Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Isoindolinone-based molecular switches

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Experimental Details

General Information. Commercially available reagents, (triisopropylsilyl)acetylene, phenylacetylene, *N*-butylamine, hydroxyamine hydrochloride, and CuCl, were purchased and used as received. All solvents were dried using a Grubbs apparatus prior to use. All reactions were performed in air unless otherwise specified. TLC analysis was performed on glass backed plates (60A) and flash chromatography was performed on ultra pure flash silica (230-400 mesh size). NMR spectra were recorded using a Varian Inova 300 MHz (^{1}H: 299.838 MHz, ^{13}C: 75.402 MHz) or Varian Unity 400 MHz spectrometer (^{1}H: 399.945 MHz, ^{13}C: 100.577 MHz) with $CDCl_3$ referenced at 7.26 ppm (^{1}H) or 77.16 ppm (^{13}C). IR spectra were recorded using KBr discs on a Nicolet Nexus 470 FTIR spectrometer. UV-Visible spectra were recorded on a Agilent 8453 spectrophotometer in $CHCl_3$. High resolution mass spectra were recorded on a Bruker Daltonics spectrometer using Electrospray Ionization (ESI).

Light Switching Experiments

Samples of enyne **4a** or **4b** were dissolved in $CDCl_3$ in an NMR tube and irradiated with 365 nm (P/N 95-0021-12 Entela UVGL-25 Compact UV Lamp), 411 nm (OSA Opto Light-OCU 400 411 OS Ultra Violet LED), or 470 nm (AND190HBB InGaN High Brightness Blue Light Emission LED) light for specific periods of time. After irradiation, the samples were quickly transferred to an NMR spectrometer and a 1D proton spectrum was acquired. Integration of the vinyl protons for each isomer was used to calculate the percentage of each isomer in the mixture.

DFT Calculations

Density functional B3LYP/6-31G* equilibrium geometry calculations were carried out in vacuum using Spartan 10. The lowest energy geometries were identified by manually searching a limited number of starting geometries. Other low energy geometries differ only in placement/geometry of butyl groups.

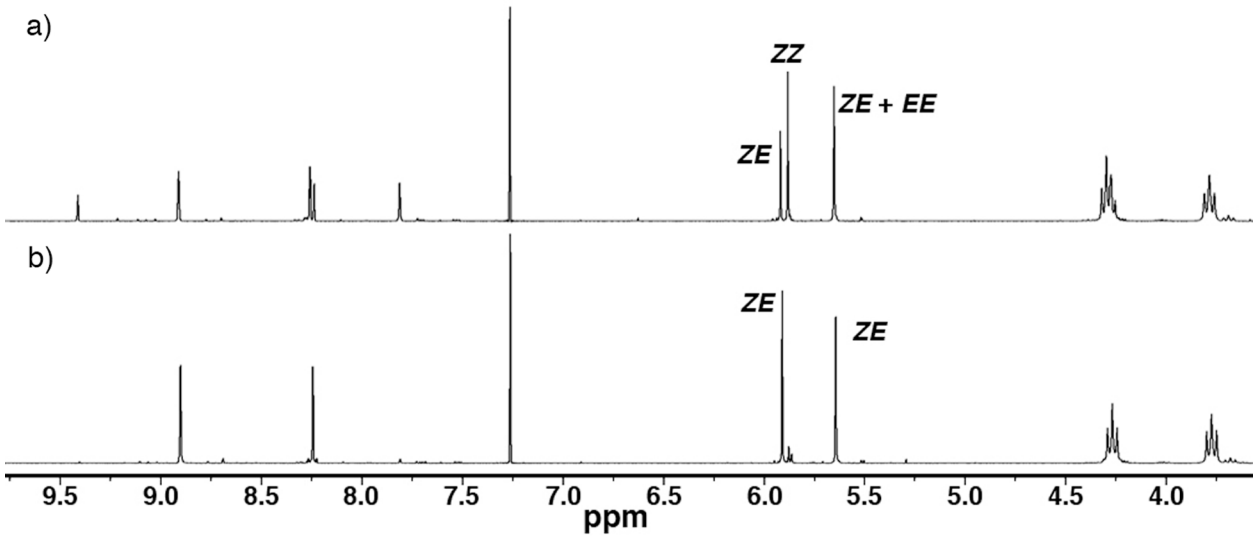


Figure S1. Isomerization experiments with compound **4a**. a) Mixture of *ZZ/ZE/EE*-**4a** that is formed after exposure of *ZZ*-**4a** to 365 nm light for 1 hour. b) Spectrum of *ZE*-**4a** that is formed after treatment of *ZZ/ZE/EE*-**4a** to TFA at rt for 2 days.

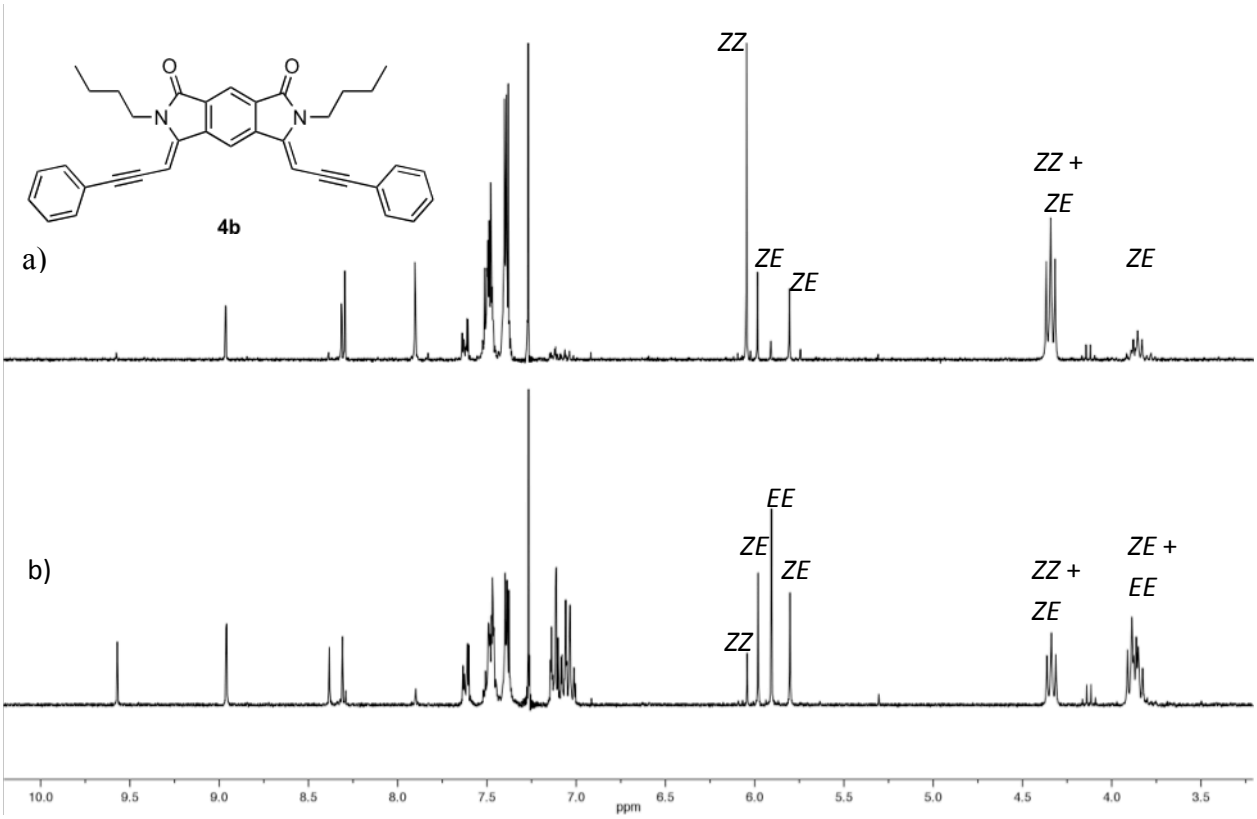


Figure S2. Response of phenyl derivative **4b** to light. a) Mixture of 2:1 *ZZ/ZE*-**4b** after column chromatography. b) Mixture of 5:5:1 *ZE/EE/ZZ*-**4b** after six hours of exposure of mixture in (a) to 365 nm light.

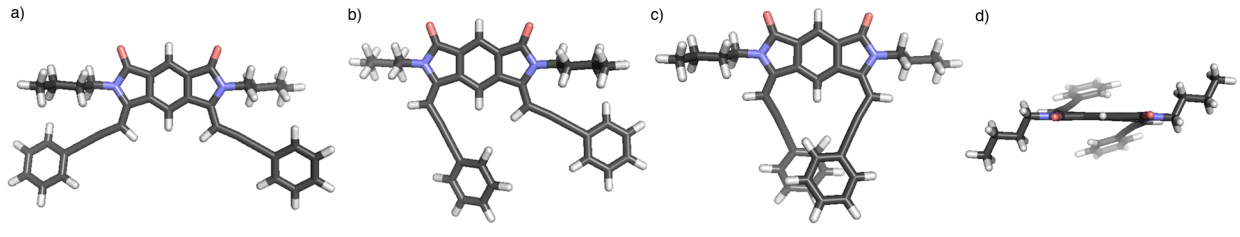


Figure S3. Computational modeling of compound **4b** in vacuum. a) *ZZ*-**4b**, b) *ZE*-**4b**, c) *EE*-**4b**, and d) *EE*-**4b**, top view. Negligible differences in energy were found between these three isomers. *EE*-**4b** was found to be 1.25 kcal/mol higher in energy than *ZE*-**4b** and *ZE*-**4b** is only 0.97 kcal/mol more stable than *ZZ*-**4b**.

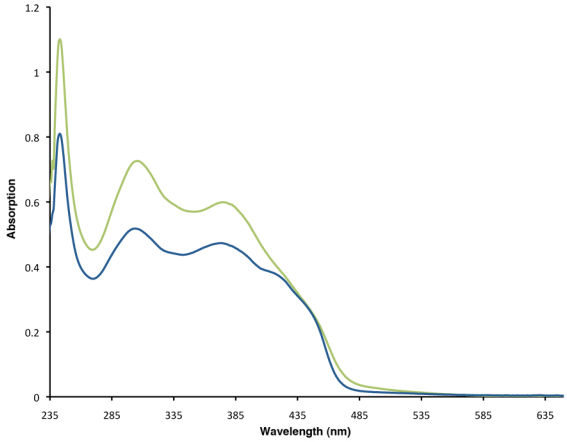


Figure S4. UV-Visible absorption spectrum of compound **4b** in $CHCl_3$. *ZZ/ZE*-blue line, *ZE/EE*-green line.

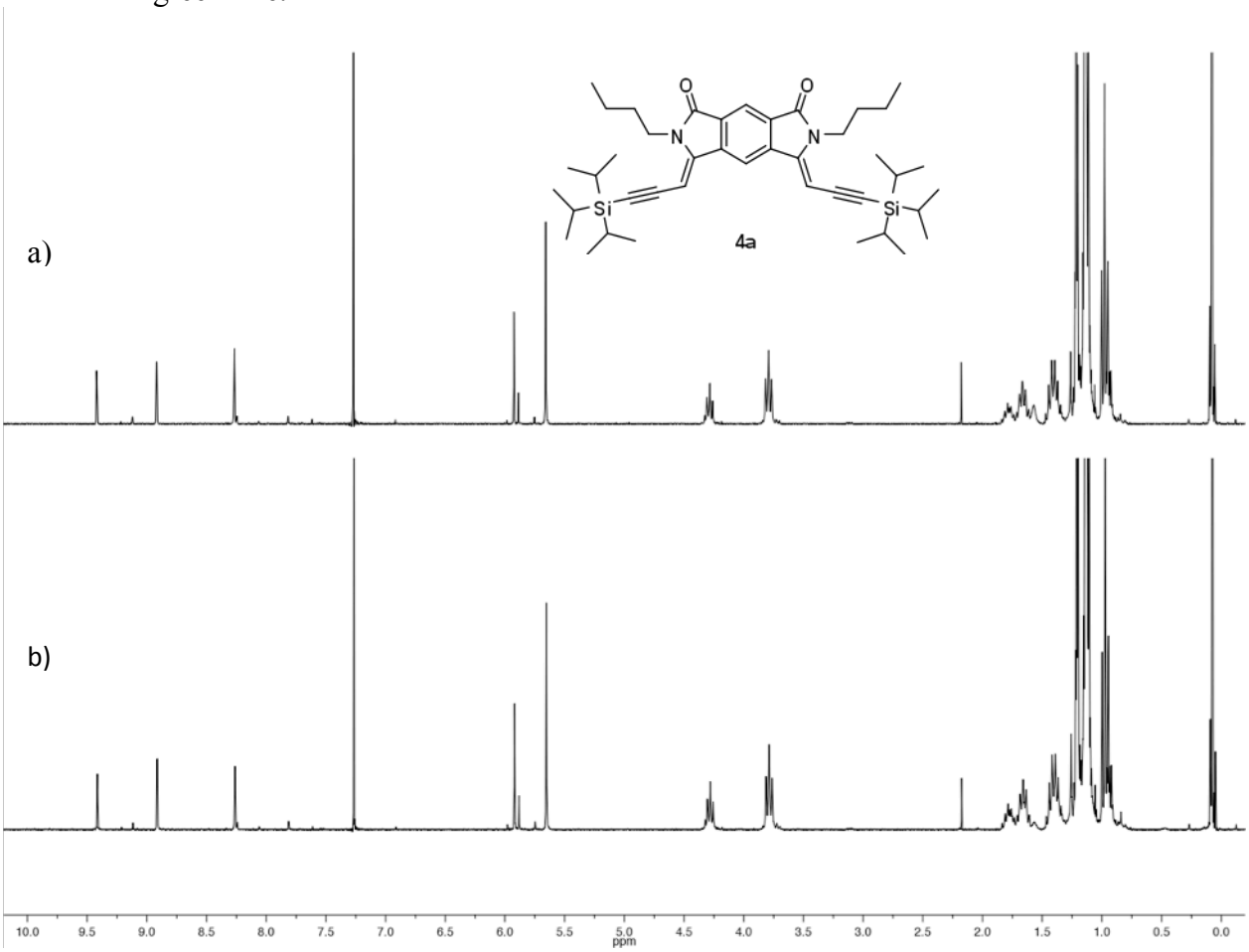
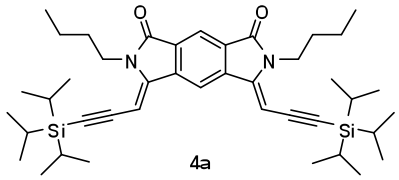


Figure S5. Thermal experiment for **4a.** a) Mixture of *ZE/EE*-**4a** in $CDCl_3$. b) After 24 hrs of heating to 60 °C.

2,6-dibutyl-3,5-bis(3-(triisopropylsilyl)prop-2-ynylidene)-2,3,5,6-tetrahydropyrrolo[3,4-*f*]isoindole-1,7-dione (4a)

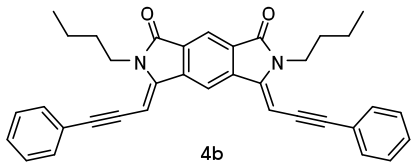


4a

N-butylamine (0.18 mL, 1.8 mmol) was added to a mixture of H_2O (3.0 mL) and MeOH (6.0 mL). This was followed by the addition of N^1,N^3-dibutyl-4,6-diethynylisophthalamide (84 mg, 0.26 mmol), CuCl (9.0 mg, 0.091 mmol), and then hydroxyamine hydrochloride (14 mg, 0.20 mmol). (Bromoethynyl)triisopropylsilane[1] (160 mg, 0.62 mmol) was diluted in 2.0 mL of MeOH and added dropwise to the mixture. The reaction was stirred at room temperature and a red precipitate formed. After 24 hours, H_2O was added to the reaction and it was extracted with Et_2O. The organic layer was washed with H_2O, brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and a red solid was obtained. Purification of crude product was accomplished by column chromatography (5% v/v Et_3N in hexanes) to give the product as a yellow solid. Yield: 108 mg (61%); R_f : 0.68 (4:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) *ZZ*-**4a**: δ 8.24 (d, *J* = 0.9 Hz, 1H), 7.81 (d, *J* = 0.9 Hz, 1H), 5.88 (s, 2H), 4.32-4.27 (m, 4H), 1.81-1.66 (m, 4H), 1.44-1.31 (m, 4H), 1.13 (s, 42 H), 0.93 (t, *J* = 7.2 Hz, 6H); *ZE*-**4a:** δ 8.91 (d, *J* = 0.9 Hz, 1H), 8.25 (d, *J* = 0.9 Hz, 1H), 5.92 (s, 1H), 5.65 (s, 1H), 4.30-4.25 (m, 2H), 3.81-3.76 (m, 2H), 1.83-1.72 (m, 2H), 1.71-1.61 (m, 2H), 1.46-1.34 (m, 4H), 1.20 (s, 21 H), 1.13 (s, 21 H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H); *EE*-**4a**: δ 9.41 (d, *J* = 0.9 Hz, 1H), 8.26 (d, *J* = 0.9 Hz, 1H), 5.65 (s, 2H), 3.81-3.76 (m, 4H), 1.71-1.60 (m, 4H), 1.46-1.34 (m, 4H), 1.12 (s, 42H), 0.97 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *ZZ*-**4a**: δ 166.4, 141.1, 140.3, 129.4, 119.2, 109.8, 103.0, 102.1, 86.6, 40.9, 32.3, 20.0, 18.8, 14.0, 11.6; *ZE*-**4a**: δ 166.4, 165.0, 143.4,

141.0, 140.8, 138.2, 130.8, 129.3, 118.8, 114.7, 103.4, 103.0, 102.7, 102.0, 89.1, 86.7, 40.9, 39.7, 32.2, 30.3, 20.4, 20.0, 18.8, 18.8, 14.0, 13.9, 11.7, 11.5; *EE*-**4a**: δ 164.9, 143.9, 138.6, 131.4, 118.5, 104.1, 102.4, 89.7, 39.5, 30.4, 20.3, 19.0, 12.1, (2 *EE* resonances buried under *ZE* isomer signals); IR (film, KBr) 2941, 2865, 2123, 1725, 1712, 1384, 1101, 1048 cm^{-1}; UV-Vis ($CHCl_3$) λ_{max} *ZZ*-**4a**: 243, 286, 353, 370, 399, 422 nm; *ZE*-**4a**: 243, 286, 357, 399, 422 nm; *ZE*-**4a**+*EE*-**4a**: 243, 286, 357, 399, 422 nm; HRMS (ESI+) for $C_{42}H_{64}N_2O_2Si_2Na$ $[M + Na]^+$: calcd. 707.4399, found 707.4376.

2,6-dibutyl-3,5-bis(3-phenylprop-2-ynylidene)-2,3,5,6-tetrahydropyrrolo[3,4-*f*]isoindole-1,7-dione (4b)



4b

N-butylamine (0.11 mL, 1.1 mmol) was added to a mixture of H_2O (2.0 mL) and MeOH (4.0 mL). This was followed by the addition of N^1,N^3-dibutyl-4,6-diethynylisophthalamide (60 mg, 0.18 mmol), CuCl (5.4 mg, 0.055 mmol), and then hydroxyamine hydrochloride (8.5 mg, 0.12 mmol). (Bromoethynyl)benzene[1] (67 mg, 0.37 mmol) was diluted in 1.0 mL of MeOH and added dropwise to the mixture. The reaction was stirred at room temperature and a red precipitate formed. After 24 hours, H_2O was added to the reaction and it was extracted with Et_2O. The organic layer was washed with H_2O, brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was a red solid. The product was purified by column chromatography (5% v/v Et_3N in 6:1 hexanes:EtOAc) to give the product as an orange solid. Yield: 51 mg (54%); R_f: 0.68 (2:1 hexanes:EtOAc); ^1H NMR (400 MHz, $CDCl_3$) *ZZ*-**4b**: δ 8.29 (d, *J* = 0.8 Hz, 1H), 7.89 (d, *J* = 1.2 Hz, 1H), 7.50-7.46 (m, 4H), 7.39-7.38 (m,

6H), 6.04 (s, 2H), 4.35-4.32 (m, 4H), 1.89-1.82 (m, 4H), 1.47-1.38 (m, 4H), 0.95 (t, *J* = 7.2 Hz, 6H); *ZE*-**4b**: δ 8.95 (d, *J* = 0.8 Hz, 1H), 8.31 (d, *J* = 0.8 Hz, 1H), 7.62-7.60 (m, 2H), 7.50-7.46 (m, 5H), 7.39-7.38 (m, 3H), 5.98 (s, 1H), 5.80 (s, 1H), 4.36-4.31 (m, 2H), 3.86-3.82 (m, 2H), 1.91-1.82 (m, 2H), 1.78-1.67 (m, 2H), 1.49-1.37 (m, 4H), 0.99 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 3H); *EE*-**4b** (300 MHz): δ 9.57 (d, *J* = 0.9 Hz, 1H), 8.38 (d, *J* = 1.2 Hz, 1H), 7.10-7.00 (m, 10H), 5.90 (s, 2H), 3.91-3.86 (m, 4H), 1.78-1.67 (m, 4H), 1.49-1.37 (m, 4H), (resonances for the Me groups are overlapping with Me groups from other isomers); ^{13}C NMR (100 MHz, $CDCl_3$) *ZZ*-**4b**: δ 166.3, 141.1, 140.1, 131.4, 129.0, 128.7, 123.1, 119.2, 110.1, 98.5, 86.5, 85.6, 41.2, 32.2, 20.3, 14.1, (1 missing resonance, likely buried under resonance from *Z,E* isomer); *ZE*-**4b** and *EE*-**4b**: δ 166.3, 165.1, 165.1, 143.0, 142.6, 141.4, 140.3, 138.4, 138.2, 131.8, 131.3, 130.8, 130.7, 129.3, 129.3, 129.2, 128.1, 127.9, 123.2, 122.7, 119.0, 118.8, 114.8, 99.9, 98.8, 98.4, 89.7, 89.0, 87.1, 86.7, 86.3, 39.8, 30.5, 30.4, 20.4, 20.4, 13.9 (12 resonances are missing, likely due to overlap with *ZZ* signals); IR (film, KBr) 2918, 2850, 1711, 1592, 1384, 1114, 1048 cm^{-1}; UV-Vis ($CHCl_3$) λ_{max} *ZZ*-**4b**+*ZE*-**4b**: 243, 304, 373 nm; *ZE*-**4b**+*EE*-**4b**: 243, 305, 375 nm; HRMS (ESI+) for $C_{36}H_{33}N_2O_2$ $[M + H]^+$: calcd 525.2537, found 525.2561.

References

1. M. X.-W. Jiang, M. Rawat and W.D. Wulff, *J. Am. Chem. Soc.*, 2004, **126**, 5970.

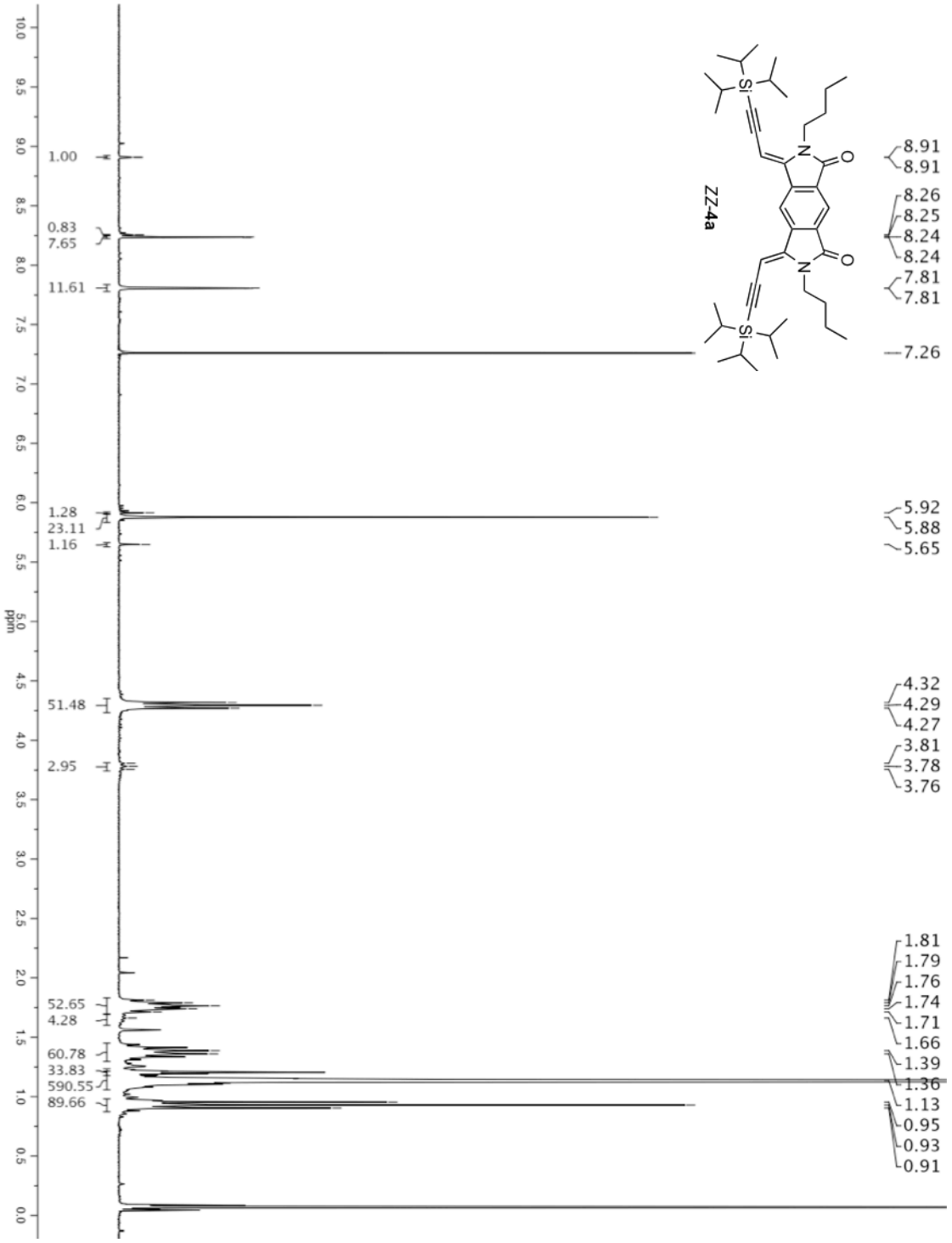


Figure S6. ^{1}H NMR spectrum in $CDCl_3$ of 12:1 mixture of *ZZ/ZE*-**4a** isolated after column chromatography.

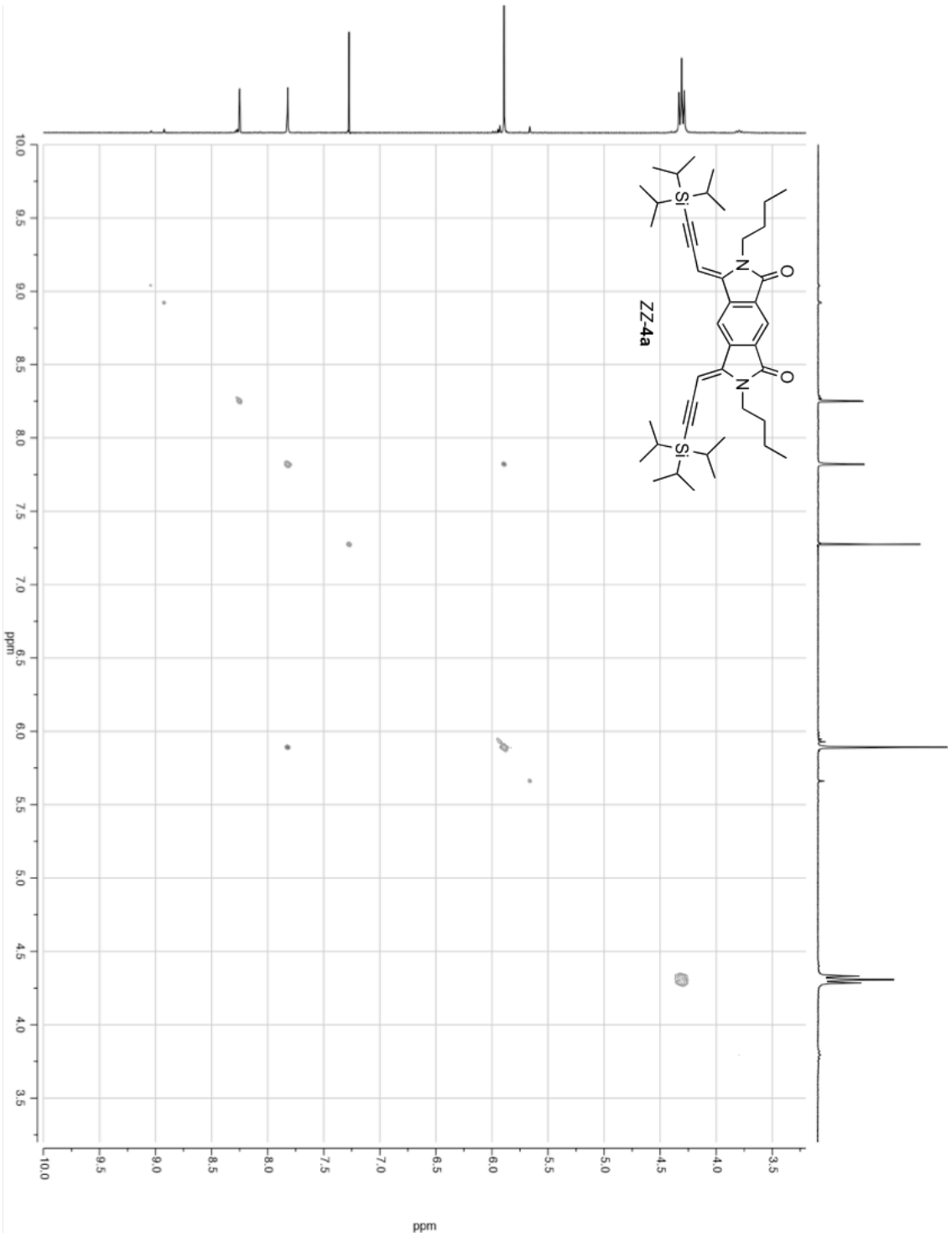


Figure S7. NOESY spectrum in $CDCl_3$ of 12:1 mixture of *ZZ/ZE*-**4a** isolated after column chromatography.

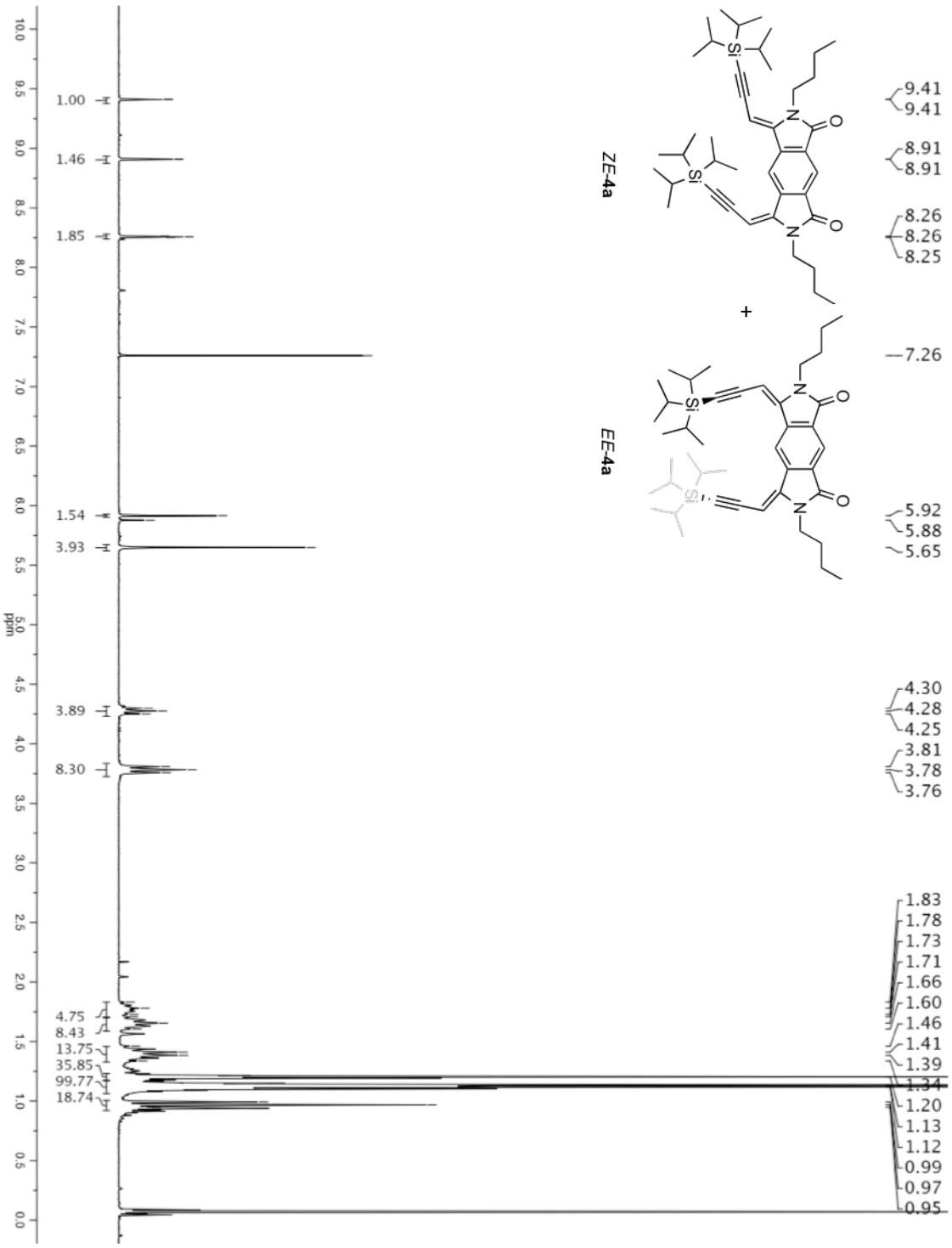


Figure S8. ^{1}H NMR spectrum of *ZE/EE*-**4a** in $CDCl_3$ after exposure of *ZZ*-**4a** to 365 nm light.

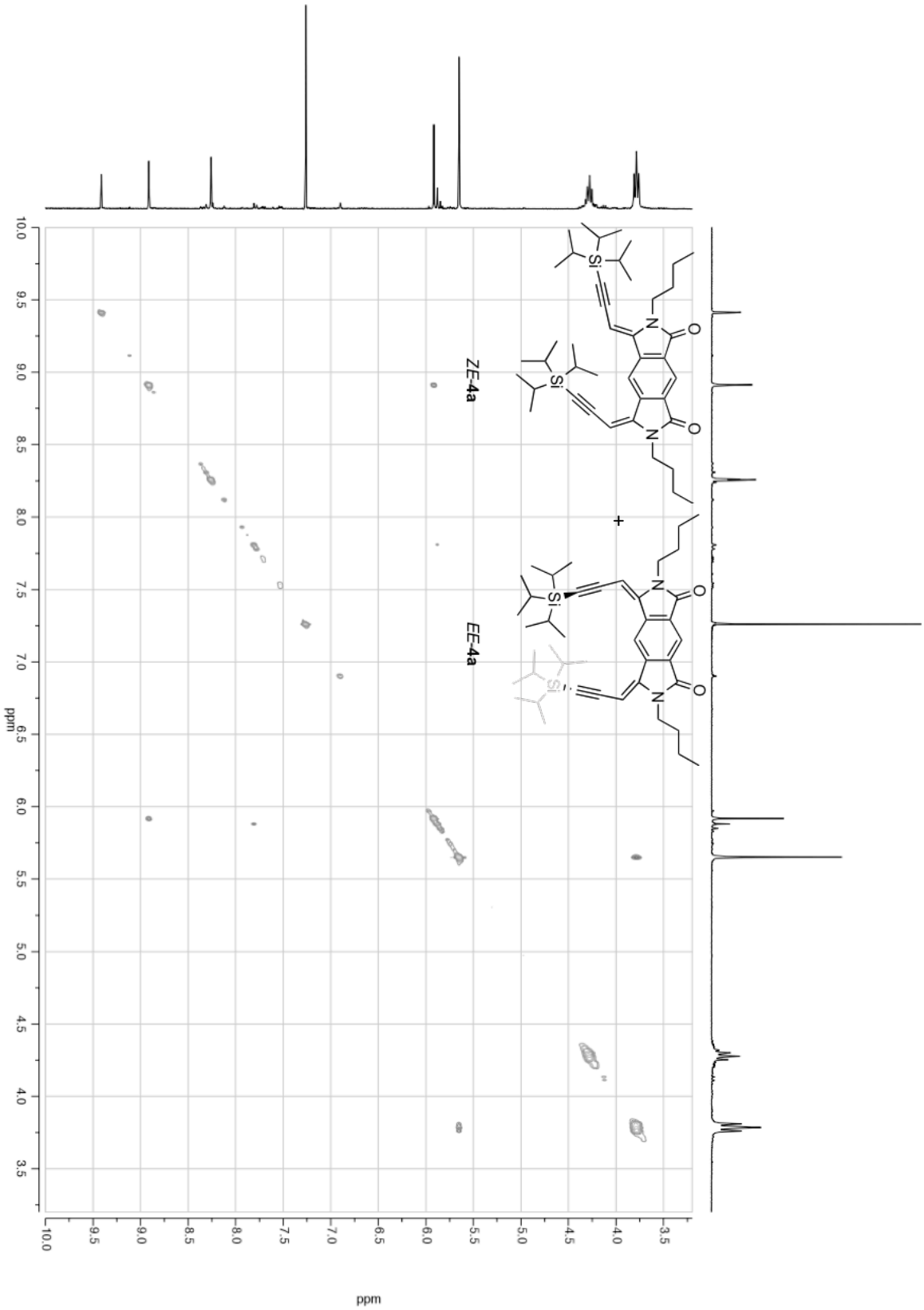


Figure S9. NOESY spectrum of *ZE/EE*-**4a** in $CDCl_3$ after exposure of *ZZ*-**4a** to 365 nm light.

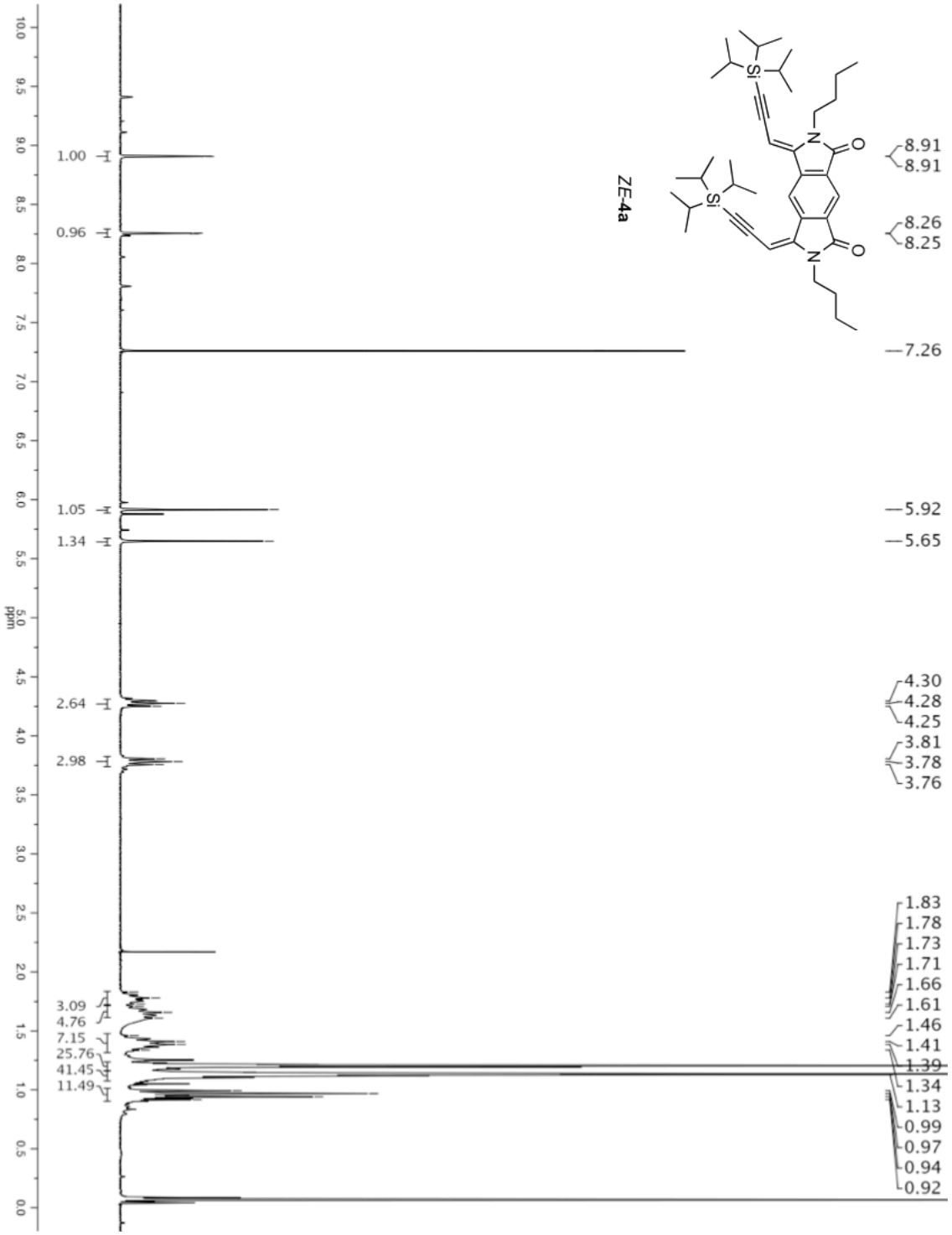


Figure S10. ^{1}H NMR spectrum of *ZE*-**4a** in $CDCl_3$ after exposure of *ZE/EE*-**4a** mixture to 470 nm light.

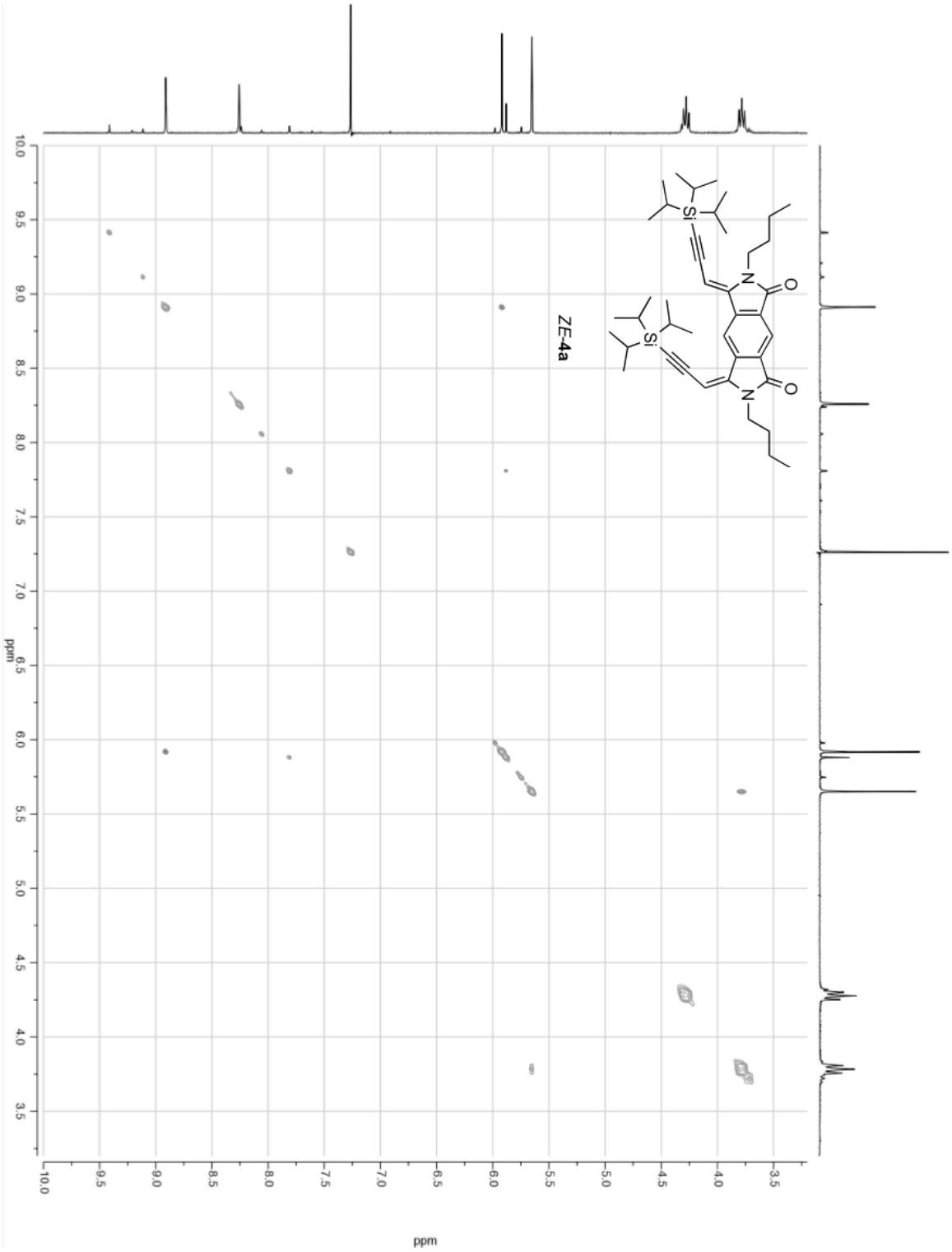


Figure S11. NOESY spectrum of *ZE*-**4a** in $CDCl_3$ after exposure of *ZE/EE*-**4a** mixture to 470 nm light.

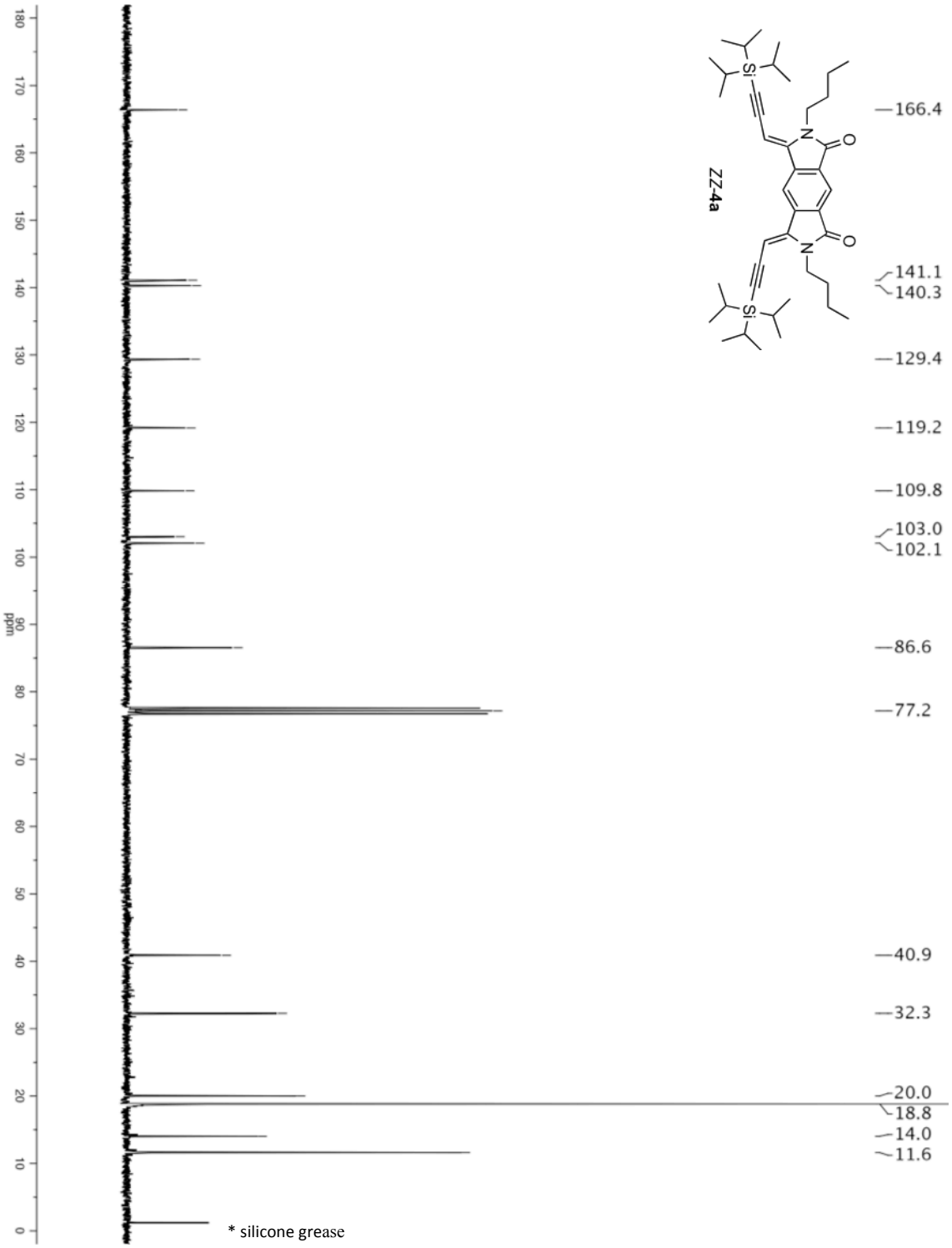


Figure S12. ^{13}C spectrum of *ZZ*-**4a**.

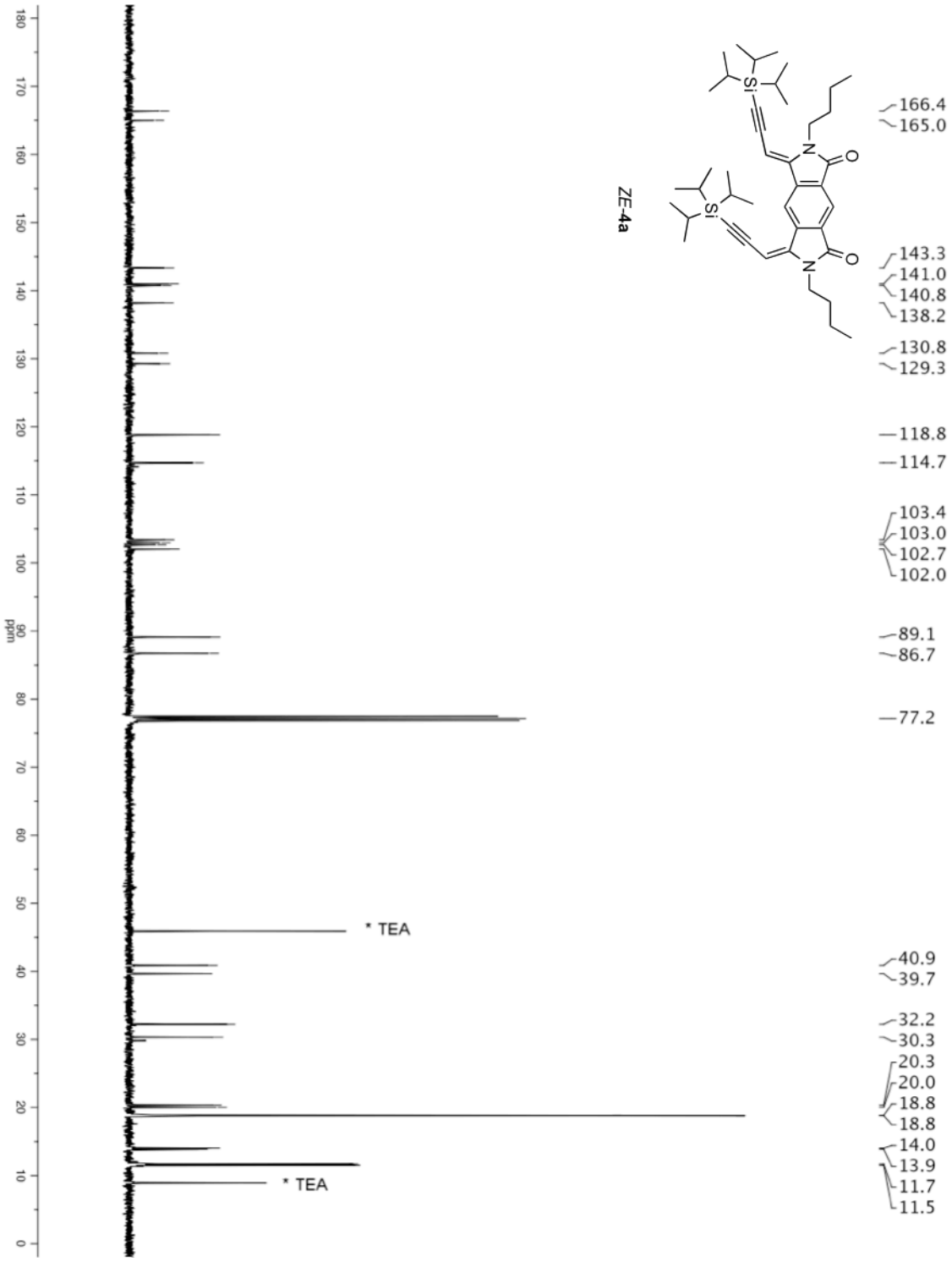


Figure S13. ^{13}C spectrum of *ZE*-**4a**.

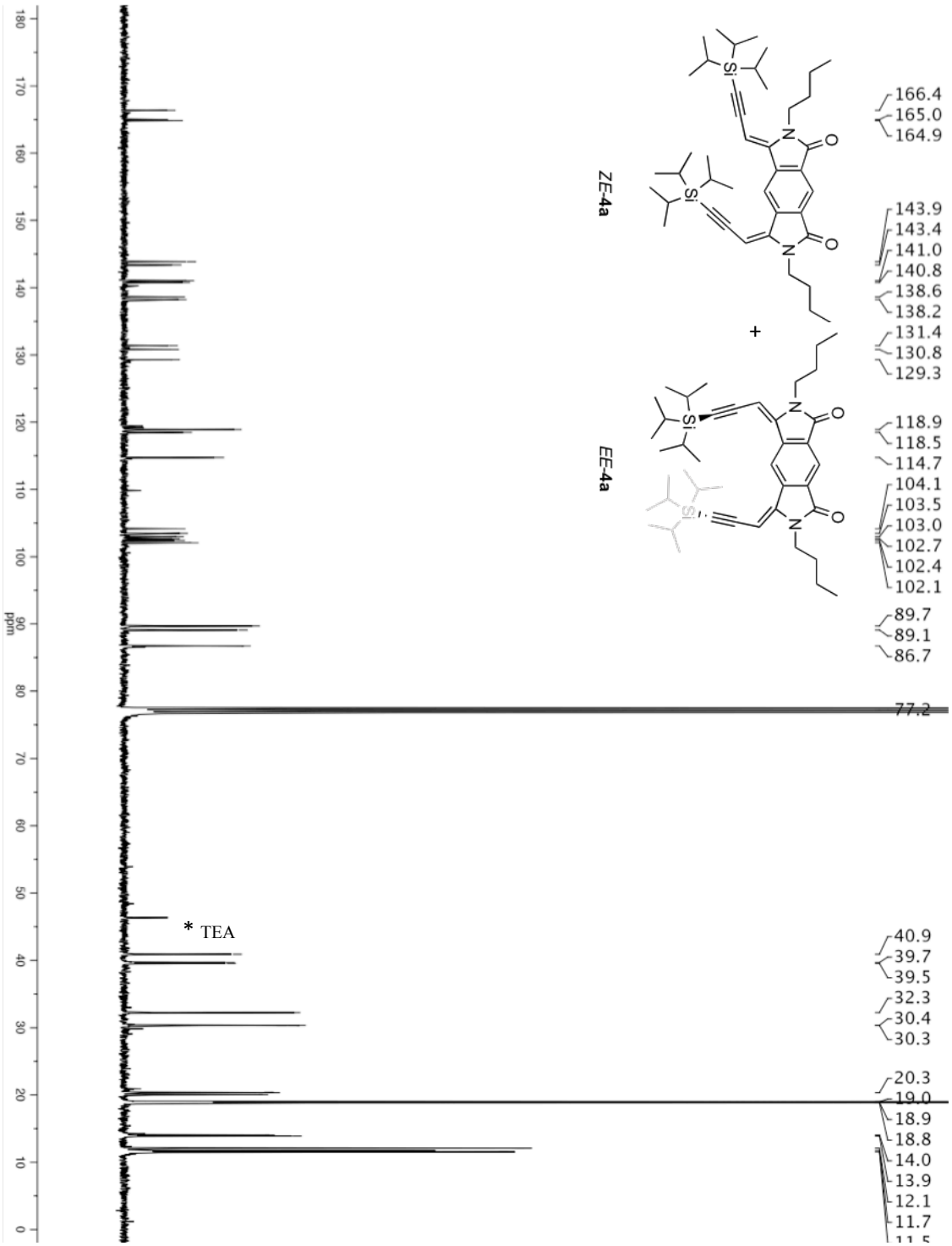


Figure S14. ^{13}C spectrum of *ZE/EE*-**4a**.

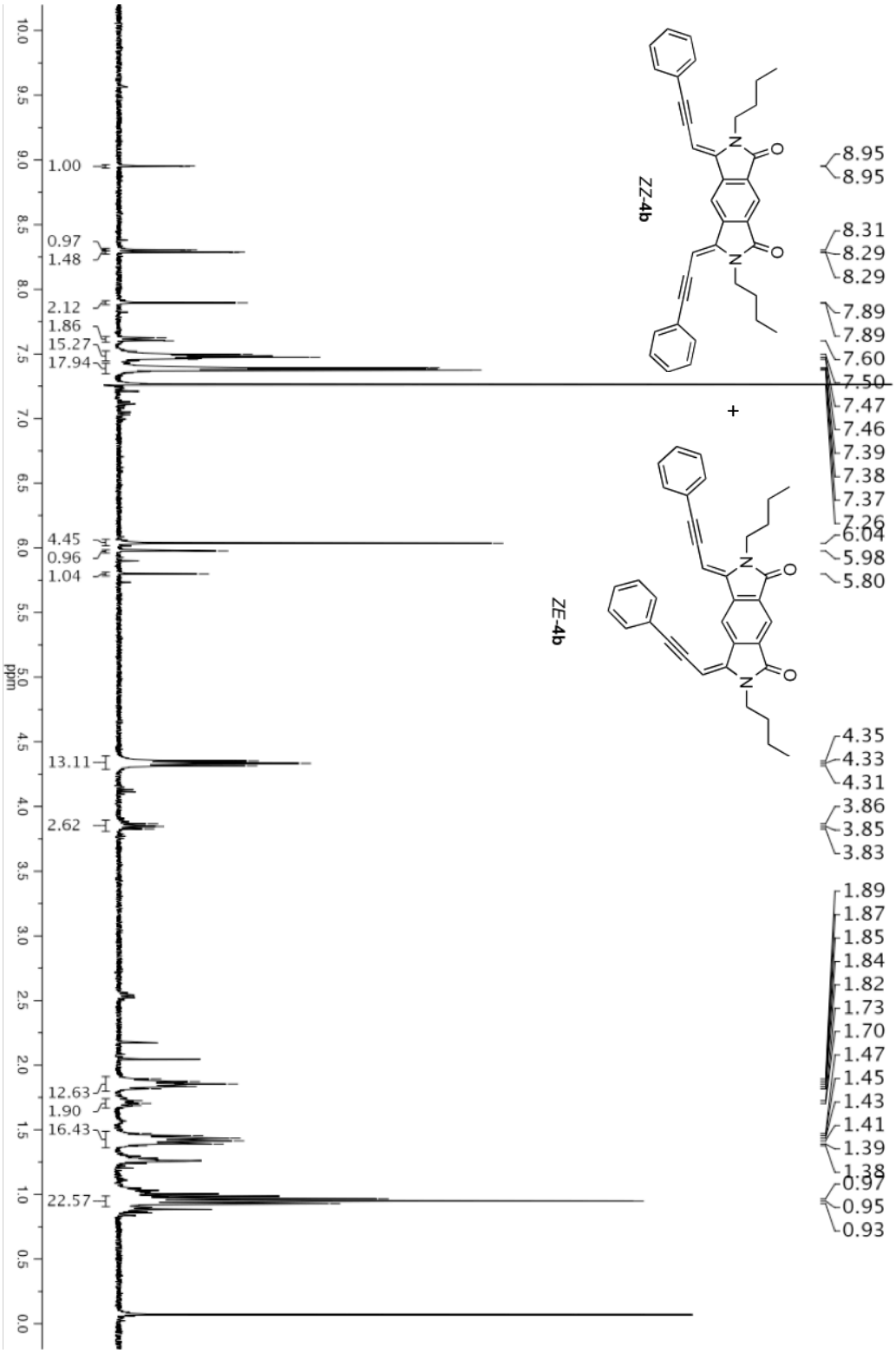


Figure S15. ^{1}H NMR spectrum of 2:1 mixture of *ZZ/ZE*-**4b** in $CDCl_3$ after column chromatography.

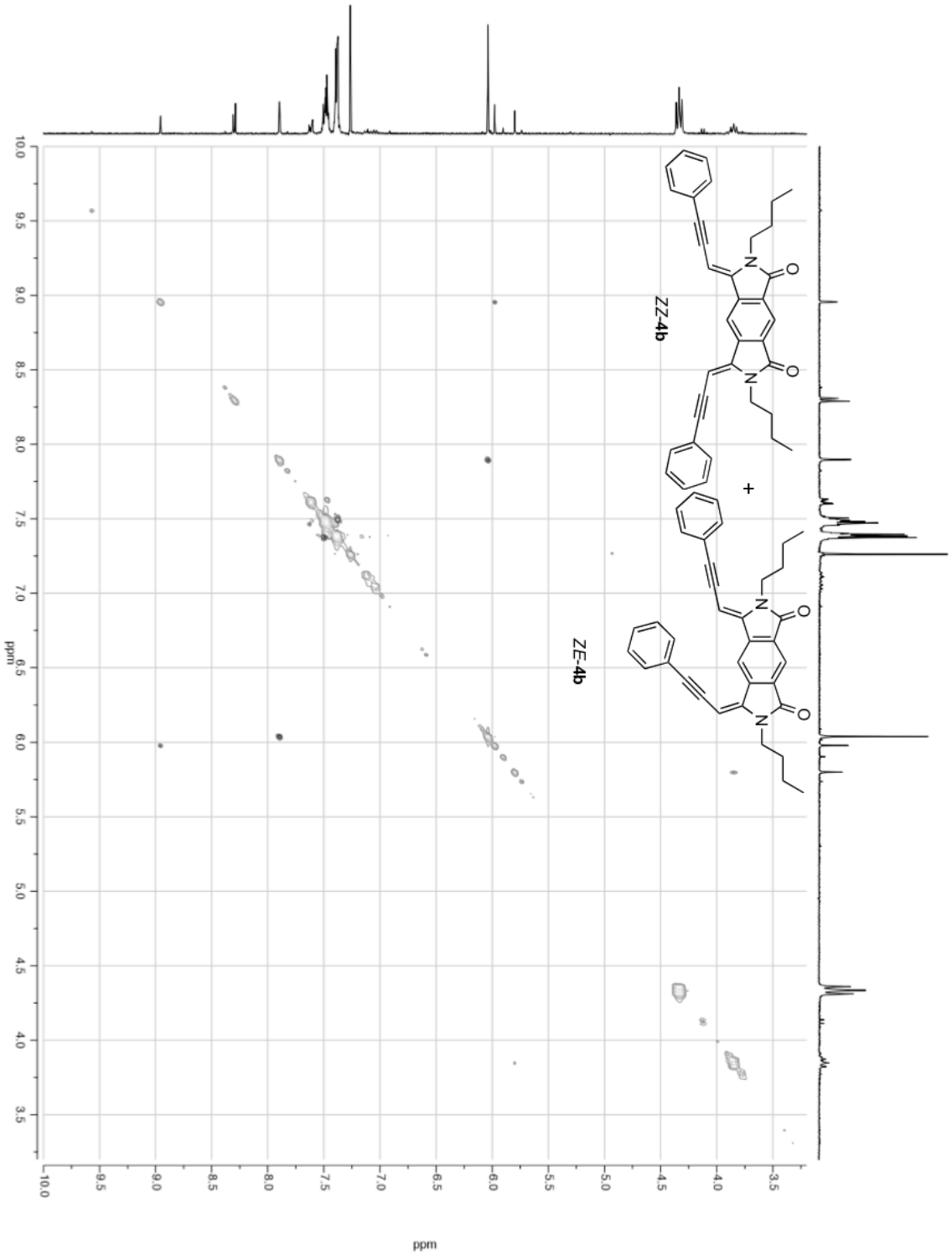


Figure S16. NOESY spectrum of 2:1 *ZZ/ZE*-**4b** in $CDCl_3$ after column chromatography.

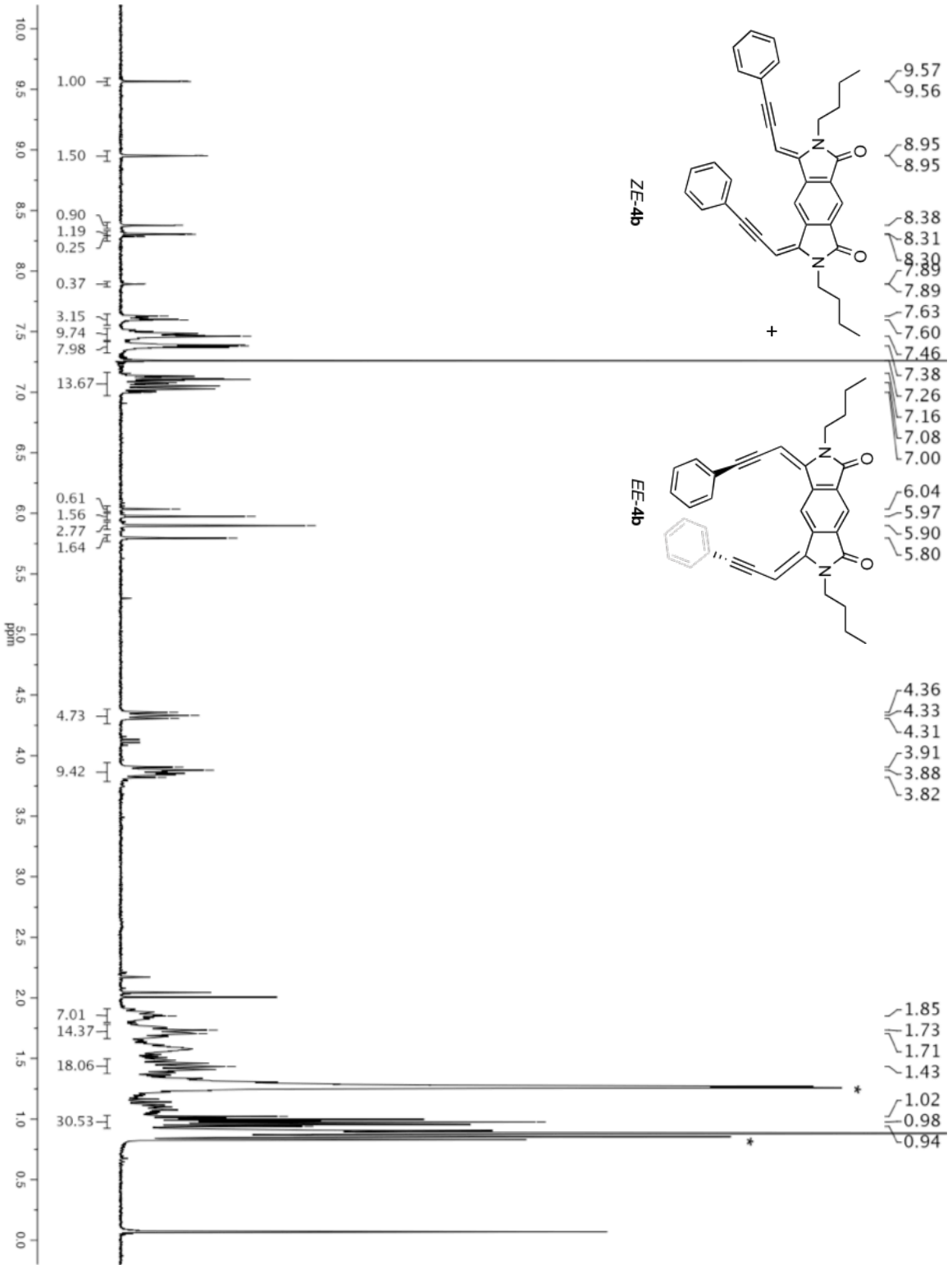


Figure S17. ^{1}H NMR spectrum of 5:5:1 *ZE/EE/ZZ*-**4b** after exposure of 2:1 *ZZ/ZE*-**4b** to 365 nm light.

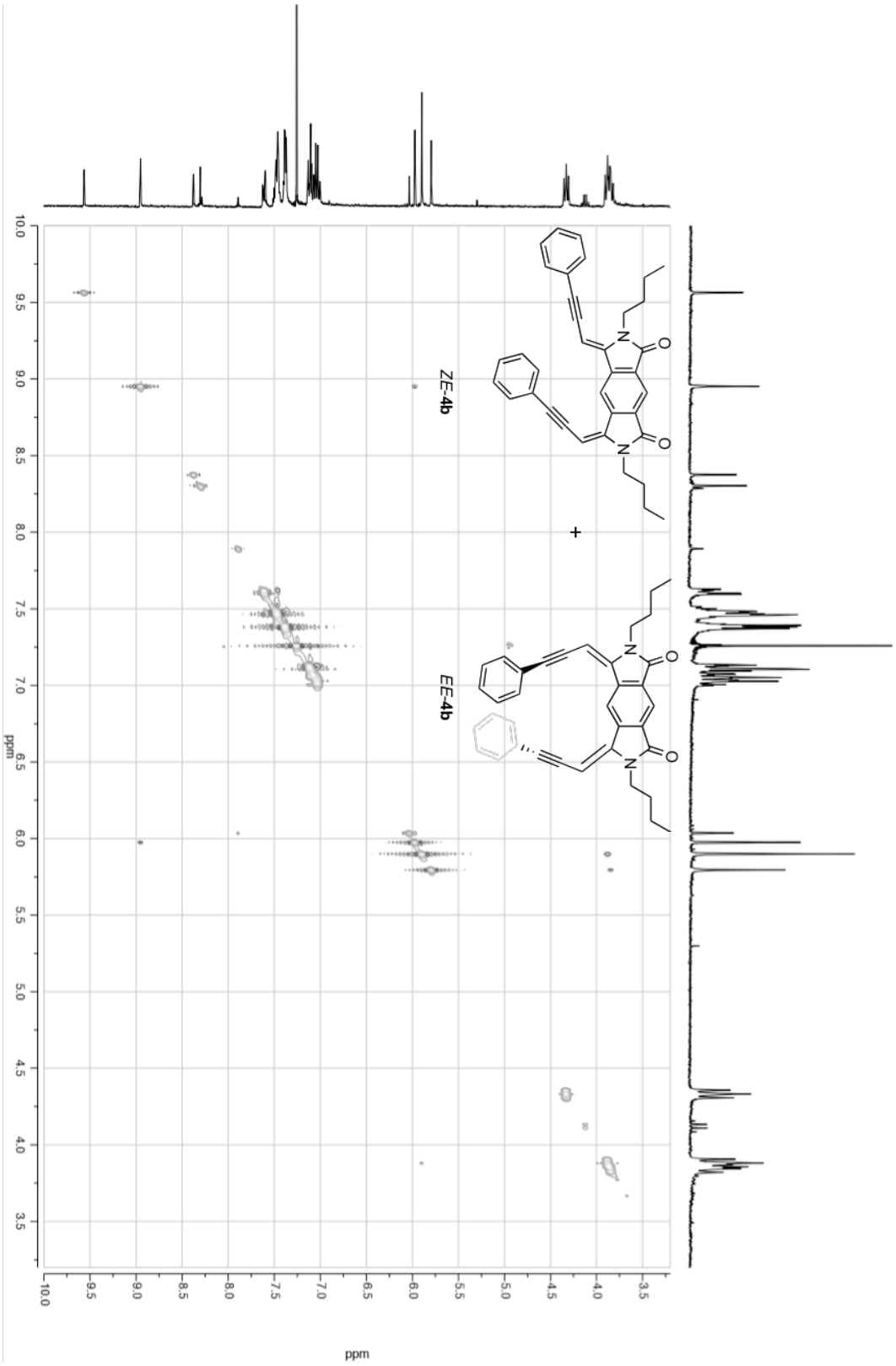


Figure S18. NOESY spectrum of 5:5:1 *ZE/EE/ZZ*-**4b**.

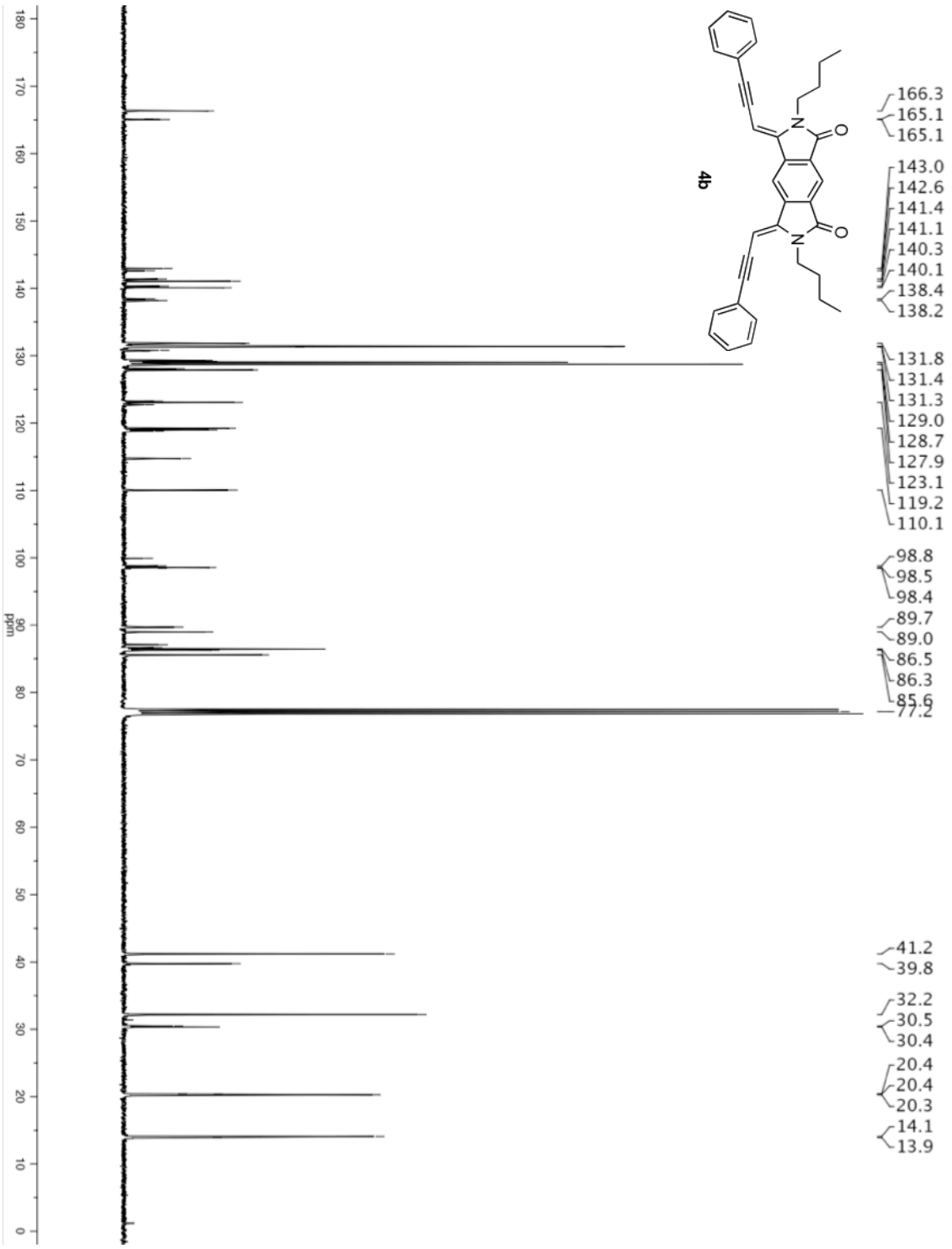


Figure S19. ^{13}C spectrum of 2:1 *ZZ*/ZE-**4b**.

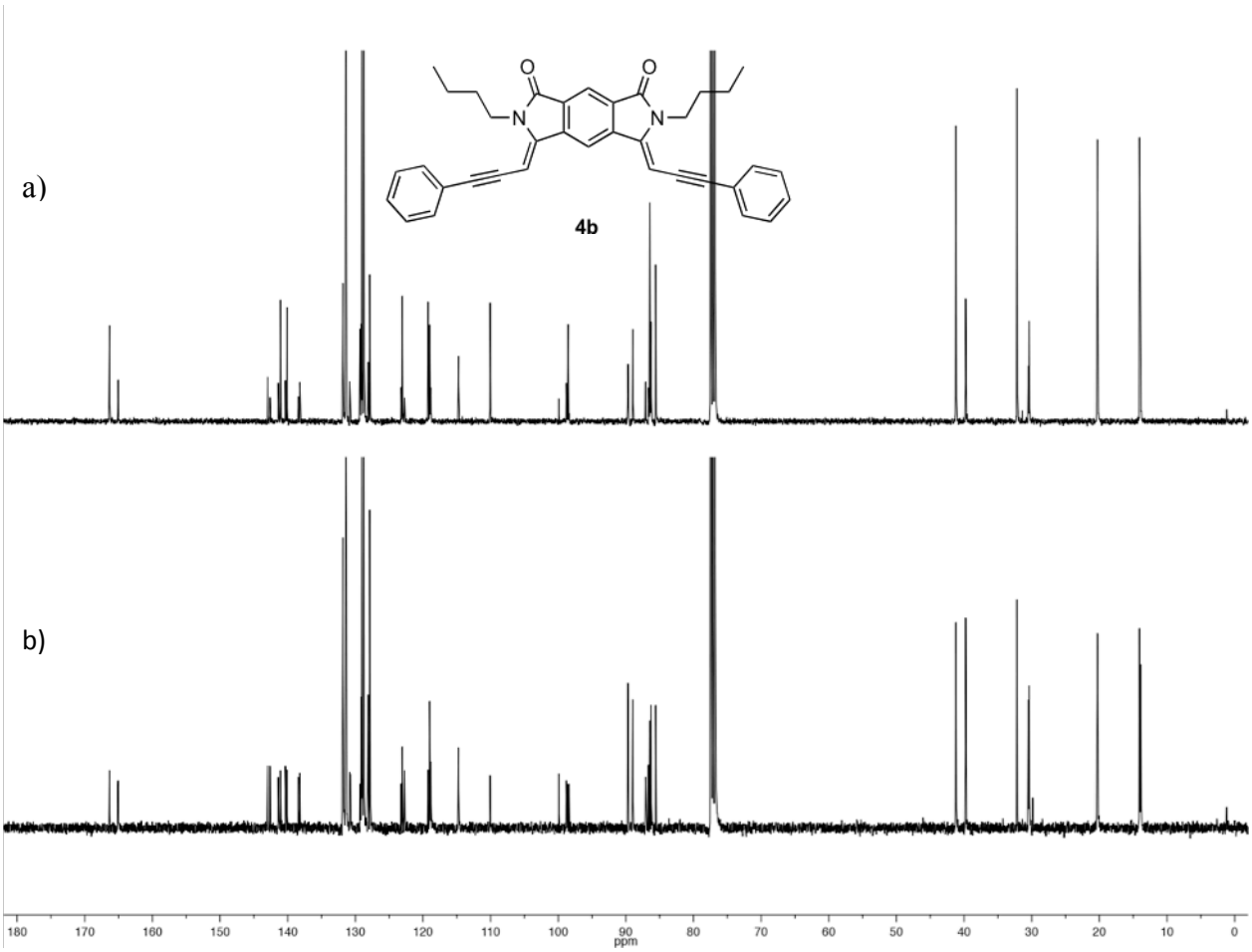


Figure S20. a) ^{13}C spectrum of 2:1 *ZZ*/ZE-**4b**. b) ^{13}C spectrum of **4b** after exposure to 365 nm light showing *ZE* and *EE* as the major isomers. Differences in signal intensity between the two spectra were used to assign ^{13}C resonances to their corresponding isomer.

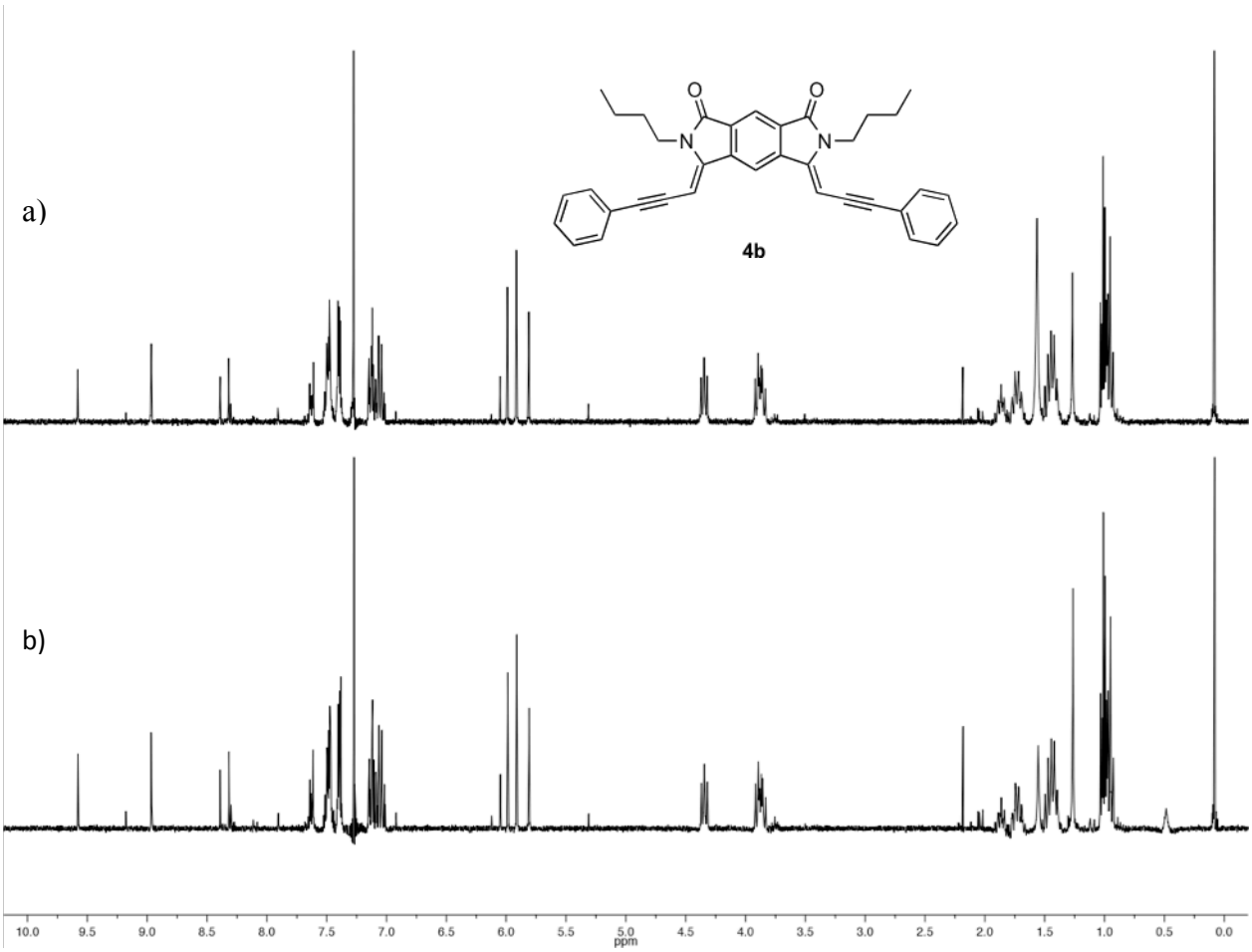


Figure S21. Thermal experiment in $CDCl_3$ for **4b**. a) 5:5:1mixture of *ZE/EE/ZZ*-**4b**. b) After 24 hours of heating to 60 °C.