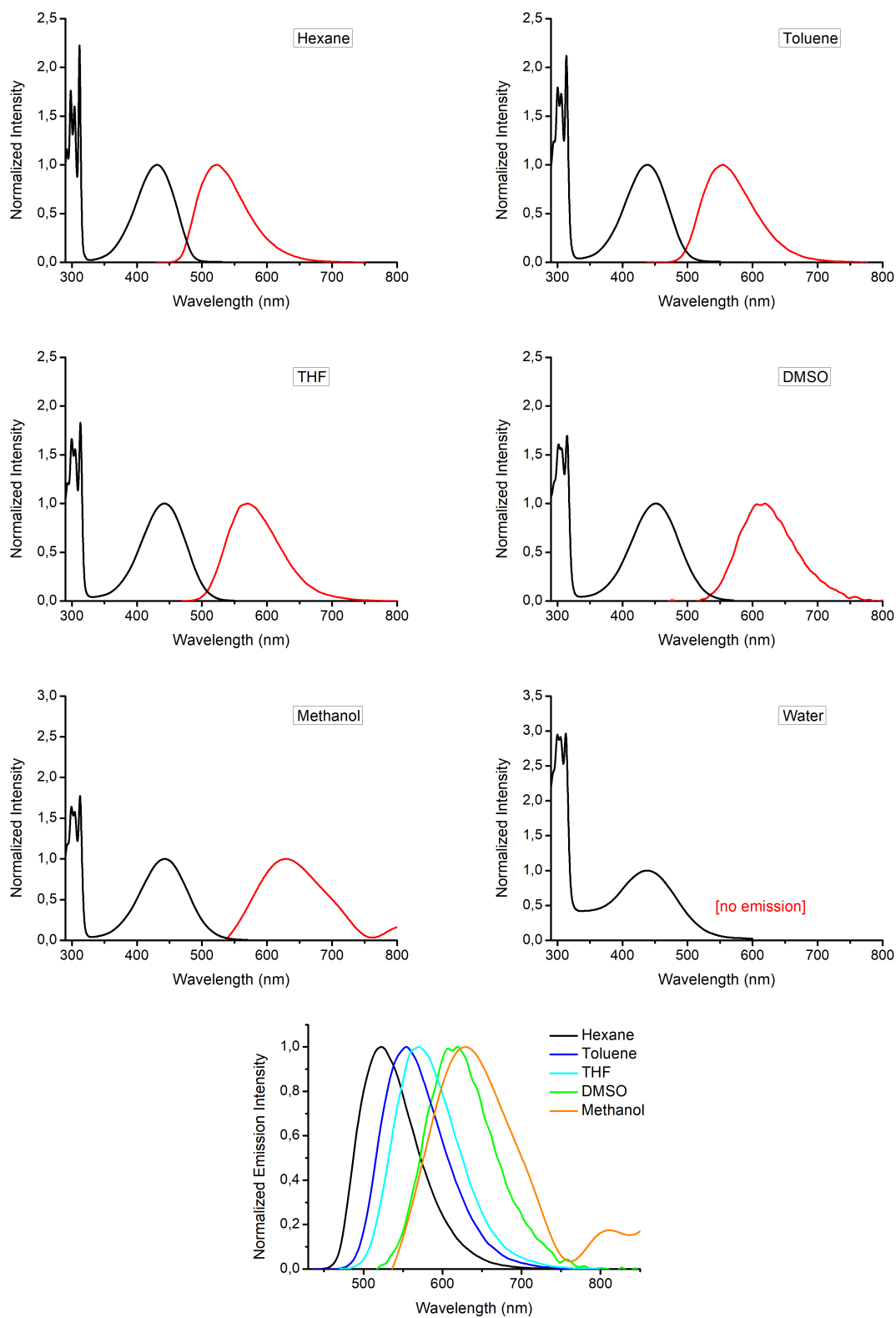
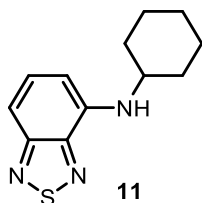


Figure S11. Normalized UV-vis absorption (black) and emission spectra (red) of **11** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

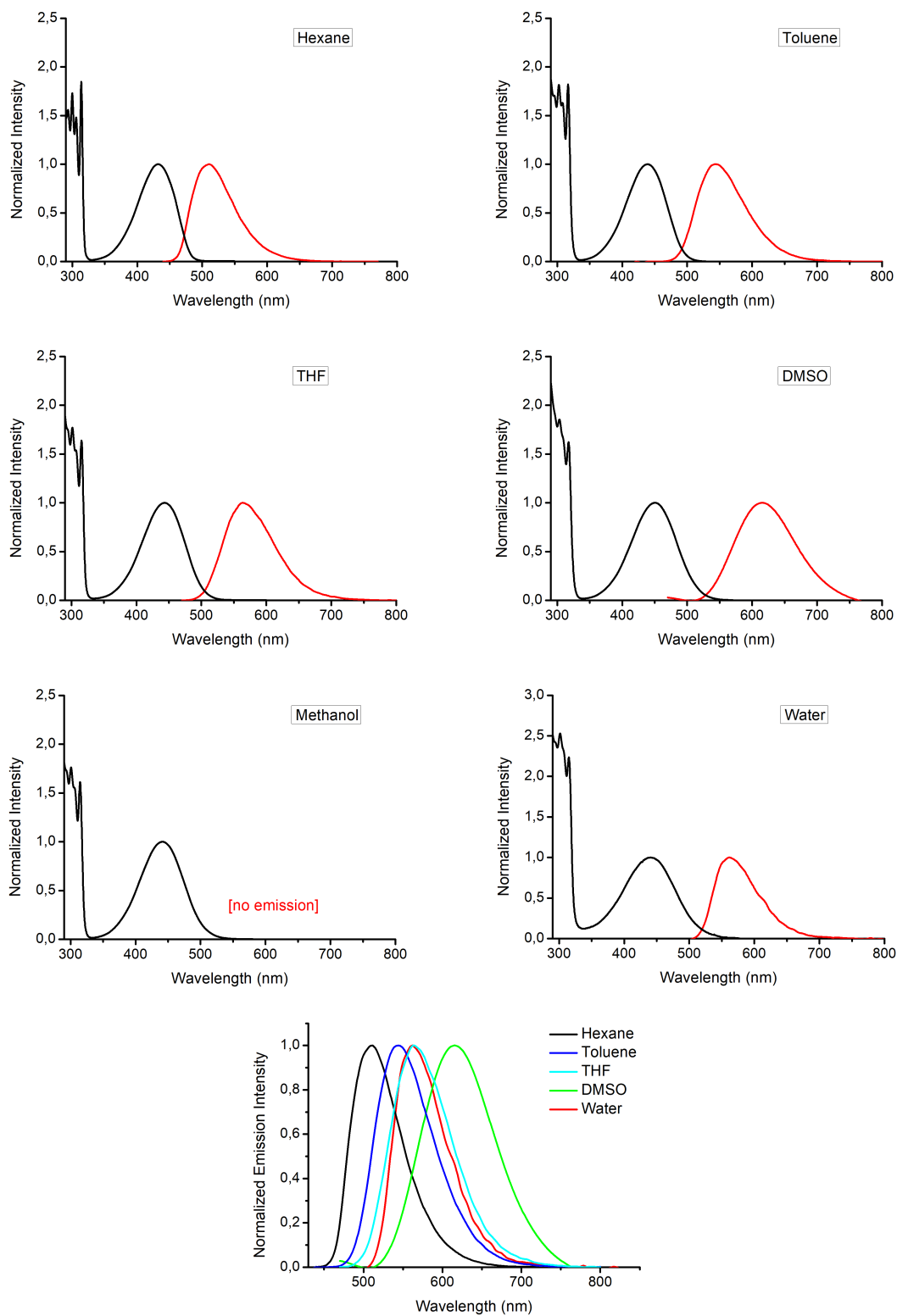
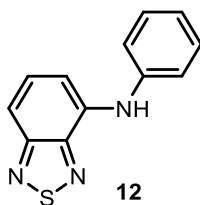


Figure S12. Normalized UV-vis absorption (black) and emission spectra (red) of **12** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission. The observed emission in water likely originated from aggregates.

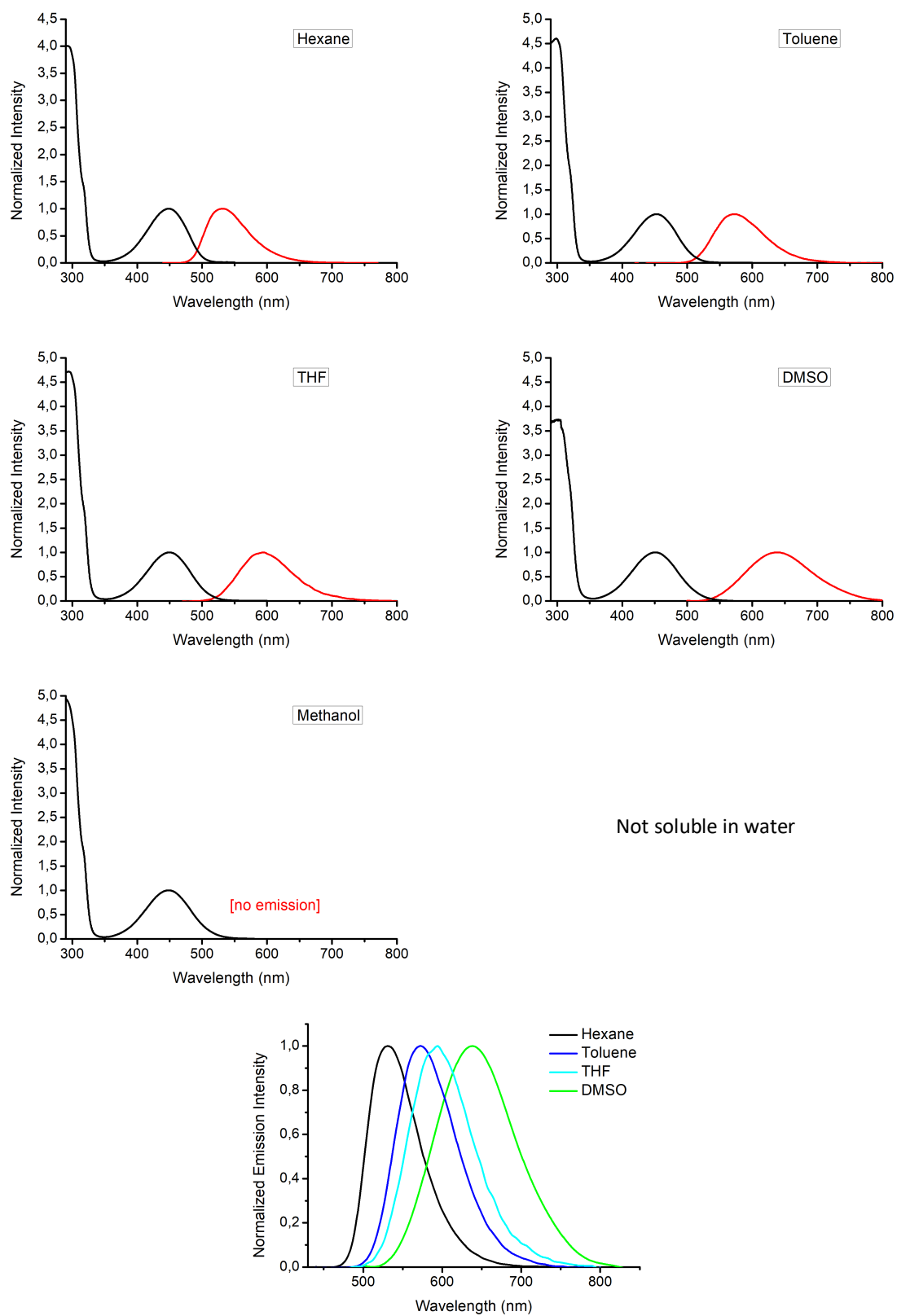
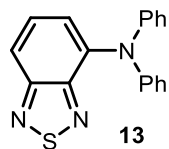


Figure S13. Normalized UV-vis absorption (black) and emission spectra (red) of **13** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

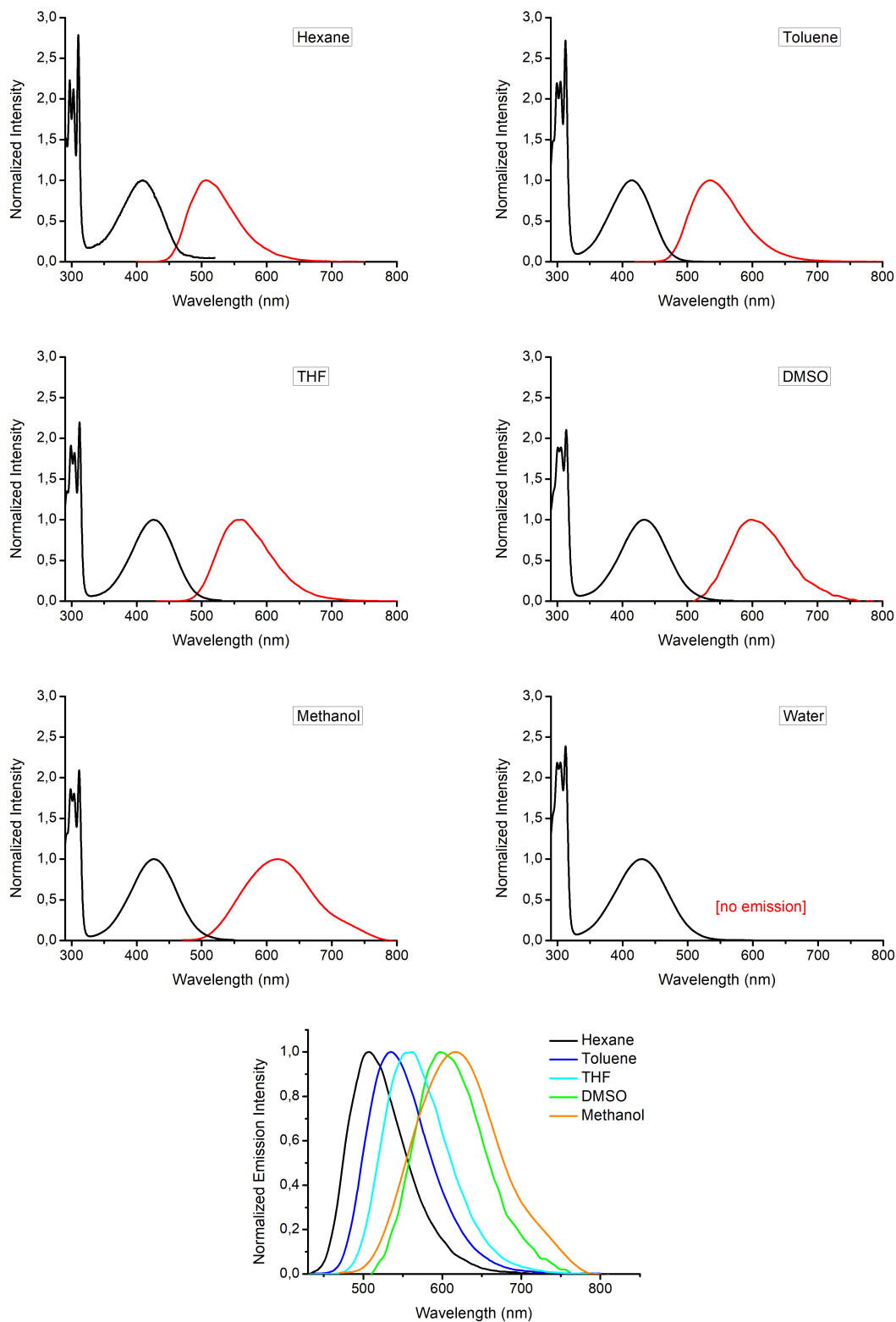
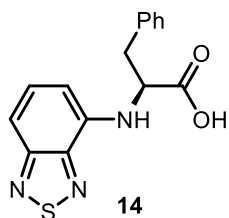


Figure S14. Normalized UV-vis absorption (black) and emission spectra (red) of **14** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

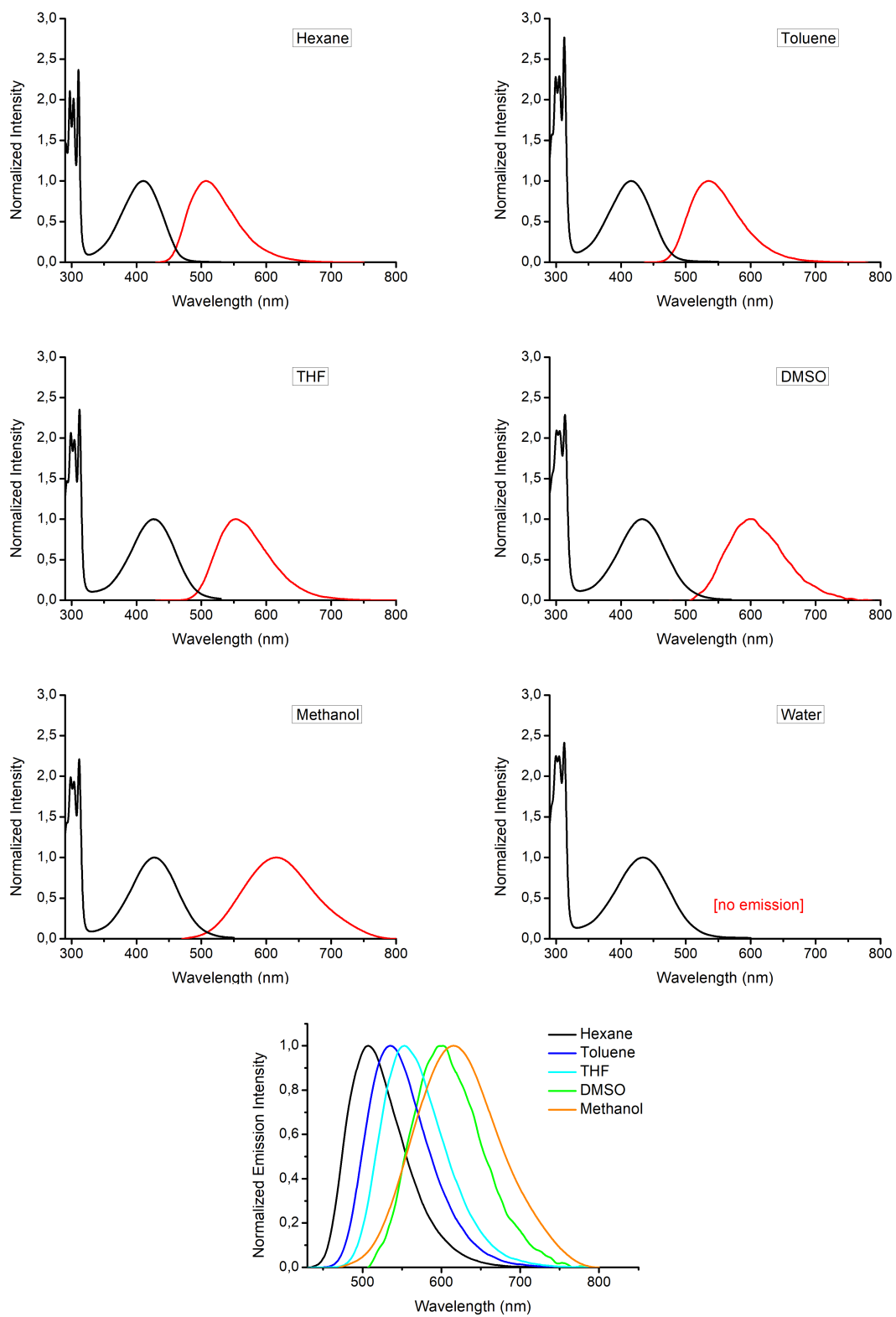
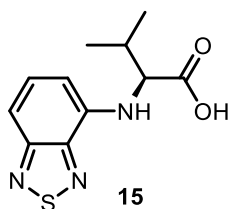


Figure S15. Normalized UV-vis absorption (black) and emission spectra (red) of **15** in solvents of different polarity. Bottom spectrum shows the solvatochromic effect on the emission.

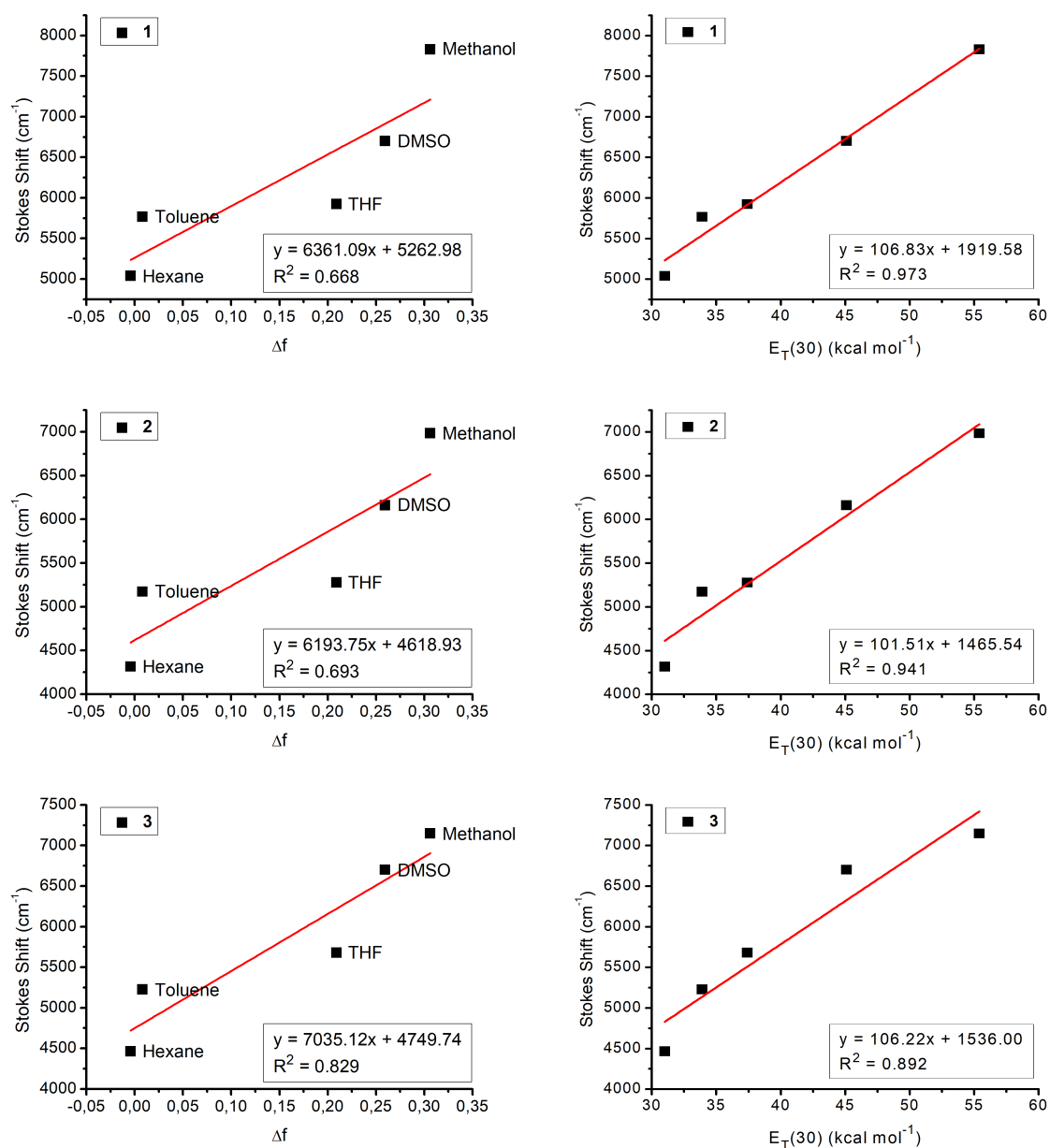


Figure S16. Lippert-Mataga plots (left) and correlation between Stokes shift and $E_T(30)$ solvent polarity parameter (right) for compounds 1-3, with the latter showing better linearity.

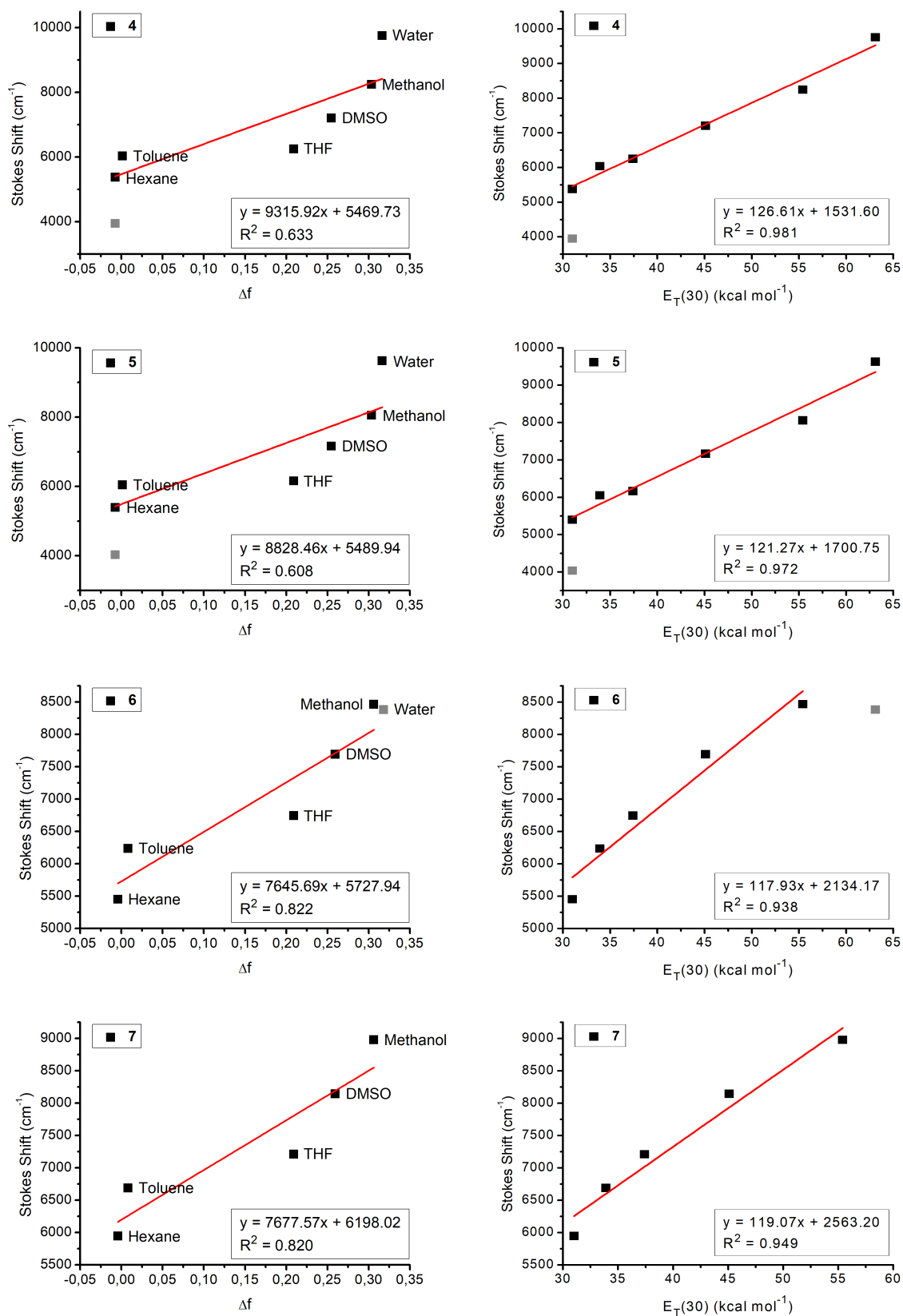


Figure S17. Lippert-Mataga plots (left) and correlation between Stokes shift and $E_T(30)$ solvent polarity parameter (right) for compounds 4-7, with the latter showing better linearity. Grey data points were not considered for the linear fit.

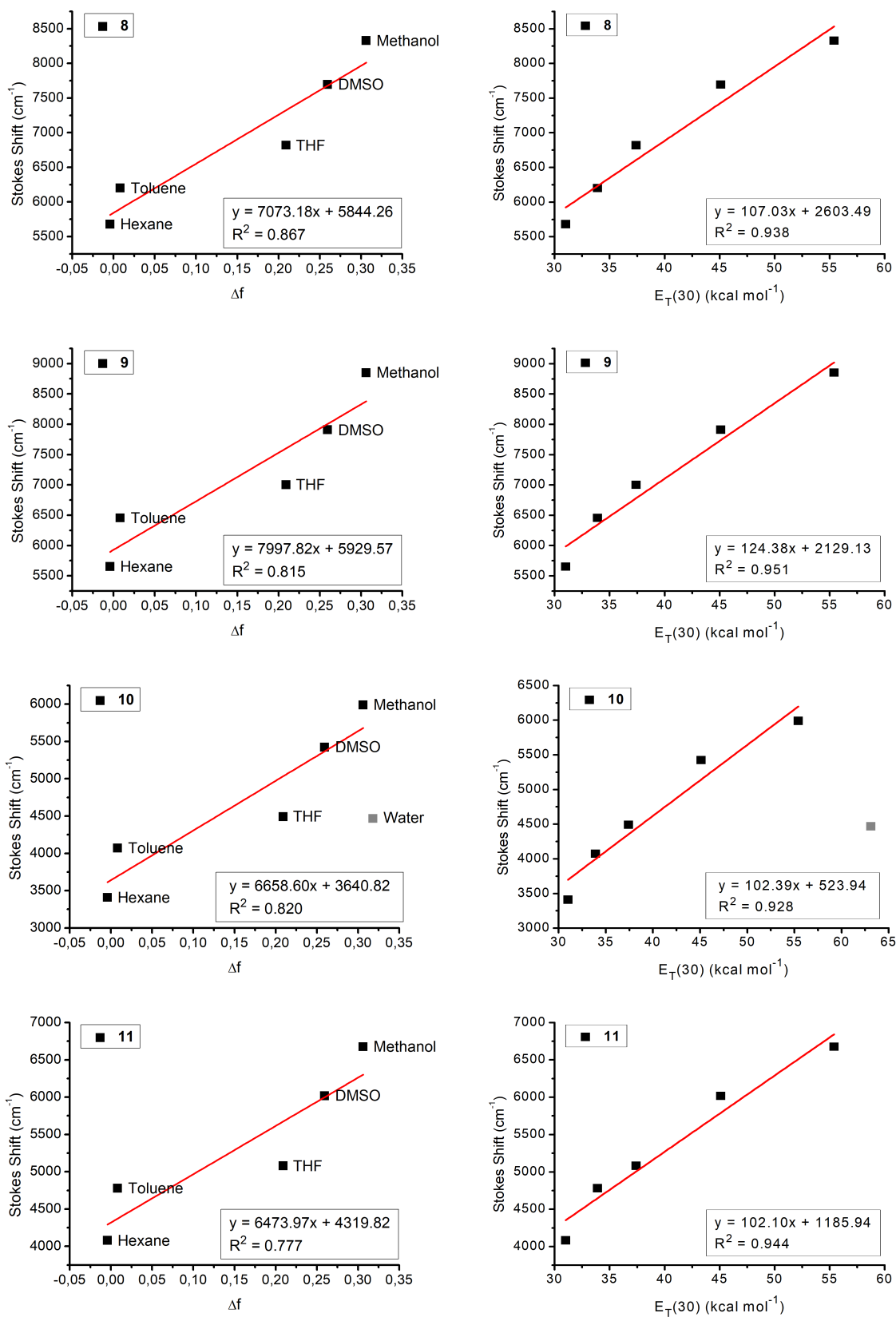


Figure S18. Lippert-Mataga plots (left) and correlation between Stokes shift and $E_T(30)$ solvent polarity parameter (right) for compounds 8-11, with the latter showing better linearity. Grey data points were not considered for the linear fit.

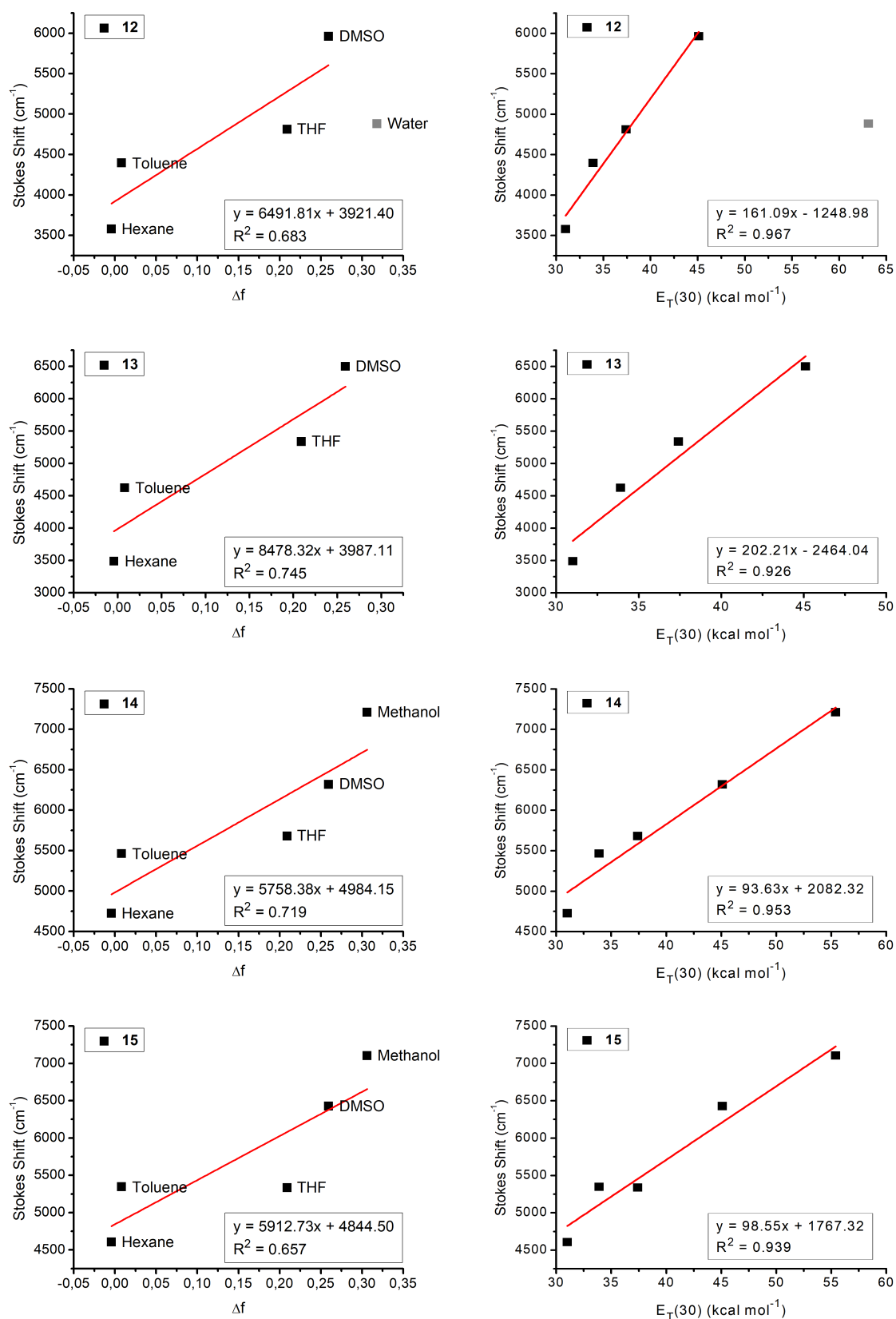


Figure S19. Lippert-Mataga plots (left) and correlation between Stokes shift and $E_T(30)$ solvent polarity parameter (right) for compounds 12-15, with the latter showing better linearity. Grey data points were not considered for the linear fit.

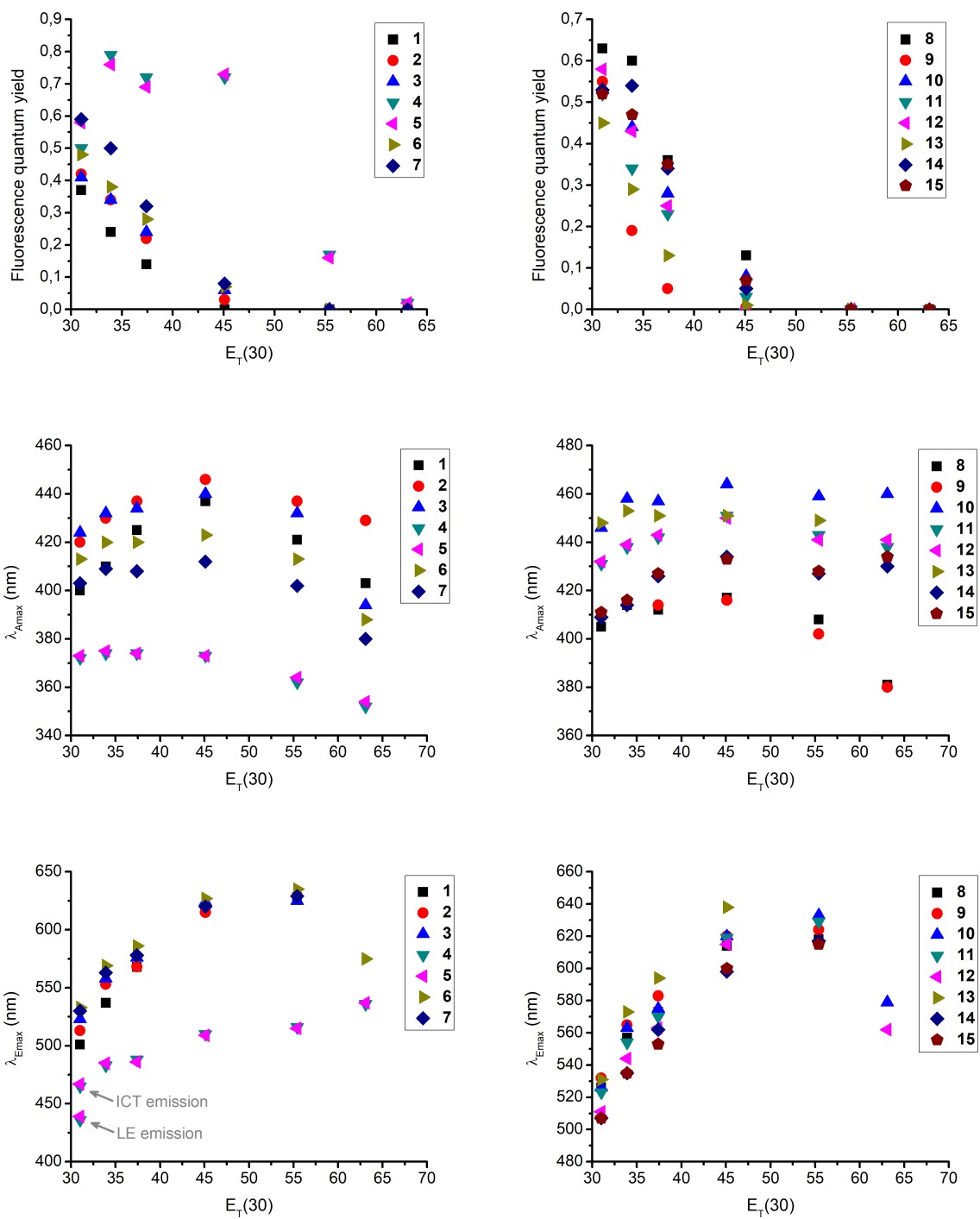
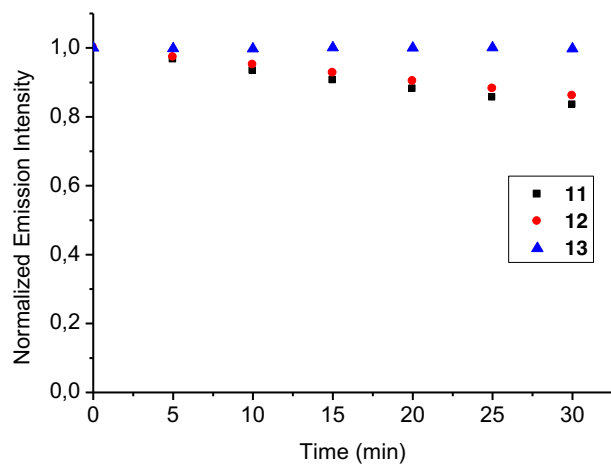


Figure S20. Correlations of fluorescence quantum yield (top), maximum absorption wavelength λ_{Amax} (middle) and maximum emission wavelength λ_{Emax} (bottom) vs $E_T(30)$ solvent polarity parameter.

A.



B.

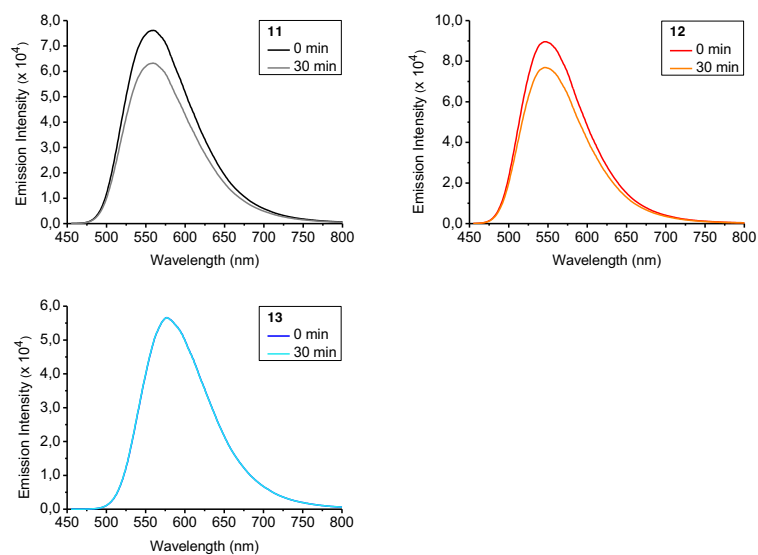


Figure S21. A) Photostability of compounds **11-13** in toluene during irradiation ($\lambda_{\text{ex}} = 445$ nm) for 30 min using the Shimadzu RF-6000 spectrofluorophotometer (ex. bandwidth = 20 nm). Each solution was prepared to give an absorbance value at 0.10 ($\lambda_{\text{abs}} = 445$ nm). B) Emission spectra ($\lambda_{\text{ex}} = 445$ nm), before and after 30 min irradiation. $\lambda_{\text{em}} = 554$ (**11**), 544 (**12**) or 573 nm (**13**).

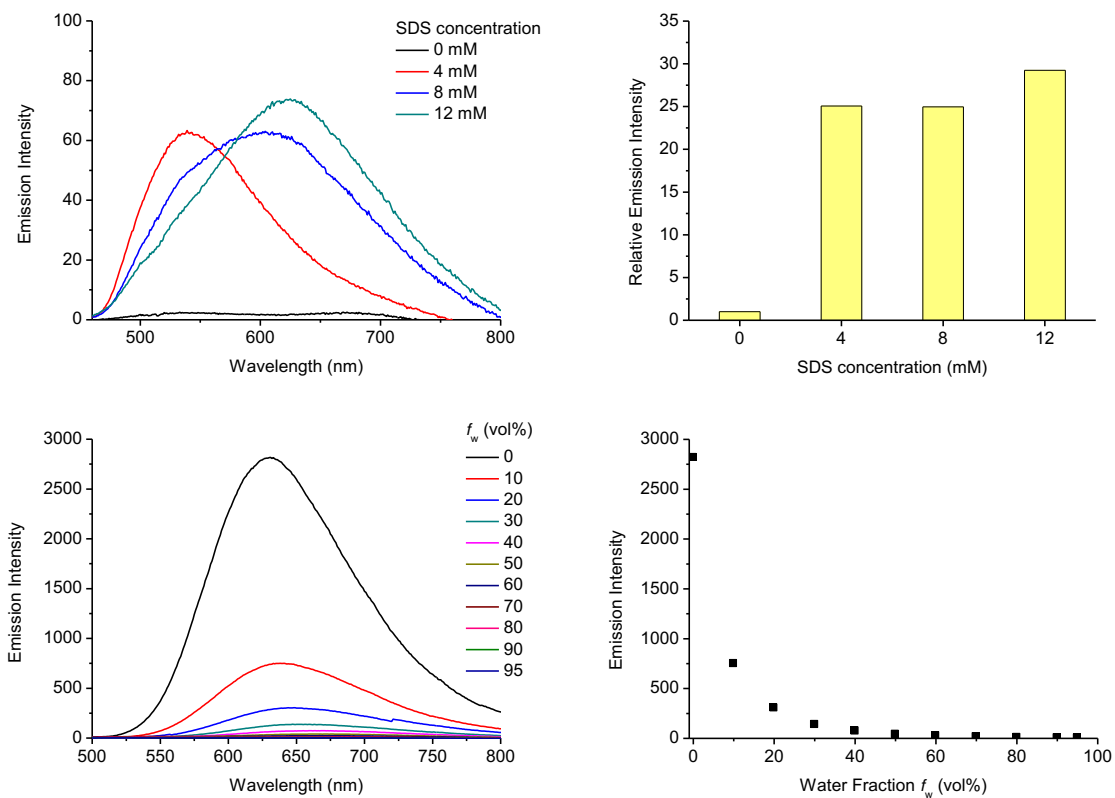
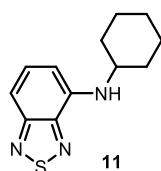


Figure S22. Top row: Emission spectra (left) ($\lambda_{\text{ex}} = 438 \text{ nm}$) and corresponding relative emission intensities (right) of **11** ($10 \mu\text{M}$) in water/DMSO 95:5 in the presence of different concentrations of sodium dodecyl sulfate (SDS). Bottom row: Emission spectra (left; $\lambda_{\text{ex}} = 451 \text{ nm}$) and corresponding emission intensities (right) of **11** ($10 \mu\text{M}$) in mixtures of DMSO/water with varying water fraction (f_w).

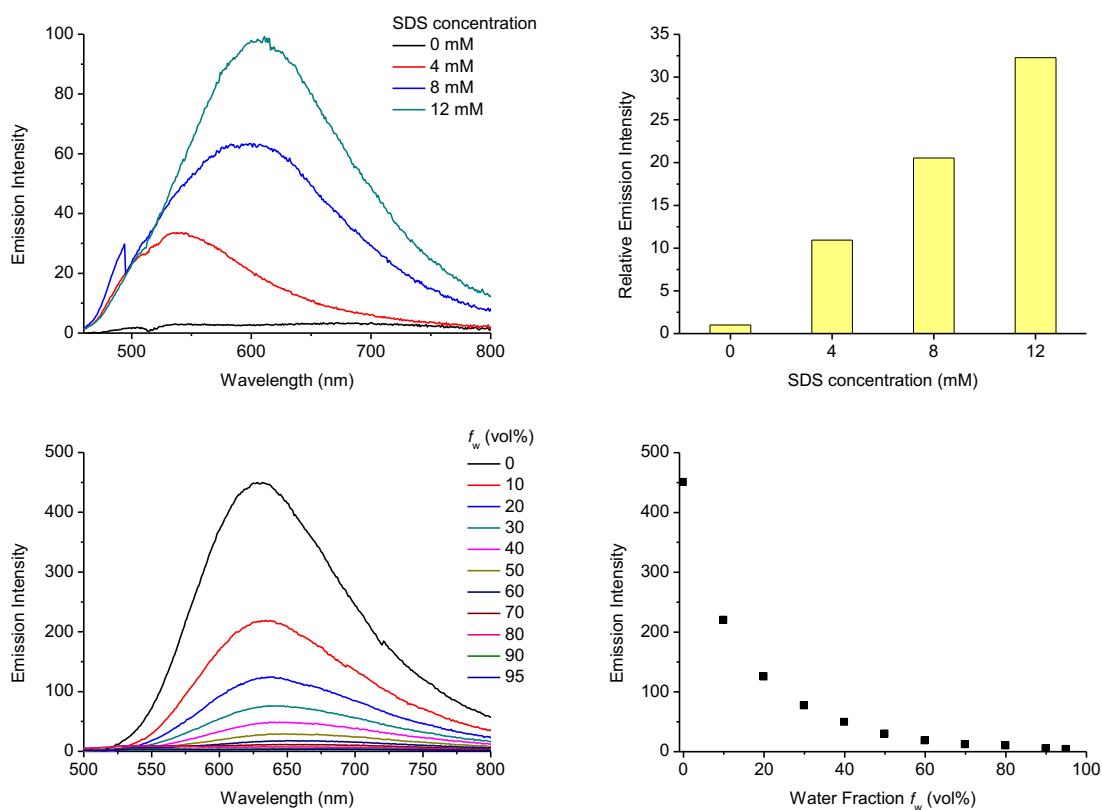
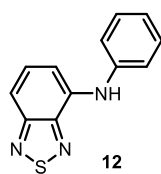


Figure S23. Top row: Emission spectra (left) ($\lambda_{\text{ex}} = 441 \text{ nm}$) and corresponding relative emission intensities (right) of **12** ($10 \mu\text{M}$) in water/DMSO 95:5 in the presence of different concentrations of sodium dodecyl sulfate (SDS). Bottom row: Emission spectra (left) ($\lambda_{\text{ex}} = 441 \text{ nm}$) and corresponding emission intensities (right) of **12** ($10 \mu\text{M}$) in mixtures of DMSO/water with varying water fraction (f_w).

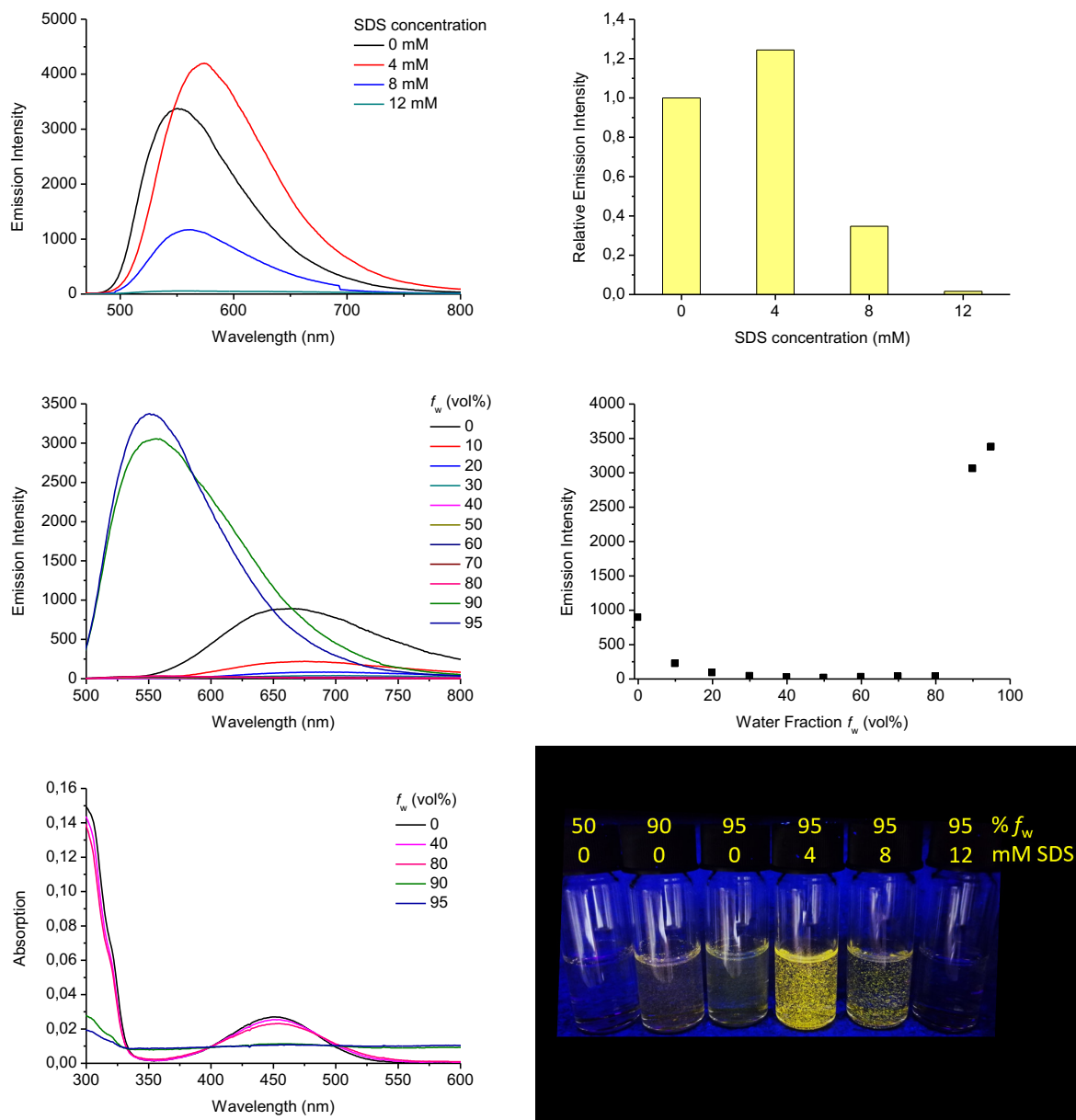
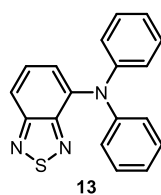


Figure S24. Top row: Emission spectra (left) ($\lambda_{\text{ex}} = 451 \text{ nm}$) and corresponding relative emission intensities (right) of **13** ($10 \mu\text{M}$) in water/DMSO 95:5 in the presence of different concentrations of sodium dodecyl sulfate (SDS). Middle row: Emission spectra (left) ($\lambda_{\text{ex}} = 451 \text{ nm}$) and corresponding emission intensities (right) of **13** ($10 \mu\text{M}$) in mixtures of DMSO/water with varying water fraction (f_w). Bottom left: Corresponding absorption spectra in selected DMSO/water mixtures, indicating aggregation effects at $f_w \geq 90\%$. Bottom right: Picture of selected samples of **13** ($10 \mu\text{M}$) exposed to UV light ($\lambda = 365 \text{ nm}$) showing weak aggregation-induced emission at high f_w and the effect of SDS concentration on aggregation and fluorescence.

IV. Lipophilicity (logP) Data

Table S1. Experimental and calculated logP values for compounds **1-15** and **LD-BTD1**^[27].

Compd.	Exp. logP	Calcd. logP ^[12]
1	1.7	1.5
2	2.4	1.8
3	2.4	2.1
4	1.4	1.2
5	2.3	2.6
6	n.d.	3.0
7	2.0	1.9
8	n.d.	2.5
9	1.5	2.0
10	n.d.	2.5
11	n.d.	4.4
12	n.d.	4.0
13	n.d.	5.5
14	1.5	2.1
15	1.5	1.4
LD-BTD1	3.3 ^[27]	3.9

n.d. = not determined due to poor water solubility.

V. Computational Results

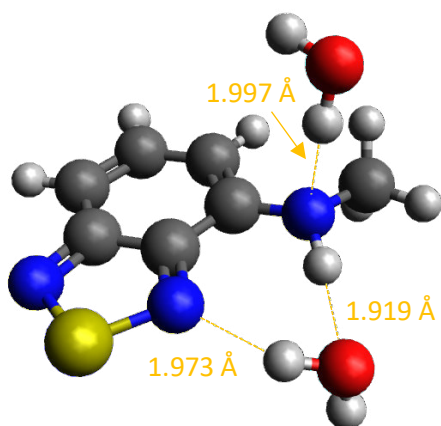
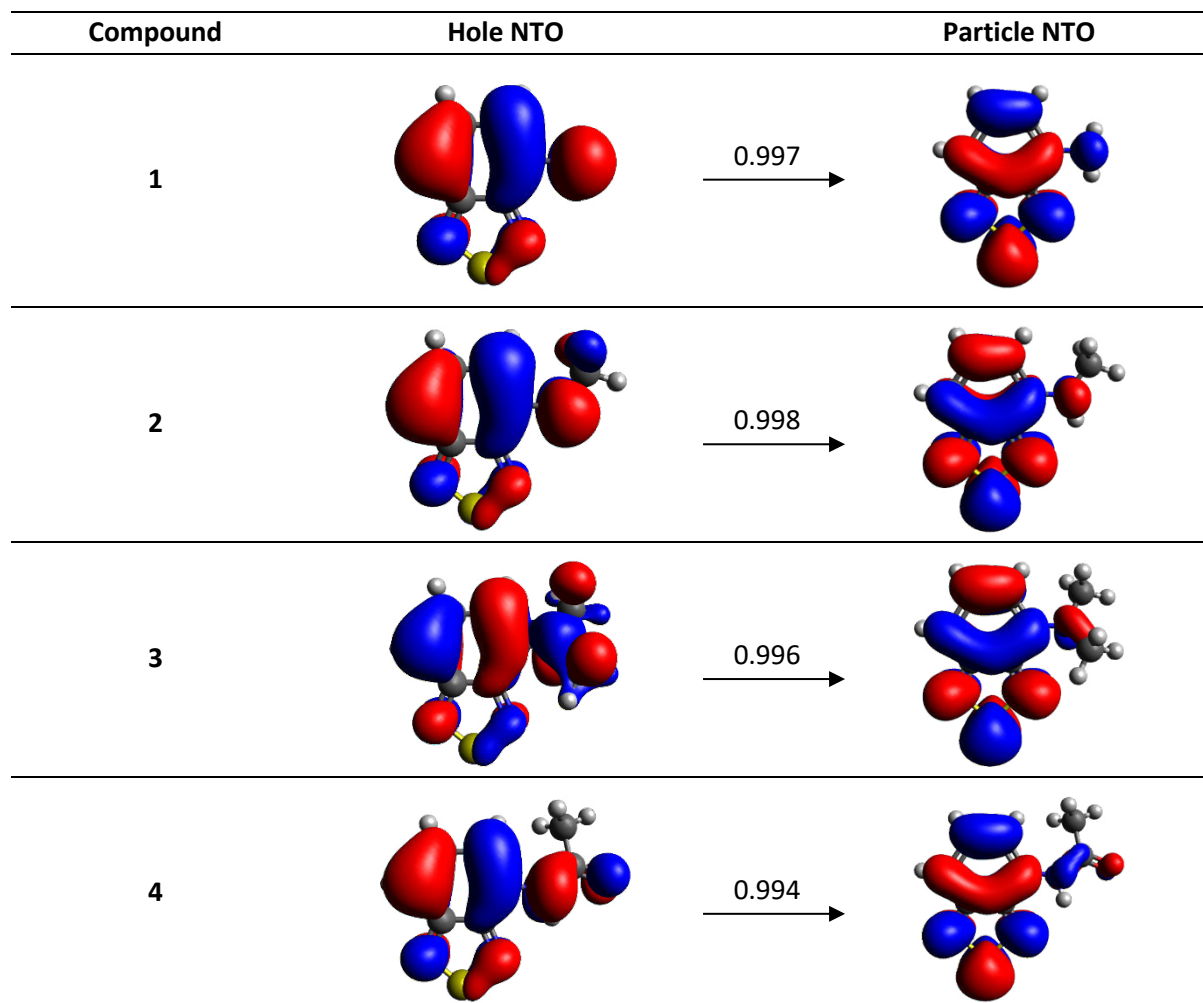


Figure S25. Optimized ground-state geometry of compound **2**. Hydrogen bonds and their lengths are indicated in yellow.

Table S2. Calculated absorption (λ_{Amax}) and emission (λ_{Emax}) in three different solvents in comparison with experimental data.

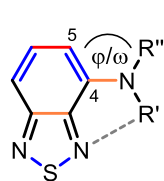
Solvent	Compd.	λ_{Amax} (nm / eV)		λ_{Emax} (nm / eV)	
		Exp.	Calcd.	Exp.	Calcd.
hexane	1	400 / 3.10	393 / 3.15	501 / 2.47	519 / 2.39
THF		425 / 2.92	422 / 2.94	568 / 2.18	674 / 1.84
H ₂ O		403 / 3.08	394 / 3.15	-	-
hexane	2	420 / 2.95	411 / 3.01	513 / 2.42	523 / 2.37
THF		437 / 2.84	430 / 2.88	568 / 2.18	638 / 1.94
H ₂ O		429 / 2.89	397 / 3.12	-	-
hexane	3	424 / 2.92	400 / 3.10	523 / 2.37	527 / 2.35
THF		434 / 2.86	412 / 3.01	576 / 2.15	645 / 1.92
H ₂ O		394 / 3.15	377 / 3.28	-	-
hexane	4	372 / 3.33	358 / 3.46	436;465 / 2.84;2.67	456 / 2.72
THF		374 / 3.32	349 / 3.55	488 / 2.54	510 / 2.43
H ₂ O		352 / 3.52	345 / 3.59	536 / 2.31	547 / 2.27

Table S3. Natural transition orbitals for compounds 1-4.



NR'R'' = NH₂ (1), NHMe (2), NMe₂ (3), NHAc (4)

Dihedral angles: $\varphi = (5,4,N,R'')$, $\omega = (5,4,N,R')$



Most significant bond length changes upon excitation from S₀ to S₁:

3-5% elongation

3-4% shortening

1-3% shortening

4-6% shortening of H-bond R'---N (1, 2, 4)

Dihedral angles (/)		
	S ₀	S ₁
1	-21 / -164	0 / -180
2	-7 / -172	0 / -180
3	-6 / 137	-7 / 167
4	-14 / 171	0 / -180

Figure S26. Calculated changes in bond lengths and dihedral angles of **1-4** upon excitation from the ground state (S₀) to the first excited state (S₁) based on optimized S₀ and S₁ structures in hexane.

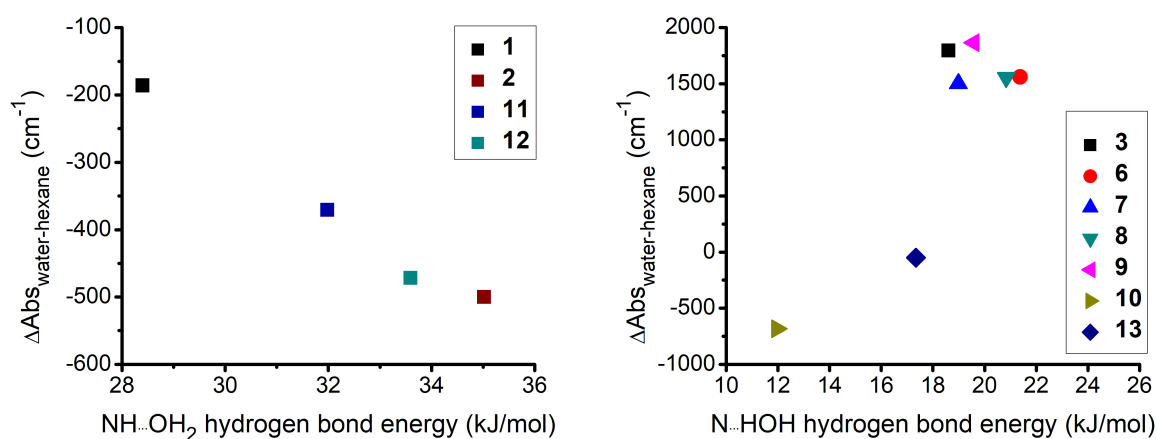


Figure S27. Correlations of hydrogen bond energy (in kJ/mol) and shift of absorption in water compared to hexane (in cm⁻¹). Left: linear red-shift of absorption with increasing hydrogen bond donor strength of the primary (**1**) or secondary (**2**, **11**, **12**) amine. Right: blue-shift of absorption with increasing hydrogen bond acceptor strength of the tertiary amine.

VI. Fluorescence Cell Imaging Pictures

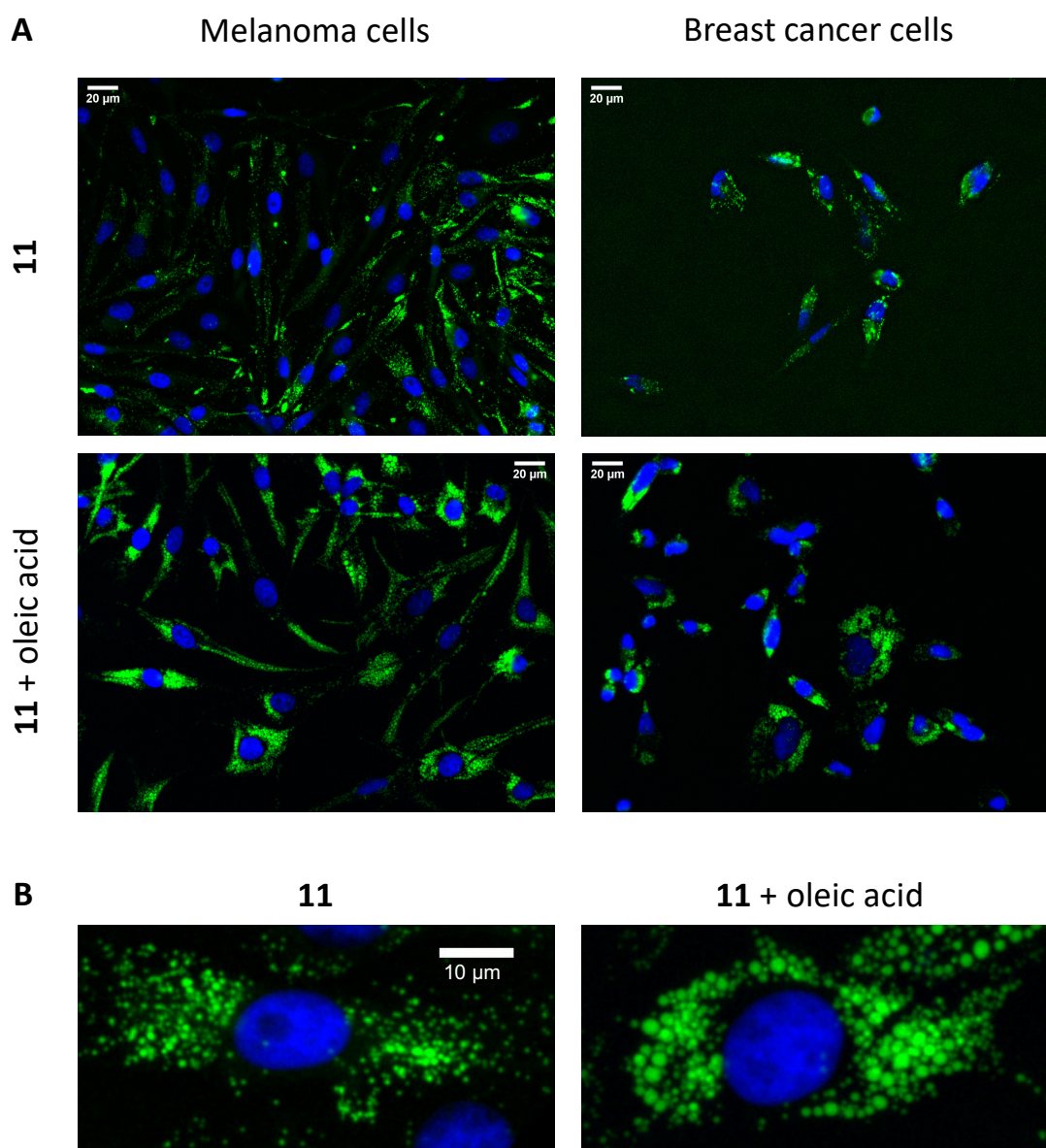


Figure S28. A) Fluorescence microscopy images of melanoma (SK-MEL-28) and breast cancer (MDA-MB-231) cells stained with **11** (seen in green; ex. 460-500 nm, em. 512-542 nm). The bottom row shows cells that have been supplemented with oleic acid (100 µM, 24 h) before fixation. B) Magnified regions of the melanoma cell images in A. Staining was performed on fixed cells (10 µM, 1 h). Cell nuclei were stained with DAPI (seen in blue; ex. 325-375 nm, em. 435-485 nm).

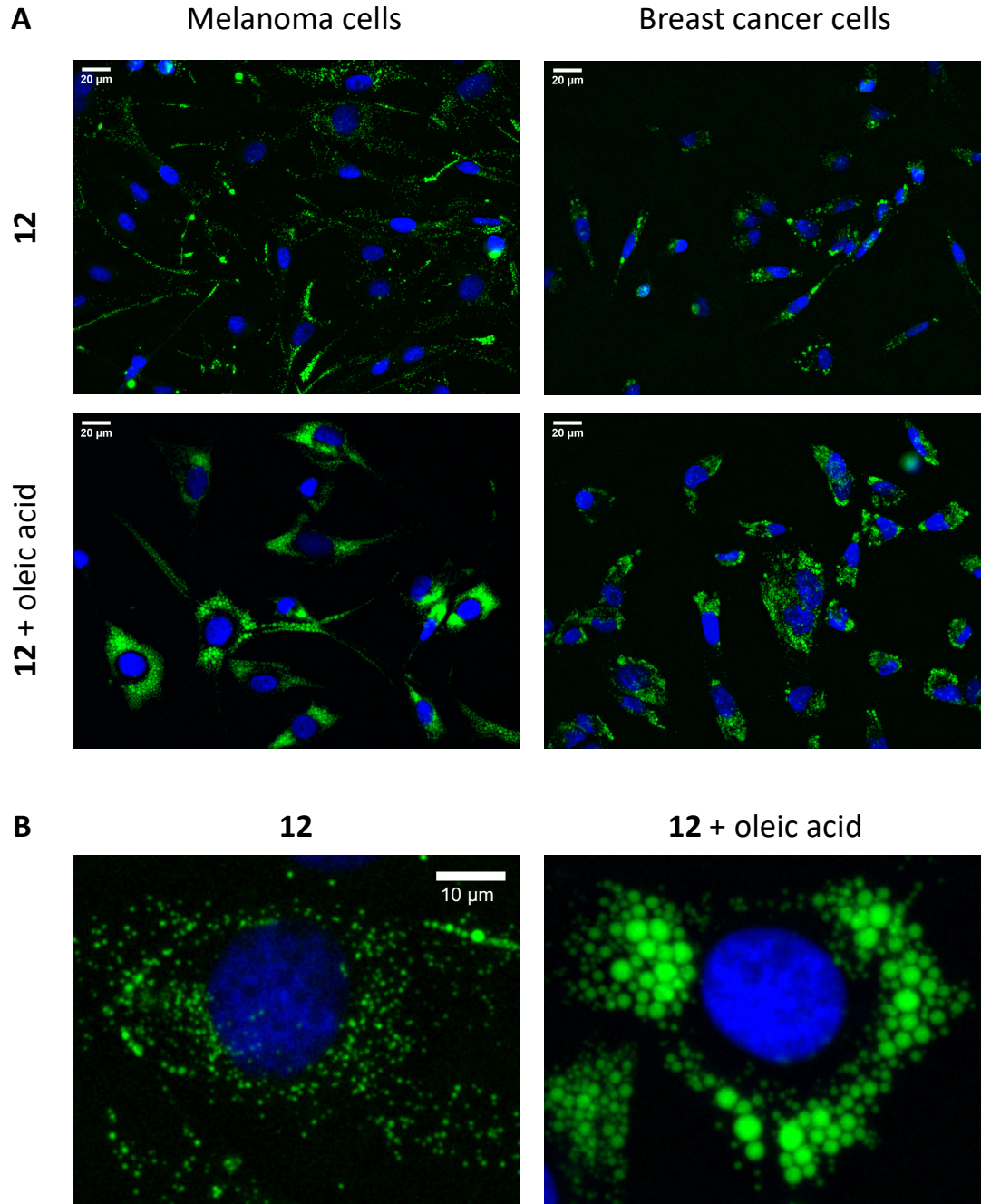


Figure S29. A) Fluorescence microscopy images of melanoma (SK-MEL-28) and breast cancer (MDA-MB-231) cells stained with **12** (seen in green; ex. 460-500 nm, em. 512-542 nm). The bottom row shows cells that have been supplemented with oleic acid (100 μ M, 24 h) before fixation. B) Magnified regions of the melanoma cell images in A. Staining was performed on fixed cells (10 μ M, 1 h). Cell nuclei were stained with DAPI (seen in blue; ex. 325-375 nm, em. 435-485 nm).

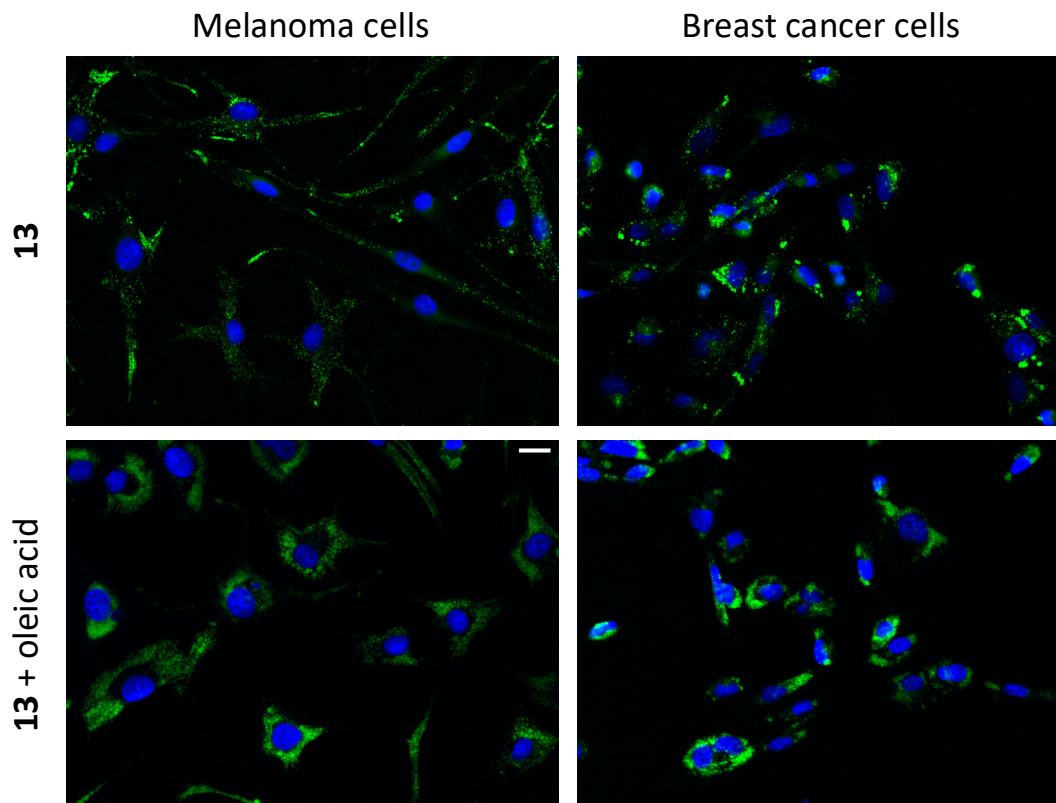


Figure S30. Fluorescence microscopy images of melanoma (SK-MEL-28) and breast cancer (MDA-MB-231) cells stained with **13** (seen in green; ex. 460-500 nm, em. 512-542 nm). The bottom row shows cells that have been supplemented with oleic acid (100 μ M, 24 h) before fixation. Scale bar 20 μ m. Staining was performed on fixed cells (10 μ M, 1 h). Cell nuclei were stained with DAPI (seen in blue; ex. 325-375 nm, em. 435-485 nm).

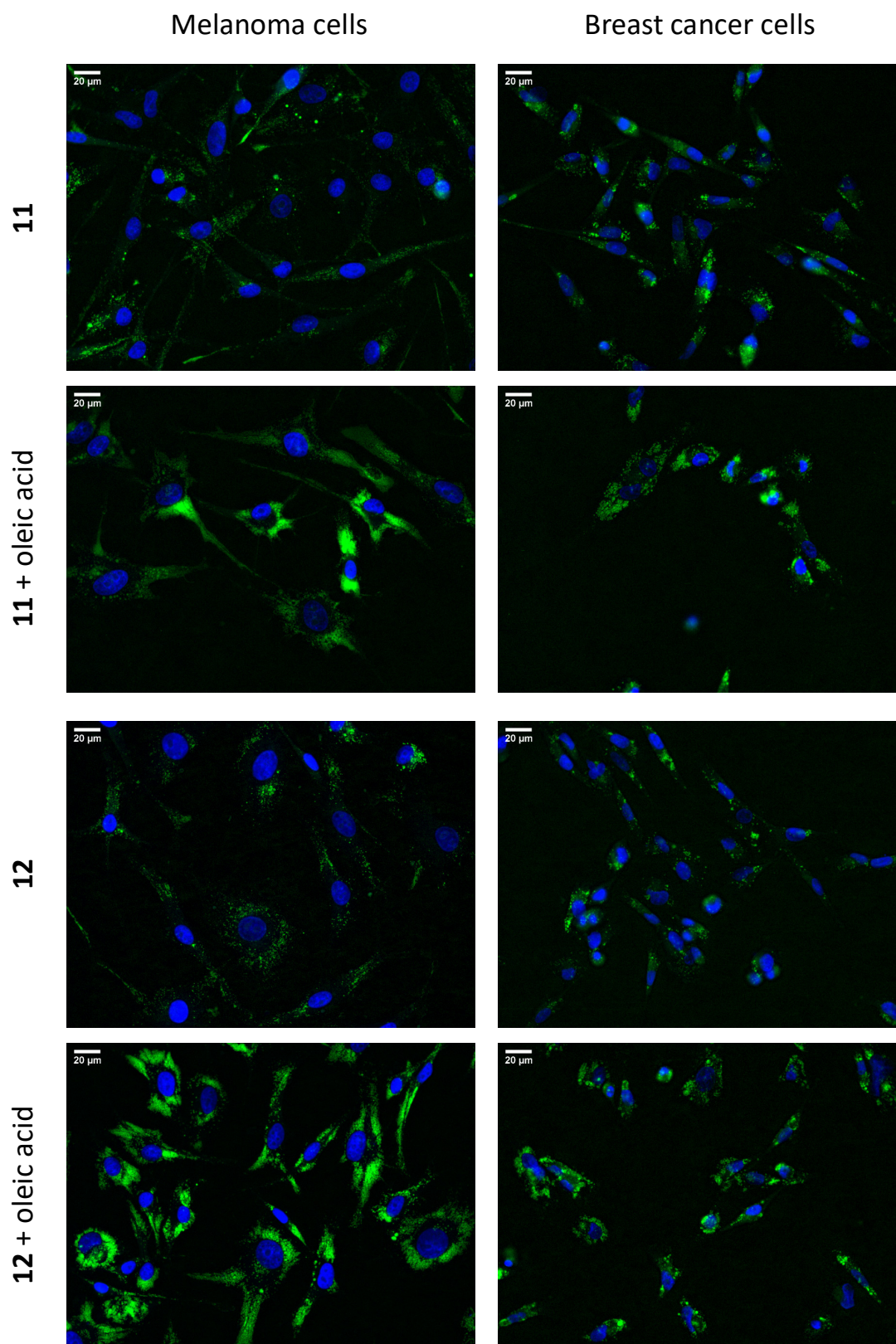


Figure S31. Fluorescence microscopy images of melanoma (SK-MEL-28) and breast cancer (MDA-MB-231) cells stained with **11** (top half) or **12** (bottom half) (seen in green; ex. 460-500 nm, em. 512-542 nm). The bottom row for each compound shows cells that have been supplemented with oleic acid (100 μ M, 24 h). Staining was performed on living cells (10 μ M, 24 h). Cell nuclei were stained with DAPI (seen in blue; ex. 325-375 nm, em. 435-485 nm).

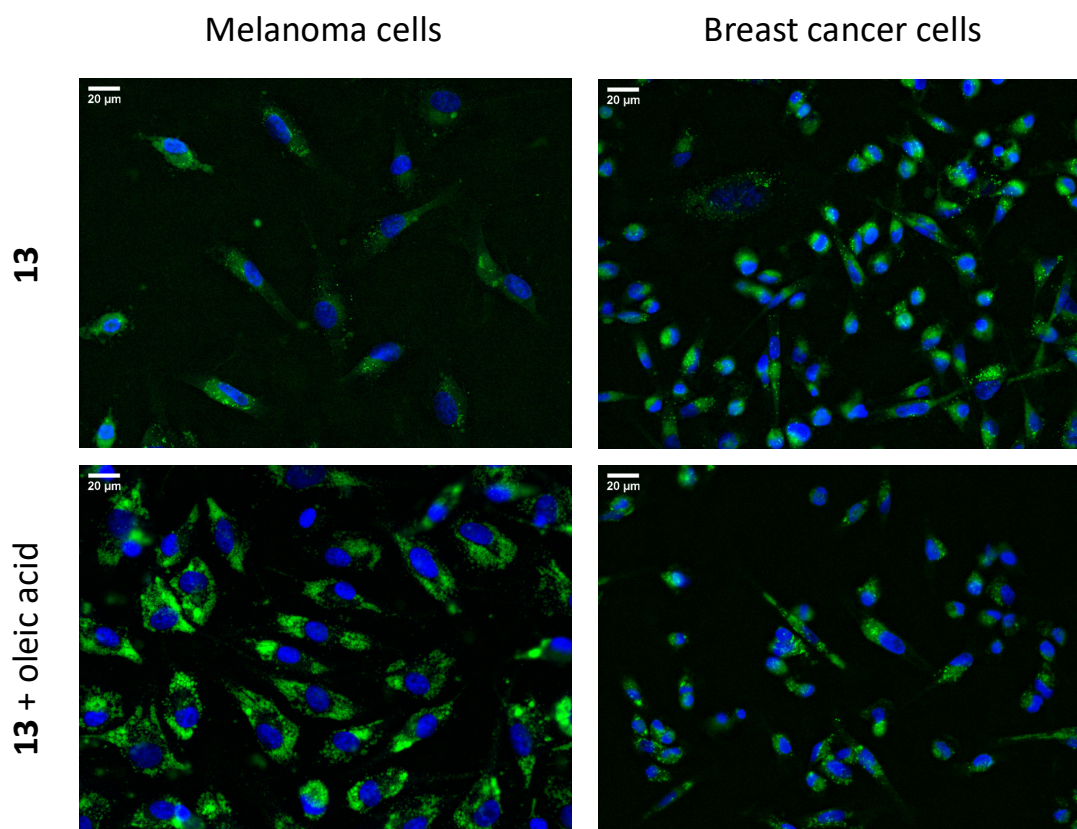


Figure S32. Fluorescence microscopy images of melanoma (SK-MEL-28) and breast cancer (MDA-MB-231) cells stained with **13** (seen in green; ex. 460-500 nm, em. 512-542 nm). The bottom row shows cells that have been supplemented with oleic acid (100 μ M, 24 h). Staining was performed on living cells (10 μ M, 24 h). Cell nuclei were stained with DAPI (seen in blue; ex. 325-375 nm, em. 435-485 nm).

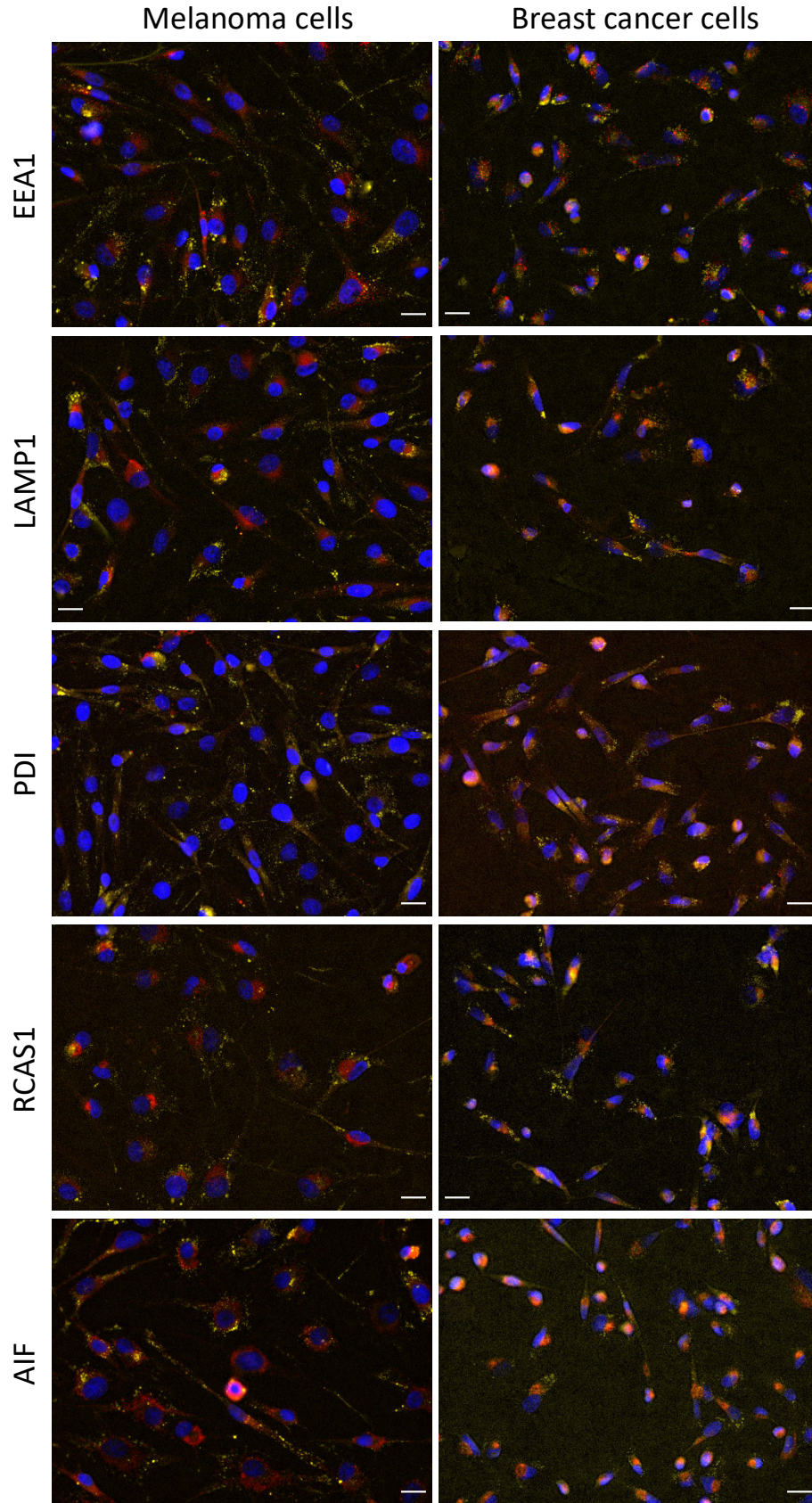


Figure S33. Colocalization experiments of **11** (30 μ M, 24 h; seen in yellow; ex. 460-500 nm, em. 512-542 nm) with EEA1 (endosomes), LAMP1 (lysosomes), PDI (endoplasmic reticulum), RCAS1 (Golgi) or AIF (mitochondria) (seen in red; ex. 590-650 nm, em. 662-738 nm). Scale bar 20 μ m. Cell nuclei were stained with DAPI (seen in blue; ex. 325-375 nm, em. 435-485 nm).

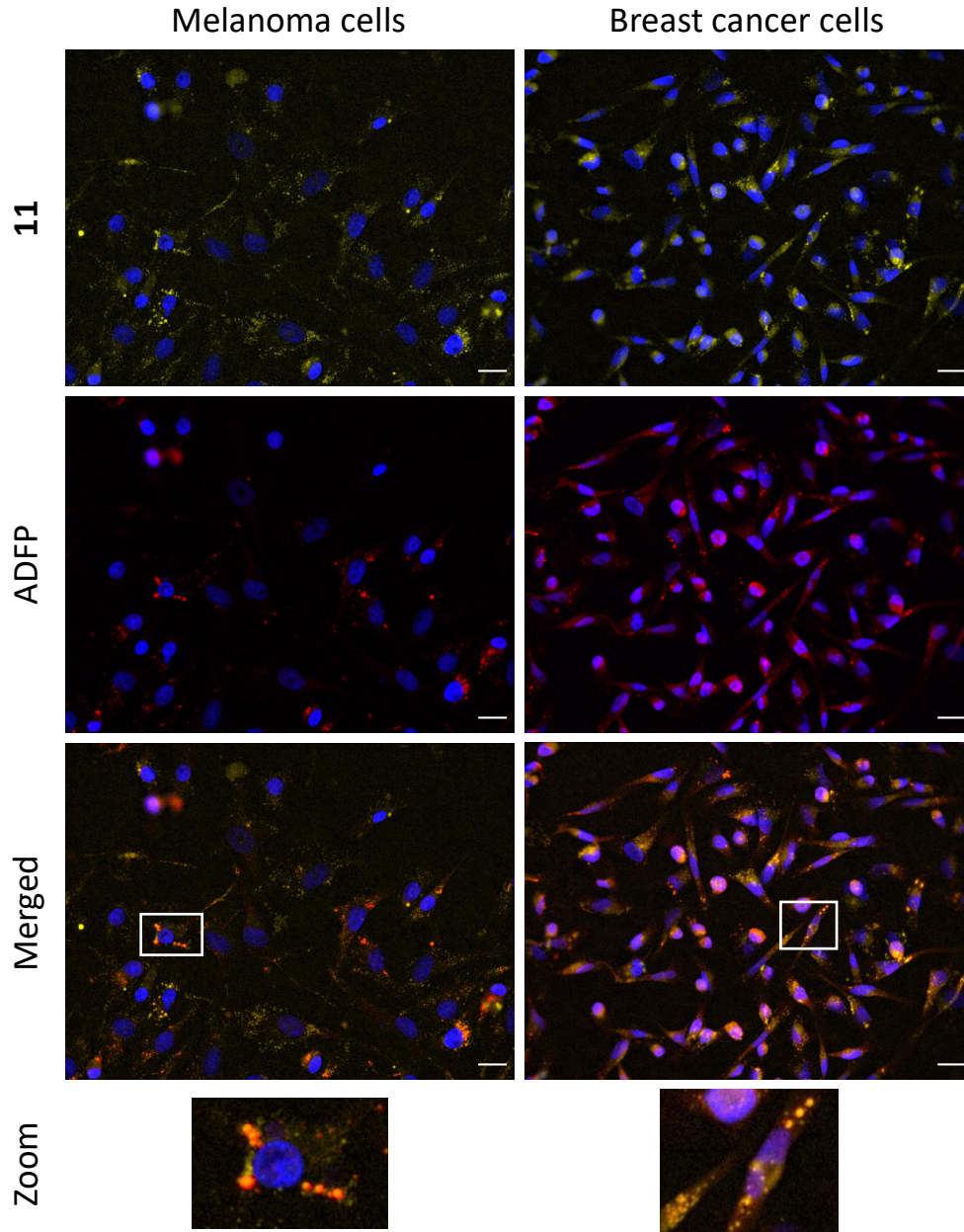


Figure S34. Fluorescence microscopy images of the colocalization of **11** (seen in yellow; ex. 460-500 nm, em. 512-542 nm) and an anti-ADFP antibody that targets the surface of lipid droplets (seen in red; ex. 590-650 nm, em. 662-738 nm) in melanoma (SK-MEL-28) and breast cancer (MDA-MB-231) cells. Scale bar 20 μm . Staining was performed on live cells, which were fixed after incubation (30 μM , 24 h) and then subjected to immunocytochemistry. Cell nuclei were stained with DAPI (seen in blue; ex. 325-375 nm, em. 435-485 nm).

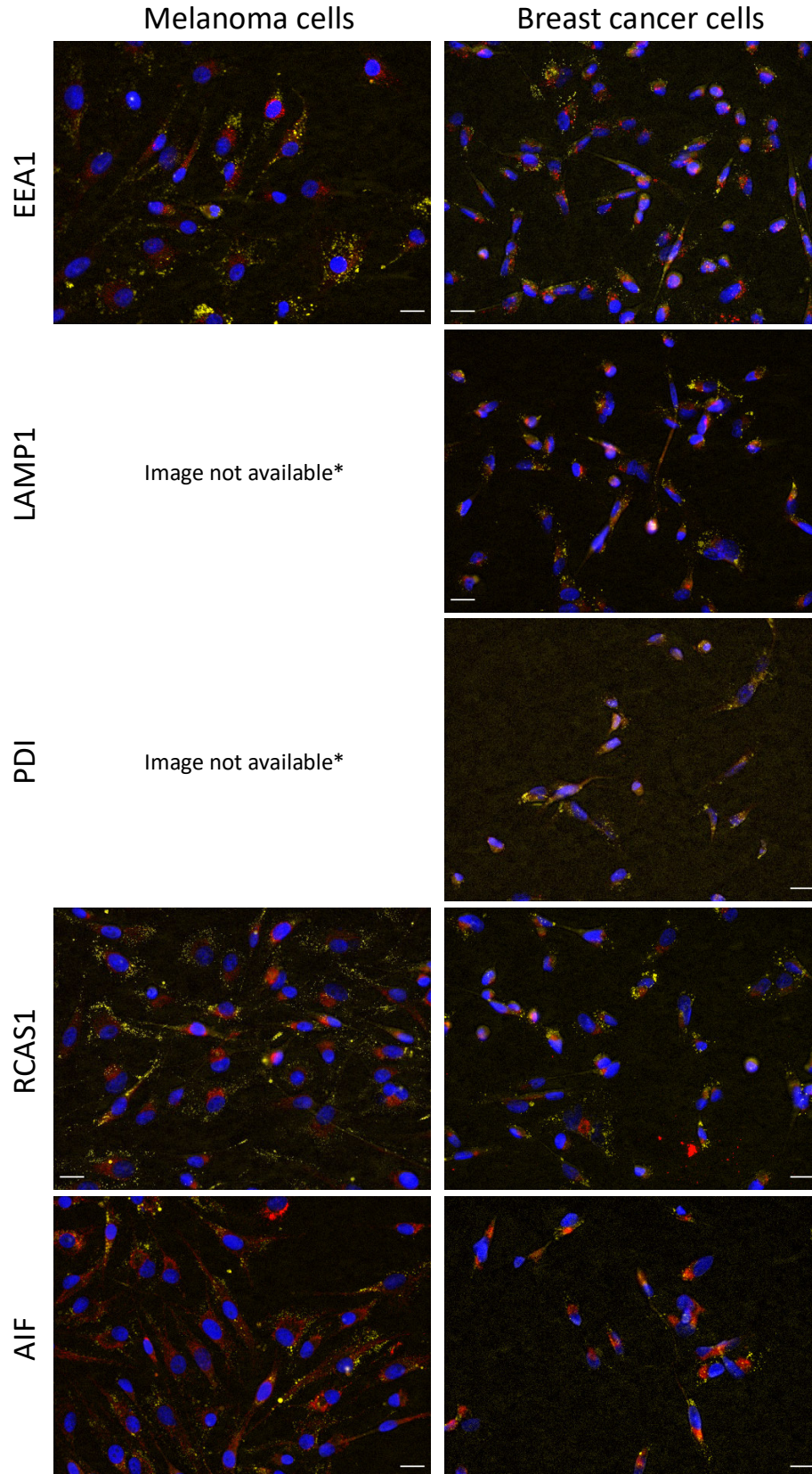


Figure S35. Colocalization experiments of **12** (30 μ M, 24 h; seen in yellow; ex. 460-500 nm, em. 512-542 nm) with EEA1 (endosomes), LAMP1 (lysosomes), PDI (endoplasmic reticulum), RCAS1 (Golgi) or AIF (mitochondria) (seen in red; ex. 590-650 nm, em. 662-738 nm). Scale bar 20 μ m. Cell nuclei were stained with DAPI (seen in blue; ex. 325-375 nm, em. 435-485 nm). *The experiment was inconclusive and not investigated further since results with breast cancer cells were obtained and good colocalization with lipid droplets was observed.

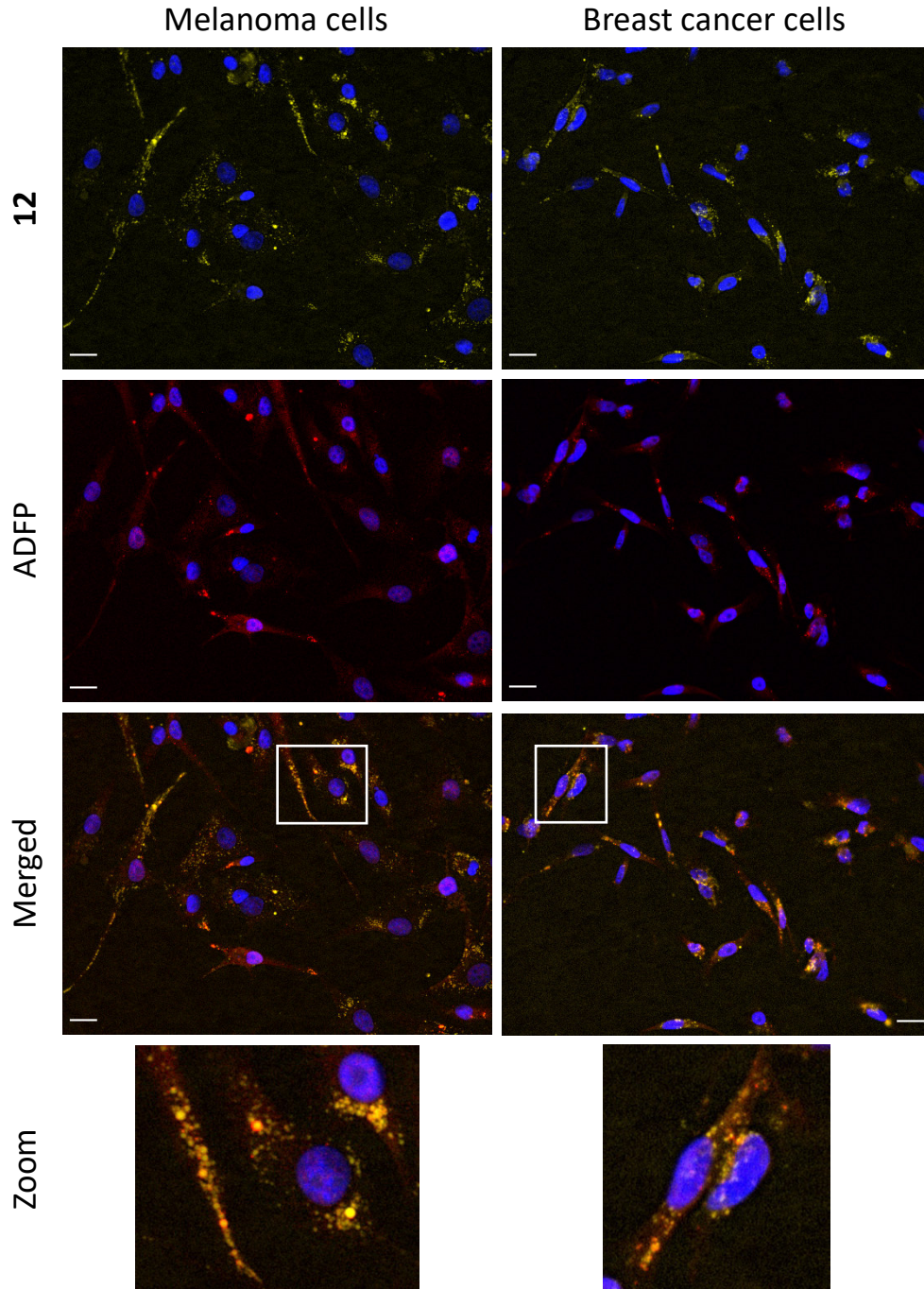


Figure S36. Fluorescence microscopy images of the colocalization of **12** (seen in yellow; ex. 460-500 nm, em. 512-542 nm) and an anti-ADFP antibody that targets the surface of lipid droplets (seen in red; ex. 590-650 nm, em. 662-738 nm) in melanoma (SK-MEL-28) and breast cancer (MDA-MB-231) cells. Scale bar 20 μm . Staining was performed on live cells, which were fixed after incubation (30 μM , 24 h) and then subjected to immunocytochemistry. Cell nuclei were stained with DAPI (seen in blue; ex. 325-375 nm, em. 435-485 nm).

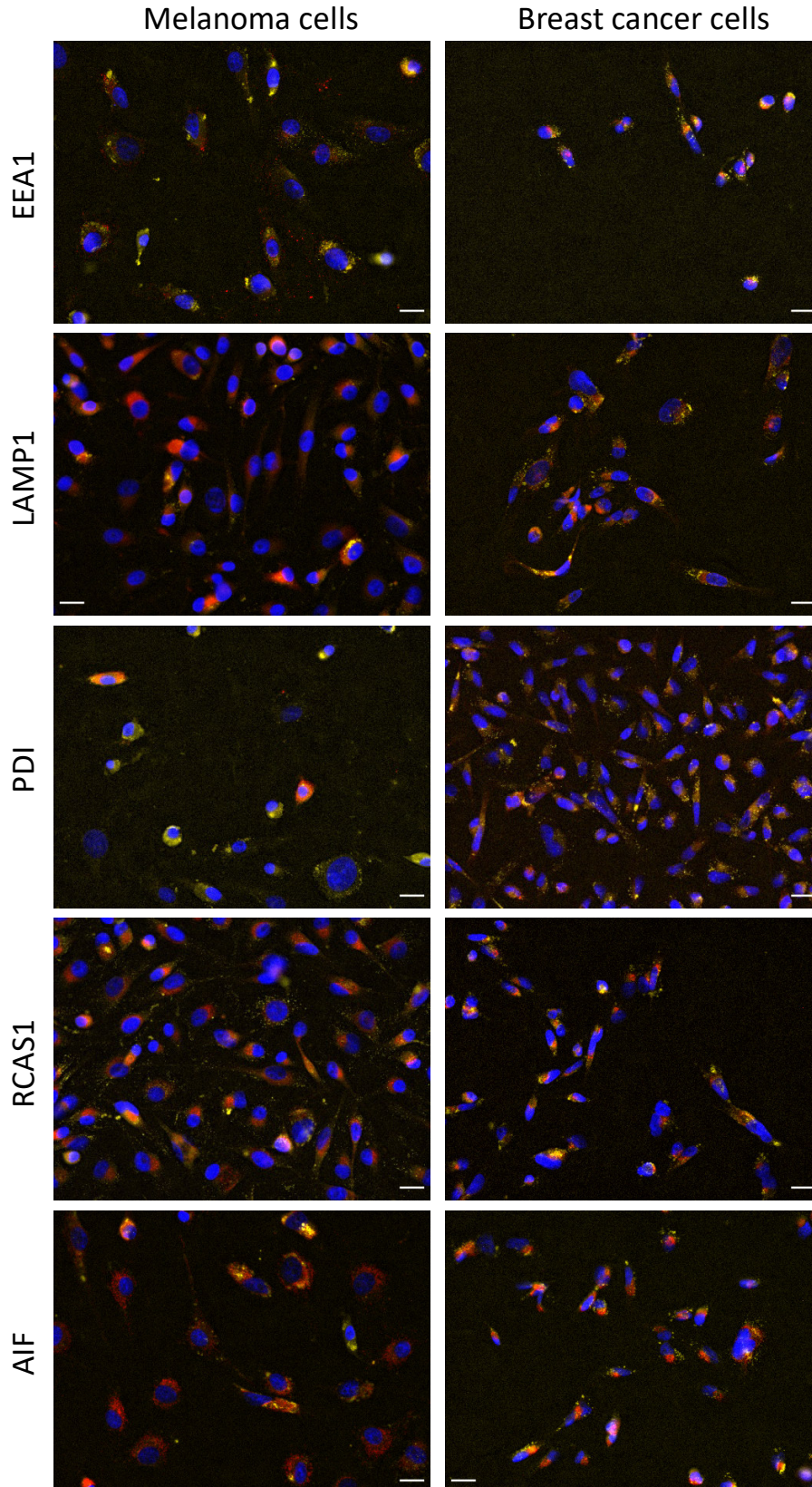


Figure S37. Colocalization experiments of **13** (10 μ M, 24 h; seen in yellow; ex. 460-500 nm, em. 512-542 nm)* with EEA1 (endosomes), LAMP1 (lysosomes), PDI (endoplasmic reticulum), RCAS1 (Golgi) or AIF (mitochondria) (seen in red; ex. 590-650 nm, em. 662-738 nm). Scale bar 20 μ m. *30 μ M of **13** was used in costaining of melanoma cells with LAMP1 and PDI. Cell nuclei were stained with DAPI (seen in blue; ex. 325-375 nm, em. 435-485 nm).

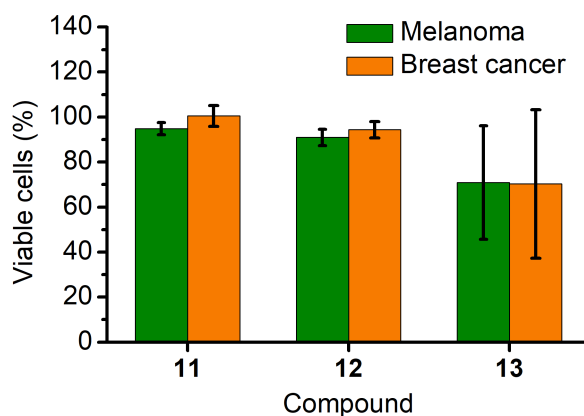


Figure S38. Cell viability of melanoma (SK-MEL-28) and breast cancer cells (MDA-MB-231) after treatment with **11**, **12** and **13** (10 μ M, 24 h), respectively. The data is presented relative to DMSO control as a mean \pm SD; n = 3 (**11**, **12**) or 4 (**13**).

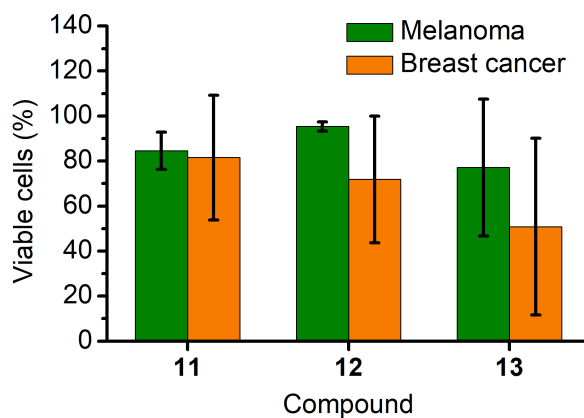


Figure S39. Cell viability of melanoma (SK-MEL-28) and breast cancer cells (MDA-MB-231) after treatment with **11**, **12** and **13** (30 μ M, 24 h), respectively. The data is presented relative to DMSO control as a mean \pm SD; n = 5 (**11**, **12**) or 6 (**13**).

VII. NMR Spectra

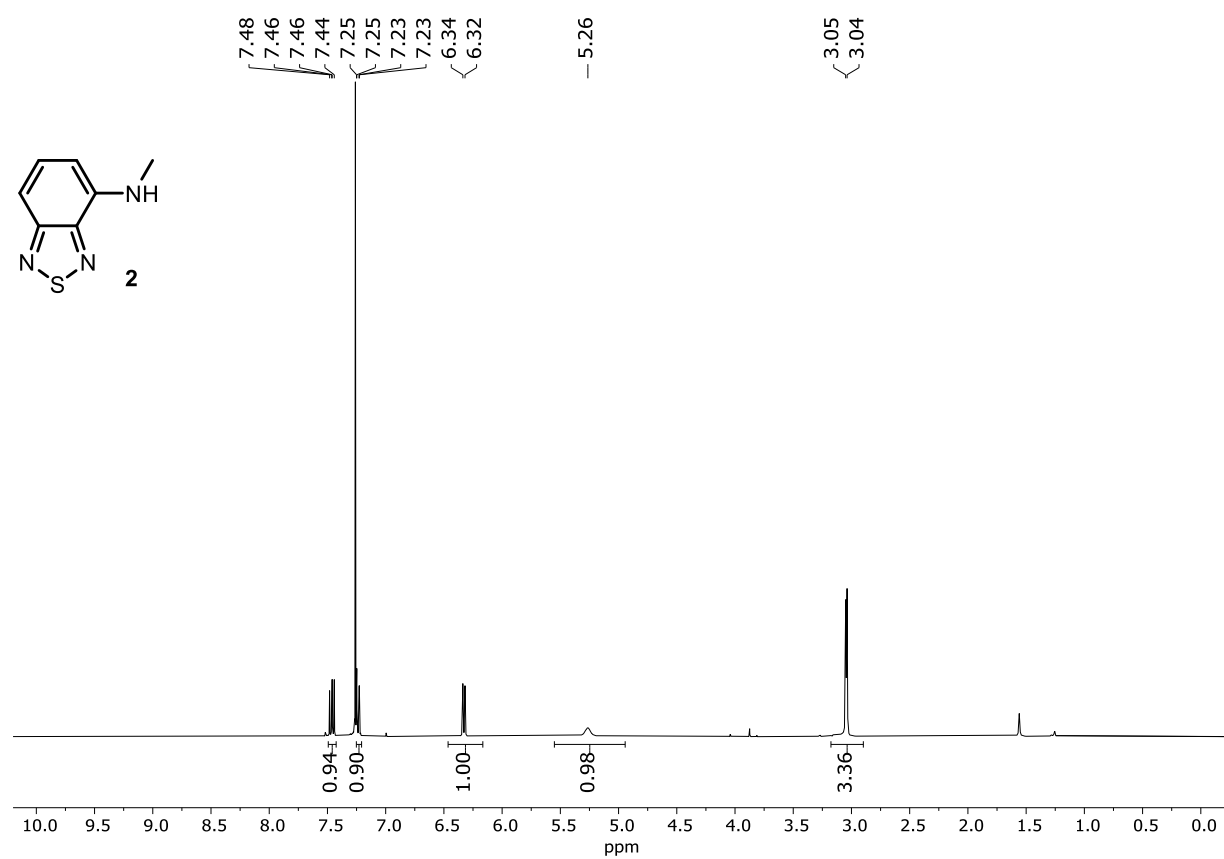


Figure S40. ¹H NMR spectrum (400 MHz, CDCl₃) of compound **2**.

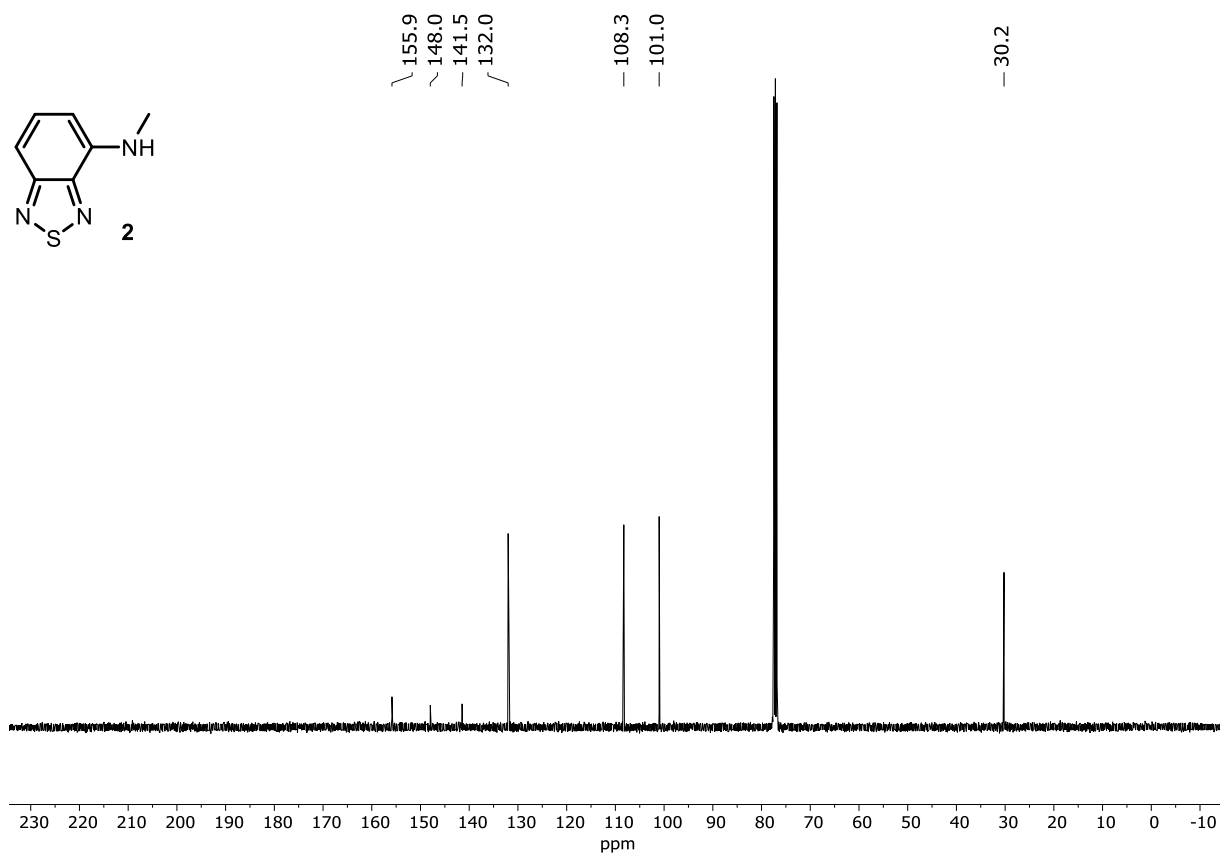


Figure S41. ¹³C NMR spectrum (101 MHz, CDCl₃) of compound **2**.

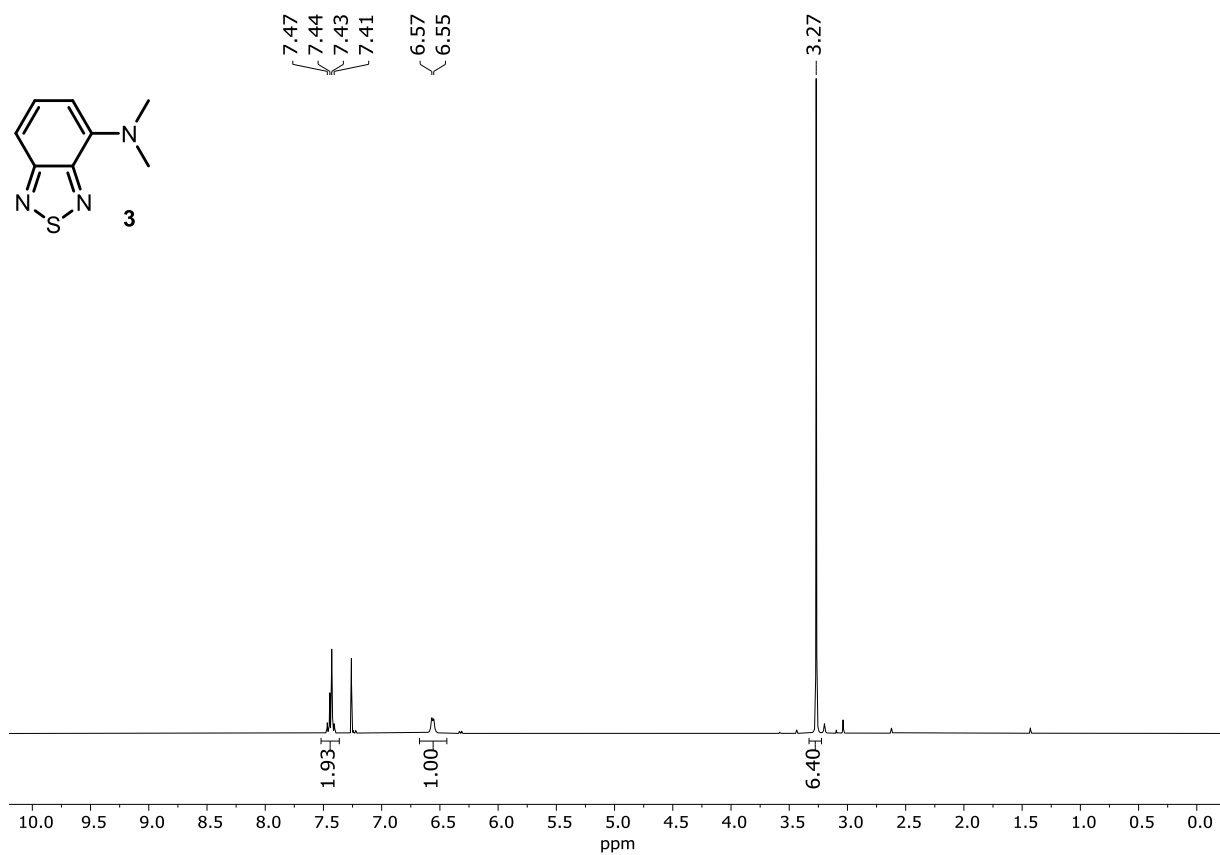


Figure S42. ¹H NMR spectrum (400 MHz, CDCl₃) of compound **3**.

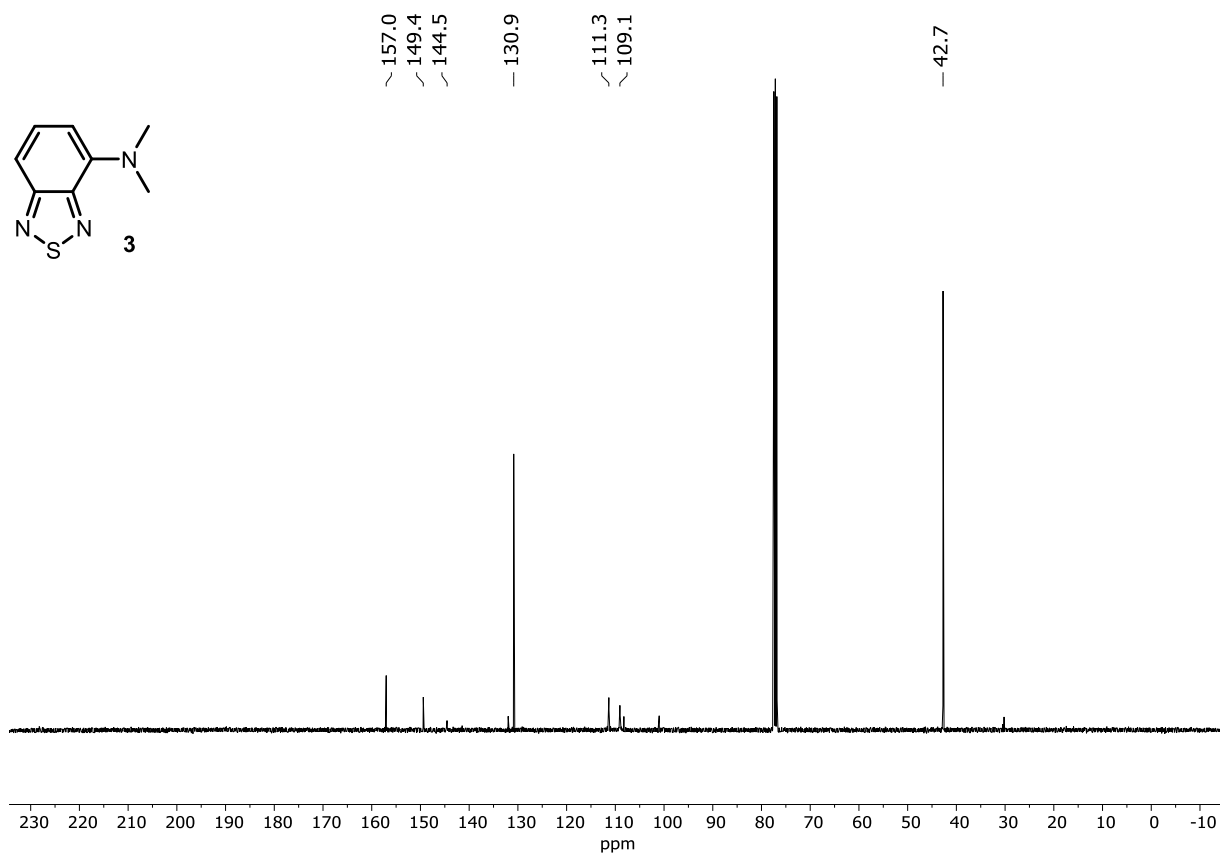


Figure S43. ^{13}C NMR spectrum (101 MHz, CDCl_3) of compound **3**. Additional peaks in the spectrum can be ascribed to **2** (cf. Figure S41), which could not be fully removed during purification (ca. 5% based on ^1H NMR).

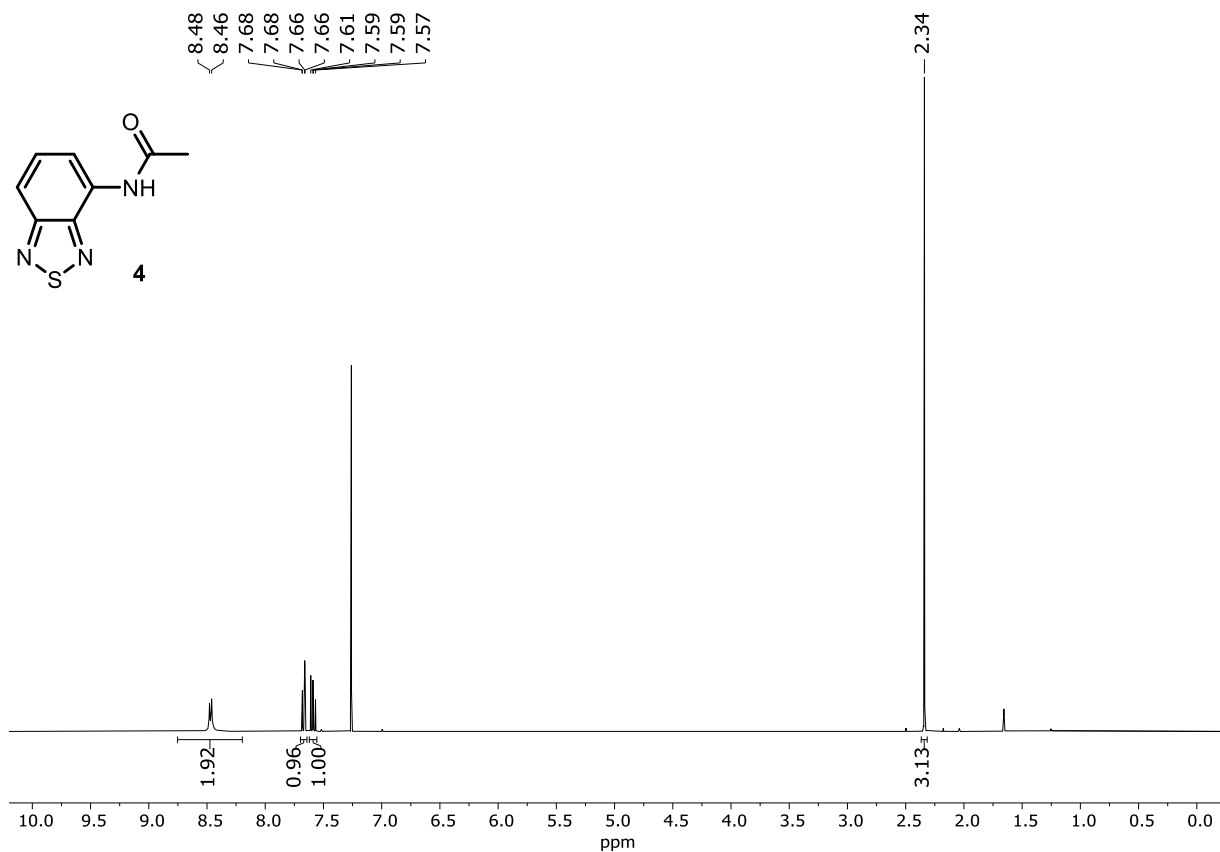


Figure S44. ^1H NMR spectrum (400 MHz, CDCl_3) of compound **4**.

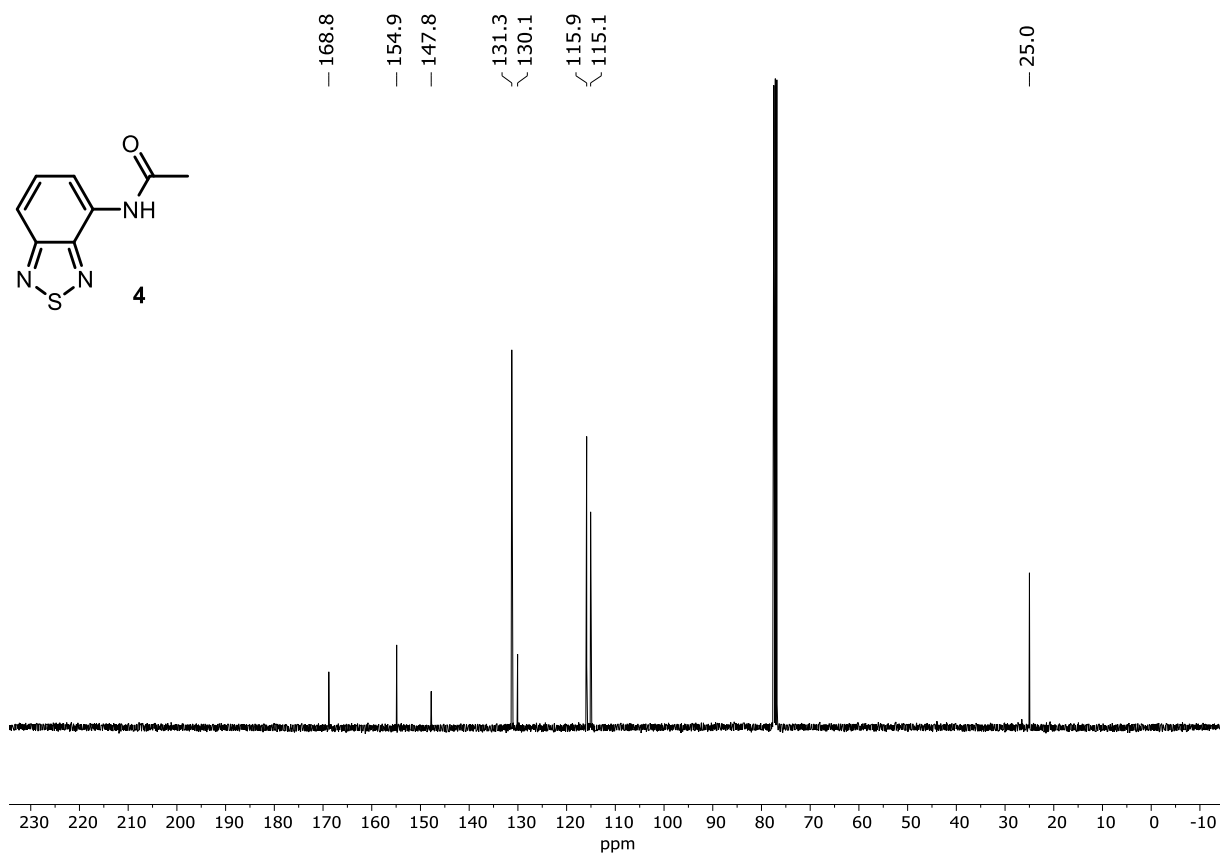


Figure S45. ^{13}C NMR spectrum (101 MHz, CDCl_3) of compound 4.

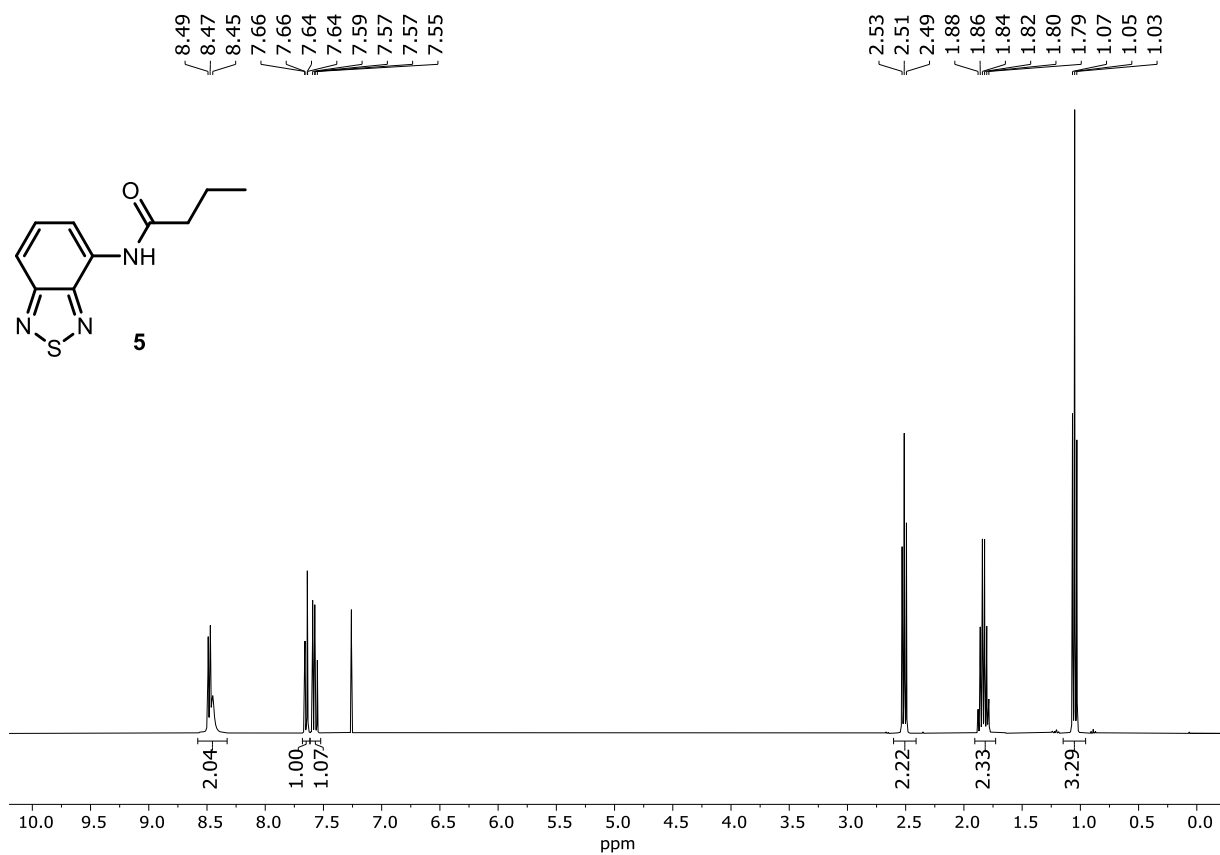


Figure S46. ^1H NMR spectrum (400 MHz, CDCl_3) of compound 5.

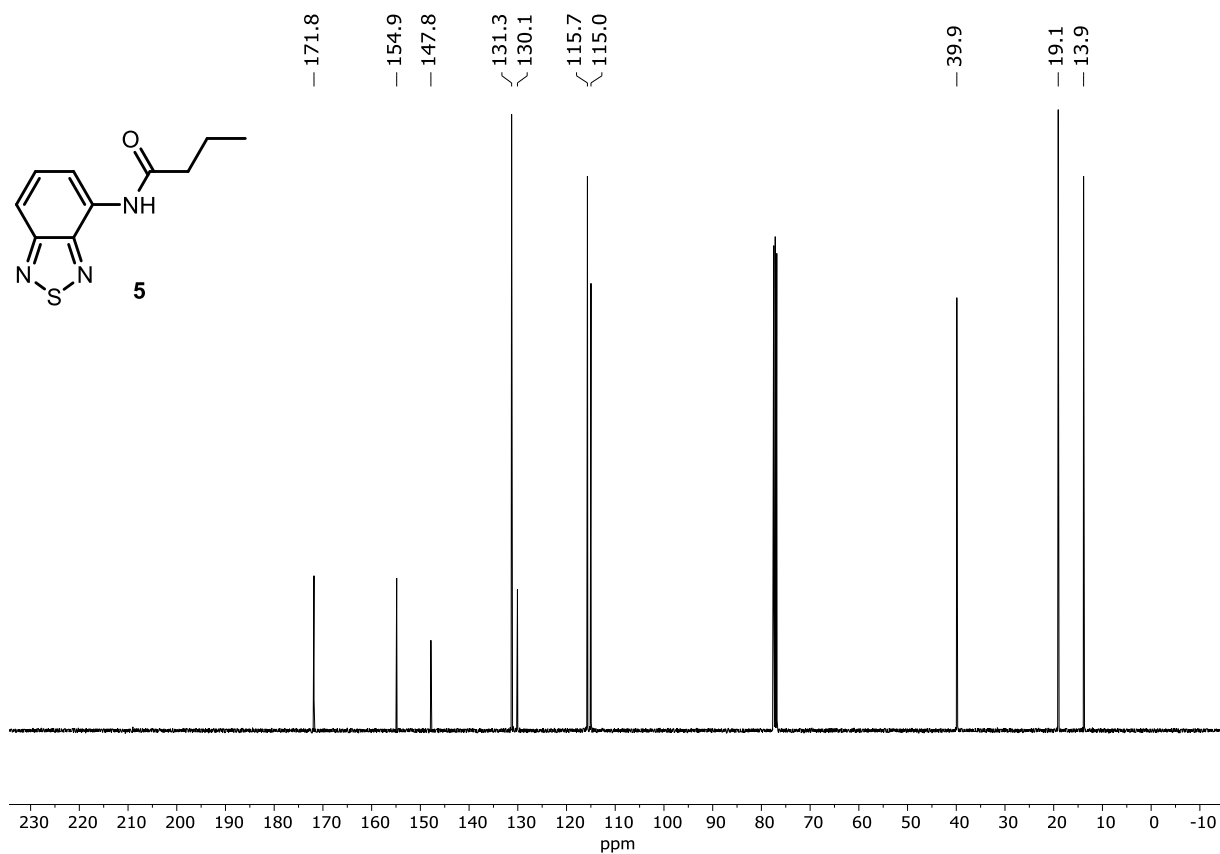


Figure S47. ^{13}C NMR spectrum (101 MHz, CDCl_3) of compound 5.

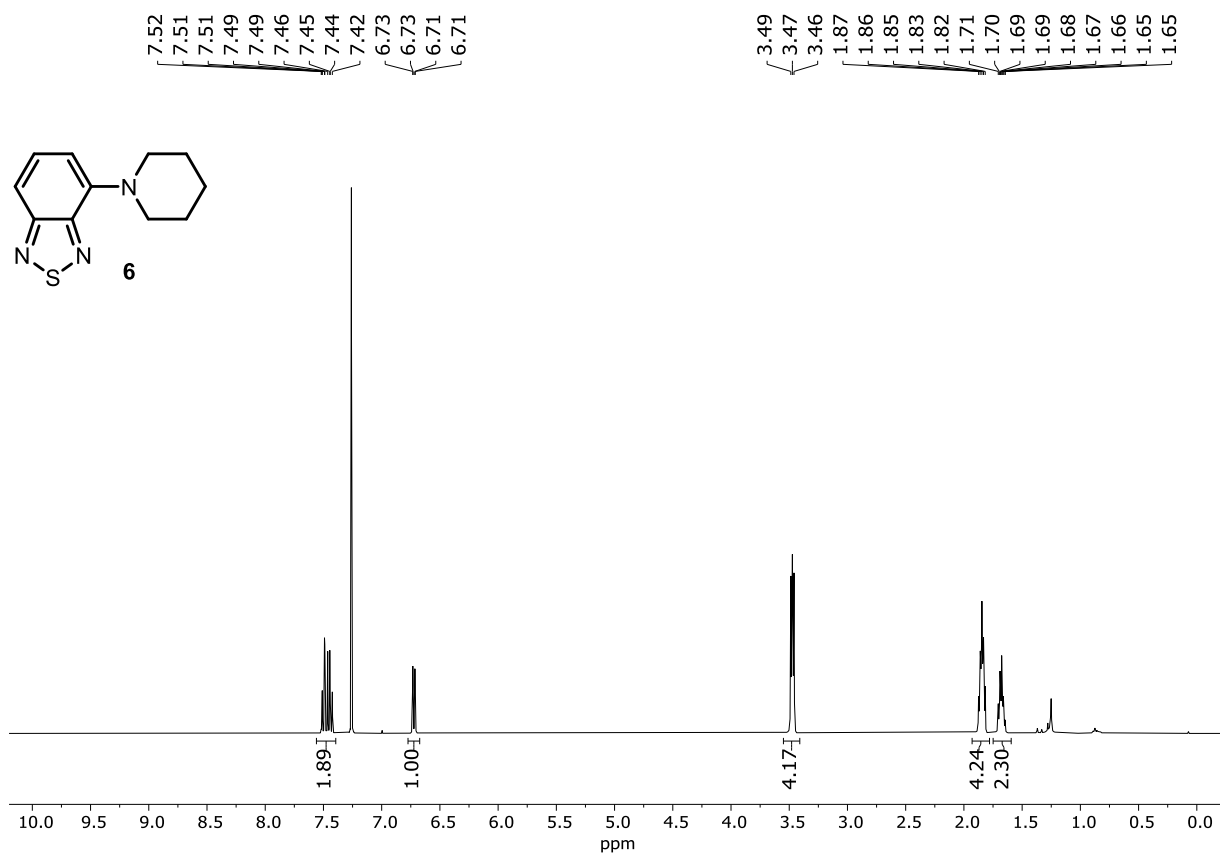


Figure S48. ^1H NMR spectrum (400 MHz, CDCl_3) of compound 6.

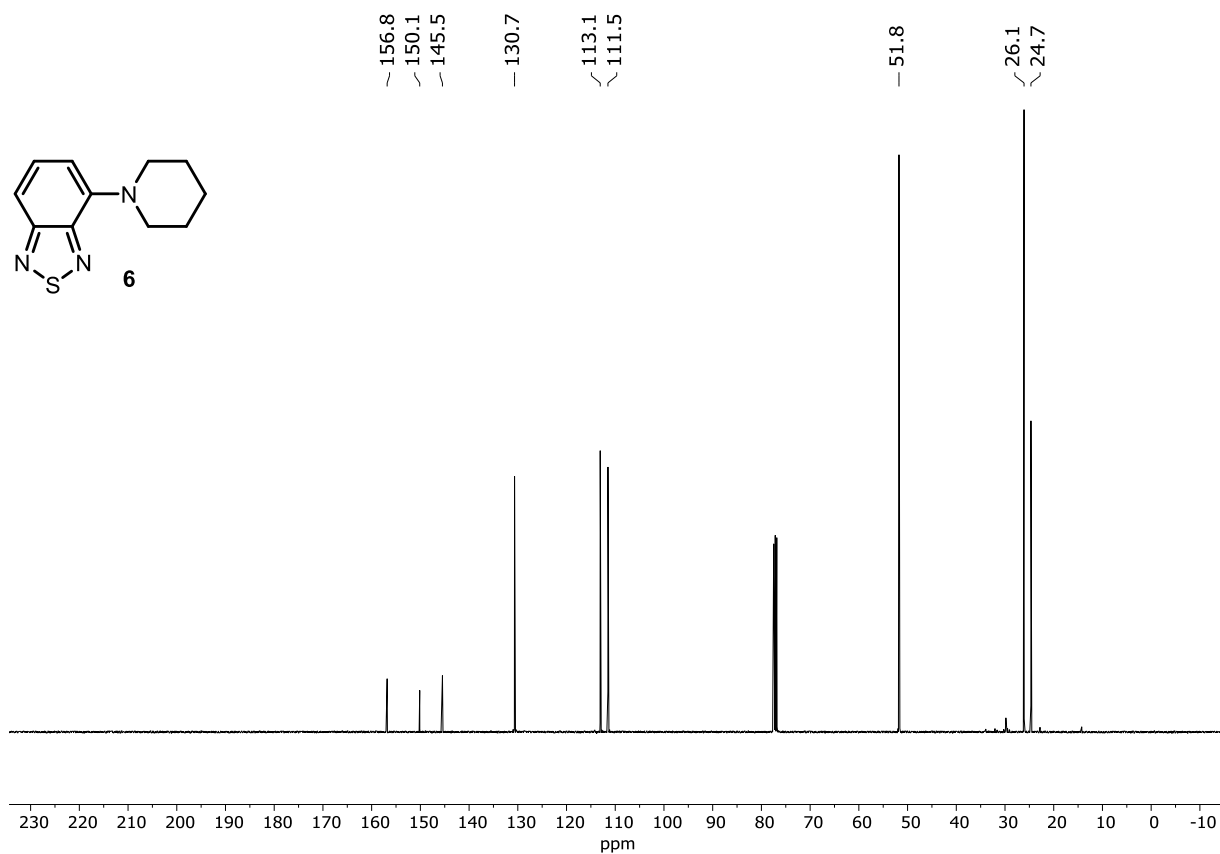


Figure S49. ^{13}C NMR spectrum (101 MHz, CDCl_3) of compound 6.

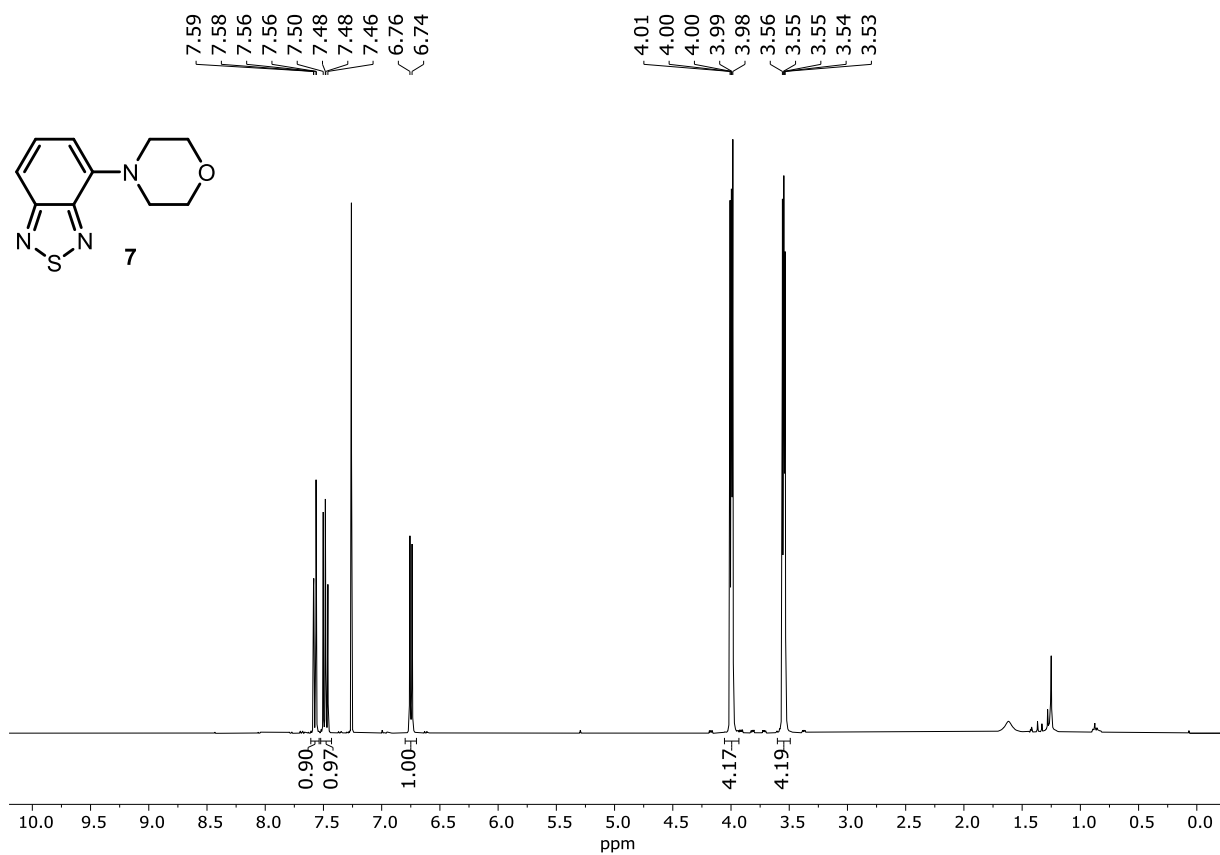


Figure S50. ^1H NMR spectrum (400 MHz, CDCl_3) of compound 7.

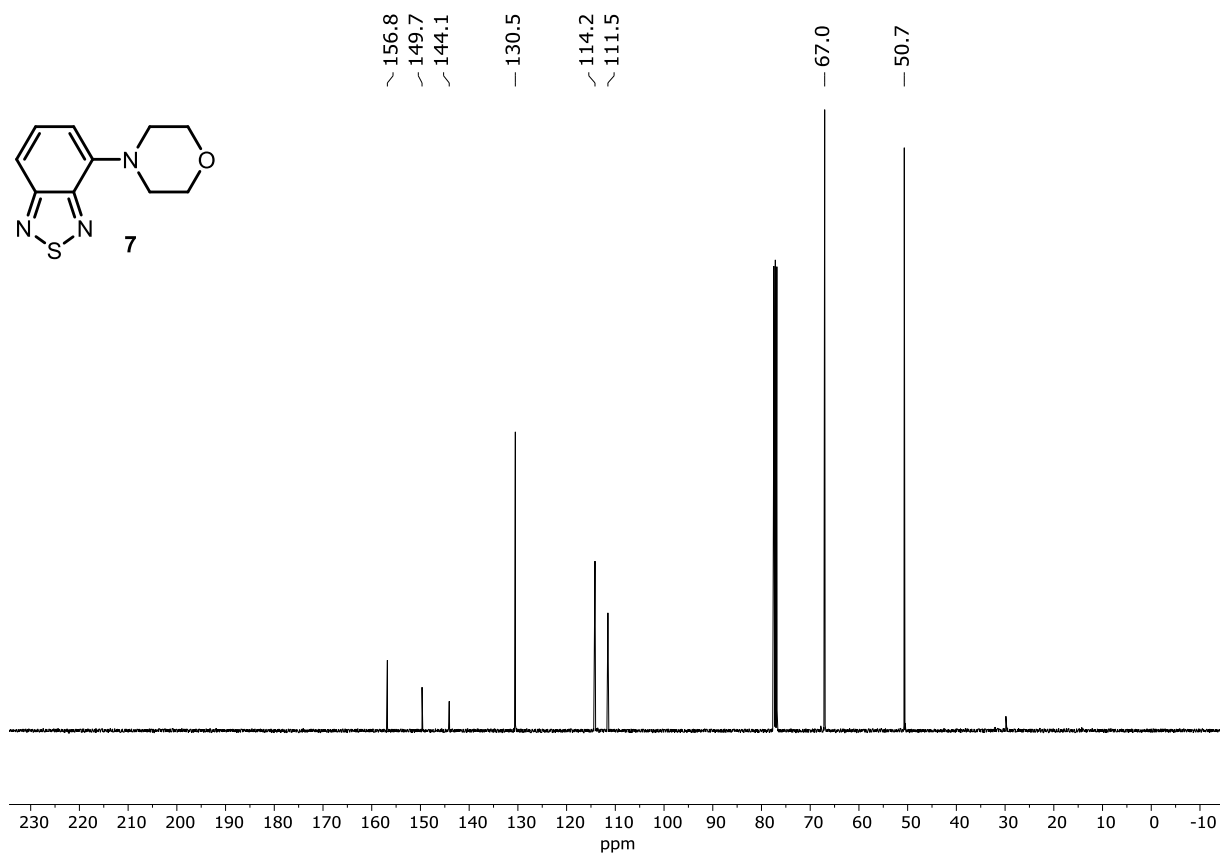


Figure S51. ^{13}C NMR spectrum (101 MHz, CDCl_3) of compound **7**.

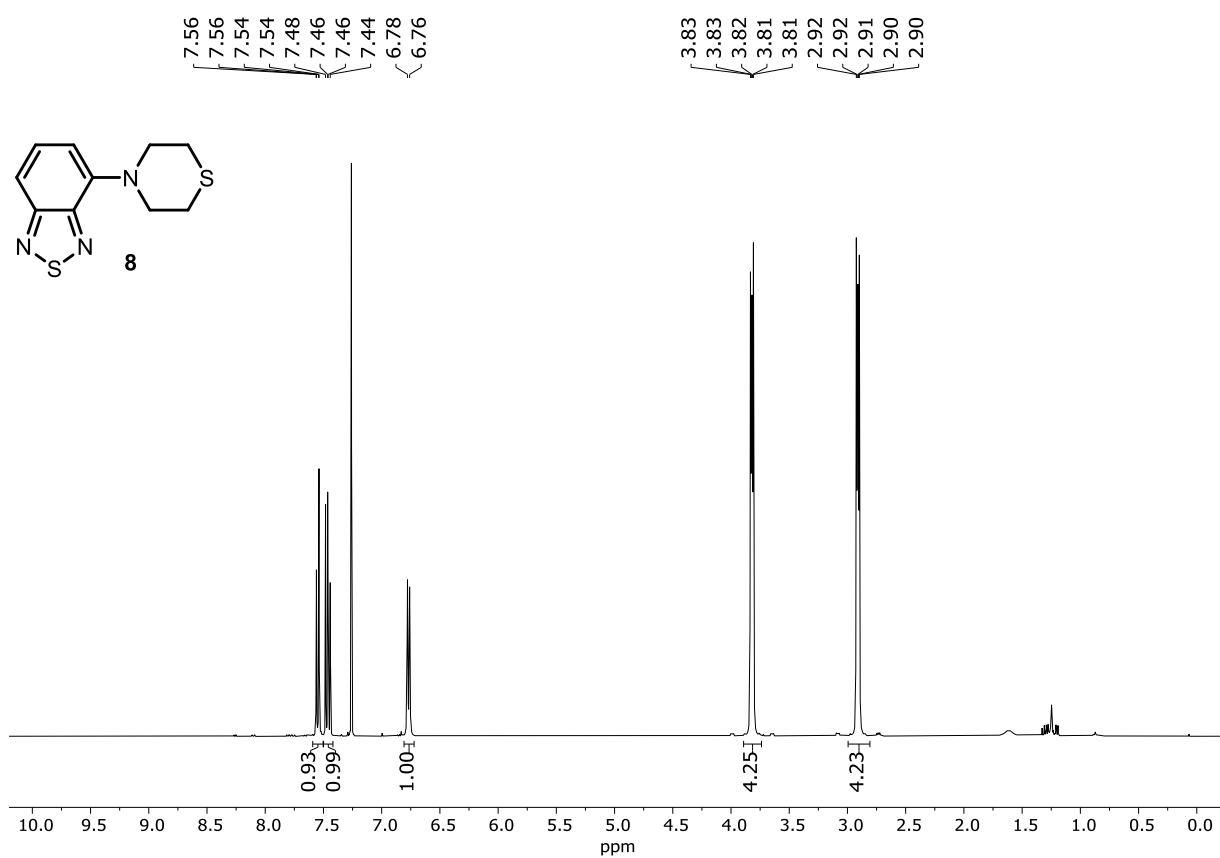


Figure S52. ^1H NMR spectrum (400 MHz, CDCl_3) of compound **8**.

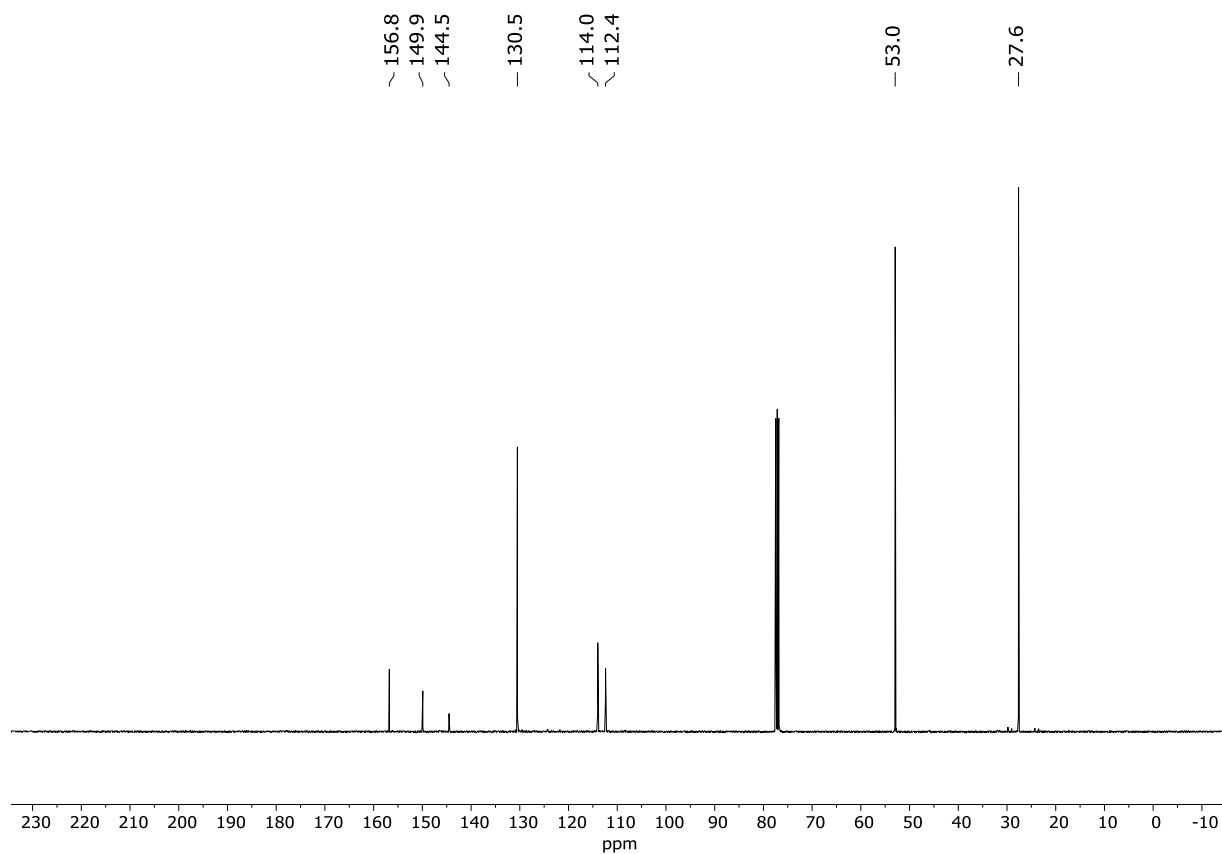


Figure S53. ^{13}C NMR spectrum (101 MHz, CDCl_3) of compound **8**.

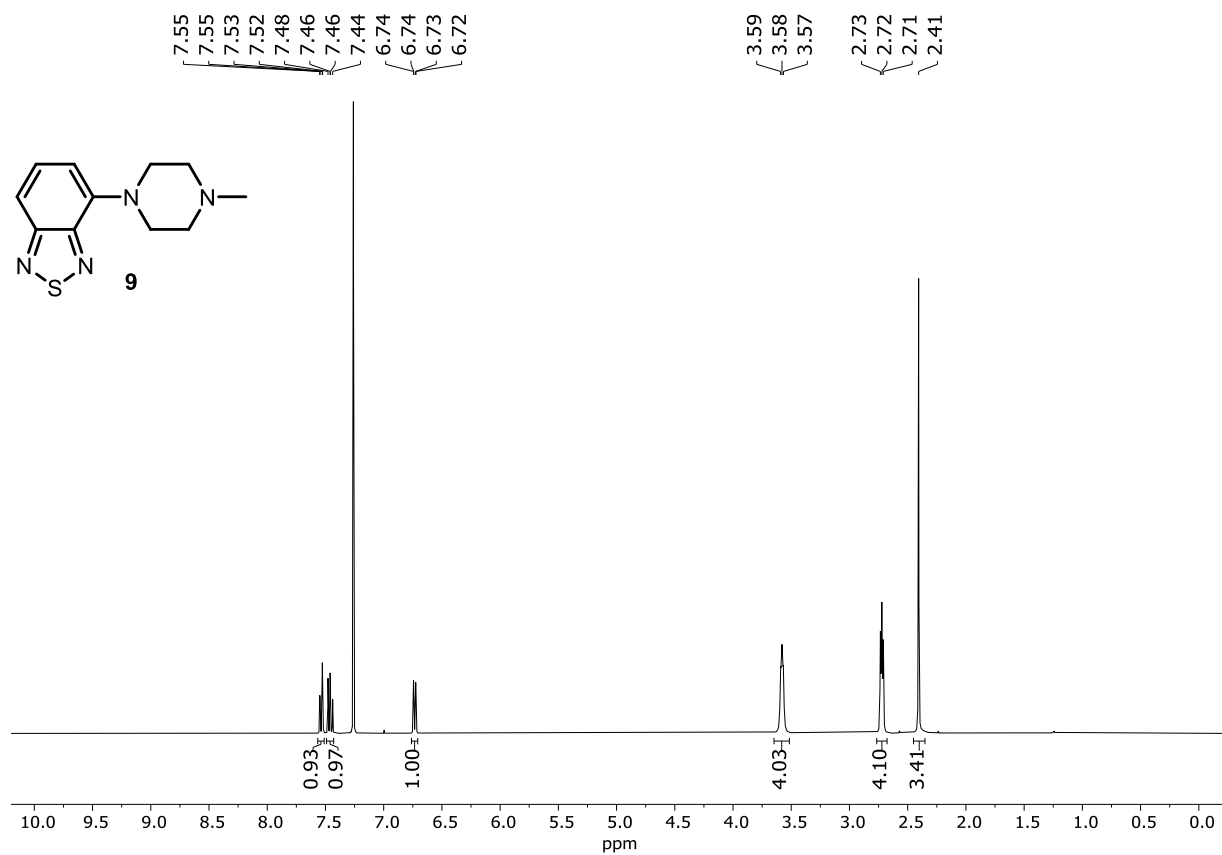


Figure S54. ^1H NMR spectrum (400 MHz, CDCl_3) of compound **9**.

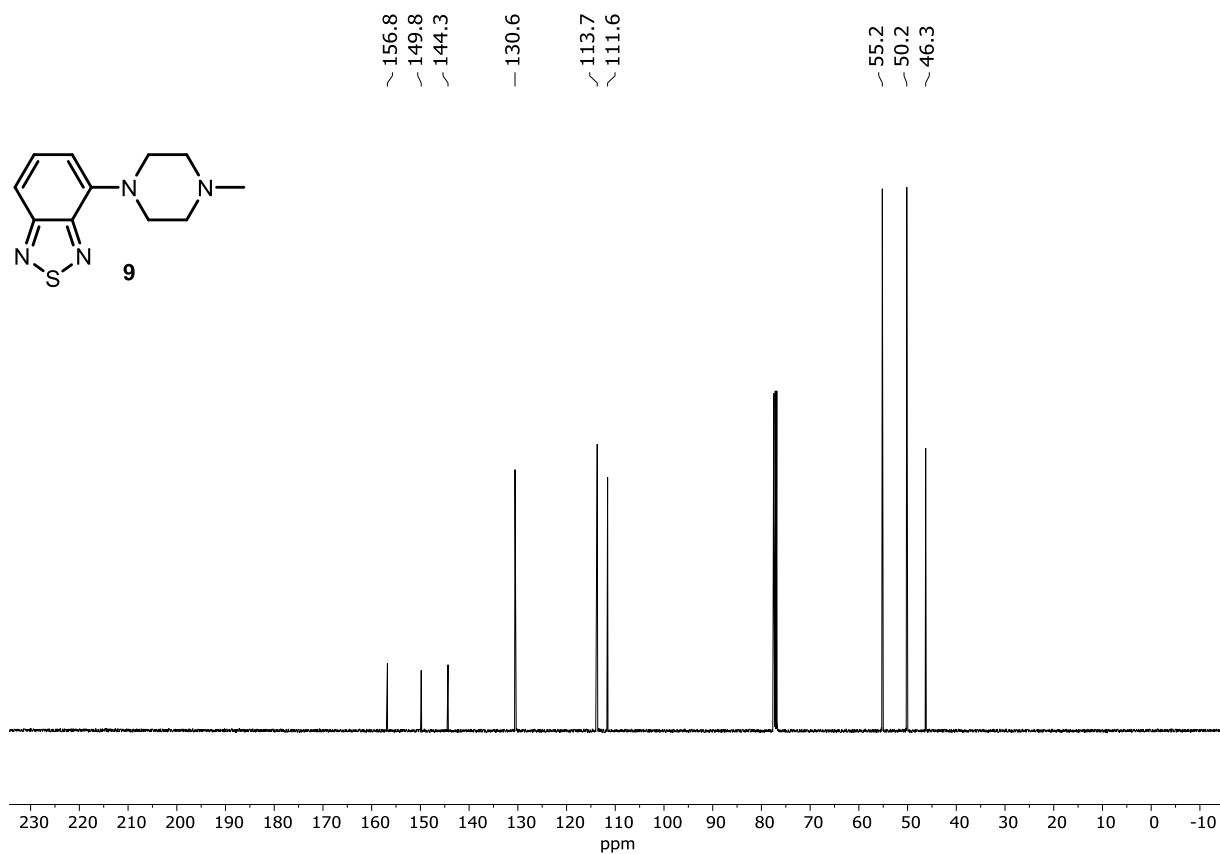


Figure S55. ^{13}C NMR spectrum (101 MHz, CDCl_3) of compound **9**.

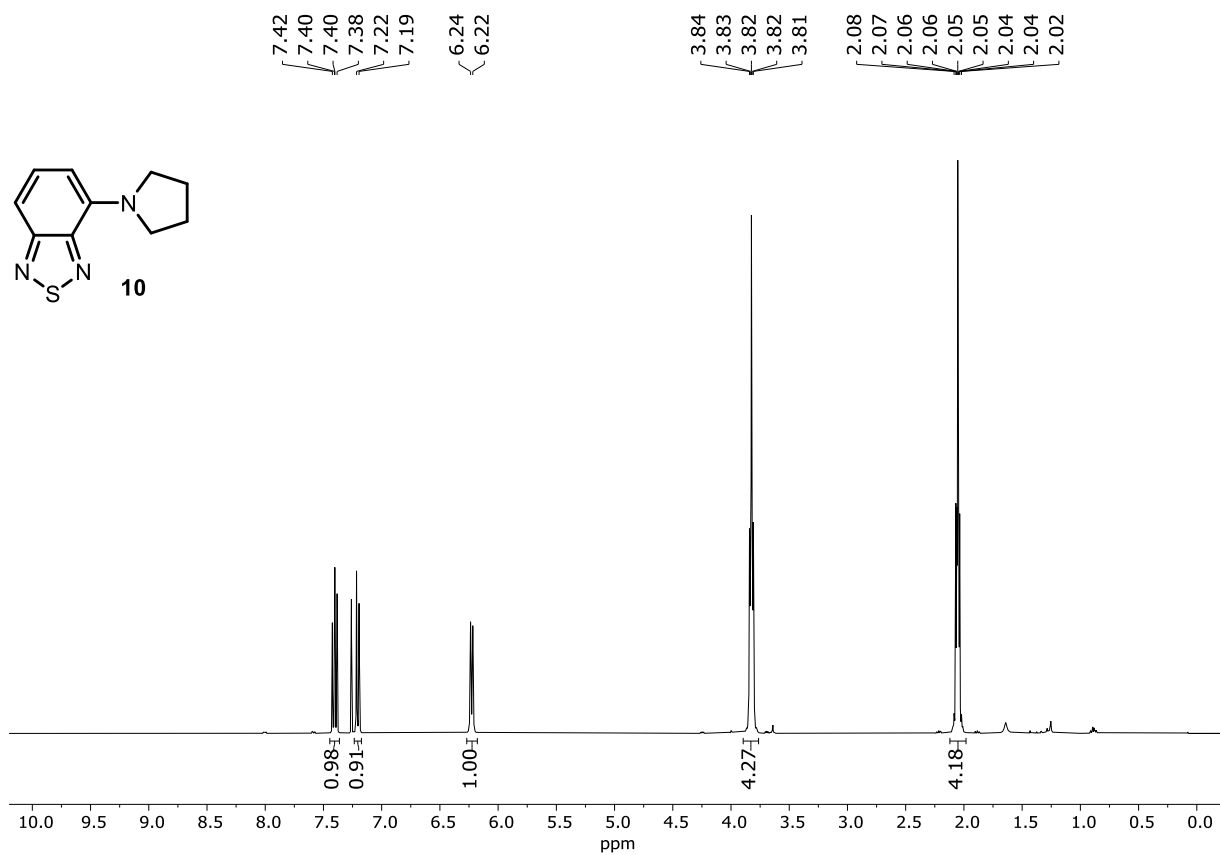


Figure S56. ^1H NMR spectrum (400 MHz, CDCl_3) of compound **10**.

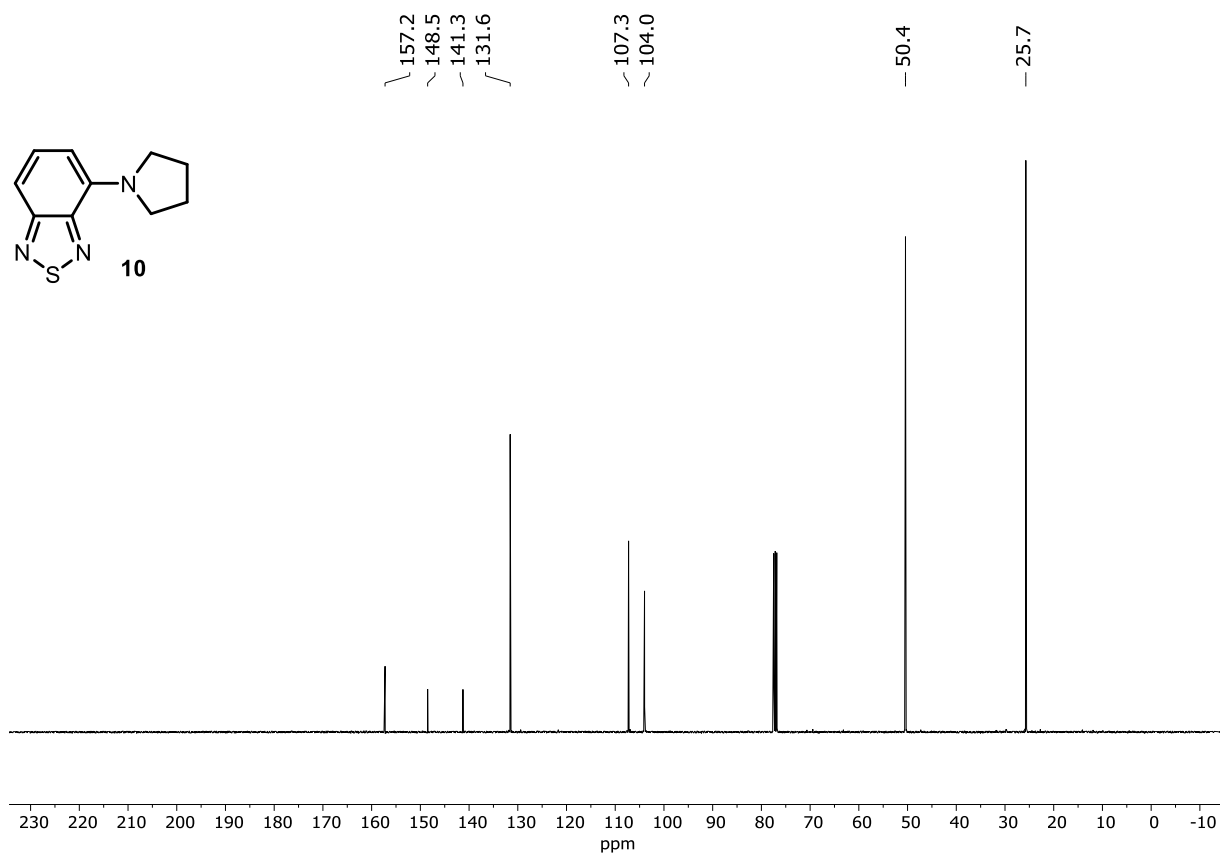


Figure S57. ^{13}C NMR spectrum (101 MHz, CDCl_3) of compound **10**.

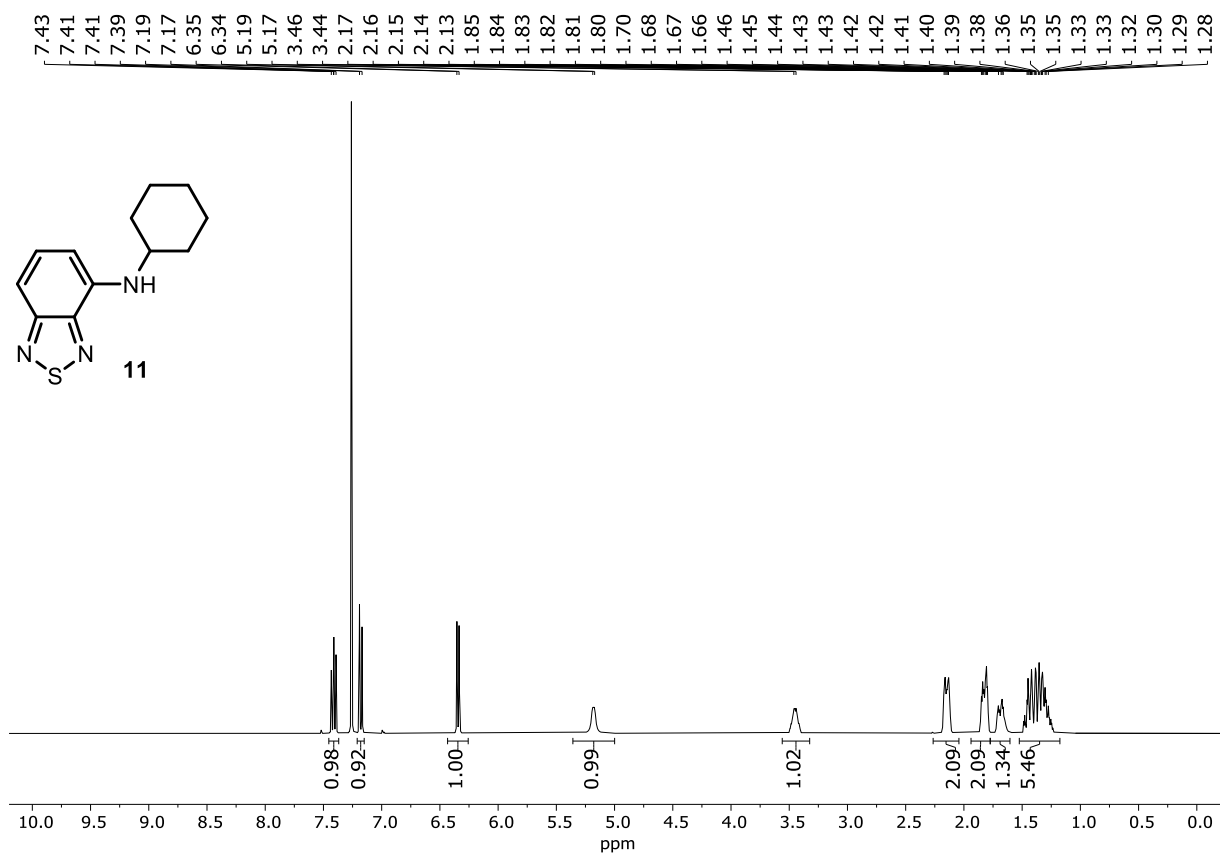


Figure S58. ^1H NMR spectrum (400 MHz, CDCl_3) of compound **11**.

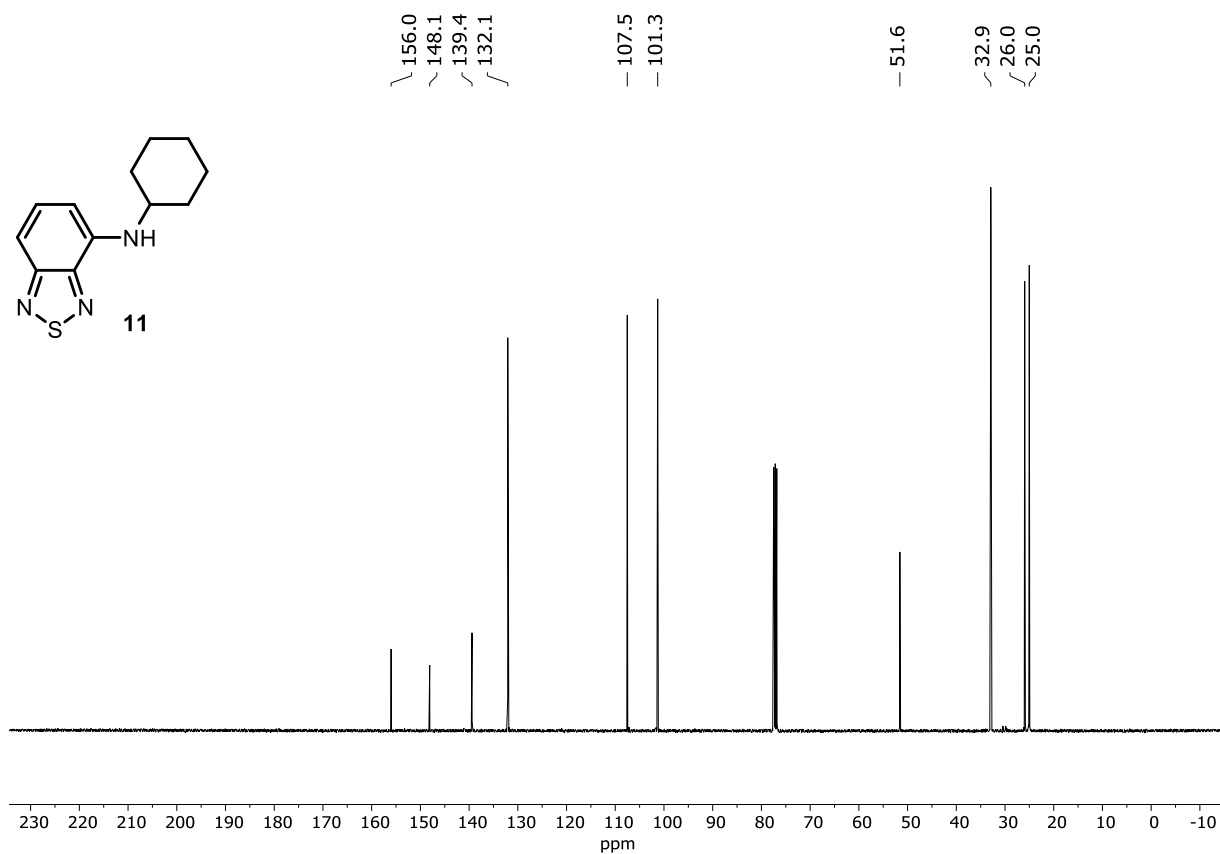


Figure S59. ¹³C NMR spectrum (101 MHz, CDCl₃) of compound **11**.

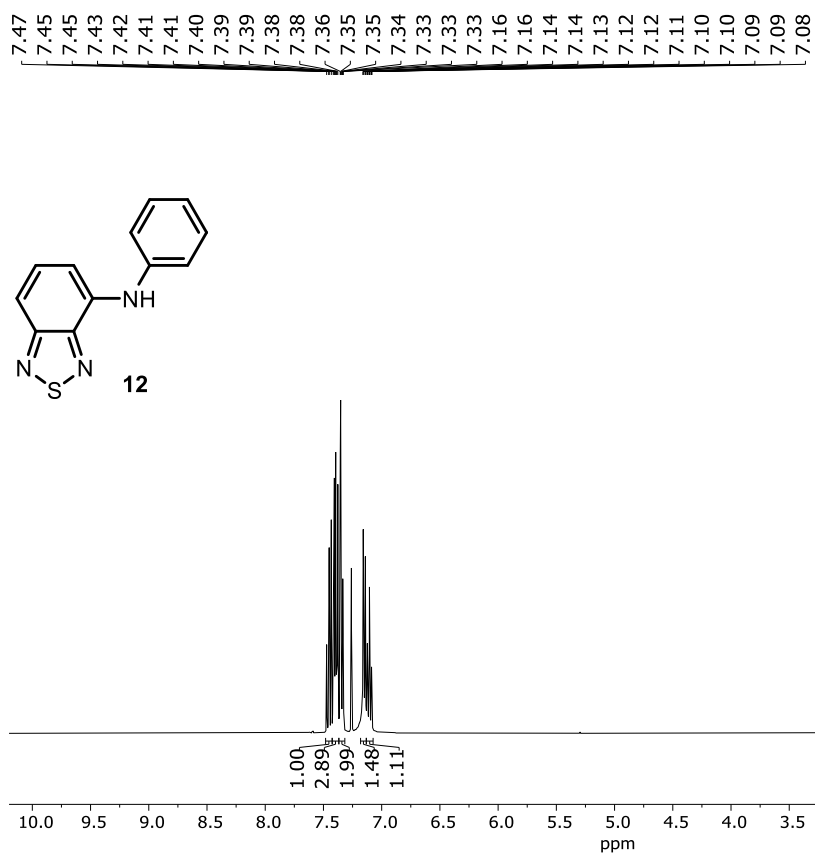


Figure S60. ¹H NMR spectrum (400 MHz, CDCl₃) of compound **12**.

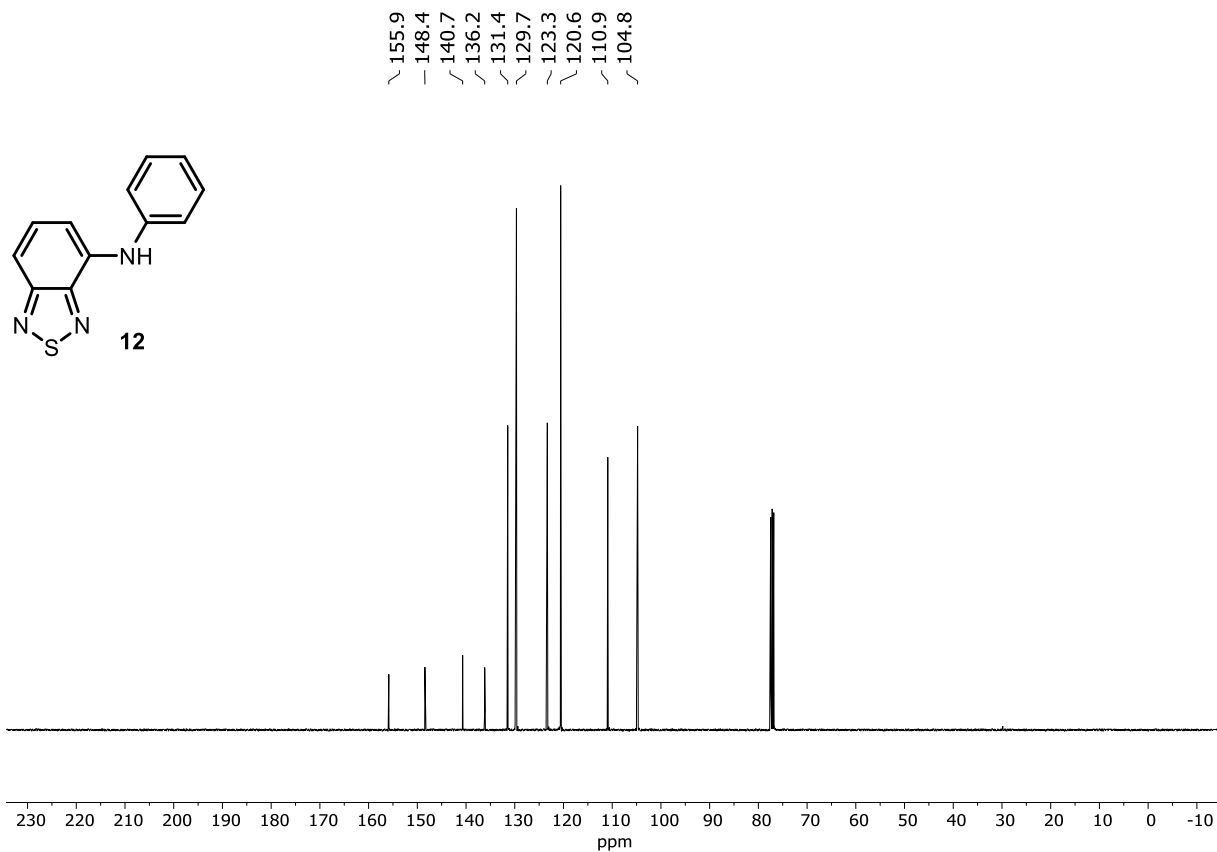


Figure S61. ^{13}C NMR spectrum (101 MHz, CDCl_3) of compound **12**.

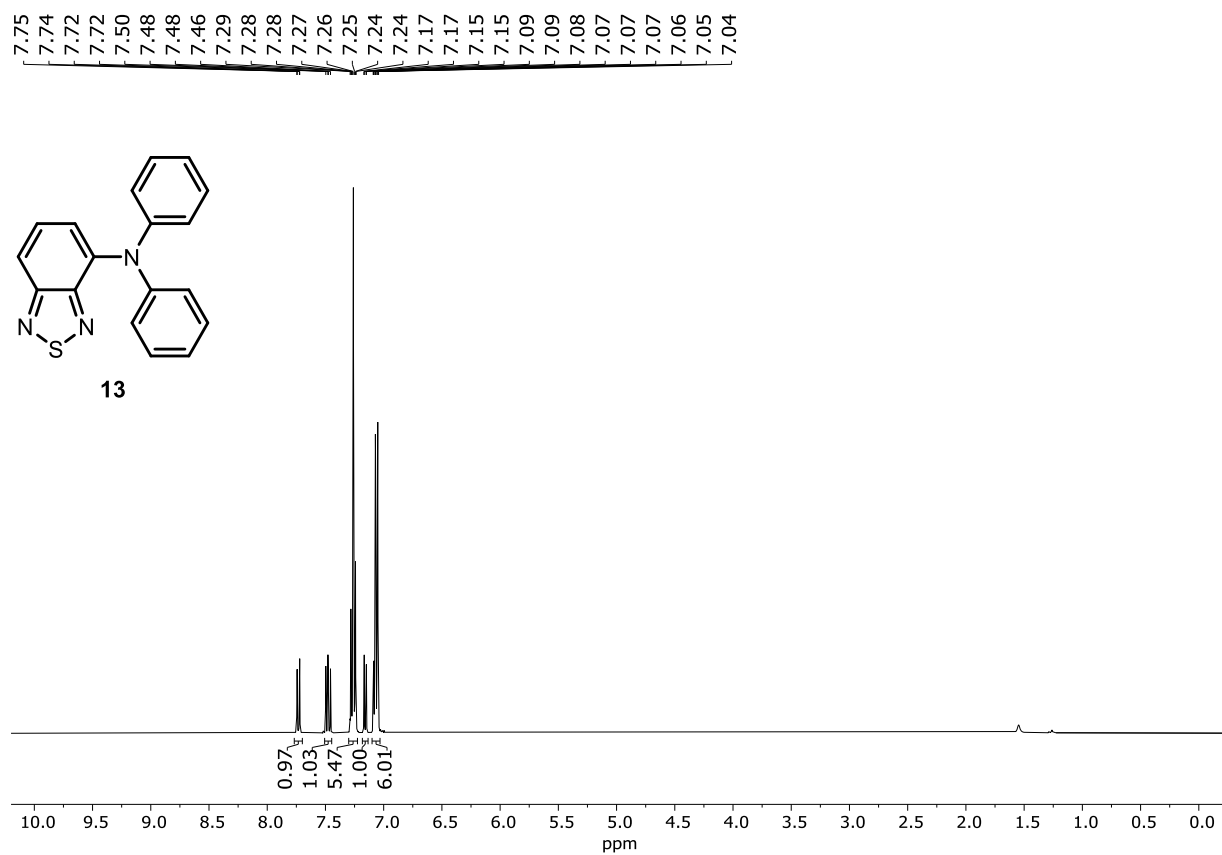


Figure S62. ^1H NMR spectrum (400 MHz, CDCl_3) of compound **13**.

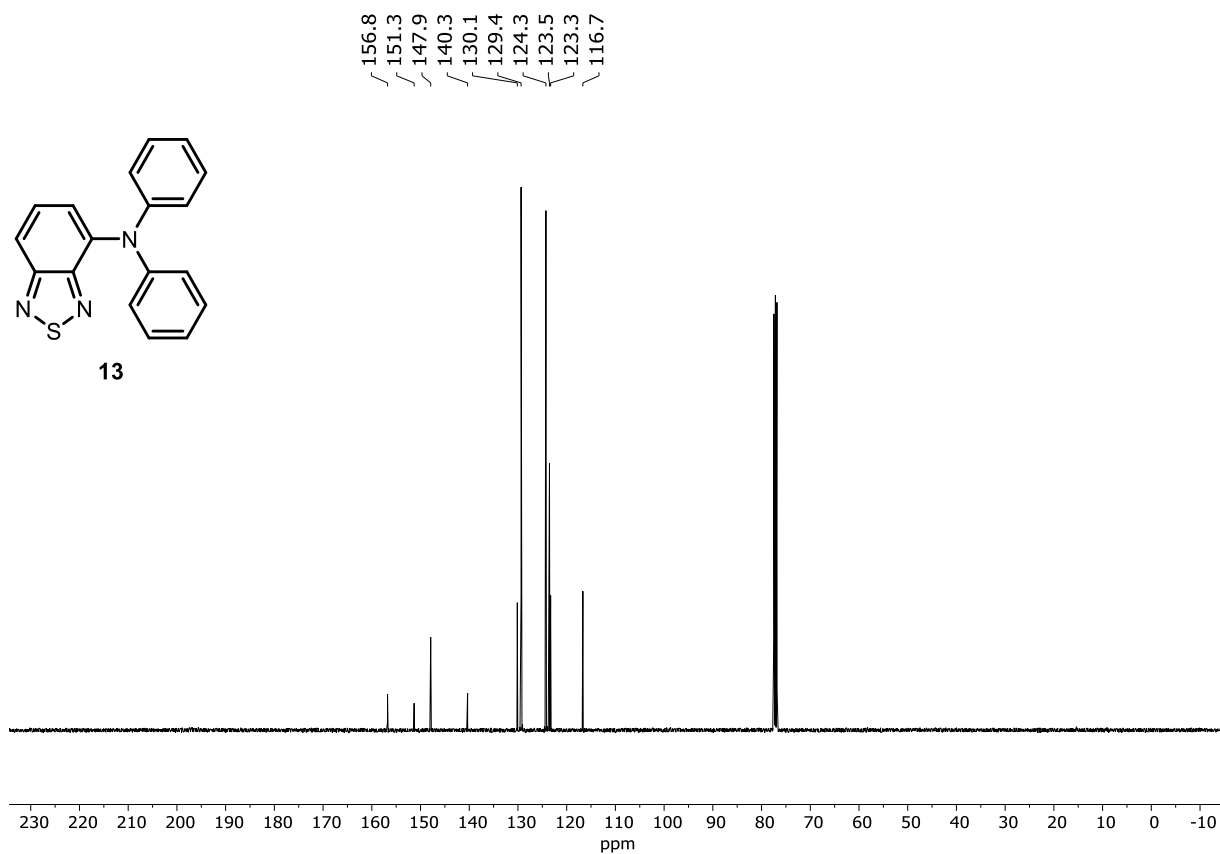


Figure S63. ¹³C NMR spectrum (101 MHz, CDCl₃) of compound **13**.

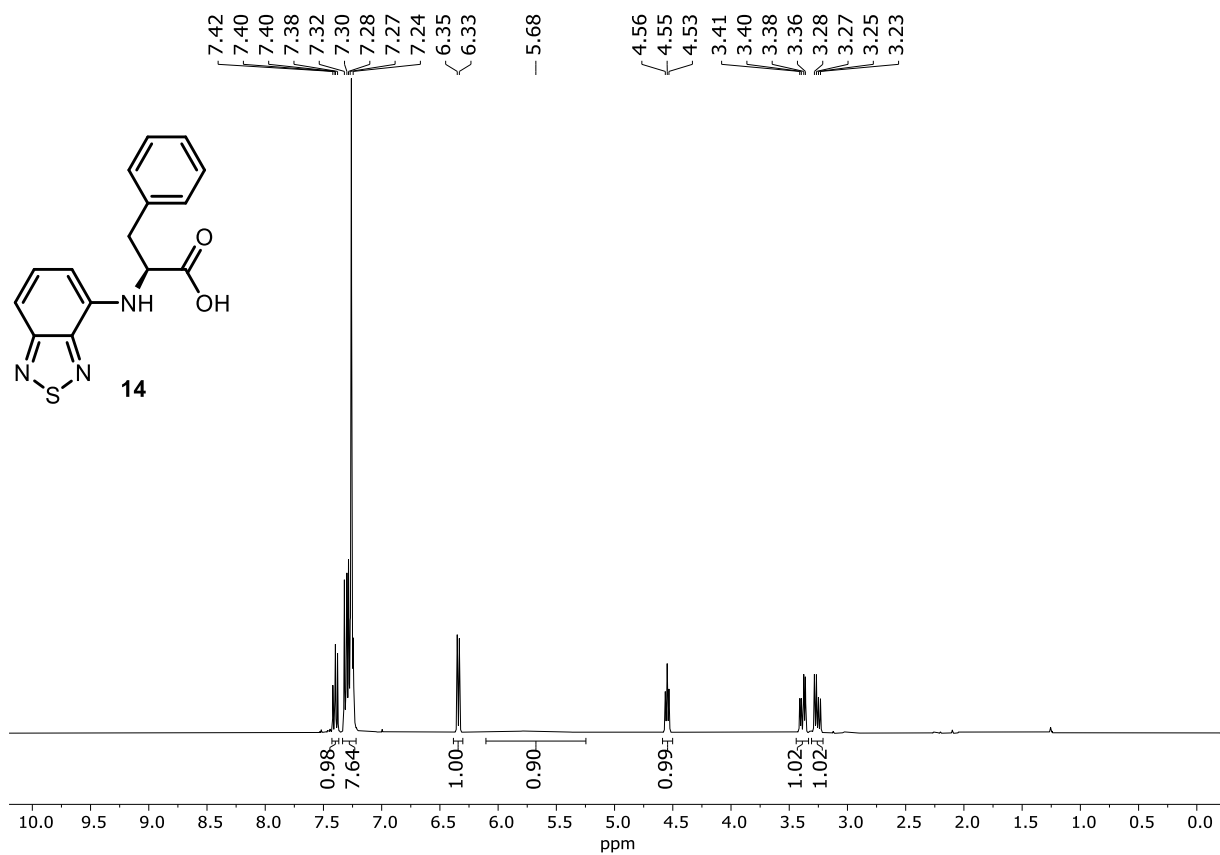


Figure S64. ¹H NMR spectrum (400 MHz, CDCl₃) of compound **14**.

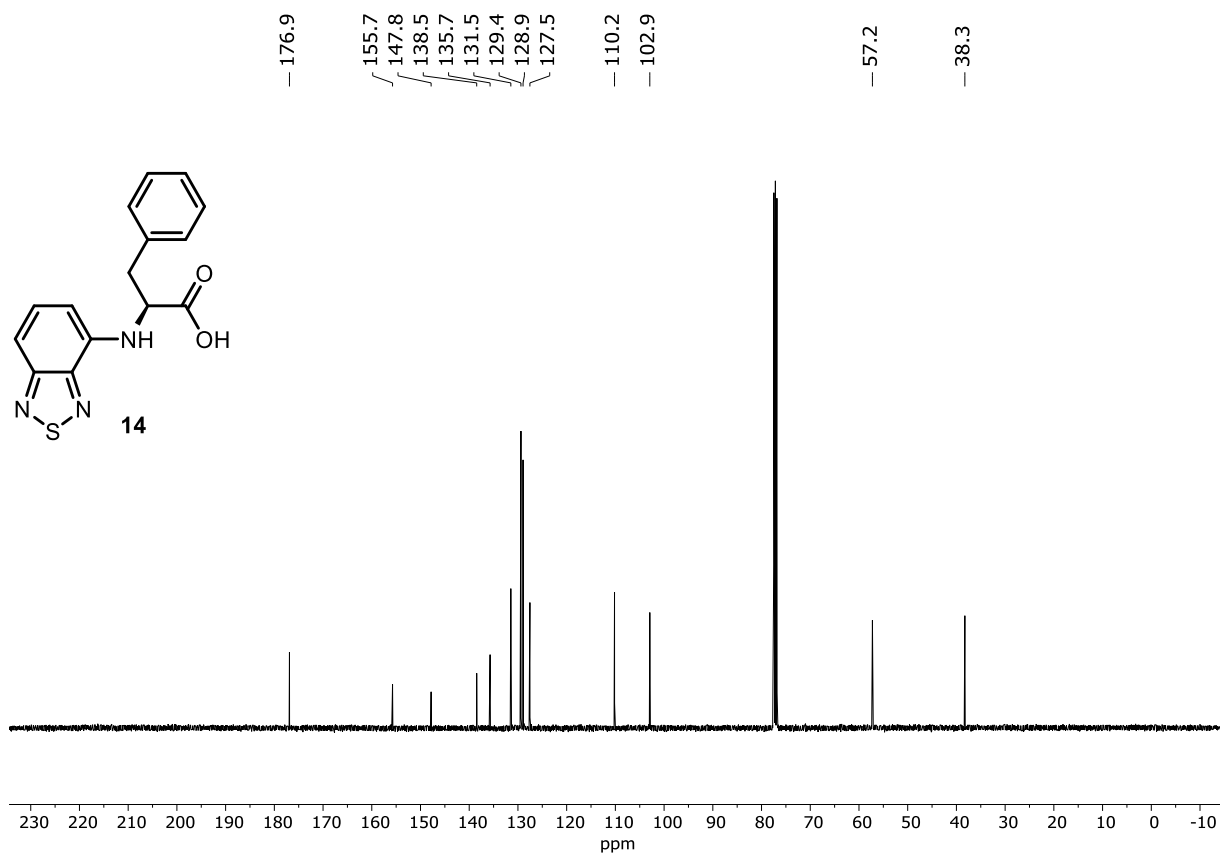


Figure S65. ^{13}C NMR spectrum (101 MHz, CDCl_3) of compound **14**.

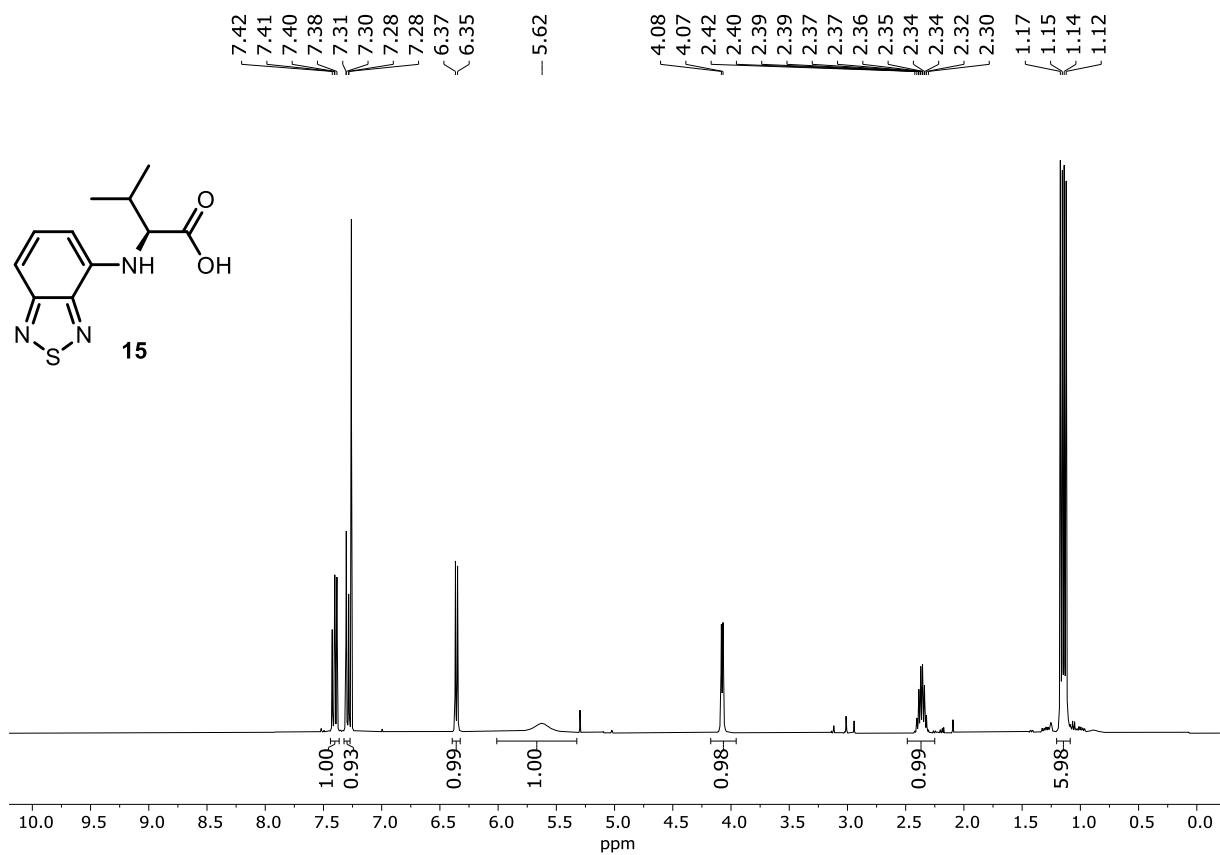


Figure S66. ^1H NMR spectrum (400 MHz, CDCl_3) of compound **15**.

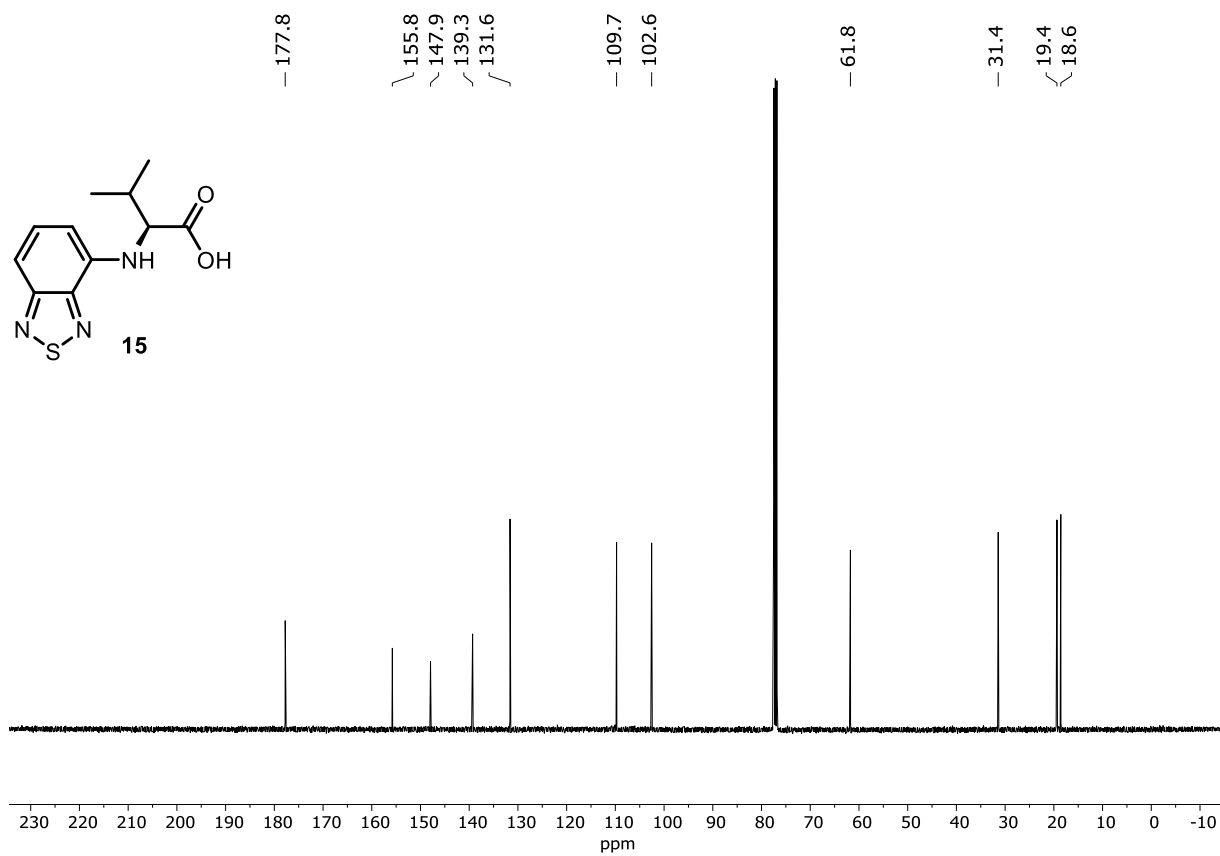


Figure S67. ¹³C NMR spectrum (101 MHz, CDCl₃) of compound **15**.

VIII. Optimized structures from computations

Cartesian coordinates and energies of optimized structures of data reported in Table S2.

Compound, solvent	1, <i>n</i> -hexane							
State	Ground state (S0)			Excited state (S1)				
Cartesian coordinates (Å)	C	-0.640942	1.984040	-0.000723	C	-0.715658	1.914849	0.000043
	C	-1.937059	1.560792	0.006645	C	-2.054549	1.489177	-0.000039
	C	-2.314744	0.184704	0.005423	C	-2.374053	0.146398	-0.000191
	C	-1.380298	-0.820579	-0.008534	C	-1.333567	-0.832097	-0.000044
	C	-0.000476	-0.414383	-0.008512	C	0.028049	-0.413946	-0.000391
	C	0.366461	0.978458	-0.005230	C	0.343334	0.962101	0.000070
	N	1.686159	1.159404	0.000693	N	1.649433	1.244831	0.000444
	N	1.032334	-1.247323	-0.000556	N	1.057177	-1.270442	-0.000459
	S	2.374728	-0.319129	0.004541	S	2.427970	-0.259669	-0.000009
	H	-3.369909	-0.069023	0.008187	H	-3.406858	-0.184758	-0.000416
	H	-0.366393	3.030906	0.000549	H	-0.474709	2.971495	0.000096
	H	-2.734341	2.297439	0.014511	H	-2.847666	2.227509	-0.000202
	N	-1.661100	-2.161770	-0.063068	N	-1.586485	-2.141915	0.000364
	H	-2.578691	-2.460038	0.227437	H	-2.524373	-2.511543	0.000873
	H	-0.905697	-2.783590	0.182751	H	-0.796117	-2.774215	0.000657
Energy (E _n)	-793.876796673			-793.767935275				
				State-specific equilibrium solvation (External iteration approach):				
				-793.775655783				
Zero-point correction	0.108983			0.106917				
<u>Thermal corrections to:</u>								
Energy	0.116427			0.114787				
Enthalpy	0.117371			0.115731				
Gibbs Free Energy	0.076799			0.074313				

Compound, solvent	2, n-hexane							
State	Ground state (S0)			Excited state (S1)				
Cartesian coordinates (Å)	C	0.576358	2.194338	0.007584	C	0.485203	2.175427	0.000017
	C	-0.781000	2.321939	0.000345	C	-0.909865	2.325697	-0.000006
	C	-1.681806	1.214798	-0.013564	C	-1.749120	1.226758	-0.000007
	C	1.099735	0.869863	0.002390	C	1.068180	0.875899	0.000014
	C	0.207130	-0.260645	-0.015324	C	0.221742	-0.252402	-0.000005
	C	-1.223896	-0.083190	-0.028024	C	-1.196226	-0.088906	0.000009
	N	2.380751	0.508178	0.015644	N	2.377622	0.603398	-0.000010
	N	0.819085	-1.435783	-0.012848	N	0.815131	-1.452646	0.000004
	S	2.423140	-1.123551	0.008271	S	2.478089	-1.085239	-0.000008
	H	-2.746640	1.412480	-0.016077	H	-2.824462	1.355960	-0.000039
	H	1.245096	3.045111	0.019491	H	1.132407	3.044764	0.000012
	H	-1.216379	3.316526	0.007262	H	-1.337067	3.321607	-0.000036
	N	-2.001735	-1.198386	-0.063745	N	-1.934961	-1.201748	0.000048
	C	-3.436863	-1.154497	0.048906	C	-3.379663	-1.270187	-0.000021
	H	-3.765062	-0.681747	0.984114	H	-3.798875	-0.789541	0.889294
	H	-3.826529	-2.171965	0.021400	H	-3.677795	-2.317102	0.000353
	H	-3.881254	-0.599166	-0.784744	H	-3.798797	-0.790192	-0.889732
	H	-1.524130	-2.078122	0.048988	H	-1.390880	-2.058410	-0.000028
Energy (E _n)	-833.161872025			-833.054889767				
				State-specific equilibrium solvation (External Iteration approach):				
				-833.062646485				
Zero-point correction	0.137278			0.135492				
<u>Thermal corrections to:</u>								
Energy	0.146444			0.144952				
Enthalpy	0.147389			0.145896				
Gibbs Free Energy	0.102418			0.100479				

Compound, solvent	3, <i>n</i> -hexane							
State	Ground state (S0)			Excited state (S1)				
Cartesian coordinates (Å)	C	-1.123899	2.213556	0.139597	C	-1.017491	2.225058	0.049682
	C	0.187693	2.569822	0.121813	C	0.326679	2.596548	0.049420
	C	1.249229	1.619543	0.041247	C	1.320016	1.638909	0.021183
	C	-1.412715	0.823043	0.055531	C	-1.367318	0.849341	0.021172
	C	-0.351196	-0.156342	-0.036871	C	-0.360755	-0.158542	-0.001482
	C	1.037565	0.261100	-0.036957	C	1.026030	0.233966	-0.003344
	N	-2.627895	0.282524	0.023038	N	-2.628980	0.411014	-0.001034
	N	-0.803908	-1.400173	-0.149813	N	-0.832479	-1.416969	-0.049972
	S	-2.431542	-1.327676	-0.122890	S	-2.519698	-1.268665	-0.052591
	H	2.260640	2.002439	0.055542	H	2.350668	1.961410	0.048857
	H	-1.930918	2.932089	0.202808	H	-1.807435	2.966530	0.069743
	H	0.458642	3.619178	0.181848	H	0.599867	3.644806	0.079587
	N	2.063596	-0.660552	-0.193914	N	2.058030	-0.640219	-0.028199
	C	3.397407	-0.136811	-0.402885	C	3.434832	-0.180432	-0.173413
	H	3.394338	0.599243	-1.209437	H	3.529162	0.534396	-0.991698
	H	4.051934	-0.960078	-0.695257	H	4.057339	-1.043840	-0.402371
	H	3.823845	0.333225	0.497459	H	3.808179	0.276221	0.749837
	C	2.055184	-1.891233	0.589423	C	1.940871	-2.074356	0.209977
	H	1.053389	-2.307250	0.635391	H	0.897439	-2.355944	0.308787
	H	2.426433	-1.722917	1.611556	H	2.495097	-2.328326	1.121101
	H	2.708198	-2.621780	0.105778	H	2.391667	-2.616343	-0.627118
Energy (E _n)	-872.437903341			-872.331402258				
				State-specific equilibrium solvation (External iteration approach):				
				-872.338465059				
Zero-point correction	0.166220			0.163897				
<u>Thermal corrections to:</u>								
Energy	0.176349			0.174652				
Enthalpy	0.177293			0.175596				
Gibbs Free Energy	0.130336			0.127172				

Compound, solvent	4, <i>n</i> -hexane							
State	Ground state (S0)			Excited state (S1)				
Cartesian coordinates (Å)	C	0.373641	2.555765	-0.065973	C	0.255169	2.588878	0.000014
	C	1.659821	2.119188	0.007455	C	1.585173	2.118054	-0.000062
	C	1.864207	0.710343	0.020171	C	1.844546	0.728786	-0.000019
	C	0.737572	-0.180454	-0.030941	C	0.747733	-0.172649	0.000007
	C	-0.611360	0.317998	-0.098168	C	-0.595802	0.314764	-0.000007
	C	-0.756832	1.679312	-0.127078	C	-0.819698	1.727698	0.000086
	N	3.027688	0.065813	0.074713	N	3.047691	0.146256	-0.000145
	N	1.066361	-1.465687	-0.015843	N	1.052021	-1.468968	0.000106
	S	2.694108	-1.528435	0.058256	S	2.750478	-1.511693	0.000042
	H	-1.733028	2.132174	-0.208080	H	-1.820829	2.127530	0.000238
	H	0.173879	3.621976	-0.086207	H	0.075151	3.657372	0.000044
	H	2.505360	2.793647	0.050252	H	2.414721	2.815699	-0.000189
	N	-1.590740	-0.667846	-0.150250	N	-1.538322	-0.661961	0.000054
	C	-2.964920	-0.667283	-0.000578	C	-2.942373	-0.708912	-0.000052
	H	-1.225129	-1.608676	-0.251568	H	-1.129790	-1.598557	-0.000022
	C	-3.681032	0.627727	0.277213	C	-3.743044	0.561189	0.000030
	O	-3.558260	-1.726764	-0.088949	O	-3.451238	-1.809110	-0.000120
	H	-3.221336	1.175621	1.102469	H	-3.531373	1.161446	0.888066
	H	-4.711524	0.382461	0.527089	H	-4.794390	0.280709	-0.000101
	H	-3.677612	1.270330	-0.607395	H	-3.531197	1.161640	-0.887836
Energy (E _n)	-946.467777082			-946.349404422				
				State-specific equilibrium solvation (External iteration approach):				
				-946.354252918				
Zero-point correction	0.148001			0.145675				
<u>Thermal corrections to:</u>								
Energy	0.158554			0.156630				
Enthalpy	0.159499			0.157574				
Gibbs Free Energy	0.109468			0.108051				

Compound, solvent	1, THF (implicit solvation and one explicit THF molecule)							
State	Ground state (S0)			Excited state (S1)				
Cartesian coordinates (Å)	C	2.670632	2.093533	-0.021778	C	2.535864	2.086840	-0.071998
	C	1.345029	2.416095	-0.089598	C	1.173987	2.427556	-0.063912
	C	0.298796	1.450916	-0.130885	C	0.196200	1.454906	-0.014152
	C	0.559739	0.098800	-0.110954	C	0.560606	0.071419	0.030653
	C	1.946985	-0.282529	-0.032344	C	1.942211	-0.288787	0.022359
	C	2.993832	0.708660	0.011875	C	2.934298	0.720097	-0.028776
	N	4.208657	0.165428	0.087733	N	4.196067	0.276590	-0.031803
	N	2.385652	-1.533826	0.012782	N	2.373926	-1.555597	0.061045
	S	4.013678	-1.455756	0.103006	S	4.072931	-1.415613	0.030335
	H	-0.733206	1.781147	-0.177072	H	-0.859015	1.703079	-0.008231
	H	3.453789	2.840073	0.009682	H	3.295745	2.858550	-0.111369
	H	1.058674	3.463336	-0.111658	H	0.887298	3.472014	-0.097486
	N	-0.391061	-0.874862	-0.194739	N	-0.364879	-0.880633	0.080017
	H	-1.357058	-0.603288	-0.022763	H	-1.364593	-0.642774	0.086026
	H	-0.111715	-1.806535	0.070173	H	-0.053491	-1.842401	0.110274
	C	-4.996170	-0.830637	-0.660797	C	-4.970942	-0.794899	-0.730506
	C	-3.802215	-0.012829	-1.131213	C	-3.720223	-0.052978	-1.174837
	O	-3.046248	0.276001	0.053743	O	-2.963011	0.166511	0.028469
	C	-3.870343	0.097238	1.218739	C	-3.819925	0.035931	1.181546
	C	-5.277330	-0.199412	0.704017	C	-5.232552	-0.160838	0.637010
	H	-4.716046	-1.882377	-0.547949	H	-4.762406	-1.863846	-0.626372
	H	-5.841608	-0.772677	-1.348855	H	-5.799539	-0.673033	-1.430317
	H	-4.122904	0.927756	-1.596511	H	-3.968295	0.915603	-1.624820
	H	-3.147951	-0.540484	-1.829487	H	-3.092789	-0.612092	-1.872683
	H	-3.818181	1.001886	1.830682	H	-3.715628	0.931639	1.798803
	H	-3.469392	-0.738651	1.803146	H	-3.484806	-0.829253	1.763547
	H	-5.843503	0.728556	0.581478	H	-5.733768	0.803823	0.516772
	H	-5.836216	-0.850853	1.378284	H	-5.844468	-0.781603	1.293610
Energy (E _n)	-1026.23190156			-1026.13129932				
				State-specific equilibrium solvation (External Iteration approach):				
				-1026.14822248				
Zero-point correction	0.228551			0.226939				
<u>Thermal corrections to:</u>								
Energy	0.242786			0.241359				
Enthalpy	0.243730			0.242304				
Gibbs Free Energy	0.182496			0.181591				

Compound, solvent	2, THF (implicit solvation and one explicit THF molecule)							
State	Ground state (S0)			Excited state (S1)				
Cartesian coordinates (Å)	C	3.749905	-0.303143	-0.081769	C	3.685113	-0.295384	0.028304
	C	3.715984	1.061685	-0.089257	C	3.711597	1.105766	0.016823
	C	2.515453	1.825793	-0.037601	C	2.542452	1.841918	0.001082
	C	2.497462	-0.975299	-0.018231	C	2.440824	-0.985432	0.023795
	C	1.267175	-0.221904	0.033983	C	1.232859	-0.244364	0.007802
	C	1.273061	1.224073	0.023625	C	1.270827	1.187978	-0.003586
	N	2.292515	-2.291242	0.001340	N	2.294532	-2.315777	0.033129
	N	0.178285	-0.974509	0.090829	N	0.098552	-0.956365	0.003742
	S	0.678029	-2.530285	0.079677	S	0.620903	-2.579129	0.022046
	H	2.588892	2.906105	-0.047511	H	2.580646	2.923828	-0.007400
	H	4.673056	-0.866751	-0.121062	H	4.607061	-0.864960	0.040463
	H	4.652079	1.610200	-0.136504	H	4.664776	1.621065	0.020396
	N	0.090582	1.877982	0.069993	N	0.119931	1.856299	-0.018346
	C	-0.004359	3.314989	0.091324	C	-0.018288	3.297379	-0.032734
	H	0.506975	3.748430	0.960443	H	0.424202	3.752219	0.858874
	H	-1.058986	3.585359	0.140910	H	-1.083075	3.523510	-0.050464
	H	0.427225	3.766389	-0.810656	H	0.450051	3.736498	-0.918850
	H	-0.778213	1.352541	0.145741	H	-0.762443	1.323377	-0.017001
	C	-3.419121	-0.927350	-0.912468	C	-3.451505	-1.038346	-0.672746
	C	-3.004290	0.519773	-1.144202	C	-2.900011	0.280220	-1.203157
	O	-2.646694	1.038329	0.145421	O	-2.545937	1.060585	-0.045789
	C	-3.090570	0.142088	1.177316	C	-2.985920	0.393269	1.149954
	C	-4.018011	-0.856177	0.493109	C	-4.015407	-0.628219	0.688615
	H	-2.537521	-1.573952	-0.917221	H	-2.635844	-1.753431	-0.542267
	H	-4.120404	-1.287658	-1.667623	H	-4.197719	-1.474970	-1.339369
	H	-3.832133	1.114461	-1.550435	H	-3.650816	0.836553	-1.776225
	H	-2.142223	0.625024	-1.808230	H	-2.006964	0.148830	-1.818647
	H	-3.582564	0.728502	1.958138	H	-3.387026	1.147359	1.831837
	H	-2.215680	-0.357756	1.607143	H	-2.124820	-0.096150	1.617966
	H	-5.039523	-0.465808	0.453105	H	-4.996761	-0.157595	0.573990
	H	-4.041703	-1.819954	1.005457	H	-4.114580	-1.462558	1.385684
Energy (E _n)	-1065.51680588			-1065.41679682				
				State-specific equilibrium solvation (External iteration approach):				
				-1065.43065146				
Zero-point correction	0.257068			0.255258				
<u>Thermal corrections to:</u>								
Energy	0.272726			0.271201				
Enthalpy	0.273670			0.272146				
Gibbs Free Energy	0.210458			0.208796				

Compound, solvent	3, THF							
State	Ground state (S0)			Excited state (S1)				
Cartesian coordinates (Å)	C	-1.121088	2.213550	0.147858	C	-1.020518	2.225201	0.054512
	C	0.191460	2.568644	0.123648	C	0.326401	2.594707	0.052635
	C	1.251769	1.617478	0.036487	C	1.318790	1.638738	0.021709
	C	-1.412006	0.823664	0.060453	C	-1.370432	0.852076	0.024083
	C	-0.351788	-0.155765	-0.039555	C	-0.360950	-0.160101	-0.001837
	C	1.037345	0.259443	-0.040764	C	1.027703	0.232291	-0.002588
	N	-2.627866	0.282776	0.028354	N	-2.632060	0.410533	0.000308
	N	-0.805804	-1.398746	-0.160451	N	-0.832742	-1.415510	-0.056898
	S	-2.433129	-1.327414	-0.128300	S	-2.522921	-1.272034	-0.057151
	H	2.263776	1.998992	0.045985	H	2.349093	1.961576	0.048429
	H	-1.925465	2.934738	0.217124	H	-1.807085	2.970213	0.076275
	H	0.463632	3.617544	0.184447	H	0.599895	3.642628	0.084117
	N	2.059149	-0.667481	-0.199771	N	2.059159	-0.639020	-0.026703
	C	3.394176	-0.146308	-0.419469	C	3.435940	-0.178478	-0.189227
	H	3.388181	0.583979	-1.231006	H	3.518075	0.537627	-1.006878
	H	4.045941	-0.972908	-0.708024	H	4.054123	-1.042052	-0.427637
	H	3.823783	0.329272	0.475764	H	3.817789	0.274672	0.731508
	C	2.058268	-1.877049	0.618454	C	1.951050	-2.070469	0.227869
	H	1.056529	-2.290031	0.689413	H	0.914233	-2.353906	0.368812
	H	2.441119	-1.679127	1.630507	H	2.540215	-2.313357	1.119181
	H	2.705397	-2.621636	0.148996	H	2.371979	-2.620666	-0.619280
Energy (E _n)	-872.440426992			-872.337590324				
				State-specific equilibrium solvation (External iteration approach):				
				-872.353809143				
Zero-point correction	0.166169			0.163924				
<u>Thermal corrections to:</u>								
Energy	0.176272			0.174662				
Enthalpy	0.177216			0.175606				
Gibbs Free Energy	0.130372			0.127318				

Compound, solvent	4, THF (implicit solvation and one explicit THF molecule)							
State	Ground state (S0)			Excited state (S1)				
Cartesian coordinates (Å)	C	3.878149	0.447362	0.567368	C	-3.867725	0.427856	-0.383912
	C	3.339309	1.678780	0.778678	C	-3.378353	1.743850	-0.523210
	C	1.944484	1.950053	0.614720	C	-2.040700	2.027250	-0.386251
	C	2.995071	-0.591452	0.156685	C	-2.975059	-0.632522	-0.122093
	C	1.593099	-0.322551	-0.036014	C	-1.576519	-0.359849	0.018253
	C	1.062012	0.992391	0.196850	C	-1.099617	0.984339	-0.096914
	N	3.320981	-1.856981	-0.100355	N	-3.311660	-1.916189	0.036611
	N	0.898266	-1.381190	-0.437374	N	-0.810496	-1.409253	0.295742
	S	1.952116	-2.618526	-0.547845	S	-1.870114	-2.734963	0.342152
	H	1.585004	2.943740	0.849542	H	-1.686184	3.032706	-0.556414
	H	4.932763	0.242076	0.702094	H	-4.926993	0.221212	-0.484924
	H	3.976461	2.495312	1.100881	H	-4.069286	2.543214	-0.762604
	N	-0.311331	1.183314	0.017495	N	0.239670	1.187065	0.003403
	C	-0.974808	2.255553	-0.518087	C	0.964227	2.339209	0.334768
	H	-0.929701	0.404473	0.288039	H	0.861228	0.368495	-0.179487
	C	-0.187704	3.388106	-1.132930	C	0.269985	3.520740	0.957134
	H	-0.812010	3.831488	-1.907943	H	0.994642	4.009340	1.607593
	H	0.764683	3.068305	-1.555560	H	-0.615934	3.245353	1.528226
	H	0.011144	4.158916	-0.383490	H	-0.016337	4.240252	0.185064
	O	-2.200846	2.273968	-0.517406	O	2.169119	2.325643	0.160053
	C	-4.368657	-0.301948	0.178905	C	4.387006	-0.353108	-0.206246
	C	-3.353360	-0.146071	1.299425	C	3.300084	-0.246275	-1.262723
	O	-2.174924	-0.828290	0.842396	O	2.122757	-0.782970	-0.642396
	C	-2.514720	-1.735137	-0.221776	C	2.492353	-1.645288	0.449927
	C	-4.036408	-1.700206	-0.343679	C	4.020717	-1.674066	0.472879
	H	-4.173157	0.454259	-0.585904	H	4.295710	0.482026	0.494105
	H	-5.399472	-0.199127	0.524148	H	5.393106	-0.346613	-0.630442
	H	-3.701436	-0.612803	2.230102	H	3.543977	-0.842413	-2.151736
	H	-3.086724	0.894293	1.491604	H	3.082291	0.779605	-1.560224
	H	-2.122891	-2.726503	0.022314	H	2.041989	-2.628101	0.291755
	H	-2.023371	-1.391528	-1.137810	H	2.074901	-1.227085	1.371229
	H	-4.490623	-2.462948	0.296190	H	4.397018	-2.517134	-0.114239
	H	-4.372600	-1.874254	-1.367829	H	4.415682	-1.766995	1.486453
Energy (E _n)	-1178.82553823			-1178.70841306 State-specific equilibrium solvation (External iteration approach): -1178.71890088				
Zero-point correction	0.267442			0.264814				
<u>Thermal corrections to:</u>								
Energy	0.284516			0.282300				
Enthalpy	0.285460			0.283244				
Gibbs Free Energy	0.219702			0.216409				

Compound, solvent	1, water (implicit solvation and two explicit H ₂ O molecules)			
State	Ground state (S0)			
Cartesian coordinates (Å)	C	-0.823262	2.392815	0.445389
	C	0.534596	2.489120	0.525611
	C	1.412566	1.396344	0.255440
	C	0.940560	0.157705	-0.097171
	C	-0.487139	0.010095	-0.173332
	C	-1.361660	1.125039	0.087120
	N	-2.650234	0.806148	-0.033419
	N	-1.129892	-1.115209	-0.471529
	S	-2.726031	-0.770944	-0.434391
	H	2.485040	1.546645	0.315542
	H	-1.481193	3.229159	0.644606
	H	0.984129	3.439097	0.796461
	N	1.746364	-0.947871	-0.319418
	H	2.735716	-0.720241	-0.443012
	H	1.392707	-1.573594	-1.033044
	H	5.092697	-0.481203	0.026713
	O	4.478622	0.062827	-0.482479
	H	4.837155	0.059687	-1.378993
	H	1.131021	-2.446023	0.969905
	O	0.479627	-3.124519	1.216845
	H	-0.284404	-2.853077	0.689359
Energy (E _n)	-946.698308665			
Zero-point correction	0.157702			
<u>Thermal corrections to:</u>				
Energy	0.172070			
Enthalpy	0.173014			
Gibbs Free Energy	0.114822			

Compound, solvent	2, water (implicit solvation and two explicit H ₂ O molecules)
State	Ground state (S0)
Cartesian coordinates (Å)	C 1.624988 -2.272905 -0.134704 C 0.384159 -2.773671 -0.389380 C -0.780809 -1.956870 -0.505844 C 1.731776 -0.861803 0.014761 C 0.565433 -0.021173 -0.096600 C -0.734290 -0.590317 -0.359654 N 2.844451 -0.170914 0.258166 N 0.833563 1.270771 0.063935 S 2.439725 1.403010 0.335321 H -1.727035 -2.442284 -0.708497 H 2.503806 -2.898912 -0.048516 H 0.258308 -3.844289 -0.514343 N -1.835931 0.236450 -0.397051 C -3.099608 -0.267600 -0.905897 H -2.998895 -0.735154 -1.893075 H -3.795702 0.567569 -0.982115 H -3.525716 -0.998642 -0.213420 H -1.651892 1.219446 -0.606415 H -0.382578 2.747255 -0.414643 O -1.222829 3.081318 -0.780099 H -1.034717 3.217374 -1.717417 H -2.446341 -0.848590 2.581393 O -2.882930 -0.025145 2.334096 H -2.433243 0.230554 1.508507
Energy (E _n)	-985.984289092
Zero-point correction	0.187155
<u>Thermal corrections to:</u>	
Energy	0.202367
Enthalpy	0.203312
Gibbs Free Energy	0.143612

Compound, solvent	3 , water (implicit solvation and one explicit H ₂ O molecule)			
State	Ground state (S0)			
Cartesian coordinates (Å)	C	1.746712	2.141255	0.204461
	C	0.545497	2.773908	0.268748
	C	-0.699138	2.081105	0.141402
	C	1.726767	0.728688	0.029103
	C	0.478070	0.014149	-0.085482
	C	-0.778514	0.725630	-0.046648
	N	2.791574	-0.069832	-0.011386
	N	0.642037	-1.302310	-0.190656
	S	2.246729	-1.594402	-0.167692
	H	-1.605171	2.670844	0.185850
	H	2.690372	2.664447	0.294326
	H	0.510618	3.849011	0.409133
	N	-1.987769	0.010486	-0.130919
	C	-3.193977	0.754659	0.206536
	H	-3.082503	1.228448	1.183096
	H	-4.028690	0.053366	0.255199
	H	-3.439600	1.526406	-0.537017
	C	-2.173162	-0.778867	-1.356023
	H	-1.276396	-1.352707	-1.576355
	H	-2.409612	-0.133688	-2.212639
	H	-2.997759	-1.477051	-1.201840
	H	-1.909160	-1.622231	1.042025
	O	-1.699193	-2.545631	1.270431
	H	-0.840642	-2.642934	0.835994
Energy (E _n)	-948.851056298			
Zero-point correction	0.191149			
<u>Thermal corrections to:</u>				
Energy	0.204213			
Enthalpy	0.205157			
Gibbs Free Energy	0.151745			

Compound, solvent	4, water (implicit solvation and one explicit H ₂ O molecule)							
State	Ground state (S0)			Excited state (S1)				
Cartesian coordinates (Å)	C	1.108381	2.643926	-0.441776	C	0.863066	2.740327	-0.324798
	C	2.272903	1.966776	-0.249760	C	2.103117	2.073846	-0.195362
	C	2.184500	0.561693	-0.036123	C	2.134814	0.674141	-0.037626
	C	0.901576	-0.088167	-0.009203	C	0.903851	-0.055548	0.008212
	C	-0.305792	0.663856	-0.206623	C	-0.344975	0.638867	-0.094795
	C	-0.171886	2.003969	-0.439641	C	-0.328974	2.060537	-0.281311
	N	3.195526	-0.283756	0.157481	N	3.231659	-0.079753	0.088916
	N	0.968683	-1.397750	0.203111	N	1.016567	-1.367058	0.173917
	S	2.549232	-1.766114	0.351425	S	2.687904	-1.667076	0.249979
	H	-1.042577	2.610753	-0.647566	H	-1.251437	2.597623	-0.434173
	H	1.132941	3.713448	-0.619483	H	0.855220	3.812242	-0.480524
	H	3.238585	2.456437	-0.261253	H	3.031522	2.632151	-0.228085
	N	-1.502149	-0.060980	-0.187121	N	-1.461476	-0.133740	-0.068258
	C	-2.748609	0.293033	0.239331	C	-2.808977	0.165345	0.145889
	H	-1.439535	-1.048677	-0.455899	H	-1.309020	-1.150271	-0.203515
	C	-2.991111	1.652971	0.833265	C	-3.236721	1.527492	0.605248
	O	-3.672481	-0.521307	0.150425	O	-3.622288	-0.735741	-0.011471
	H	-2.138655	2.017809	1.406491	H	-2.534684	1.968964	1.312492
	H	-3.869213	1.578884	1.473079	H	-4.213715	1.416983	1.072816
	H	-3.208495	2.375563	0.042143	H	-3.347020	2.199434	-0.250243
	H	-2.170637	-3.286518	-0.055484	H	-1.825201	-3.392958	0.202907
	O	-2.371989	-2.732340	-0.819886	O	-1.978427	-2.874142	-0.596842
	H	-3.068553	-2.121634	-0.500252	H	-2.824862	-2.418082	-0.439594
Energy (E _n)	-1022.88925903			-1022.77190569				
				State-specific equilibrium solvation (External Iteration approach):				
				-1022.78670651				
Zero-point correction	0.173141			0.170433				
<u>Thermal corrections to:</u>								
Energy	0.186425			0.184258				
Enthalpy	0.187369			0.185202				
Gibbs Free Energy	0.132414			0.129422				

Cartesian coordinates and energies of optimized structures of data reported in Figure 2.

Solvent, state	<i>n</i> -hexane, ground state (S0)							
Compound	6			10				
Cartesian coordinates (Å)	C	-2.699333	1.815042	0.140814	C	-2.294979	1.931446	-0.085755
	C	-1.602033	2.615438	0.195529	C	-1.137536	2.650455	-0.088047
	C	-0.267828	2.106244	0.159227	C	0.153386	2.056826	-0.047962
	C	-2.471267	0.414864	0.024664	C	-2.168398	0.517590	-0.031434
	C	-1.127784	-0.116645	-0.025081	C	-0.864894	-0.114592	0.012355
	C	0.018262	0.765774	0.052958	C	0.343950	0.686218	-0.002290
	N	-3.409602	-0.522840	-0.077564	N	-3.170489	-0.358147	-0.001110
	N	-1.095371	-1.435926	-0.177478	N	-0.929441	-1.439097	0.083011
	S	-2.640630	-1.950678	-0.233643	S	-2.507647	-1.845281	0.083518
	H	0.541122	2.820988	0.234332	H	1.011931	2.714474	-0.064964
	H	-3.711208	2.198552	0.171277	H	-3.275060	2.389093	-0.116688
	H	-1.726873	3.690075	0.283039	H	-1.185836	3.734516	-0.126585
	N	1.306549	0.248262	-0.056999	N	1.583960	0.121582	0.053415
	C	2.388060	1.194071	-0.302586	C	2.781398	0.947413	0.154045
	C	1.689497	-0.822540	0.874216	C	1.907212	-1.297610	-0.132904
	C	3.625046	0.477895	-0.839461	C	3.907393	-0.065092	0.349226
	H	2.649865	1.745678	0.618296	H	2.697049	1.651882	0.988646
	H	2.045382	1.927840	-1.035525	H	2.928589	1.538859	-0.762008
	C	2.899494	-1.590239	0.357435	C	3.407156	-1.282641	-0.427861
	H	0.845719	-1.496101	1.000818	H	1.321603	-1.732117	-0.943587
	H	1.926334	-0.383006	1.858849	H	1.679900	-1.872173	0.772030
	C	4.069619	-0.647232	0.091127	H	4.008480	-0.309776	1.411129
	H	2.618499	-2.105347	-0.567747	H	4.869710	0.311285	-0.002865
	H	3.174033	-2.357113	1.088660	H	3.575147	-1.137271	-1.499769
	H	4.425937	1.211032	-0.978688	H	3.894488	-2.214719	-0.135078
	H	3.387039	0.064660	-1.825898				
	H	4.917235	-1.189243	-0.339237				
	H	4.415574	-0.219670	1.041338				
Energy (E _n)	-989.118222538			-949.825174841				
Zero-point correction	0.233254			0.203367				
<u>Thermal corrections to:</u>								
Energy	0.244961			0.214370				
Enthalpy	0.245905			0.215314				
Gibbs Free Energy	0.194923			0.165624				

Cartesian coordinates and energies of optimized structures of data reported in Figure S27.

State	ground state (S0)			
Compound	H ₂ O (gas phase)			
Cartesian coordinates (Å)	H	0.759951	-0.473674	0.000000
	O	0.000000	0.118418	0.000000
	H	-0.759951	-0.473674	0.000000
Energy (E _n)	-76.3910447721			
Zero-point correction	0.021558			
<u>Thermal corrections to:</u>				
Energy	0.024393			
Enthalpy	0.025337			
Gibbs Free Energy	0.003253			

State	ground state (S0)							
Compound	1 (gas phase)			1 + 2 H ₂ O				
Cartesian coordinates (Å)	C	-0.642984	1.983358	-0.001027	C	-0.862905	-2.509433	-0.003569
	C	-1.938301	1.559500	0.007528	C	0.494520	-2.639270	-0.069309
	C	-2.314784	0.182708	0.005836	C	1.388995	-1.537035	-0.120704
	C	-1.379350	-0.820636	-0.009106	C	0.949153	-0.227801	-0.112301
	C	-0.000213	-0.414077	-0.009150	C	-0.483340	-0.048043	-0.037348
	C	0.365838	0.978787	-0.006215	C	-1.375701	-1.185240	0.015398
	N	1.684598	1.160796	-0.000717	N	-2.658146	-0.831735	0.082889
	N	1.031570	-1.247414	0.000245	N	-1.118413	1.119038	-0.007225
	S	2.373399	-0.317114	0.005424	S	-2.720987	0.793160	0.082210
	H	-3.369763	-0.072346	0.007574	H	2.457179	-1.719538	-0.169959
	H	-0.368169	3.030044	0.000405	H	-1.537280	-3.354439	0.035529
	H	-2.736107	2.295581	0.016012	H	0.928421	-3.634786	-0.083088
	N	-1.655958	-2.163091	-0.061526	N	1.773782	0.845130	-0.188403
	H	-2.570304	-2.467387	0.230413	H	2.770829	0.678078	-0.118815
	H	-0.892740	-2.781939	0.165613	H	1.423181	1.788428	-0.049007
					H	5.316400	0.301807	-0.322573
					O	4.580248	-0.055294	0.186845
					H	4.827926	0.060960	1.111205
					H	0.479497	3.769333	-0.883355
					O	0.480527	3.494155	0.040873
					H	-0.261454	2.862608	0.099138
Energy (E _n)	-793.874208097			-946.687849569				
				Counterpoise corrected energy:				
				-946.677933025144				
Zero-point correction	0.109003			0.158233				
<u>Thermal corrections to:</u>								
Energy	0.116462			0.172592				
Enthalpy	0.117407			0.173536				
Gibbs Free Energy	0.076804			0.115338				

State	ground state (S0)																																																																																																																																			
Compound	2 (gas phase)			2 + 1 H ₂ O																																																																																																																																
Cartesian coordinates (Å)	C	0.578399	2.194132	0.006917	C	1.441051	2.228229	0.017231	C	0.197130	2.784759	0.020591	C	-1.006546	2.024354	0.014391	C	1.505846	0.808094	0.005615	C	0.298262	0.014193	0.000307	C	-1.005408	0.643447	0.006714	N	2.380718	0.505888	0.014459	N	2.611013	0.066826	-0.003159	N	0.815091	-1.436448	-0.011772	N	0.530688	-1.293309	-0.011970	S	2.419869	-1.125229	0.008039	S	2.157006	-1.494276	-0.018974	H	-2.745284	1.415945	-0.014752	H	-1.949610	2.555914	0.016906	H	1.249117	3.043212	0.018044	H	2.351077	2.813182	0.021133	H	-1.212182	3.318953	0.007372	H	0.102448	3.866363	0.027646	N	-2.000564	-1.197143	-0.059368	N	-2.121761	-0.125973	0.008199	C	-3.434774	-1.155493	0.046054	C	-3.442505	0.442853	-0.043812	H	-3.768690	-0.679382	0.977844	H	-3.651316	1.070387	0.832088	H	-3.824032	-2.173477	0.021503	H	-4.170834	-0.368050	-0.063989	H	-3.877577	-0.604528	-0.791872	H	-3.589887	1.058961	-0.940634	H	-2.038528	-1.139215	-0.040636	H	-0.827279	-2.697602	-0.111791	O	-1.746296	-3.019097	-0.047884	H	-1.834360	-3.307139	0.868216
Energy (E _n)	-833.159737850			-909.570497793			Counterpoise corrected energy: -909.564121585136																																																																																																																													
Zero-point correction	0.137365			0.163037																																																																																																																																
<u>Thermal corrections to:</u>																																																																																																																																				
Energy	0.146526			0.174855																																																																																																																																
Enthalpy	0.147470			0.175799																																																																																																																																
Gibbs Free Energy	0.102456			0.124898																																																																																																																																

State	ground state (S0)																																																																																																																																																															
Compound	3 (gas phase)			3 + 1 H ₂ O																																																																																																																																																												
Cartesian coordinates (Å)	C	-1.125746	2.213216	0.134683	C	-1.881067	2.054135	-0.203328	C	-0.718913	2.755510	-0.255326	C	0.563127	2.136252	-0.123699	C	-1.780459	0.644002	-0.035032	C	-0.492899	0.002279	0.085973	C	0.721208	0.786048	0.057014	N	-2.627807	0.281837	0.019775	N	-2.797611	-0.212665	-0.007415	N	-0.802153	-1.401194	-0.143971	N	-0.578039	-1.321493	0.183210	S	-2.430009	-1.327998	-0.120021	S	-2.164834	-1.702128	0.144867	H	2.258576	2.004454	0.062541	H	1.435015	2.776616	-0.158899	H	-1.934621	2.929864	0.193959	H	-2.854650	2.517647	-0.298396	H	0.455123	3.620251	0.181062	H	-0.746615	3.831858	-0.390127	N	2.065902	-0.656746	-0.190180	N	1.964668	0.142826	0.130190	C	3.398310	-0.131940	-0.395841	C	3.129516	0.939616	-0.211712	H	3.395158	0.606946	-1.200011	H	2.982910	1.426476	-1.177676	H	4.053974	-0.953475	-0.691133	H	3.991549	0.274073	-0.288821	H	3.825316	0.335879	0.505904	H	3.359190	1.709058	0.541701	C	2.053753	-1.897688	0.574917	C	2.208487	-0.695587	1.308973	H	1.052061	-2.315379	0.607275	H	1.315407	-1.261203	1.560594	H	2.418264	-1.745091	1.602264	H	2.506212	-0.085137	2.173221	H	2.710687	-2.620605	0.084679	H	2.998861	-1.410051	1.074817	H	2.012711	-1.565057	-1.096336	O	1.986101	-2.531082	-1.171117	H	1.130833	-2.725771	-0.768095
Energy (E _n)	-872.436069595			-948.840141554			Counterpoise corrected energy: -948.834199676822																																																																																																																																																									
Zero-point correction	0.166332			0.191336																																																																																																																																																												
<u>Thermal corrections to:</u>																																																																																																																																																																
Energy	0.176439			0.204538																																																																																																																																																												
Enthalpy	0.177383			0.205482																																																																																																																																																												
Gibbs Free Energy	0.130498			0.151633																																																																																																																																																												

State	ground state (S0)							
Compound	6 (gas phase)			6 + 1 H ₂ O				
Cartesian coordinates (Å)	C	-2.701259	1.813464	0.131795	C	2.859058	1.868180	0.042018
	C	-1.605803	2.615274	0.191655	C	1.790409	2.703174	0.118487
	C	-0.270817	2.107590	0.162816	C	0.439874	2.232974	0.082203
	C	-2.470838	0.413292	0.019808	C	2.588362	0.473607	-0.054507
	C	-1.126447	-0.116826	-0.021951	C	1.230689	-0.015640	-0.078648
	C	0.017713	0.767682	0.058302	C	0.118920	0.904849	-0.021770
	N	-3.407797	-0.524825	-0.083884	N	3.496671	-0.497156	-0.098121
	N	-1.091470	-1.436413	-0.168839	N	1.154619	-1.342571	-0.123908
	S	-2.636581	-1.951909	-0.230627	S	2.686260	-1.905717	-0.152634
	H	0.537034	2.823198	0.242168	H	-0.349489	2.971795	0.129967
	H	-3.714259	2.194121	0.155825	H	3.883205	2.218190	0.064951
	H	-1.732415	3.689920	0.277111	H	1.949415	3.773498	0.199451
	N	1.307468	0.253399	-0.047481	N	-1.193794	0.399638	-0.010384
	C	2.388613	1.198282	-0.290872	C	-2.241085	1.332948	0.408097
	C	1.689690	-0.826425	0.871983	C	-1.581354	-0.355566	-1.221868
	C	3.622821	0.483942	-0.836994	C	-3.545790	0.591277	0.683586
	H	2.655095	1.745253	0.631876	H	-2.410510	2.103315	-0.364676
	H	2.044239	1.936478	-1.018610	H	-1.901005	1.843333	1.312628
	C	2.896195	-1.592485	0.344530	C	-2.871314	-1.133850	-0.992235
	H	0.844558	-1.499180	0.992920	H	-0.770850	-1.036704	-1.475609
	H	1.930281	-0.397577	1.860761	H	-1.707117	0.350945	-2.059511
	C	4.067702	-0.649870	0.082793	C	-3.995927	-0.205836	-0.538710
	H	2.609993	-2.098530	-0.583994	H	-2.683421	-1.888728	-0.222743
	H	3.171586	-2.366547	1.067921	H	-3.140325	-1.651795	-1.918325
	H	4.425176	1.216261	-0.973081	H	-4.308111	1.318963	0.979382
	H	3.380344	0.079157	-1.825777	H	-3.396282	-0.088172	1.529394
	H	4.913312	-1.189664	-0.354402	H	-4.899312	-0.778630	-0.309458
	H	4.417523	-0.230997	1.035552	H	-4.255053	0.486062	-1.351286
					H	-1.207738	-1.109476	1.360901
					O	-1.272455	-1.981780	1.785285
					H	-0.557451	-2.462966	1.351763
	Energy (E _n)	-989.116430733			-1065.52311174 Counterpoise corrected energy: -1065.515618082224			
	Zero-point correction	0.233357			0.258575			
<u>Thermal corrections to:</u>								
Energy	0.245060			0.273314				
Enthalpy	0.246004			0.274258				
Gibbs Free Energy	0.195019			0.216616				

State	ground state (S0)							
Compound	7 (gas phase)			7 + 1 H ₂ O				
Cartesian coordinates (Å)	C	-2.673249	1.834499	0.128237	C	2.829934	1.892160	0.050112
	C	-1.568211	2.623679	0.176186	C	1.752708	2.714469	0.140792
	C	-0.239747	2.099577	0.139913	C	0.407549	2.229049	0.109762
	C	-2.460351	0.431197	0.022956	C	2.574082	0.495683	-0.056161
	C	-1.123170	-0.115810	-0.025581	C	1.222254	-0.009621	-0.075026
	C	0.030504	0.756030	0.040025	C	0.101505	0.898284	-0.003080
	N	-3.409225	-0.496425	-0.066640	N	3.493292	-0.464048	-0.114234
	N	-1.105888	-1.437211	-0.161874	N	1.162612	-1.337343	-0.131192
	S	-2.657793	-1.933543	-0.208210	S	2.700890	-1.881599	-0.175264
	H	0.577037	2.806137	0.207679	H	-0.389346	2.958787	0.169084
	H	-3.681475	2.227217	0.157543	H	3.850296	2.253208	0.068624
	H	-1.681177	3.700133	0.256509	H	1.899871	3.785782	0.229456
	N	1.315109	0.229436	-0.073976	N	-1.206818	0.382219	0.014242
	C	2.412573	1.165666	-0.263383	C	-2.269570	1.316230	0.384290
	C	1.695482	-0.875743	0.813224	C	-1.595230	-0.407356	-1.173056
	C	3.649278	0.416087	-0.739082	C	-3.574494	0.555675	0.575676
	H	2.649646	1.707080	0.667885	H	-2.414102	2.084537	-0.392274
	H	2.130657	1.900845	-1.021635	H	-1.994158	1.816530	1.316780
	C	2.954783	-1.542639	0.289822	C	-2.929277	-1.091012	-0.923055
	H	0.887247	-1.602873	0.853177	H	-0.828945	-1.156101	-1.369431
	H	1.885308	-0.495057	1.829663	H	-1.676376	0.256813	-2.046839
	O	4.012248	-0.612973	0.154655	O	-3.931493	-0.144468	-0.595615
	H	2.741004	-2.017377	-0.679647	H	-2.811350	-1.821961	-0.112344
	H	3.295142	-2.309553	0.989249	H	-3.261203	-1.602896	-1.829093
	H	4.500322	1.098318	-0.803188	H	-4.384411	1.257114	0.789658
	H	3.455661	-0.000260	-1.739592	H	-3.477246	-0.138809	1.423090
				H	-1.188677	-1.150845	1.402241	
				O	-1.231297	-2.053682	1.757354	
				H	-0.496630	-2.478531	1.298127	
Energy (E _n)	-1025.00767608			-1101.41337691				
				Counterpoise corrected energy:				
				-1101.405952529418				
Zero-point correction	0.209304			0.234429				
<u>Thermal corrections to:</u>								
Energy	0.220719			0.248923				
Enthalpy	0.221663			0.249867				
Gibbs Free Energy	0.171186			0.192586				

State	ground state (S0)							
Compound	8 (gas phase)			8 + 1 H ₂ O				
Cartesian coordinates (Å)	C	-3.070395	1.718259	0.134596	C	3.158371	1.822933	-0.018852
	C	-2.022053	2.578456	0.220006	C	2.110050	2.683435	0.057140
	C	-0.660577	2.143654	0.205899	C	0.748555	2.242173	0.051244
	C	-2.763154	0.333465	0.012396	C	2.856711	0.432661	-0.084640
	C	-1.392228	-0.121003	-0.015803	C	1.489014	-0.025258	-0.077811
	C	-0.301087	0.823649	0.088641	C	0.400458	0.920059	-0.019828
	N	-3.644779	-0.654427	-0.112894	N	3.741121	-0.560109	-0.125091
	N	-1.279977	-1.435277	-0.172891	N	1.378946	-1.350326	-0.098848
	S	-2.793612	-2.034496	-0.261256	S	2.896689	-1.949464	-0.142257
	H	0.107192	2.900187	0.306840	H	-0.024673	2.998563	0.095791
	H	-4.102817	2.043313	0.147555	H	4.190012	2.151152	-0.018401
	H	-2.208500	3.643325	0.315695	H	2.293922	3.751179	0.114304
	N	1.016144	0.372204	-0.009676	N	-0.923193	0.434384	0.023398
	C	2.043943	1.362929	-0.295231	C	-1.930303	1.379294	0.512256
	C	1.439638	-0.666050	0.936854	C	-1.341755	-0.281604	-1.201125
	C	3.260092	0.732486	-0.964056	C	-3.218269	0.671274	0.913060
	H	2.359489	1.898168	0.615365	H	-2.155948	2.149690	-0.241562
	H	1.623009	2.096466	-0.987394	H	-1.515323	1.876529	1.393541
	C	2.578289	-1.508874	0.385949	C	-2.574144	-1.142358	-0.968726
	H	0.591039	-1.318362	1.132977	H	-0.517583	-0.925624	-1.507906
	H	1.752848	-0.203470	1.885808	H	-1.535048	0.444363	-2.004695
	S	4.073168	-0.523211	0.067567	S	-4.023317	-0.150870	-0.493981
	H	2.259731	-2.005881	-0.534059	H	-2.368131	-1.874169	-0.184362
	H	2.859312	-2.274446	1.112307	H	-2.835867	-1.665259	-1.890863
	H	4.008559	1.501409	-1.167781	H	-3.929954	1.402954	1.301012
	H	2.962726	0.283278	-1.915555	H	-3.017464	-0.065760	1.694789
					H	-0.913086	-1.062878	1.361290
				O	-1.100733	-1.873165	1.866229	
				H	-0.409179	-2.473383	1.564528	
Energy (E _n)	-1348.00288398			-1424.40949928				
				Counterpoise corrected energy:				
				-1424.401866181308				
Zero-point correction	0.205642			0.230947				
<u>Thermal corrections to:</u>								
Energy	0.217678			0.245997				
Enthalpy	0.218623			0.246941				
Gibbs Free Energy	0.166357			0.188196				

State	ground state (S0)							
Compound	9 (gas phase)			9 + 1 H ₂ O				
Cartesian coordinates (Å)	C	-3.182111	1.667838	0.089497	C	3.263082	1.768401	-0.005335
	C	-2.147149	2.546247	0.148400	C	2.235635	2.651482	0.091316
	C	-0.779514	2.134667	0.138498	C	0.864913	2.243407	0.086148
	C	-2.851373	0.286490	-0.000317	C	2.926496	0.387810	-0.091347
	C	-1.472354	-0.147917	-0.022858	C	1.547768	-0.039979	-0.083892
	C	-0.395246	0.817371	0.054267	C	0.480754	0.930896	-0.005241
	N	-3.718679	-0.716969	-0.097418	N	3.789142	-0.622812	-0.152440
	N	-1.343739	-1.464008	-0.148663	N	1.412873	-1.362709	-0.124442
	S	-2.848177	-2.087929	-0.215585	S	2.916964	-1.993871	-0.185417
	H	-0.026051	2.907475	0.215049	H	0.112084	3.018368	0.146811
	H	-4.219825	1.975487	0.099367	H	4.302485	2.070845	-0.006120
	H	-2.350450	3.610175	0.218017	H	2.444766	3.713664	0.164755
	N	0.929833	0.400560	-0.033911	N	-0.853814	0.492093	0.039147
	C	1.945376	1.424489	-0.218949	C	-1.852816	1.488174	0.419866
	C	1.386264	-0.660900	0.869297	C	-1.307944	-0.280971	-1.133938
	C	3.247686	0.796861	-0.694967	C	-3.190994	0.813819	0.681968
	H	2.131268	1.982582	0.713683	H	-1.981883	2.244289	-0.370862
	H	1.599047	2.132552	-0.975480	H	-1.514828	1.993387	1.328148
	C	2.691905	-1.254178	0.370316	C	-2.656084	-0.923160	-0.855304
	H	0.629101	-1.439577	0.917062	H	-0.572612	-1.053381	-1.352289
	H	1.542459	-0.250973	1.879659	H	-1.390675	0.388047	-2.003523
	N	3.705477	-0.220858	0.233589	N	-3.638556	0.091592	-0.496792
	H	2.509131	-1.774418	-0.588527	H	-2.532231	-1.675338	-0.058249
	H	3.041783	-1.999404	1.091829	H	-2.993720	-1.434883	-1.762338
	H	4.010399	1.578756	-0.769989	H	-3.929003	1.584431	0.927173
	H	3.094078	0.381679	-1.709208	H	-3.098119	0.149372	1.560620
	C	4.987432	-0.768932	-0.158575	C	-4.955546	-0.482744	-0.305034
	H	5.733779	0.029041	-0.204647	H	-5.674861	0.308957	-0.077224
	H	4.960881	-1.269564	-1.143647	H	-4.989247	-1.223838	0.512895
	H	5.319489	-1.500229	0.583368	H	-5.278933	-0.977979	-1.224749
					H	-0.907514	-1.022533	1.468871
					O	-0.940150	-1.918963	1.840356
				H	-0.245034	-2.359733	1.336347	
Energy (E _n)	-1044.43090582			-1120.83681257				
				Counterpoise corrected energy:				
				-1120.829409771097				
Zero-point correction	0.249855			0.275157				
<u>Thermal corrections to:</u>								
Energy	0.262848			0.291206				
Enthalpy	0.263792			0.292150				
Gibbs Free Energy	0.209929			0.231671				

State	ground state (S0)							
Compound	10 (gas phase)			10 + 1 H ₂ O				
Cartesian coordinates (Å)	C	2.296948	1.929502	0.081845	C	-2.445890	2.003437	0.083905
	C	1.141539	2.650152	0.087624	C	-1.318839	2.742969	0.265687
	C	-0.150797	2.057487	0.051167	C	-0.007754	2.181132	0.248588
	C	2.168417	0.515440	0.028871	C	-2.274524	0.602934	-0.093841
	C	0.864174	-0.114604	-0.011014	C	-0.955440	0.012628	-0.099365
	C	-0.342452	0.688255	0.005305	C	0.221869	0.838807	0.045637
	N	3.169096	-0.360904	-0.002503	N	-3.247340	-0.295384	-0.225461
	N	0.925511	-1.439326	-0.079066	N	-0.975857	-1.312728	-0.208678
	S	2.503965	-1.846225	-0.082614	S	-2.542685	-1.757506	-0.324552
	H	-1.008574	2.716199	0.070823	H	0.829129	2.852071	0.390129
	H	3.278430	2.384128	0.109693	H	-3.440285	2.430388	0.090513
	H	1.191292	3.734126	0.125851	H	-1.402117	3.814084	0.419921
	N	-1.584309	0.123514	-0.048888	N	1.482610	0.269955	0.043851
	C	-2.780065	0.948789	-0.151736	C	2.648540	1.120505	0.278847
	C	-1.906181	-1.295986	0.132574	C	1.838824	-0.846084	-0.872140
	C	-3.905872	-0.063285	-0.352069	C	3.820568	0.183842	0.019024
	H	-2.693550	1.654662	-0.985290	H	2.626650	1.528572	1.293768
	H	-2.931234	1.540189	0.764221	H	2.674374	1.968737	-0.423627
	C	-3.407153	-1.282810	0.423110	C	3.321753	-0.619220	-1.182671
	H	-1.322349	-1.732674	0.943400	H	1.215267	-0.828796	-1.769070
	H	-1.674437	-1.868999	-0.772325	H	1.681190	-1.796049	-0.361852
	H	-4.003927	-0.305642	-1.414871	H	3.973105	-0.473289	0.880646
	H	-4.869809	0.311642	-0.002386	H	4.750975	0.722275	-0.171688
H	-3.578843	-1.140392	1.494942	H	3.434809	-0.026496	-2.096152	
H	-3.893884	-2.214269	0.126907	H	3.856446	-1.559978	-1.326794	
				H	1.300744	-1.196428	1.744490	
				O	1.116978	-2.121821	1.959311	
				H	0.336320	-2.299025	1.418049	
Energy (E _n)	-949.823240186			-1026.22534753			Counterpoise corrected energy: -1026.218840696475	
Zero-point correction	0.203479			0.228574				
<u>Thermal corrections to:</u>								
Energy	0.214475			0.242668				
Enthalpy	0.215419			0.243612				
Gibbs Free Energy	0.165736			0.186806				

State	ground state (S0)																																																																																																																																																																																																																																											
Compound	11 (gas phase)			11 + 1 H ₂ O																																																																																																																																																																																																																																								
Cartesian coordinates (Å)	C	2.824285	2.046062	-0.194412	C	-2.759374	-2.329769	-0.195297	C	-1.480231	-2.781897	-0.324133	C	-0.337508	-1.932938	-0.318052	C	-2.927093	-0.926129	-0.048013	C	-1.782784	-0.043588	-0.045119	C	-0.437725	-0.560848	-0.191903	N	4.073752	-0.057045	0.137954	N	-4.080035	-0.277730	0.098285	N	-2.108335	1.235583	0.102415	S	3.653542	-1.628110	0.271530	S	-3.740278	1.306915	0.229980	H	-0.571885	2.208419	-0.478320	H	0.638043	-2.391096	-0.416796	H	3.703225	2.677119	-0.186038	H	-3.621472	-2.983251	-0.197297	H	1.424195	3.607148	-0.466758	H	-1.305760	-3.847873	-0.434584	N	-0.583407	-0.521055	-0.260947	N	0.602697	0.311492	-0.215479	C	-1.980057	-0.140762	-0.275727	C	1.995329	-0.087062	-0.270785	H	-0.352675	-1.476224	-0.028667	H	0.417240	1.294640	-0.032629	C	-2.500618	0.352559	1.079303	C	2.535149	-0.605478	1.067632	C	-2.826216	-1.325577	-0.773105	C	2.842161	1.103484	-0.758265	H	-2.080840	0.680569	-0.996745	H	2.079446	-0.897136	-1.007533	C	-3.920234	0.933028	0.939475	C	3.947406	-1.194023	0.895125	H	-1.817386	1.097219	1.496425	H	1.854695	-1.351215	1.487509	H	-2.497201	-0.495020	1.774873	H	2.549097	0.232575	1.773686	C	-4.732291	0.226627	-0.164542	C	4.749702	-0.468618	-0.203780	H	-3.865006	2.004802	0.722101	H	3.881173	-2.260488	0.654741	H	-4.439201	0.842943	1.898858	H	4.479914	-1.129322	1.849215	C	-4.293776	-1.229532	-0.316681	C	4.314269	0.991567	-0.321088	H	-4.592459	0.741598	-1.122501	H	4.595988	-0.963730	-1.170205	H	-5.801819	0.285414	0.057189	H	5.821634	-0.536602	0.003966	H	-4.938816	-1.758227	-1.024184	H	4.953590	1.532162	-1.025077	H	-4.417526	-1.736938	0.646887	H	4.450690	1.479728	0.650639	H	-2.389733	-2.257826	-0.394269	H	2.411415	2.028244	-0.359562	H	-2.761434	-1.376876	-1.864079	H	2.769570	1.166867	-1.848851	H	-0.880027	2.759264	0.252092	O	-0.012467	3.195552	0.159464	H	-0.007146	3.518563	-0.749199
Energy (E _n)	-1028.41364085			-1104.82395723			Counterpoise corrected energy: -1104.816866626463																																																																																																																																																																																																																																					
Zero-point correction	0.261940			0.287336																																																																																																																																																																																																																																								
<u>Thermal corrections to:</u>																																																																																																																																																																																																																																												
Energy	0.275373			0.303662																																																																																																																																																																																																																																								
Enthalpy	0.276318			0.304606																																																																																																																																																																																																																																								
Gibbs Free Energy	0.220517			0.242537																																																																																																																																																																																																																																								

State	ground state (S0)							
Compound	12 (gas phase)			12 + 1 H ₂ O				
Cartesian coordinates (Å)	C	2.617377	2.047590	-0.230152	C	2.569496	2.322118	-0.263184
	C	1.347398	2.523924	-0.354419	C	1.287532	2.760773	-0.399558
	C	0.181431	1.699530	-0.305175	C	0.151044	1.903509	-0.335414
	C	2.763653	0.642734	-0.052379	C	2.748824	0.926780	-0.060571
	C	1.599452	-0.201393	0.004624	C	1.610783	0.040340	0.009075
	C	0.270258	0.342352	-0.115232	C	0.262469	0.548186	-0.119184
	N	3.898620	-0.041094	0.069766	N	3.910254	0.291712	0.076454
	N	1.871261	-1.489059	0.162537	N	1.950144	-1.231627	0.193968
	S	3.498540	-1.612831	0.235866	S	3.584746	-1.287996	0.270974
	H	-0.784244	2.165940	-0.444185	H	-0.827059	2.339607	-0.484015
	H	3.490471	2.685803	-0.268171	H	3.428043	2.978842	-0.310149
	H	1.194278	3.588054	-0.504336	H	1.103450	3.816625	-0.571566
	N	-0.754106	-0.572450	-0.061209	N	-0.767324	-0.353797	-0.039597
	C	-2.137093	-0.358042	-0.006025	C	-2.145402	-0.099963	0.011033
	H	-0.447244	-1.533994	-0.104642	H	-0.528956	-1.340299	-0.142816
	C	-2.705816	0.739332	0.645736	C	-2.699671	0.998296	0.674532
	C	-2.977872	-1.317387	-0.578668	C	-2.999580	-1.043436	-0.571328
	C	-4.087221	0.878029	0.695147	C	-4.079181	1.157761	0.722258
	C	-4.920687	-0.072781	0.119694	C	-4.925233	0.227042	0.132682
	C	-4.355360	-1.177077	-0.509069	C	-4.374589	-0.880141	-0.504886
	H	-2.539451	-2.171483	-1.086305	H	-2.566590	-1.904305	-1.071172
	H	-5.998122	0.041489	0.165124	H	-6.000978	0.358434	0.174913
	H	-4.990888	-1.932874	-0.959150	H	-5.020963	-1.621781	-0.963375
	H	-2.071486	1.463982	1.140044	H	-2.056969	1.709309	1.178276
	H	-4.513490	1.735752	1.205620	H	-4.493828	2.016484	1.240826
					H	-0.370329	-3.511230	0.694652
					O	-0.110589	-3.192955	-0.177994
				H	0.772481	-2.801722	-0.045729	
Energy (E _n)	-1024.79437809			-1101.20495978				
				Counterpoise corrected energy:				
				-1101.198215871613				
Zero-point correction	0.191388			0.216691				
<u>Thermal corrections to:</u>								
Energy	0.203224			0.231412				
Enthalpy	0.204168			0.232356				
Gibbs Free Energy	0.151778			0.173662				

State	ground state (S0)							
Compound	13 (gas phase)			13 + 1 H ₂ O				
Cartesian coordinates (Å)	C	2.710778	-2.455587	1.046273	C	-3.041837	-1.865656	-1.533141
	C	1.461753	-2.728155	1.512444	C	-1.872003	-2.116344	-2.182728
	C	0.331724	-1.912314	1.203243	C	-0.635909	-1.513637	-1.792091
	C	2.860297	-1.319519	0.201463	C	-2.996474	-1.000023	-0.403257
	C	1.722434	-0.497935	-0.137026	C	-1.750221	-0.409959	0.011554
	C	0.420642	-0.807404	0.398151	C	-0.545346	-0.658845	-0.728656
	N	3.988145	-0.913449	-0.376865	N	-4.014951	-0.684254	0.394599
	N	2.015635	0.494864	-0.968058	N	-1.851762	0.313871	1.122133
	S	3.611138	0.392623	-1.274020	S	-3.418578	0.262188	1.573741
	H	-0.633668	-2.180471	1.616582	H	0.261717	-1.737064	-2.358443
	H	3.571790	-3.067996	1.282657	H	-3.982831	-2.310140	-1.832385
	H	1.304324	-3.586892	2.156830	H	-1.865590	-2.780015	-3.040867
	N	-0.690066	-0.020645	0.055055	N	0.652942	-0.034645	-0.325440
	C	-0.622552	1.393256	0.192687	C	0.718585	1.392286	-0.423527
	C	-1.954373	-0.641671	-0.137087	C	1.820514	-0.797823	-0.110873
	C	-1.268512	2.212923	-0.733810	C	1.189055	2.145613	0.652275
	C	0.075553	1.972642	1.250867	C	0.305559	2.028417	-1.591801
	C	-1.215395	3.591718	-0.597620	C	1.261364	3.526861	0.540857
	C	-0.506291	4.171549	0.450158	C	0.849320	4.166746	-0.624716
	C	0.141218	3.355330	1.368742	C	0.363321	3.414339	-1.686232
	H	0.565266	1.336553	1.980354	H	-0.059728	1.435233	-2.423373
	H	-0.459732	5.250861	0.548189	H	0.899978	5.247902	-0.700707
	H	0.692475	3.794319	2.194143	H	0.036581	3.903717	-2.598081
	H	-1.804754	1.760092	-1.560141	H	1.448838	1.641710	1.577518
	H	-1.720498	4.218997	-1.325091	H	1.624013	4.109762	1.381303
	C	-3.095521	-0.157720	0.503810	C	3.085827	-0.284209	-0.410287
	C	-2.064409	-1.745530	-0.986351	C	1.726604	-2.084464	0.436247
	C	-4.326190	-0.766222	0.290422	C	4.223395	-1.039582	-0.160683
	C	-4.432697	-1.870260	-0.546286	C	4.128838	-2.317984	0.376331
	C	-3.293739	-2.357963	-1.179560	C	2.871835	-2.833961	0.668861
	H	-3.364171	-3.214223	-1.842641	H	2.775989	-3.828180	1.093456
	H	-1.179553	-2.115775	-1.492048	H	0.751700	-2.497740	0.671076
	H	-3.013981	0.698109	1.163987	H	3.174078	0.708051	-0.835189
	H	-5.205721	-0.377843	0.793834	H	5.196214	-0.621629	-0.399286
	H	-5.394305	-2.345928	-0.706375	H	5.021718	-2.903130	0.566450
					H	-0.170756	0.222568	2.464677
					O	0.598300	0.023216	3.020525
					H	1.080737	-0.647234	2.521972
Energy (E _n)	-1255.70209234			-1332.10651123				
				Counterpoise corrected energy:				
				-1332.099742501843				
Zero-point correction	0.272246			0.297109				
<u>Thermal corrections to:</u>								
Energy	0.288716			0.316777				
Enthalpy	0.289660			0.317721				
Gibbs Free Energy	0.225963			0.246864				

IX. References and Notes

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