Supplementary Information for

# C–H Activation-Enabled Synthesis of A Piperazine-Embedded Azadibenzo[*a,g*]corannulene Analogue

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## 1. General materials and methods

Unless otherwise stated, all chemicals were of reagent grade or higher, obtained from commercial sources and used without further purification. Flash chromatography was performed on silica gel 200–300 mesh or neutral $Al_2O_3$. Thin layer chromatography (TLC) was performed on glass backed plates pre-coated with silica (GF254), which were developed using standard visualizing agents.

$^1H$ and $^{13}C$ NMR spectra were recorded on a 400 MHz or 600 MHz BRUKER AVANCE spectrometer at 298 K. Chemical shifts($\delta$) are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$ $^1H$: *$\delta$ 7.26*, $^{13}C$: *$\delta$ 77.16;* $CD_2Cl_2$ $^1H$: *$\delta$ 5.32*, $^{13}C$: *$\delta$ 53.84*; $(CD_3)_2SO$ $^1H$: *$\delta$ 2.50*, $^{13}C$: *$\delta$ 39.52*). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet, sept = septet), integration, coupling constants (*J*) in Hz.

IR absorption spectra were recorded using a Bruker Tensor II FTIR spectrometer (MCT detector, 4000–400 $cm^{-1}$ range, resolution of 4 $cm^{-1}$, averaging by 16 scans).

Melting points were recorded on a national standard melting point apparatus without correction.

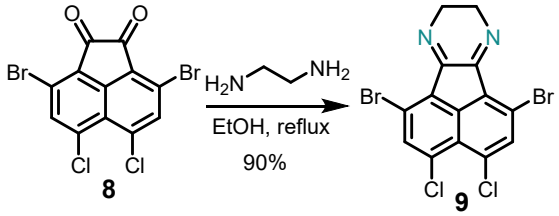
High-resolution mass spectra (HRMS) recorded for accurate mass analysis, were performed on a Q-TOF micro (Bruker Compass Data Analysis 4.0) spectrometer.

Single crystals of compounds suitable for X-ray diffraction were mounted in inert oil and transferred to the cold gas stream of a Rigaku XtaLAB FRX diffractometer equipped with the Hypix6000HE detector. X-ray diffraction intensity data were recorded using mirror-focused Cu *K$\alpha$* radiation ($\lambda$ = 1.54184 Å) and reduced by using the software package CrysAlisPro, applying an empirical absorption correction. The structure was solved by intrinsic phasing method using SHELXT[1] structure solution program, then refined with the SHELXL[2] refinement package using Least Squares minimization in and OLEX2.[2]

## 2. Synthesis and characterization

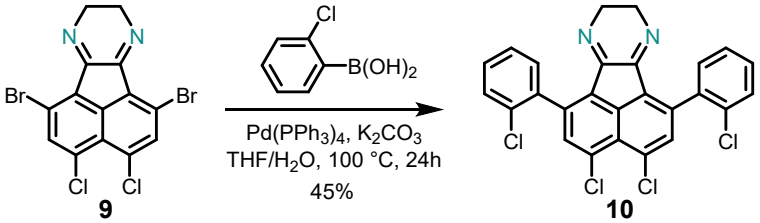
3,8-Dibromo-5,6-dichloroacenaphthenequinone **8** was synthesized according to the reported procedure.[3]

### Synthesis of compound 9




To a 100 mL round-bottom flask with a condensing unit were added 3,8-dibromo-5,6-dichloroacenaphthenequinone **8** (1.2 g, 3 mmol, 1.0 equiv.), ethylenediamine (0.22 g, 0.24 mL, 3.6 mmol, 1.2 equiv.) and EtOH (20 mL). The resulting mixture was heated to reflux for 5 hours. After cooling to room temperature, the solvent was removed under reduced pressure. The residual was solved to 50 mL DCM then washed with water and dried with anhydrous $Na_2SO_4$. After being concentrated through rotary evaporation, the crude product **9** was obtained as a gay solid (1.2 g, 90 %). The crude product was used for next step without further purification. **m. p.** > 300 °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ = 7.89 (s, 2H), 4.00 (s, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ = 156.4, 145.6, 136.5, 133.3, 128.3, 123.7, 116.0, 45.2. **IR** (KBr) ν [$cm^{-1}$] 2942, 2841, 1628, 1588, 1564, 1255, 1127, 1005, 966, 876, 852. **HRMS** (ESI) *m/z* calcd for $C_{14}H_7Br_2Cl_2N_2$ {$[M+H]^+$} 430.8353, found 430.8348.

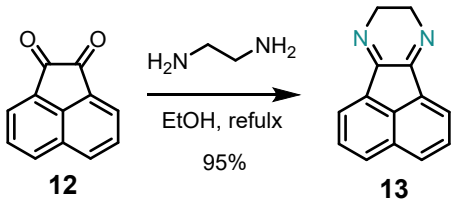
### Synthesis of compound 10




To a 100 mL round-bottom flask with a condensing unit were added 1,6-dibromo-3,4-dichloro-8,9-dihydroacenaphtho[1,2-*b*]pyrazine **9** (216 mg, 0.5 mmol, 1.0 equiv.), 2-chloroboronic acid (234 mg, 1.5 mmol, 3 equiv.), $Pd(PPh_3)_4$ (57 mg, 10 mol %), $Cs_2CO_3$ (978 mg, 3 mmol, 6.0 equiv.), THF (12.5 mL) and water (2.5 mL). The solution was purged with argon for 15 min, then heated to 100 °C and stirred at this temperature for 24 hours. The reaction mixture was allowed to cool to room temperature, the solvent was removed under reduced pressure. Afterwards, the reaction mixture was diluted with water, and extracted with EtOAc (15 mL × 3). The combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$, and filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (silica, hexane/EtOAc 8:2) to obtain desired compound **10** (110 mg, 45%) as a solid. **m. p.** 80–82 °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ = 7.70 (s, 2H), 7.52–

7.50 (m, 2H), 7.44–7.36 (m, 6H), 3.68–3.54 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ =157.0, 136.0, 134.8, 133.6, 133.1, 131.7, 131.2, 129.8, 129.6, 128.9, 126.6, 124.7, 45.3. A peak is missing in $^{13}$C NMR spectrum, possibly due to overlap of peaks. **IR** (KBr) ν [$cm^{-1}$] 3212, 3052, 1569, 1479, 1436, 1405, 1332, 1114, 1058, 1035, 1010, 759, 739. **HRMS** (ESI) *m/z* calcd for $C_{26}H_{15}Cl_4N_2$ {$[M+H]^+$} 494.9989, found 494.9798.

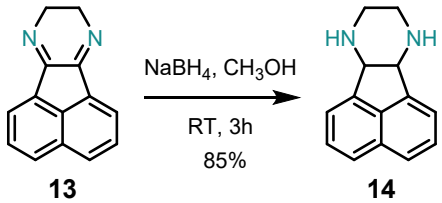
**Synthesis of 8,9-dihydroacenaphtho[1,2-*b*]pyrazine 13**




**12** **13**

To a 250 mL round-bottom flask with a condensing unit were added acenaphthoquinone (1.82 g, 10 mmol, 1.0 equiv.), ethylenediamine (0.72 g, 0.8 mL, 12 mmol, 1.2 equiv.) and EtOH (60 mL). The resulting mixture was heated to reflux for 4 hours. After cooling to room temperature, the solvent was removed under reduced pressure. The residual was solved to 200 mL DCM then washed with water and dried with anhydrous $Na_2SO_4$. After being concentrated through rotary evaporation, the crude product **13** was obtained as a solid. The crude product (1.96 g, 95%) was used for next step without further purification. **m. p.** 86–88 °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ = 7.83 (t, *J* = 7.3 Hz, 4H), 7.59 (dd, *J* = 8.2, 7.1 Hz, 2H), 3.85 (s, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ = 158.4, 141.3, 131.7, 130.5, 128.4, 128.2, 118.5, 44.9. **IR** (KBr) ν [$cm^{-1}$] 3402, 3043, 2938, 2838, 1632, 1433, 1346, 1292, 1118, 964, 825, 778. **HRMS** (ESI) *m/z* calcd for $C_{14}H_{11}N_2$ {$[M+H]^+$} 207.0922, found 207.0920.

**Synthesis of 6b,7,8,9,10,10a-hexahydroacenaphtho[1,2-*b*]pyrazine 14**

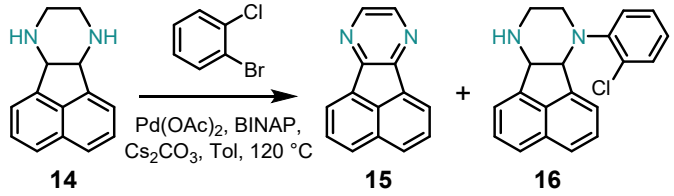



**13** **14**

To a 250 mL round-bottom flask were added 8,9-dihydroacenaphtho[1,2-*b*]pyrazine **13** (1.9 g, 9.2 mmol, 1.0 equiv.) and MeOH (55 mL). $NaBH_4$ (1.4 g, 37 mmol, 4.0 equiv.) was added in 3 portions over 1 hour to the vigorously stirred solution resulting a color change form colorless to dark bule immediately. After the additions were complete, the solution was stirred at room temperature for 6 hours. When the TLC plate showed all the starting material was consumed, most of the MeOH was removed under reduced pressure then acidified with 1 M HCl to pH neutral. The mixture was extracted with DCM (25 mL × 3). The combined organic layers were washed with water and brine, dried over $Na_2SO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified via flash chromatography (silica, $CH_2Cl_2$/MeOH 20:1) to obtain hexahydroacenaphtho[1,2-*b*]pyrazine **14** (1.65 g, 85 %) as a colorless solid. **m. p.** 282–284 °C **$^1$H NMR** (400 MHz, $CDCl_3$) δ = 7.71 (d, *J* = 8.1 Hz, 2H), 7.53 (t, *J* = 6.9 Hz, 2H), 7.47 (d, *J* = 6.8 Hz, 2H), 4.55 (s, 2H), 2.94–2.75 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ = 143.7, 137.3, 131.4, 128.1, 124.2, 120.6, 59.1, 42.0. **IR** (KBr) ν [$cm^{-1}$] 3196, 2943, 2851, 2750, 2501, 2424, 1669, 1597, 1496, 1461, 1306, 1101, 988, 951,

824, 780, 688. **HRMS** (ESI) *m/z* calcd for $C_{14}H_{15}N_2$ {[M+H]$^+$} 211.1235, found 211.1231.

**Synthesis of compounds 15 and 16**



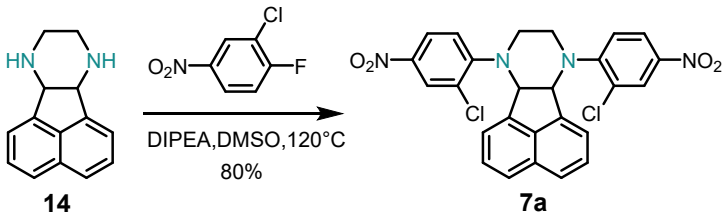

**14** **15** **16**

To a 35 mL sealed reaction vessel were added compound **14** (105 mg, 0.5 mmol, 1.0 equiv.), 1-bromo-2-chlorobenzene (210 mg, 1.1 mmol, 128 µL 2.2 equiv.), $Pd(OAc)_2$ (12 mg, 10 mol %), BINAP (62 mg, 20 mol %), $Cs_2CO_3$ (391 mg, 1.2 mmol, 2.4 equiv.), and anhydrous toluene (2.5 mL). The solution was purged with argon for 10 min, then heated to 120 °C and stirred at this temperature for 24 h. The reaction mixture was allowed to cool to room temperature, diluted with DCM (20 mL) and washed with water (10 mL × 3). The organic layer was dried with anhydrous $Na_2SO_4$, and the solvent was removed under reduced pressure. The crude product was purified via flash chromatography (silica, $CH_2Cl_2$/MeOH 99:1) to obtain acenaphtho[1,2-*b*]pyrazine **15** (56 mg, 55 %) as a colorless solid and mono-substituted product **16** (14 mg, 9%) as a colorless oil.

acenaphtho[1,2-*b*]pyrazine **15**: **m. p.** 142–143 °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ = 8.45 (s, 2H), 8.26 (d, *J* = 6.9 Hz, 2H), 8.03 (d, *J* = 8.2 Hz, 2H), 7.75 (t, *J* = 7.3 Hz, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ = 153.9, 141.5, 132.4, 131.8. 129.6, 129.6, 128.4, 122.6. **IR** (KBr) ν [cm$^{-1}$] 3850, 3042, 1482, 1430, 1334, 1310, 1118, 823, 774, 438. **HRMS** (ESI) *m/z* calcd for $C_{14}H_9N_2$ {[M+H]$^+$} 205.0766, found 205.0760.

mono-substituted product **16**: **$^1$H NMR** (400 MHz, $CDCl_3$) δ = 7.73 (t, *J* = 4.3 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.58–7.54 (m, 2H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 6.8 Hz, 1H), 5.55 (d, *J* = 6.6 Hz, 1H), 5.02 (d, *J* = 6.6 Hz, 1H), 3.10–2.96 (m, 3H), 2.72–2.59 (m, 1H), 2.37 (s, 1H, N-H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ = 148.5, 142.7, 141.5, 138.0, 131.1, 130.9, 128.6, 128.1, 127.7, 127.4, 124.4, 124.0, 123.6, 123.2, 121.7, 121.0, 62.6, 58.6, 45.0, 40.4. **HRMS** (ESI) *m/z* calcd for $C_{20}H_{18}ClN_2$ {[M+H]$^+$} 321.1158, found 321.1153.

**Synthesis of compound 7a**

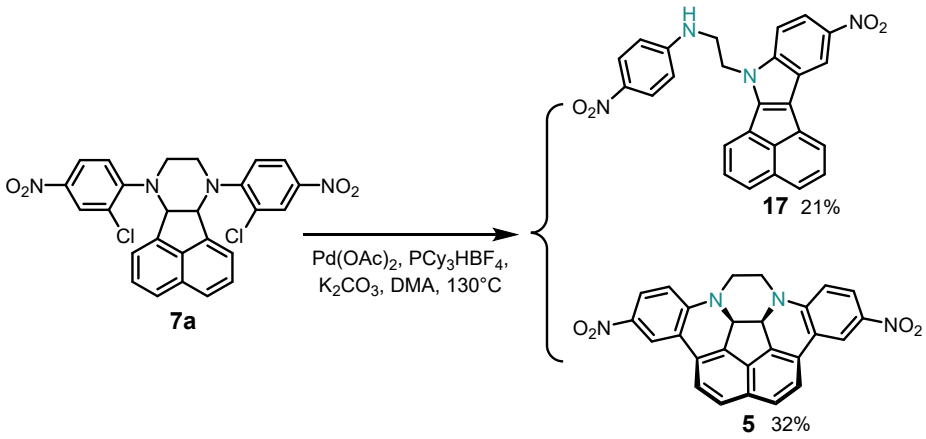



**14** **7a**

To a 135 mL sealed reaction vessel were added compound **14** (1.02 g, 4.84 mmol, 1.0 equiv.), 3-chloro-4-fluoronitrobenzene (4.25 g, 24.2 mmol, 5.0 equiv.), DIPEA (4.2 mL, 24.2 mmol, 5.0 equiv.), and anhydrous dimethyl sulfoxide (DMSO, 16 mL) under an inert atmosphere. The reaction was heated to 120 °C and stirred at this temperature for 48 h. Then the reaction mixture was allowed to cool to room temperature, diluted with DCM (100 mL) and washed with water for three times. The organic layer was

dried with anhydrous $Na_2SO_4$, and the solvent was removed under reduced pressure. The crude product was purified via column chromatography (silica, hexane/DCM 1:1) to obtain compound **7a** (2.0 g, 80%) as an orange solid. **m. p.** 256–258 °C. **$^1$H NMR** (400 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 2.6 Hz, 2H), 8.11 (dd, *J* = 8.9, 2.6 Hz, 2H), 7.81 (d, *J* = 8.2 Hz, 2H), 7.53 (t, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 6.9 Hz, 2H), 7.14 (d, *J* = 9.0 Hz, 2H), 6.12 (s, 2H), 3.48–3.37 (m, 2H), 3.21–3.05 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ = 154.1, 142.2, 139.0, 138.2, 131.0, 128.2, 127.0, 126.8, 125.2, 123.2, 121.7, 121.6, 62.4, 43.2. **IR** (KBr) ν [$cm^{-1}$] 3094, 2917, 285, 1581, 1511, 1498, 1336, 1293, 1254, 1128, 893, 826, 787, 746, 719. **HRMS** (ESI) *m/z* calcd for $C_{26}H_{19}Cl_2N_4O_4$ {[M+H]$^+$} 521.0783, found 521.0786.

**Synthesis of compounds 5 and 17**




To a Schlenk tube were added **7a** (156 mg, 0.3 mmol, 1.0 equiv.), $Pd(OAc)_2$ (67 mg, 0.3 mmol, 1.0 equiv.), $PCy_3{\cdot}HBF_4$ (221 mg, 0.6 mmol, 2.0 equiv.), $K_2CO_3$ (408 mg, 3.0 mmol, 10.0 equiv.) and anhydrous N,N-dimethylacetamide (DMA, 15 mL) via a syringe and argon gas was bubbled to the solution for 10 min. After the bubbling, the solution was heated for 24 h at 130 °C. The crude solution was cooled to room temperature and poured into DCM (40 mL). The organic phase was washed with degassed water (20 mL × 3), dried over $Na_2SO_4$. After the volatile matters were evaporated under reduced pressure, the crude product was purified via column chromatography (silica, hexane/DCM 1:1) to obtain compound **5** (43 mg, 32%) as a yellow solid, and compound **17** (28 mg, 21%) as a papaya solid. (Note: compound **5** was found to be sensitive to oxygen and moisture in both solution and solid state).

Azacorannulene analogue **5**: **$^1$H NMR** (600 MHz, DMSO-$d_6$) δ = 8.72 (d, *J* = 2.7 Hz, 2H), 8.16 (dd, *J* = 9.2, 2.7 Hz, 2H), 7.97 (d, *J* = 8.7 Hz, 2H), 7.92 (d, *J* = 8.6 Hz, 2H), 7.10 (d, *J* = 9.3 Hz, 2H), 5.38 (s, 2H), 4.01–3.92 (m, 2H), 3.87–3.79 (m, 2H). **$^{13}$C NMR** (151 MHz, DMSO-$d_6$) δ = 149.0, 138.4, 137.7, 135.9, 132.9, 127.1, 126.0, 125.4, 124.6, 123.0, 119.3, 112.8, 58.2, 43.2. **HRMS** (ESI) *m/z* calcd for $C_{26}H_{17}N_4O_4$ {[M+H]$^+$} 449.1250, found 449.1246.

By-product **17**: **m. p.** 252–254 °C. **$^1$H NMR** (400 MHz, DMSO-$d_6$) δ = 8.93 (d, *J* = 2.3 Hz, 1H), 8.20 (d, *J* = 6.8 Hz, 1H), 8.02 (dd, *J* = 9.2, 2.3 Hz, 1H), 7.92–7.89 (m, 3H), 7.84 (d, *J* = 7.0 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.71 (d, *J* = 9.2 Hz, 1H), 7.61 (t, *J* = 6.9 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.38 (t, *J* = 6.5 Hz, 1H, N-H), 6.54 (d, *J* = 8.8 Hz, 2H), 4.83 (t, *J* = 5.5 Hz, 2H), 3.84–3.79 (m, 2H). Due to the poor solubility of **17**, no $^{13}$C NMR spectrum was obtained. **IR** (KBr) ν [$cm^{-1}$] 3041, 2928, 1600, 1506, 1336, 1321, 1283, 1113, 816, 768, 750. **HRMS** (ESI) *m/z* calcd for $C_{26}H_{17}N_4O_4$ {[M−H]$^-$} 449.1250, found 449.1255.

## 3. X-ray crystal data

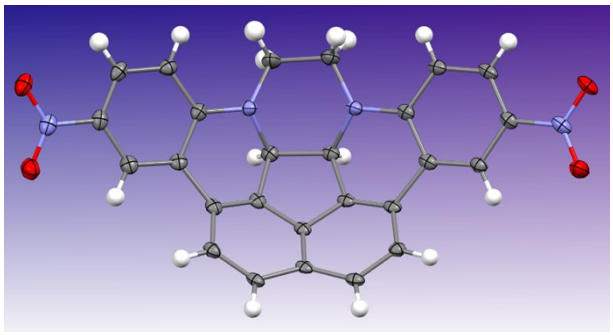


**Figure S1**. Crystal structure of **5** with thermal ellipsoids of 50% probability.

**Table S1.** Crystal data of **5**

| Identification code | **5** |
|---|---|
| Empirical formula | $C_{26}H_{16}N_4O_4$ |
| Formula weight | 448.43 |
| Temperature/K | 100.00(10) |
| Crystal system | monoclinic |
| Space group | $P2_1/n$ |
| a/Å | 11.6003(3) |
| b/Å | 7.7459(2) |
| c/Å | 22.1452(6) |
| α/° | 90 |
| β/° | 90.835(2) |
| γ/° | 90 |
| Volume/Å$^3$ | 1989.63(9) |
| Z | 4 |
| $\rho_{calc}$g/cm$^3$ | 1.497 |
| μ/mm$^{-1}$ | 0.856 |
| F(000) | 928 |
| Crystal size/mm$^3$ | 0.1 × 0.08 × 0.08 |
| Radiation | CuKα (λ = 1.54184) |
| 2Θ range for data collection/° | 7.986 to 145.214 |
| Index ranges | $-12 \leq h \leq 13$, $-9 \leq k \leq 9$, $-27 \leq l \leq 25$ |
| Reflections collected | 10166 |
| Independent reflections | 3742 [$R_{int}$ = 0.0559, $R_{sigma}$ = 0.0682] |
| Data/restraints/parameters | 3742/0/307 |
| Goodness-of-fit on $F^2$ | 1.045 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0500, $wR_2$ = 0.1248 |
| Final R indexes [all data] | $R_1$ = 0.0643, $wR_2$ = 0.1333 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.21/-0.37 |

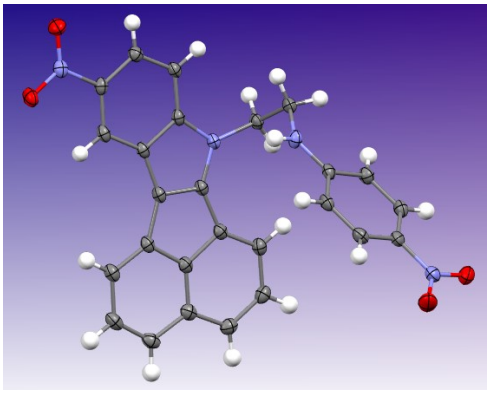


**Figure S2**. Crystal structure of **17** with thermal ellipsoids of 50% probability.

**Table S2.** Crystal data of **17**

| Identification code | **17** |
|---|---|
| Empirical formula | $C_{26}H_{18}N_4O_4$ |
| Formula weight | 450.44 |
| Temperature/K | 100.01(10) |
| Crystal system | monoclinic |
| Space group | $P2_1/n$ |
| a/Å | 10.30850(10) |
| b/Å | 9.13480(10) |
| c/Å | 21.6558(3) |
| α/° | 90 |
| β/° | 96.3680(10) |
| γ/° | 90 |
| Volume/Å$^3$ | 2026.66(4) |
| Z | 4 |
| $\rho_{calc}$g/cm$^3$ | 1.476 |
| μ/mm$^{-1}$ | 0.84 |
| F(000) | 936 |
| Crystal size/mm$^3$ | 0.25 × 0.2 × 0.15 |
| Radiation | CuKα (λ = 1.54184) |
| 2Θ range for data collection/° | 8.216 to 145.382 |
| Index ranges | $-11 \le h \le 12$, $-11 \le k \le 10$, $-26 \le l \le 26$ |
| Reflections collected | 24851 |
| Independent reflections | 3817 [$R_{int}$ = 0.0453, $R_{sigma}$ = 0.0240] |
| Data/restraints/parameters | 3817/0/307 |
| Goodness-of-fit on $F^2$ | 1.042 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0384, $wR_2$ = 0.1018 |
| Final R indexes [all data] | $R_1$ = 0.0411, $wR_2$ = 0.1041 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.20/-0.33 |

## 4. $^{1}H$ and $^{13}C$ NMR spectra

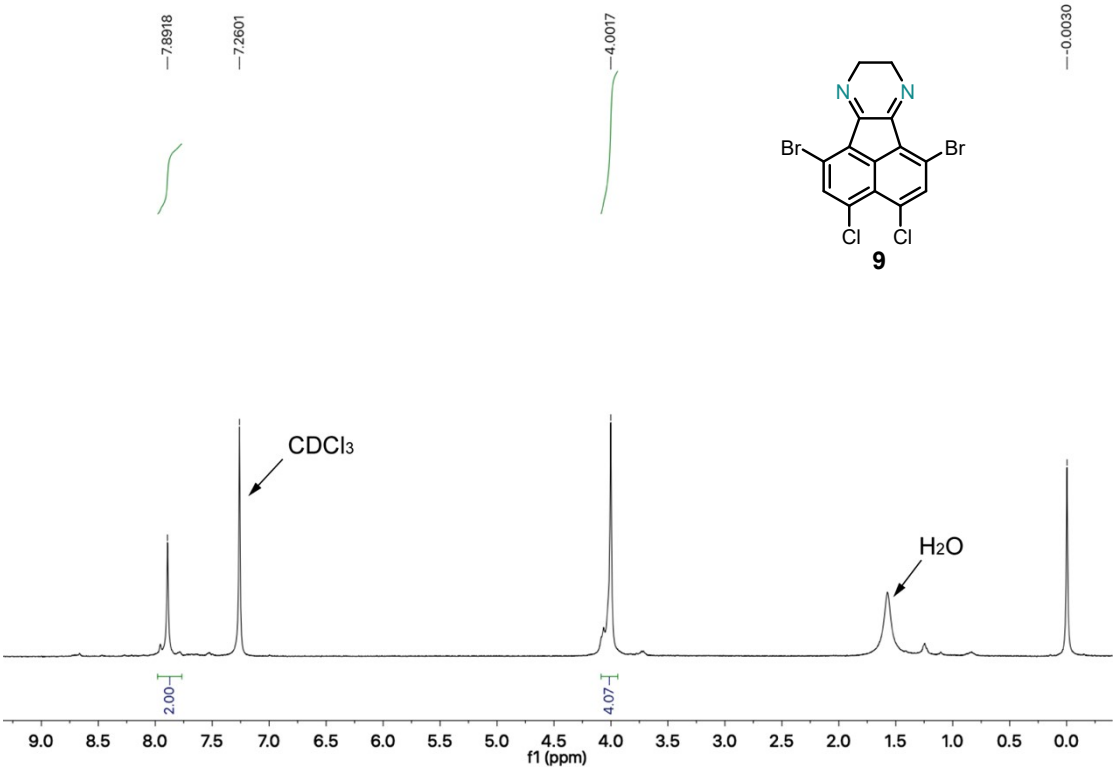



**Figure S3**. $^{1}H$ NMR spectrum of compound **9**.

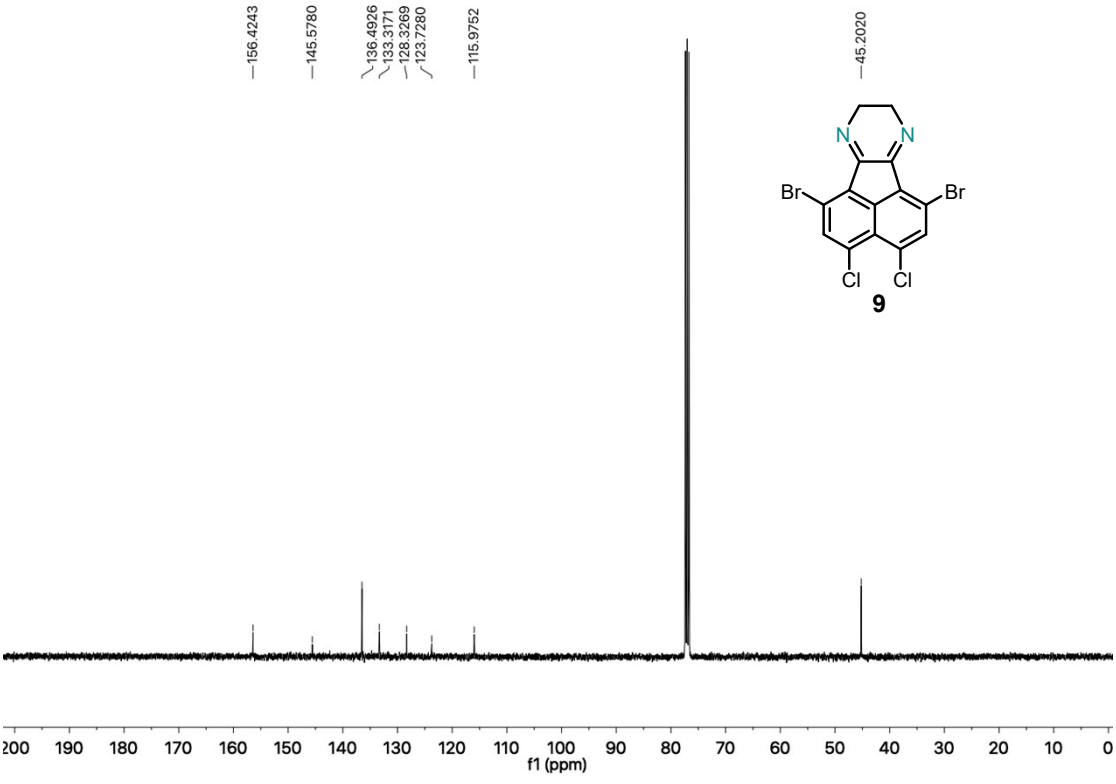



**Figure S4**. $^{13}C$ NMR spectrum of compound **9**.

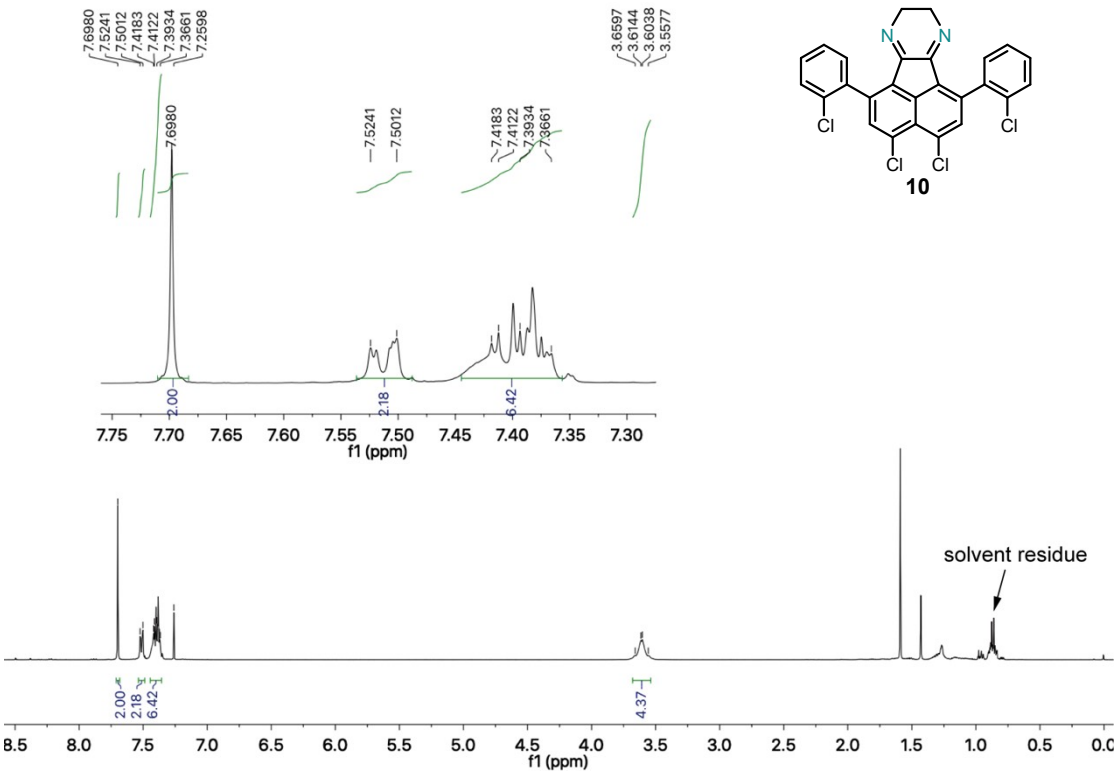



**Figure S5**. [1]H NMR spectrum of compound **10**.

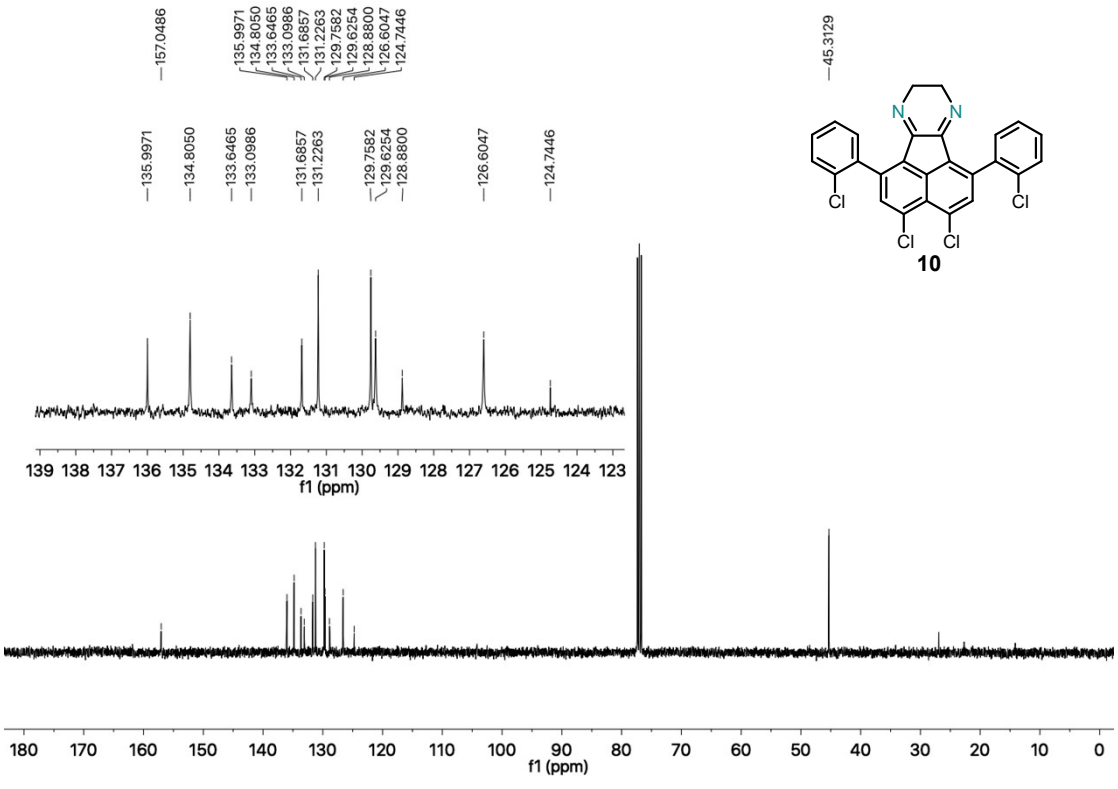



**Figure S6**. [13]C NMR spectrum of compound **10**.

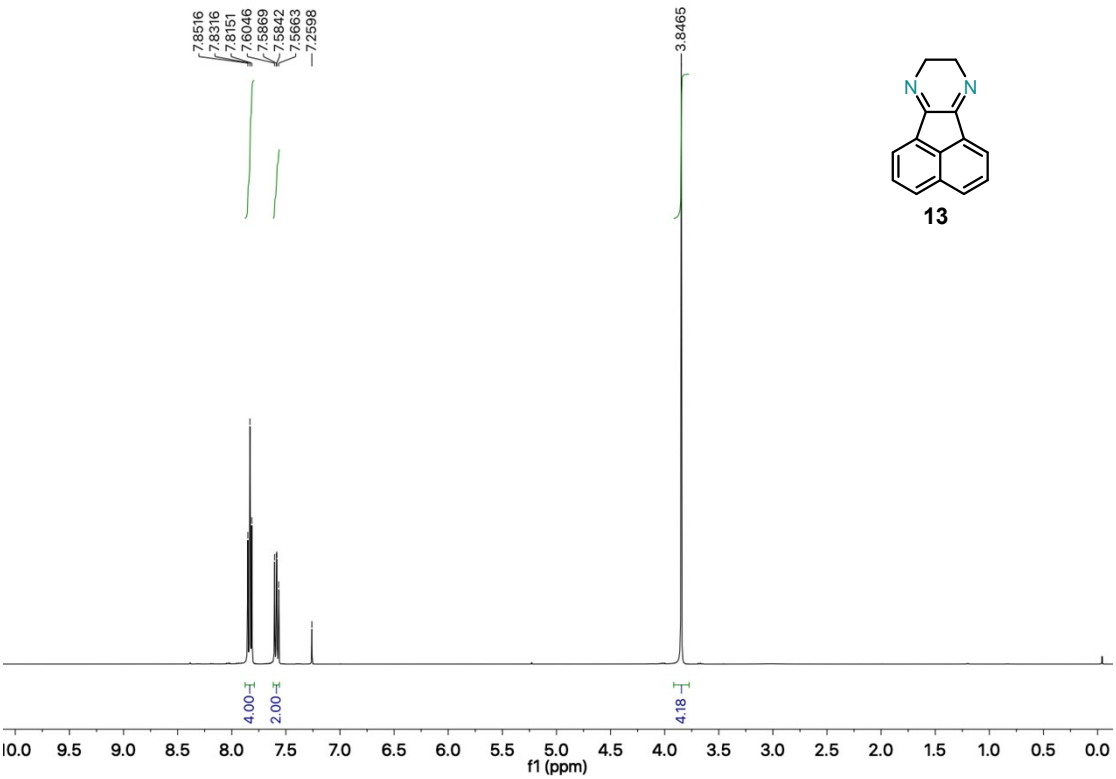



**Figure S7**. [1]H NMR spectrum of compound **13**.

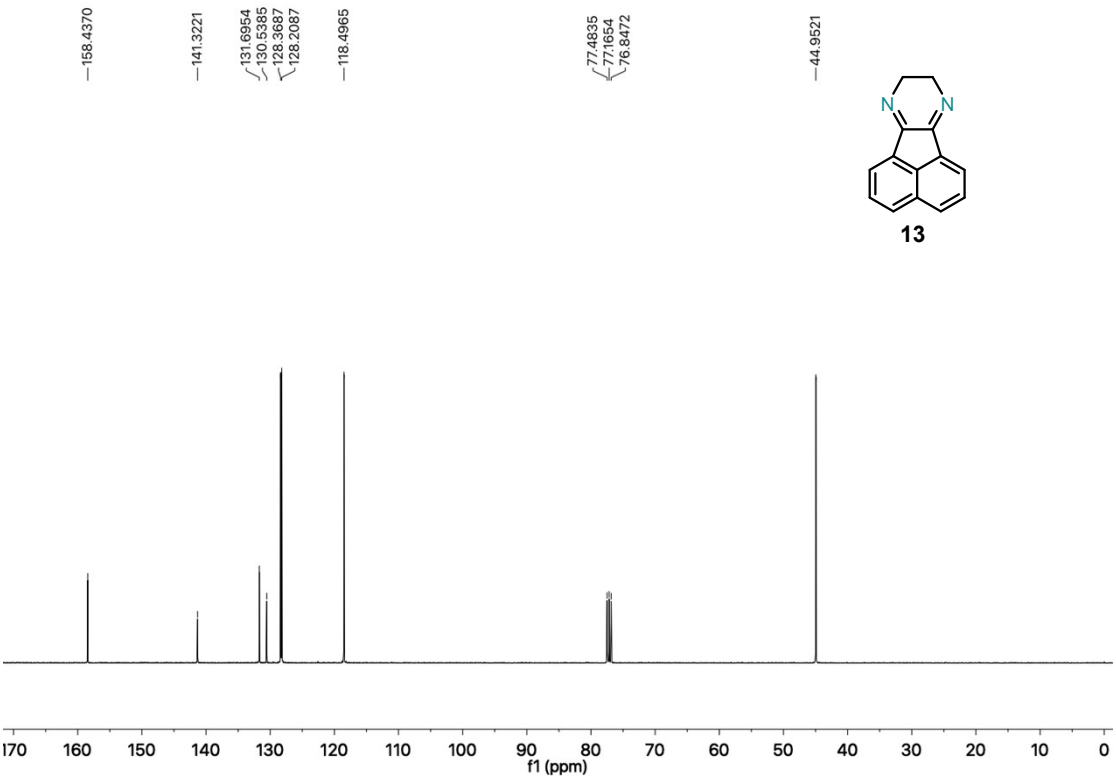



**Figure S8**. [13]C NMR spectrum of compound **13**.

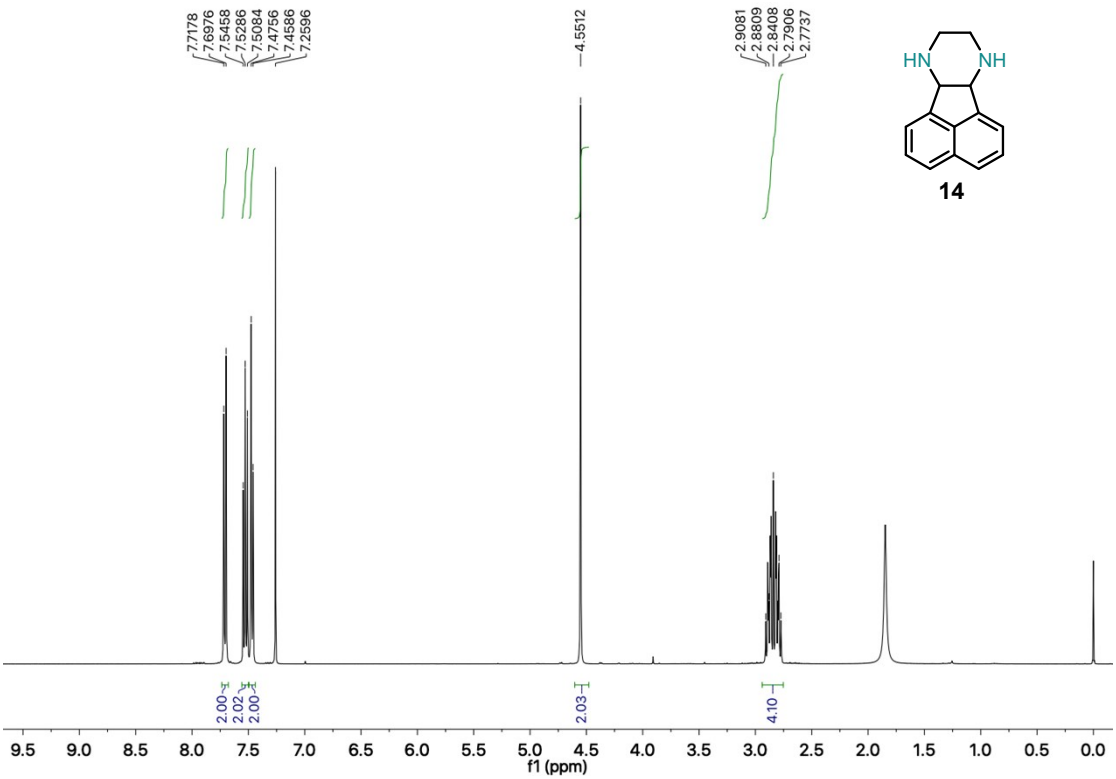



**Figure S9**. [1]H NMR spectrum of compound **14**.

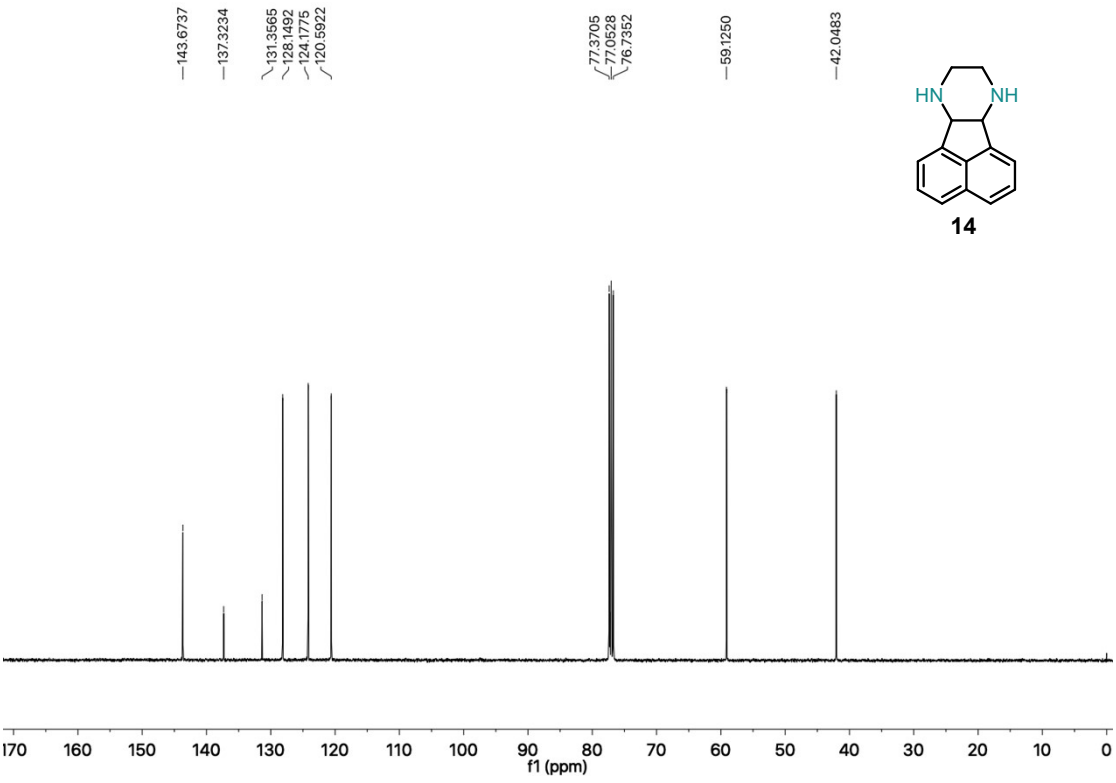



**Figure S10**. [13]C NMR spectrum of compound **14**.

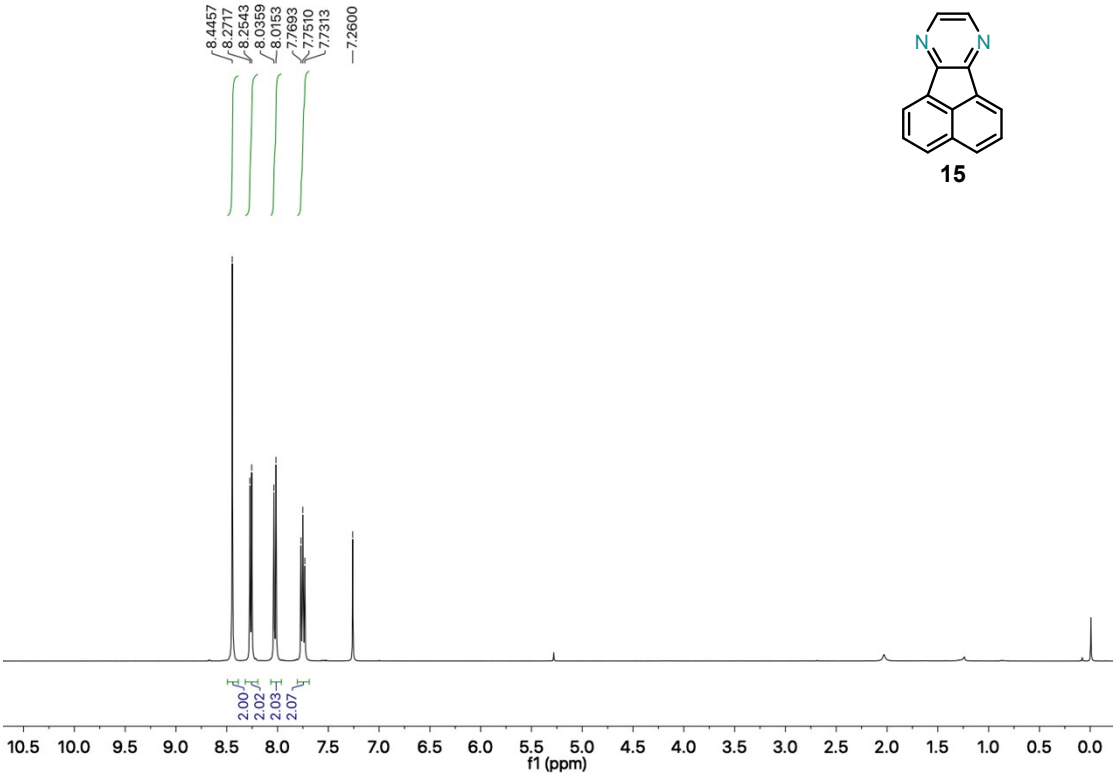



**Figure S11**. [1]H NMR spectrum of compound **15**.

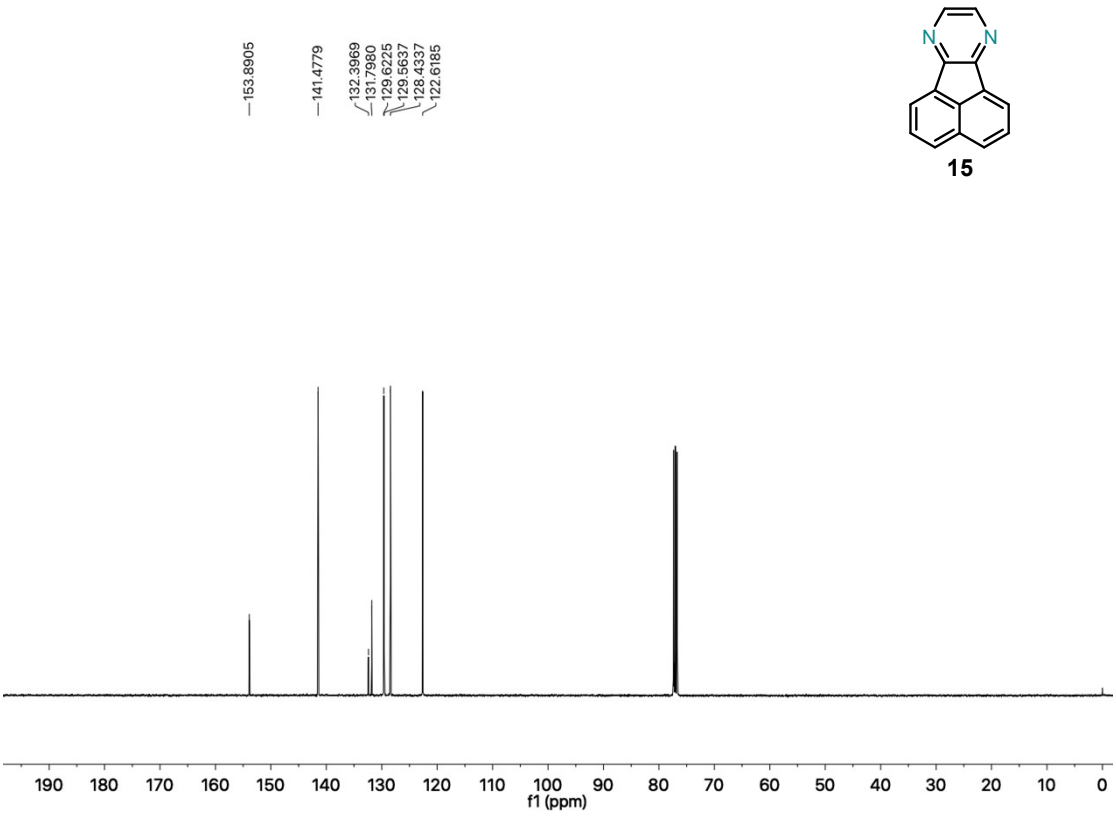



**Figure S12**. [13]C NMR spectrum of compound **15**.

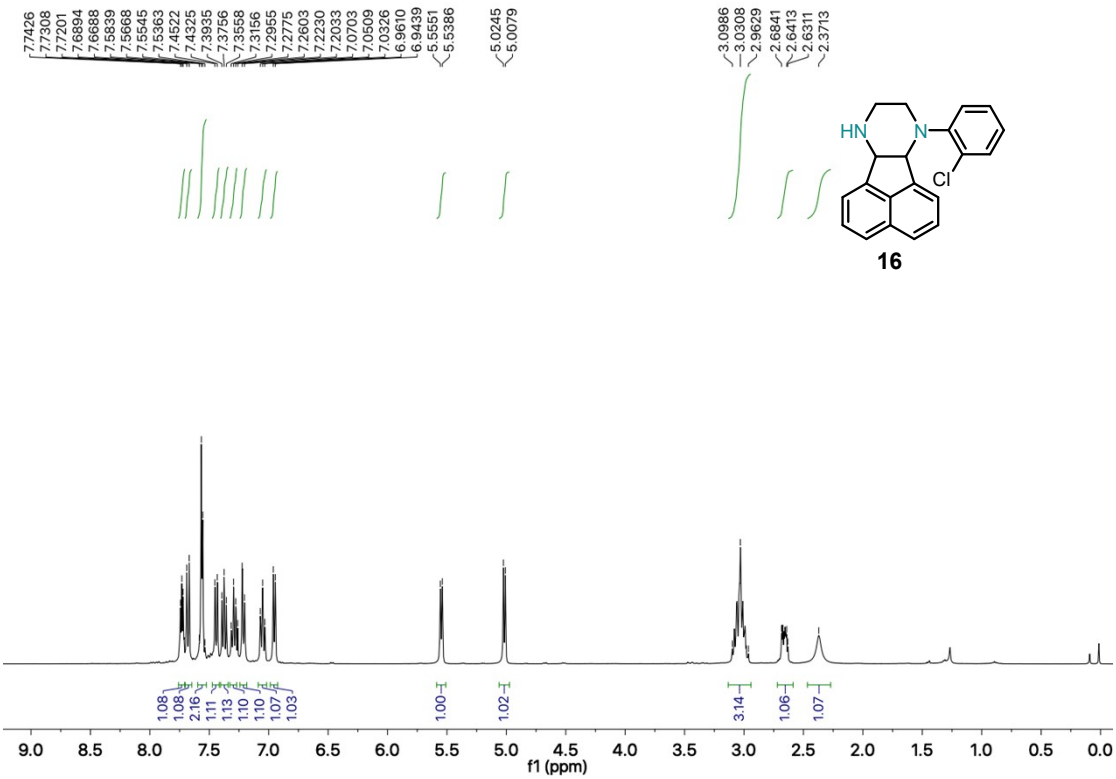



**Figure S13**. [1]H NMR spectrum of compound **16**.

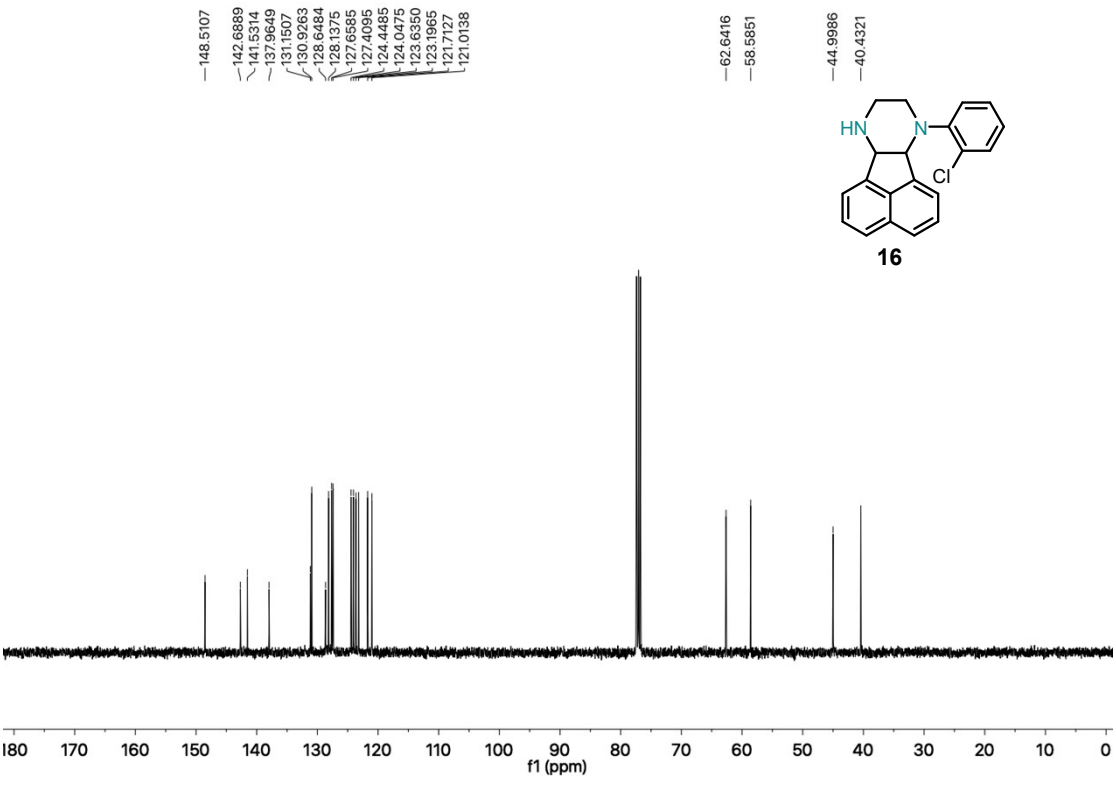



**Figure S14**. [13]C NMR spectrum of compound **16**.

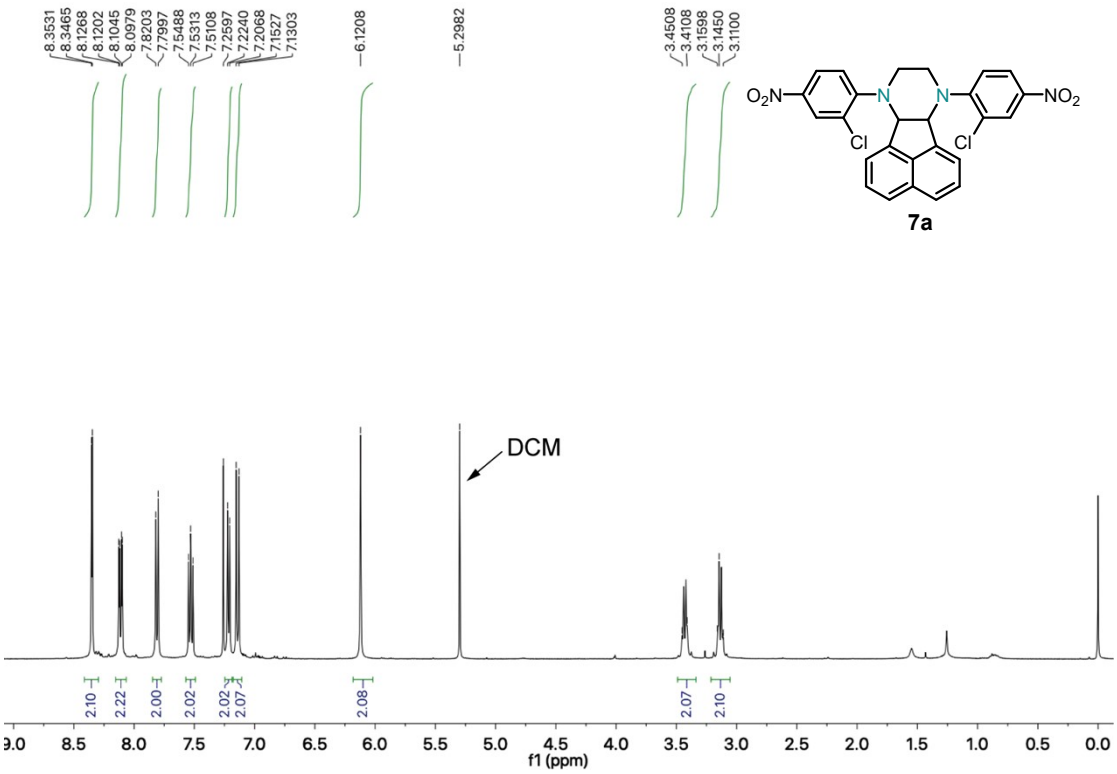



**Figure S15**. [1]H NMR spectrum of compound **7a**.

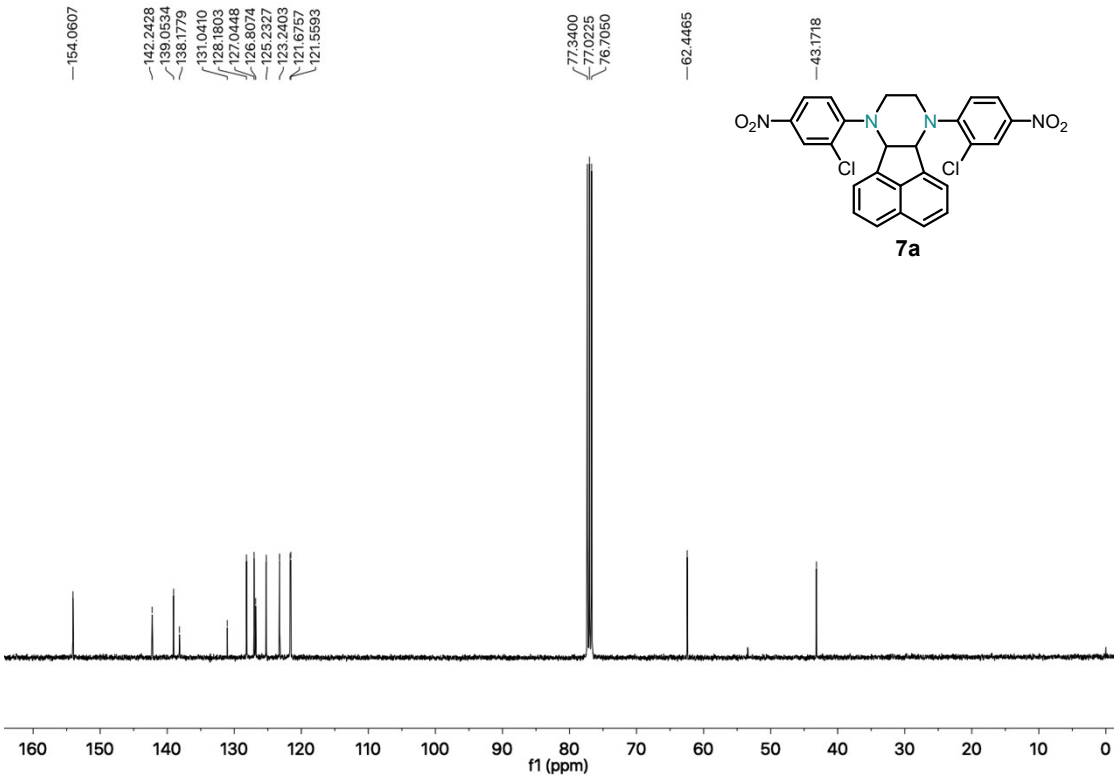



**Figure S16**. [13]C NMR spectrum of compound **7a**.

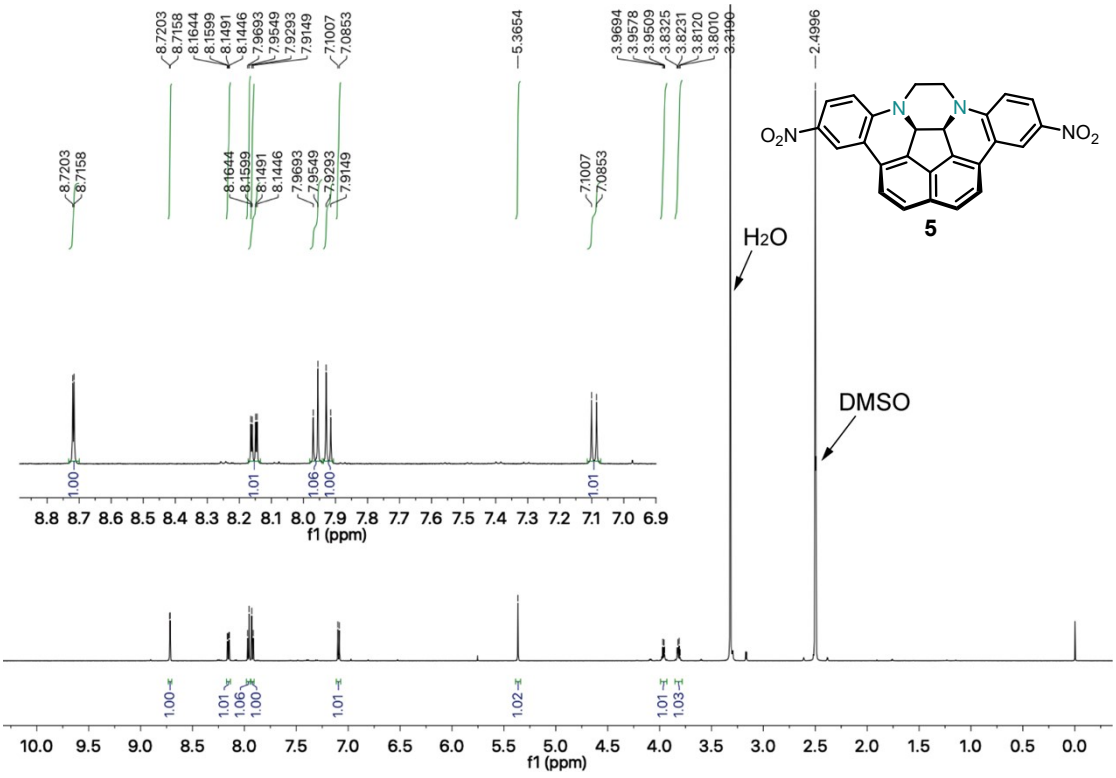



**Figure S17**. [1]H NMR spectrum of compound **5**.

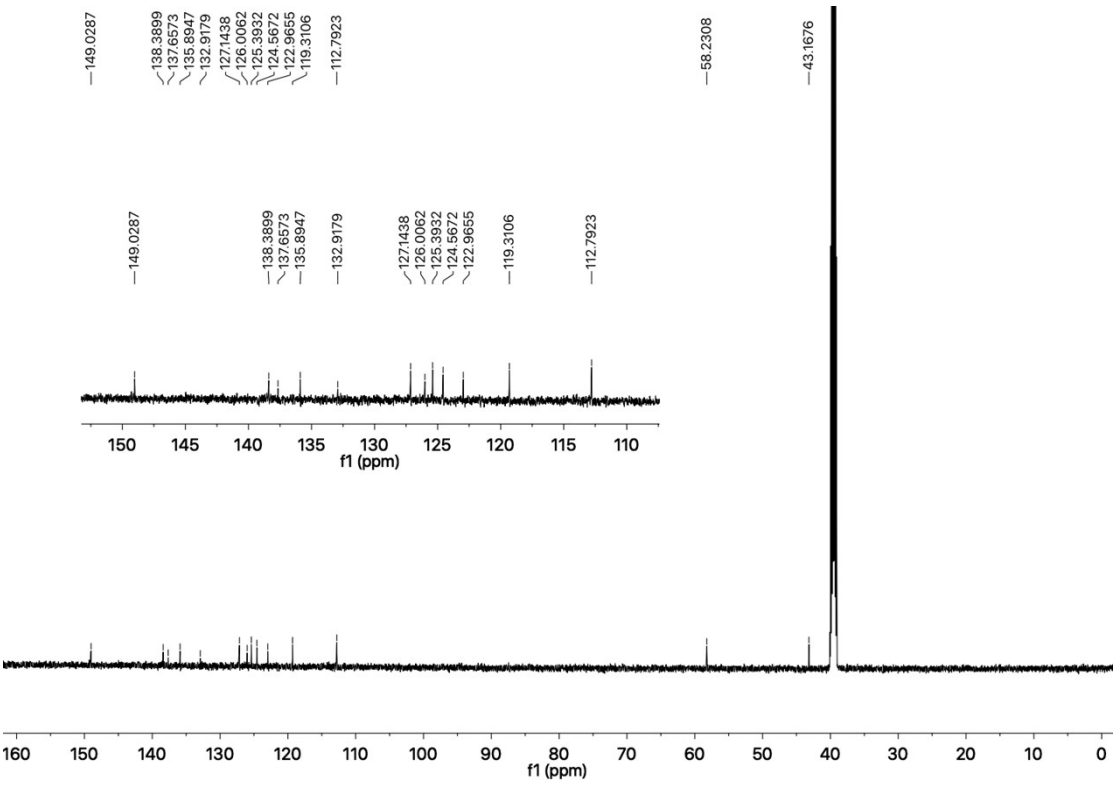



**Figure S18**. [13]C NMR spectrum of compound **5**.

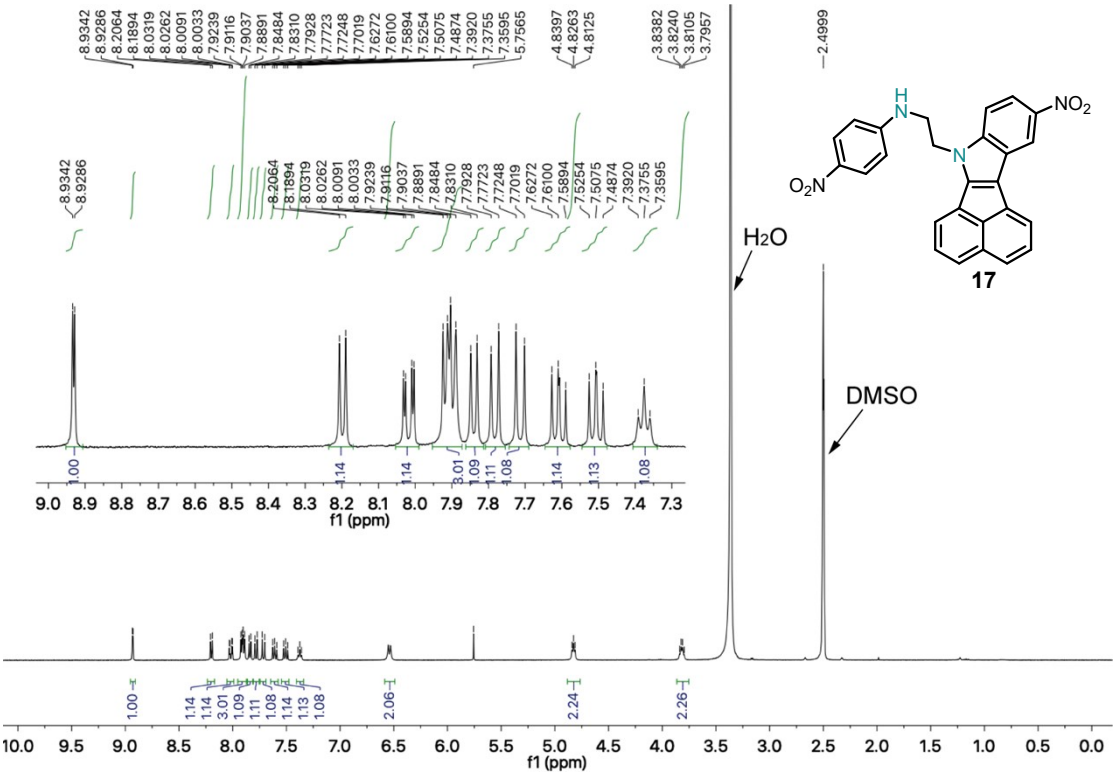



**Figure S19**. $^{1}$H NMR spectrum of compound **17**.

## 5. References

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