

Transition Metal-Free Construction of Trinuclear N-Fused Hybrid Scaffolds by Double Nucleophilic Aromatic Substitution under Microwave Irradiation

Pham Duy Quang Dao,^a Ho-Jin Lim,^b and Chan Sik Cho^{*,a}

^a Department of Applied Chemistry, Kyungpook National University, 80 Daehakro, Bukgu, Daegu 41566, Republic of Korea.

^b Department of Environmental Engineering, Kyungpook National University. 80 Daehakro, Bukgu, Daegu 41566, Republic of Korea

E-mail: cscho@knu.ac.kr

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1. General Information

All reactions were carried out in a sealed tube under microwave irradiation (CEM, Discover LabMate) and the reaction temperature was maintained by an external infrared sensor. ^1H (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a Bruker Avance Digital 500 spectrometer using TMS as an internal standard in CDCl_3 or $\text{DMSO-}d_6$. Melting points were measured on a microscopic melting point apparatus (Stanford Research Inc. MPA100 automated melting point apparatus). High-resolution mass data were obtained using electronic ionization (HRMS, magnetic sector-electric sector double focusing mass analyzer) at the Korea Basic Science Center (Daegu). The products were isolated by TLC (a glass plate coated with Kieselgel 60 GF₂₅₄, Merck). The starting materials **1** were prepared from the corresponding aldehydes and *o*-phenylenediamine¹ or 3,6-dimethoxybenzene-1,2-diamine² according to the reported methods. Other commercially available organic and inorganic reagents were used without further purification.

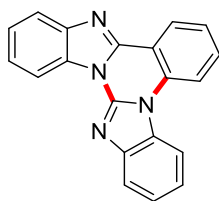
2. Experimental Procedures

a. Synthesis and Characterization of **3**

General Procedure:

To a 10 mL microwave reaction tube, **1** (0.3 mmol), **2** (0.45 mmol), K_3PO_4 (0.128 g, 0.6 mmol), and DMF (3 mL) were added. After stirring the reaction mixture at room temperature for 10 min, it was heated at 130 °C for 1.5 h under microwave irradiation (100 W of initial power). The reaction mixture was cooled and filtered through a short silica gel column to eliminate inorganic salts using ethyl acetate. Removal of the eluent under reduced pressure left a crude mixture, which was purified by TLC (dichloromethane/MeOH = 97/3) to give **3**. All new products were characterized spectroscopically as shown below.

Benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (**3a**).



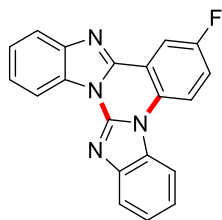
According to the general procedure, the product **3a** was obtained as a white solid (77.7 mg, 84%); mp 229-231 °C.

^1H NMR (CDCl_3 , 500 MHz) δ 8.73-8.69 (m, 1H), 8.66 (dd, $J = 7.9$ and 1.5 Hz, 1H), 8.22 (d, $J = 8.4$ Hz, 1H), 8.01 (d, $J = 8.0$ Hz, 1H), 7.94-7.91 (m, 1H), 7.84-7.82 (m, 1H), 7.72-7.68 (m, 1H), 7.53-7.49 (m, 1H), 7.48-7.45 (m, 1H), 7.40-7.37 (m, 1H), 7.35-7.32 (m, 1H).

^{13}C NMR (CDCl_3 , 125 MHz) δ 144.6, 143.8, 142.5, 141.7, 134.1, 132.0, 130.4, 130.1, 126.6, 125.3, 124.4, 123.1, 120.1, 119.6, 115.0, 114.9, 114.5, 112.7.

NMR data correspond to the reported article.³

7-Fluorobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3b).



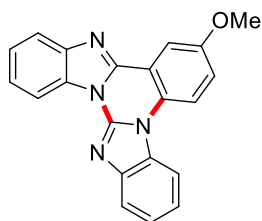
According to the general procedure, the product **3b** was obtained as a white solid (71.5 mg, 73%); mp 302-303 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.82 (d, *J* = 7.1 Hz, 1H), 8.46 (dd, *J* = 8.3 and 2.8 Hz, 1H), 8.39 (dd, *J* = 9.1 and 4.1 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 1H), 7.61-7.45 (m, 5H).

¹³C NMR (CDCl₃, 125 MHz) δ 144.0 (⁴*J*_{C-F} = 3.2 Hz), 142.8, 141.7, 130.9 (⁴*J*_{C-F} = 2.9 Hz), 130.5 (²*J*_{C-F} = 28.4 Hz), 125.8, 125.1, 124.7, 123.5, 120.5, 120.1, 119.8 (²*J*_{C-F} = 23.8 Hz), 117.1 (³*J*_{C-F} = 8.2 Hz), 116.7 (³*J*_{C-F} = 8.8 Hz), 115.3, 113.1, 112.9 (112.92), 112.9 (112.91), 112.6.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₀H₁₁FN₄ 326.0968; found: 326.0970.

7-Methoxybenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3c).



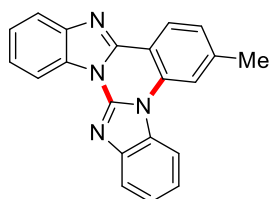
According to the general procedure, the product **3c** was obtained as a white solid (71.1 mg, 70%); mp 267-269 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.77-8.74 (m, 1H), 8.21 (d, *J* = 9.2 Hz, 1H), 8.08 (d, *J* = 3.0 Hz, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 7.93-7.89 (m, 1H), 7.88-7.86 (m, 1H), 7.52-7.47 (m, 2H), 7.42-7.38 (m, 1H), 7.37-7.34 (m, 1H), 7.28 (dd, *J* = 9.1 and 3.0 Hz, 1H), 3.93 (s, 3H).

¹³C NMR (CDCl₃, 125 MHz) δ 157.1, 144.8, 143.9, 142.7, 141.7, 130.7, 130.3, 128.5, 125.6, 124.7, 124.3, 123.2, 121.0, 120.9, 119.8, 116.7, 115.8, 115.3, 112.6, 108.2, 56.2.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₁H₁₄N₄O 338.1168; found: 338.1171.

8-Methylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3d).



According to the general procedure, the product **3d** was obtained as a white solid (72.5 mg, 75%);

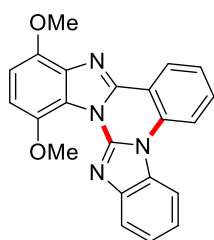
mp 238-240 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.81-8.78 (m, 1H), 8.60 (d, *J* = 8.0 Hz, 1H), 8.13 (d, *J* = 7.5 Hz, 1H), 8.12 (s, 1H), 7.97-7.94 (m, 1H), 7.93-7.91 (m, 1H), 7.57-7.53 (m, 2H), 7.48-7.41 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 2.62 (s, 3H).

¹³C NMR (CDCl₃, 125 MHz) δ 144.9, 143.9, 143.2, 142.6, 141.9, 134.3, 130.4, 130.2, 126.6, 126.5, 125.3, 124.3, 124.2, 123.0, 120.1, 119.5, 114.9, 112.8, 112.0, 22.4.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₁H₁₄N₄ 322.1218; found: 322.1220.

1,4-Dimethoxybenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3e).



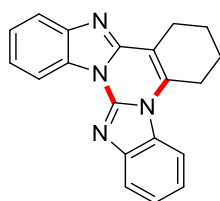
According to the general procedure, the product **3e** was obtained as a white solid (85.4 mg, 71%); mp 247-249 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.94 (dd, *J* = 8.0 and 1.4 Hz, 1H), 8.42 (d, *J* = 8.4 Hz, 1H), 8.22-8.20 (m, 1H), 8.00-7.98 (m, 1H), 7.83-7.80 (m, 1H), 7.58-7.54 (m, 1H), 7.51-7.45 (m, 2H), 7.02 (d, *J* = 8.7 Hz, 1H), 6.91 (d, *J* = 8.7 Hz, 1H), 4.16 (s, 3H), 4.11 (s, 3H).

¹³C NMR (CDCl₃, 125 MHz) δ 146.3, 145.0, 142.4, 142.2, 134.2, 132.1, 130.9, 128.5, 127.3, 125.3, 124.2, 123.3, 120.8, 115.0, 114.8, 112.7, 109.9, 105.8, 59.0, 56.2.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₂H₁₆N₄O₂ 368.1273; found: 368.1270.

6,7,8,9-Tetrahydrobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3f).



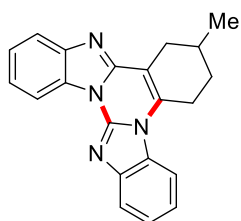
According to the general procedure, the product **3f** was obtained as a white solid (71.2 mg, 76%); mp 262-265 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.74-8.71 (m, 1H), 7.94-7.91 (m, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.53-7.48 (m, 2H), 7.40-7.37 (m, 1H), 7.24-7.20 (m, 1H), 3.33-3.31 (m, 2H), 3.07-3.04 (m, 2H), 2.14-2.09 (m, 2H), 2.01-1.96 (m, 2H).

¹³C NMR (CDCl₃, 125 MHz) δ 146.5, 144.2, 142.5, 142.1, 137.8, 129.9, 129.8, 125.4, 124.2, 123.6, 122.1, 119.8, 119.5, 114.9, 113.4, 109.4, 27.3, 23.2, 22.2, 21.0.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₀H₁₆N₄ 312.1375; found: 312.1372.

7-Methyl-6,7,8,9-tetrahydrobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3g).



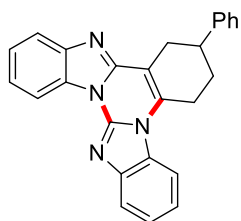
According to the general procedure, the product **3g** was obtained as a white solid (76.4 mg, 78%); mp 287-288 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.72-8.69 (m, 1H), 7.93-7.89 (m, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.52-7.47 (m, 2H), 7.38-7.35 (m, 1H), 7.21-7.18 (m, 1H), 3.43-3.39 (m, 1H), 3.29-3.23 (m, 2H), 2.54-2.49 (m, 1H), 2.21-2.17 (m, 1H), 2.06-1.99 (m, 1H), 1.71-1.62 (m, 1H), 1.22 (d, *J* = 6.6 Hz, 3H).

¹³C NMR (CDCl₃, 125 MHz) δ 146.4, 144.1, 142.4, 142.0, 137.4, 129.8, 129.7, 125.3, 124.2, 123.5, 122.1, 119.7, 119.4, 114.8, 113.3, 108.9, 31.1, 30.0, 27.2 (27.24), 27.2 (27.22), 21.1.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₁H₁₈N₄ 326.1531; found: 326.1530.

7-Phenyl-6,7,8,9-tetrahydrobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3h).



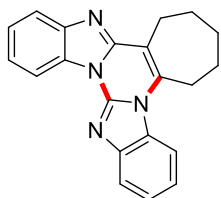
According to the general procedure, the product **3h** was obtained as a white solid (83.9 mg, 72%); mp 272-273 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.74-8.71 (m, 1H), 7.90-7.86 (m, 2H), 7.79 (d, *J* = 8.6 Hz, 1H), 7.52-7.48 (m, 2H), 7.40-7.35 (m, 5H), 7.30-7.26 (m, 1H), 7.23-7.20 (m, 1H), 3.50-3.45 (m, 2H), 3.40-3.33 (m, 1H), 3.18-3.12 (m, 1H), 3.06-2.99 (m, 1H), 2.47-2.43 (m, 1H), 2.22-2.14 (m, 1H).

¹³C NMR (CDCl₃, 125 MHz) δ 146.1, 144.2, 144.1, 142.4, 142.0, 137.1, 129.8, 129.7, 128.7, 126.9, 126.8, 125.3, 124.3, 123.7, 122.2, 119.8, 119.5, 114.8, 113.3, 109.0, 38.1, 30.3, 29.0, 27.6.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₆H₂₀N₄ 388.1688; found: 388.1689.

7-Phenyl-6,7,8,9-tetrahydrobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3i).



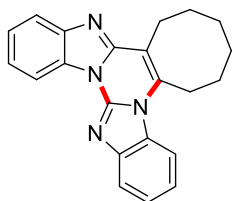
According to the general procedure, the product **3i** was obtained as a white solid (57.8 mg, 59%); mp 247-249 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.77-8.75 (m, 1H), 7.93-7.91 (m, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.54-7.48 (m, 2H), 7.43-7.40 (m, 1H), 7.29-7.26 (m, 1H), 3.59-3.57 (m, 2H), 3.34-3.31 (m, 2H), 2.03-2.01 (m, 4H), 1.94-1.90 (m, 2H).

¹³C NMR (CDCl₃, 125 MHz) δ 146.9, 144.0, 142.6, 142.4, 142.2, 130.1, 129.9, 125.3, 124.3, 123.4, 122.0, 119.8, 119.2, 115.1, 114.9, 113.4, 30.4, 30.1, 26.2, 25.2, 24.1.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₁H₁₈N₄ 326.1531; found: 326.1534.

6,7,8,9,10,11-Hexahydrobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]cycloocta[e]pyrimidine (3j).



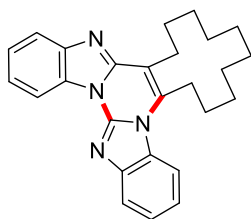
According to the general procedure, the product **3j** was obtained as a white solid (63.3 mg, 62 %); mp 258-259 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.73-8.72 (m, 1H), 7.93-7.91 (m, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.52-7.46 (m, 2H), 7.42-7.39 (m, 1H), 7.29-7.26 (m, 1H), 3.37-3.35 (m, 2H), 3.17-3.14 (m, 2H), 2.03-1.98 (m, 2H), 1.90-1.85 (m, 2H), 1.61-1.57 (m, 2H), 1.50-1.46 (m, 2H).

¹³C NMR (CDCl₃, 125 MHz) δ 146.3, 144.1, 142.5, 142.2, 139.1, 129.9, 129.3, 125.2, 124.2, 123.4, 122.3, 119.7, 119.3, 114.9, 113.1, 112.4, 30.1, 27.9, 26.8, 26.4, 25.7.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₂H₂₀N₄ 340.1688; found: 340.1686.

6,7,8,9,10,11,12,13,14,15-Decahydrobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]cyclododeca[e]pyrimidine (3k).



According to the general procedure, the product **3k** was obtained as a white solid (61.9 mg, 52%);

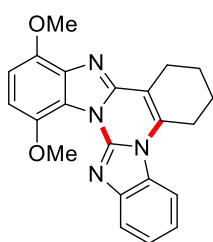
mp 208-209 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.80-8.76 (m, 1H), 7.97-7.94 (m, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.54-7.49 (m, 2H), 7.42-7.39 (m, 1H), 7.30-7.27 (m, 1H), 3.34-3.31 (m, 2H), 3.05-3.02 (m, 2H), 2.04-1.98 (m, 2H), 1.66-1.56 (m, 2H), 1.50-1.46 (m, 4H).

¹³C NMR (CDCl₃, 125 MHz) δ 146.8, 144.2, 142.6, 142.3, 139.8, 129.7, 129.5, 125.2, 124.2, 123.4, 122.2, 119.7, 119.3, 115.0, 113.4, 112.9, 26.9, 26.8, 26.3, 26.1, 26.0 (26.04), 26.0 (25.98), 25.5, 24.9, 22.2, 21.9.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₆H₂₈N₄ 396.2314; found: 396.2317.

1,4-Dimethoxy-6,7,8,9-tetrahydrobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3l).



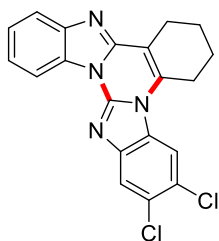
According to the general procedure, the product **3l** was obtained as a white solid (42.4 mg, 38%); mp 273-275 °C.

¹H NMR (CDCl₃, 500 MHz) δ 7.93 (d, *J* = 8.9 Hz, 2H), 7.43-7.40 (m, 1H), 7.30-7.26 (m, 1H), 6.95 (d, *J* = 8.7 Hz, 1H), 6.87 (d, *J* = 8.7 Hz, 1H), 4.13 (s, 3H), 4.06 (s, 3H), 3.41-3.39 (m, 2H), 3.16-3.13 (m, 2H), 2.14-2.10 (m, 2H), 1.99-1.96 (m, 2H).

¹³C NMR (CDCl₃, 125 MHz) δ 146.6, 146.0, 142.2, 142.0, 137.3, 136.6, 130.3, 123.9, 122.1, 121.8, 120.3, 113.4, 109.6, 108.5, 105.4, 58.8, 56.0, 27.3, 23.4, 22.3, 20.9.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₂H₂₀N₄O₂ 372.1586; found: 372.1588.

12,13-Dichloro-6,7,8,9-tetrahydrobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3m).



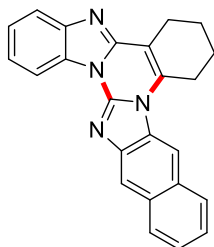
According to the general procedure, the product **3m** was obtained as a pale yellow solid (57.2 mg, 50%); mp 269-271 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.51 (d, *J* = 7.6 Hz, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.821 (s, 1H), 7.817 (s, 1H), 7.48-7.41 (m, 2H), 3.16-3.14 (m, 2H), 3.03-3.00 (m, 2H), 2.13-2.09 (m, 2H), 2.00-1.95 (m, 2H).

^{13}C NMR (CDCl_3 , 125 MHz) δ 145.9, 144.0, 142.9, 141.7, 136.8, 129.3, 128.6, 128.2, 125.6, 125.5, 123.8, 120.5, 119.5, 114.6, 114.5, 110.3, 26.8, 23.0, 21.9, 20.7.

HRMS (EI): m/z [M^+] calcd for $\text{C}_{20}\text{H}_{14}\text{Cl}_2\text{N}_4$ 380.0596; found: 380.0597.

6,7,8,9-Tetrahydrobenzo[4,5]imidazo[1,2-*c*]naphtho[2',3':4,5]imidazo[1,2-*a*]quinazoline (3n).



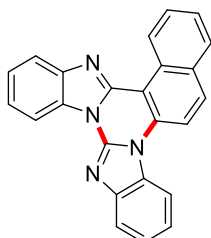
According to the general procedure, the product **3n** was obtained as a pale yellow solid (47.8 mg, 44%); mp 289-291 °C.

^1H NMR (CDCl_3 , 500 MHz) δ 8.80-8.76 (m, 1H), 8.28 (s, 1H), 8.21 (s, 1H), 7.99 (d, $J = 8.3$ Hz, 1H), 7.95-7.93 (m, 1H), 7.87 (d, $J = 8.3$ Hz, 1H), 7.54-7.53 (m, 2H), 7.48-7.45 (m, 1H), 7.41-7.38 (m, 1H), 3.48-3.46 (m, 2H), 3.08-3.06 (m, 2H), 2.20-2.16 (m, 2H), 2.04-1.99 (m, 2H).

^{13}C NMR (CDCl_3 , 125 MHz) δ 142.1, 130.9, 130.7, 129.5, 127.9, 127.7, 125.5, 124.8, 124.4, 123.7, 119.4, 115.9, 114.9, 110.3, 27.3, 23.0, 22.1, 20.9.

HRMS (EI): m/z [M^+] calcd for $\text{C}_{24}\text{H}_{18}\text{N}_4$ 362.1531; found: 362.1534.

Benzo[*f*]benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3o).



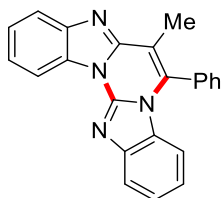
According to the general procedure, the product **3o** was obtained as a white solid (67.7 mg, 63%); mp 299-301 °C.

^1H NMR (CDCl_3 , 500 MHz) δ 10.57 (d, $J = 8.7$ Hz, 1H), 8.91-8.87 (m, 1H), 8.45 (d, $J = 9.1$ Hz, 1H), 8.19 (d, $J = 8.2$ Hz, 1H), 8.11 (d, $J = 9.1$ Hz, 1H), 8.06-8.04 (m, 1H), 7.95 (d, $J = 7.4$ Hz, 1H), 7.87 (d, $J = 8.0$ Hz, 1H), 7.82-7.78 (m, 1H), 7.61-7.55 (m, 3H), 7.50-7.47 (m, 1H), 7.44-7.40 (m, 1H).

^{13}C NMR (CDCl_3 , 125 MHz) δ 144.7, 144.1, 143.0, 141.9, 133.9, 133.3, 130.4, 130.2 (130.22), 130.2 (130.18), 129.3 (129.34), 129.3 (129.27), 128.3, 127.8, 126.5, 125.3, 124.5, 124.4, 122.7, 120.1, 119.9, 115.1, 113.7, 113.3, 108.2.

HRMS (EI): m/z [M^+] calcd for $\text{C}_{24}\text{H}_{14}\text{N}_4$ 358.1218; found: 358.1220.

6-Methyl-7-phenylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]pyrimidine (3p).



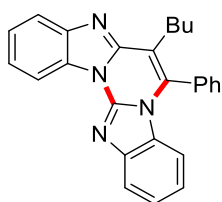
According to the general procedure, the product **3m** was obtained as a white solid (70.0 mg, 67%); mp 236-238 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.87-8.83 (m, 1H), 8.02-7.98 (m, 1H), 7.86-7.84 (m, 1H), 7.74-7.67 (m, 3H), 7.59-7.54 (m, 4H), 7.32-7.29 (m, 1H), 6.92-6.89 (m, 1H), 5.92 (d, *J* = 8.4 Hz, 1H), 2.39 (s, 3H).

¹³C NMR (CDCl₃, 125 MHz) δ 147.1, 144.1, 142.3, 142.1, 137.5, 131.8, 130.5, 129.9, 129.7 (129.71), 129.7 (129.70), 129.6, 125.4, 124.2, 123.9, 121.8, 119.6, 119.3, 115.0, 112.8, 109.4, 12.8.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₃H₁₆N₄ 348.1375; found: 348.1378.

6-Butyl-7-phenylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]pyrimidine (**3q**).



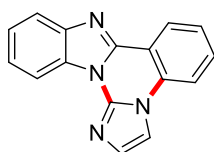
According to the general procedure, the product **3n** was obtained as a white solid (83.2 mg, 71%); mp 209-211 °C.

¹H NMR (CDCl₃, 500 MHz) δ 8.89-8.87 (m, 1H), 8.04-8.01 (m, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.74-7.66 (m, 3H), 7.60-7.53 (m, 4H), 7.34-7.31 (m, 1H), 6.94-6.90 (m, 1H), 5.84 (d, *J* = 8.4 Hz, 1H) 2.79(t, *J* = 8.0 Hz, 2H). 1.76-1.70 (m, 2H), 1.31-1.29 (m, 2H), 0.81 (t, *J* = 7.4 Hz, 3H).

¹³C NMR (CDCl₃, 125 MHz) δ 146.6, 144.3, 142.4, 137.4, 131.7, 130.5, 129.8, 129.5, 129.2 (129.23), 129.2 (129.18), 125.4, 124.2, 123.9, 121.8, 119.7, 119.4, 115.0, 114.3, 112.9, 31.8, 26.9, 22.7, 13.8.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₃H₁₆N₄ 390.1844; found: 390.1846.

Benzo[4,5]imidazo[1,2-*c*]imidazo[1,2-*a*]quinazoline (**3r**).



According to the general procedure, the product **3r** was obtained as a pale yellow solid (53.5 mg, 69%); mp 190-191 °C.

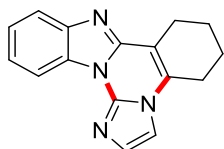
¹H NMR (CDCl₃, 500 MHz) δ 8.60-8.58 (m, 1H), 8.54-8.50 (m, 1H), 7.92-7.85 (m, 1H), 7.63-

7.57 (m 3H), 7.46-7.42 (m, 3H), 7.31 (d, $J = 1.7$ Hz, 1H).

^{13}C NMR (CDCl_3 , 125 MHz) δ 144.1, 143.7, 137.9, 132.2, 131.9, 130.0, 129.2, 126.3, 125.1, 124.3, 119.8, 115.1, 114.9, 114.4, 110.2.

NMR data correspond to the reported article.^{3b}

5,6,7,8-Tetrahydrobenzo[4,5]imidazo[1,2-*c*]imidazo[1,2-*a*]quinazoline (3s).



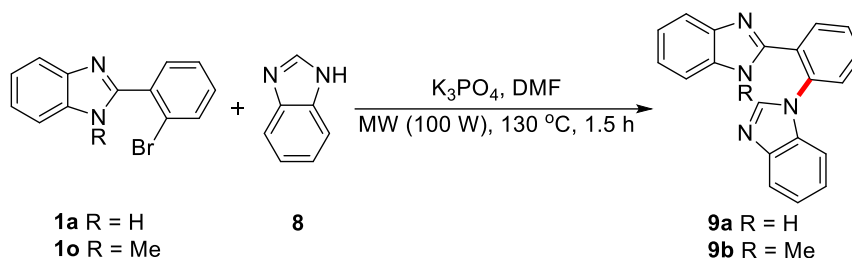
According to the general procedure, the product **3s** was obtained as a pale yellow solid (53.5 mg, 68%); mp 160-162 °C.

^1H NMR (CDCl_3 , 500 MHz) δ 8.59-8.58 (m, 1H), 7.95-7.93 (m, 1H), 7.52-7.46 (m, 2H), 7.37 (d, $J = 1.6$ Hz, 1H), 7.28 (d, $J = 1.6$ Hz, 1H), 3.06-3.04 (m, 2H), 2.85-2.82 (m, 2H), 2.09-2.04 (m, 2H), 1.98-1.94 (m, 2H).

^{13}C NMR (CDCl_3 , 125 MHz) δ 145.9, 143.7, 138.0, 134.4, 129.1, 128.5, 124.9, 123.2, 119.4, 114.2, 110.7, 109.2, 25.1, 22.6, 21.6, 21.4.

HRMS (EI): m/z [M^+] calcd for $\text{C}_{16}\text{H}_{14}\text{N}_4$ 262.1218; found: 262.1215.

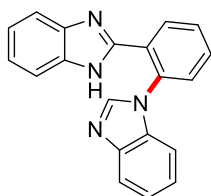
b. Experiments for mechanism study



Procedure for mechanism study:

A 10 mL microwave reaction tube was added **1a** or **1o** (0.3 mmol), **8** (0.45 mmol), K_3PO_4 (0.128 g, 0.6 mmol), and DMF (3 mL). After stirring the reaction mixture at room temperature for 10 min, it was heated at 130 °C for 1.5 h under microwave irradiation (100 W of initial power). The reaction mixture was cooled and filtered through a short silica gel column to eliminate inorganic salts using ethyl acetate. Removal of the eluent under reduced pressure left a crude mixture, which was purified by TLC (dichloromethane/MeOH = 49/1) to give **9a** or **9b**.

2-(2-(1H-Benzo[*d*]imidazol-1-yl)phenyl)-1H-benzo[*d*]imidazole (9a).



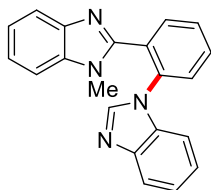
The product **9a** was obtained as a white solid (36.3 mg, 39%); mp 174-176 °C.

¹H NMR (DMSO-*d*₆, 500 MHz) δ 12.60 (s, 1H), 8.25 (s, 1H), 8.05-8.03 (m, 1H), 7.78-7.72 (m, 2H), 7.69-7.66 (m, 2H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.18-7.06 (m, 5H).

¹³C NMR (CDCl₃, 125 MHz) δ 148.8, 144.5, 143.5, 143.1, 134.4, 134.0, 131.5, 131.1, 129.0, 128.2, 127.8, 123.0, 122.6, 121.9, 124.5, 119.5, 119.0, 111.4, 110.0.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₀H₁₄N₄ 310.1218; found: 310.1214.

2-(2-(1*H*-Benzo[*d*]imidazol-1-yl)phenyl)-1-methyl-1*H*-benzo[*d*]imidazole (**9b**).



The product **9b** was obtained as a white solid (43.8 mg, 45%); mp 182-183 °C.

¹H NMR (DMSO-*d*₆, 500 MHz) δ 8.05 (s, 1H), 7.90-7.84 (m, 2H), 7.81 (dd, *J* = 8.0 and 1.1 Hz, 1H), 7.78-7.74 (m, 1H), 7.64-7.60 (m, 1H), 7.56-7.54 (m, 1H), 7.43-7.41 (m, 1H), 7.34-7.30 (m, 1H), 7.22-7.15 (m, 4H), 3.35 (s, 3H).

¹³C NMR (CDCl₃, 125 MHz) δ 149.9, 143.7, 142.9, 142.4, 135.4, 134.9, 133.8, 132.7, 131.7, 128.8, 127.4, 126.9, 123.3, 122.5, 122.3, 121.9, 119.7, 119.1, 110.5, 110.1, 30.6.

HRMS (EI): *m/z* [*M*⁺] calcd for C₂₁H₁₆N₄ 324.1375; found: 324.1372.

c. Evolution of NH₃ gas test

Detection of ammonia gas by Nessler's test:

Nessler's reagent was prepared by known procedure.⁴ Potassium iodide (5 g) was dissolved in 5 mL cold distilled water and saturated solution of mercury(II) chloride was added until an excess was indicated by the formation of orange precipitate. Then NaOH 5 N aqueous solution (20 mL) was added to the mixture, which was diluted to 100 mL with distilled water. After the reaction of **1a** and **2a** was finished, the evolution of NH₃ gas was identified by using Nessler's reagent solution (3 mL). Nessler's reagent was changed from colorless liquid to yellow mixture when connected with reaction tube (Figure S1). The color change indicates the formation of ammonia during the reaction course.

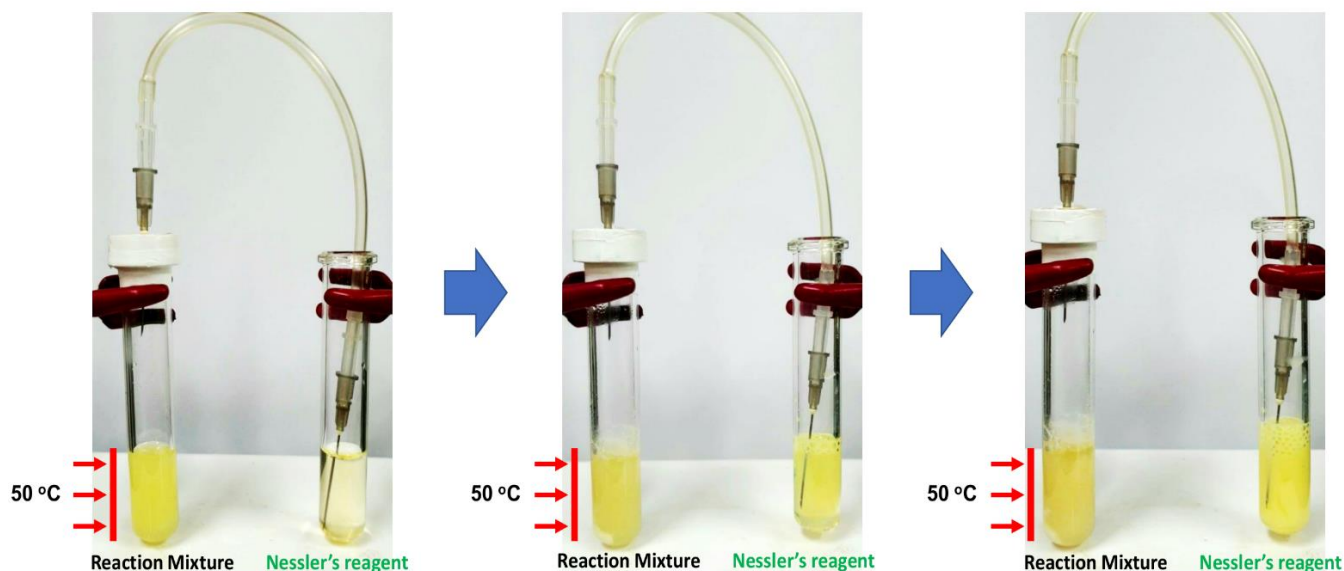


Figure S1. Detection of evolution of ammonia by Nessler's test.

Detection of ammonia gas with NH₃ monitor:

The formation of ammonia gas was also detected by using LSE- NH₃ Monitor (LSE Monitors, Netherlands), which is a highly sensitive ammonia gas analyzer based on laser photoacoustic spectroscopy (detection range 0-15 ppm). Ammonia gas evolved in a reaction tube was carried with N₂ at 10 mL/min and introduced into the monitor at 50 mL/min for 90 minutes after dilution with N₂ gas (5 L N₂/min). Significant amount of ammonia gas was detected as shown in the graph (Figure S2).

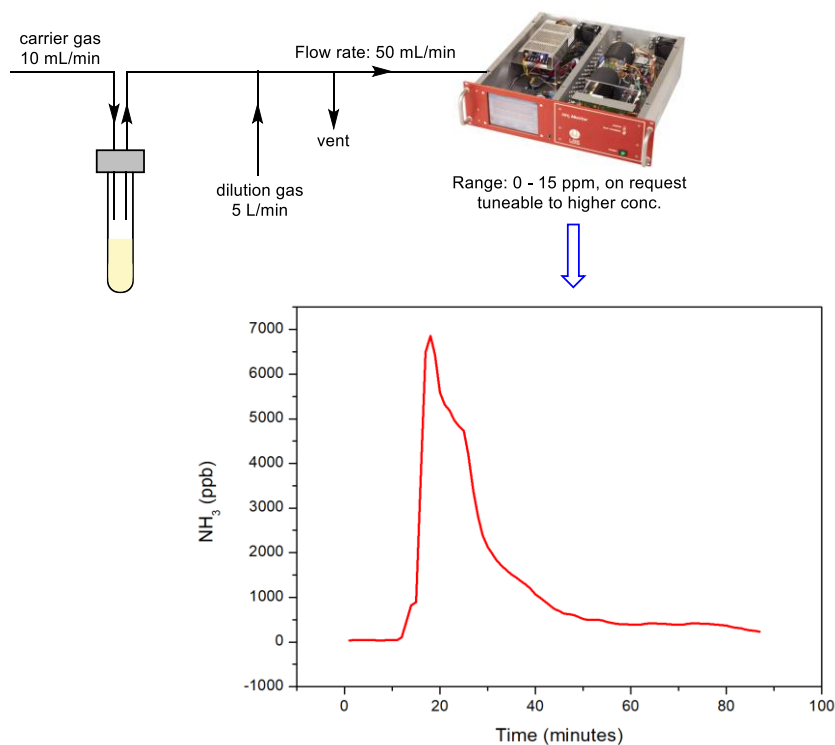
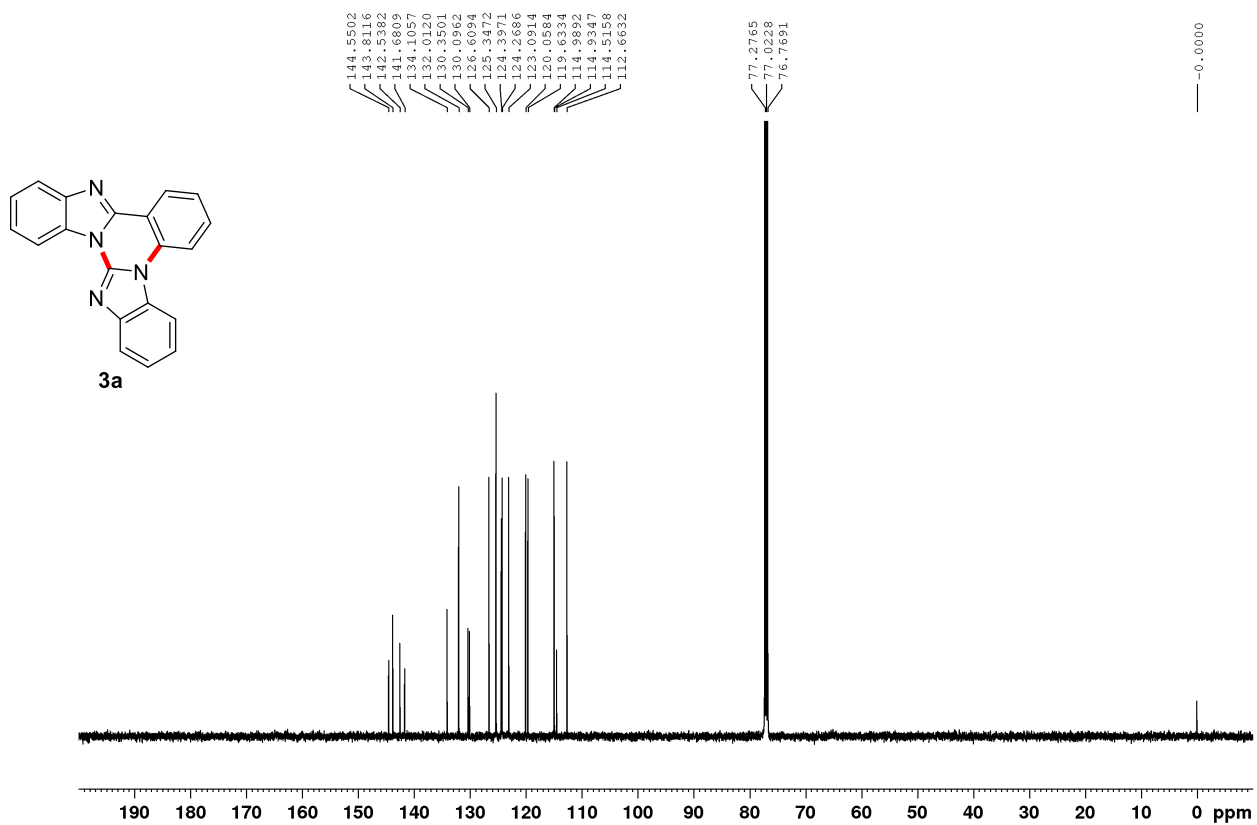
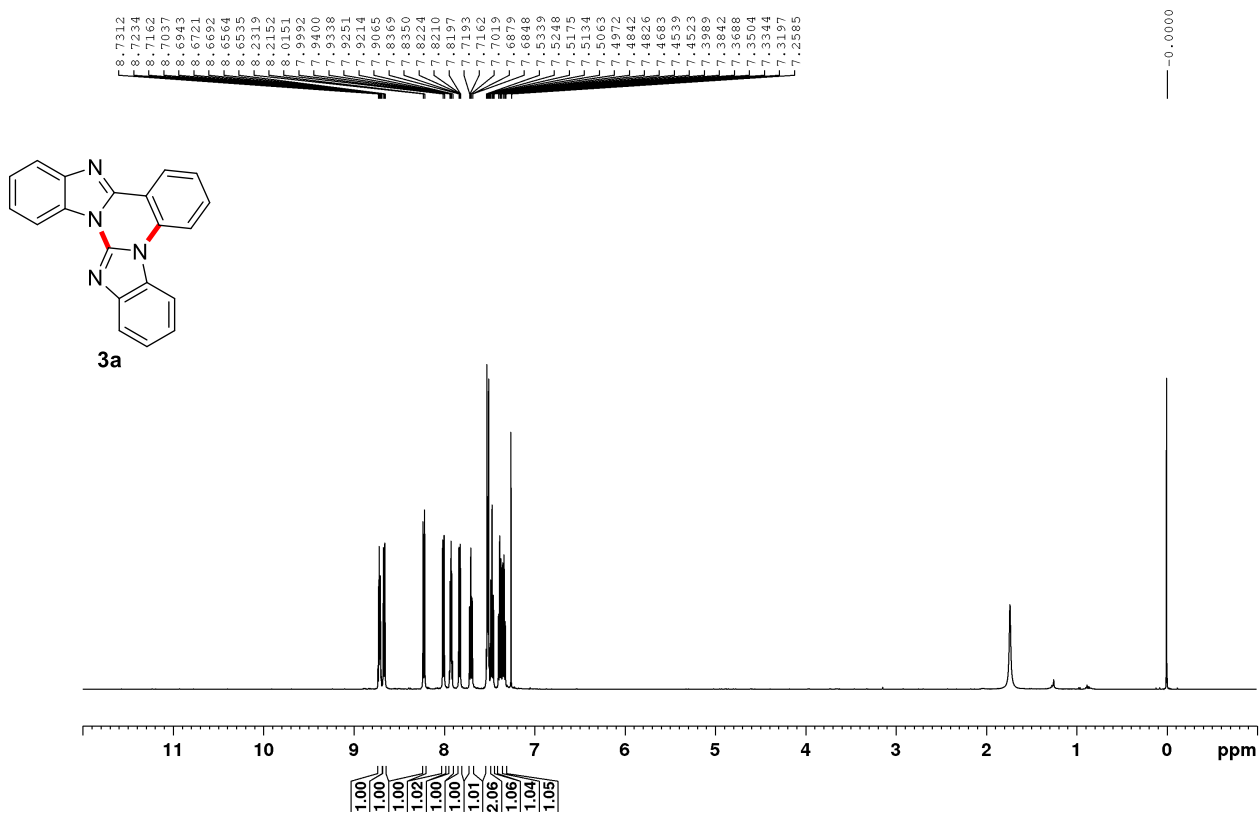


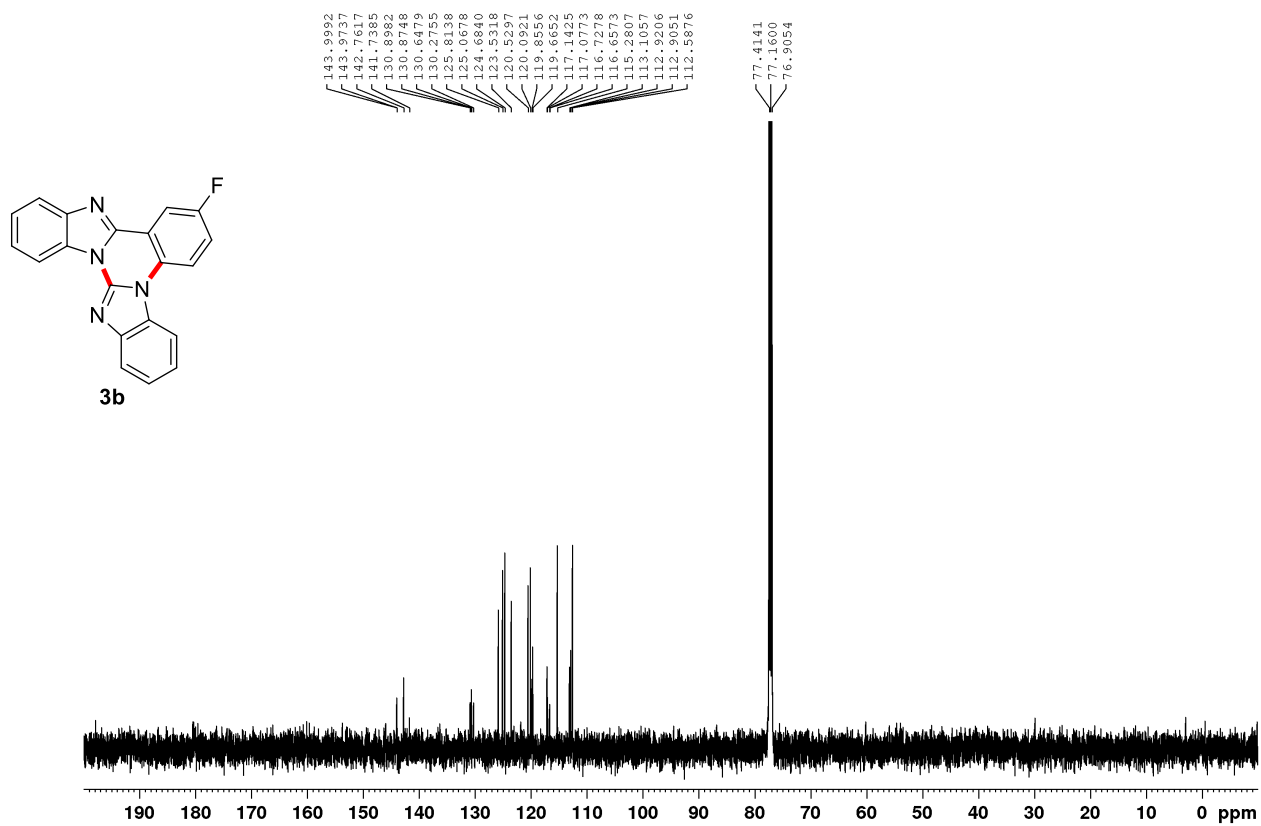
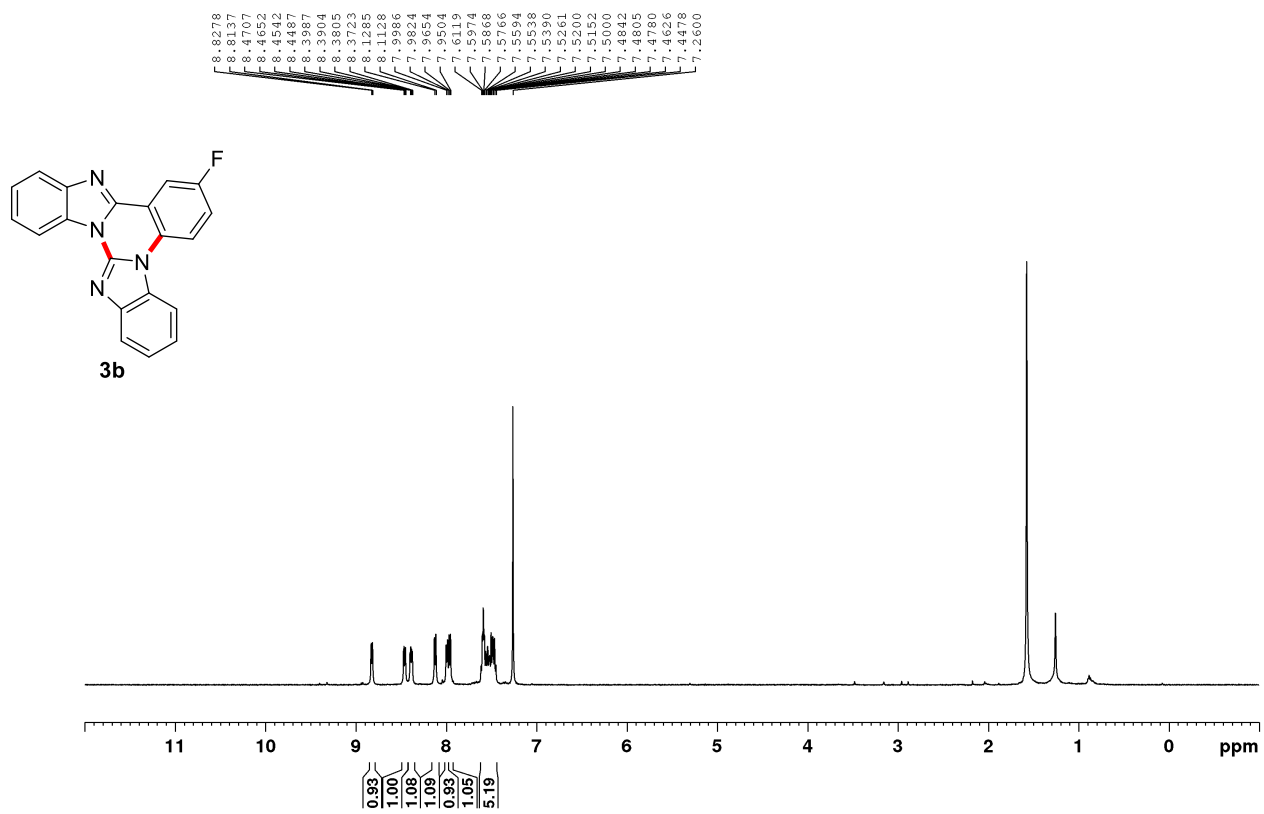
Figure S2. Detection of ammonia gas with LSE- NH₃ monitor.

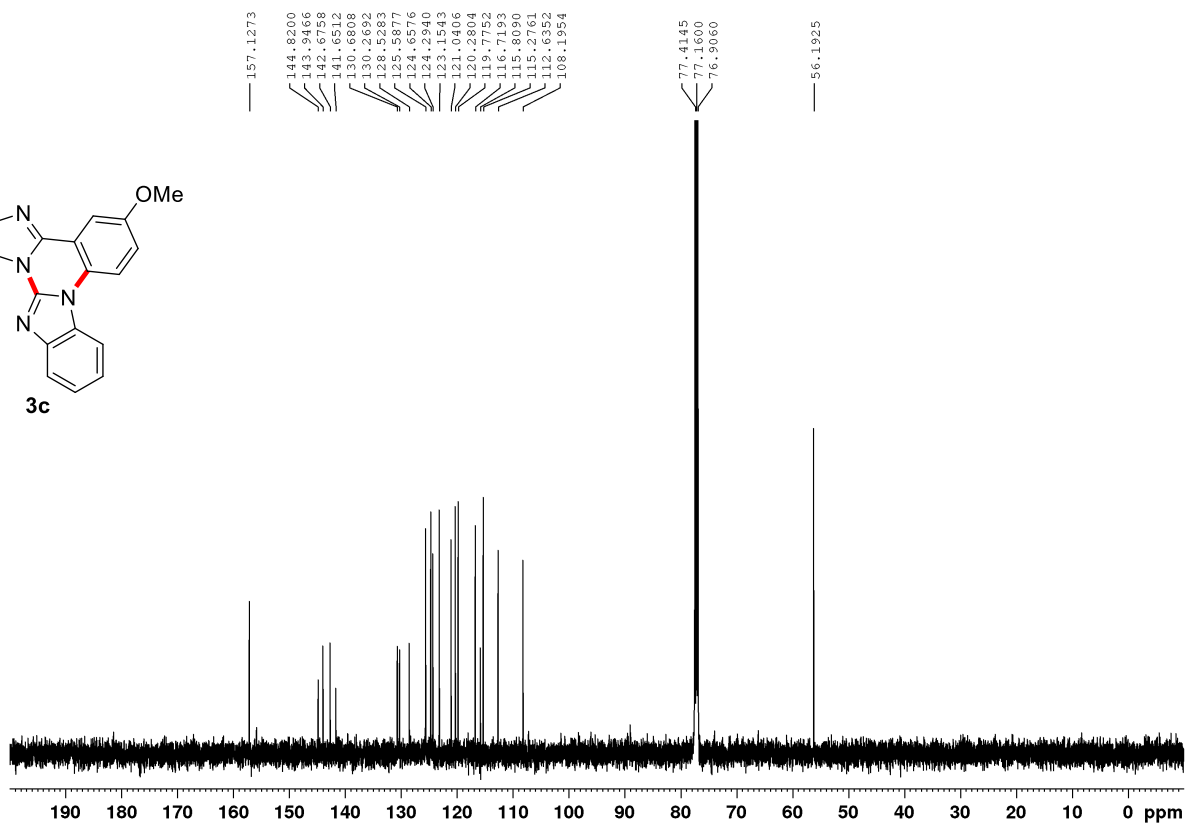
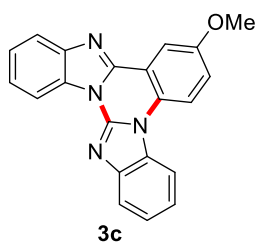
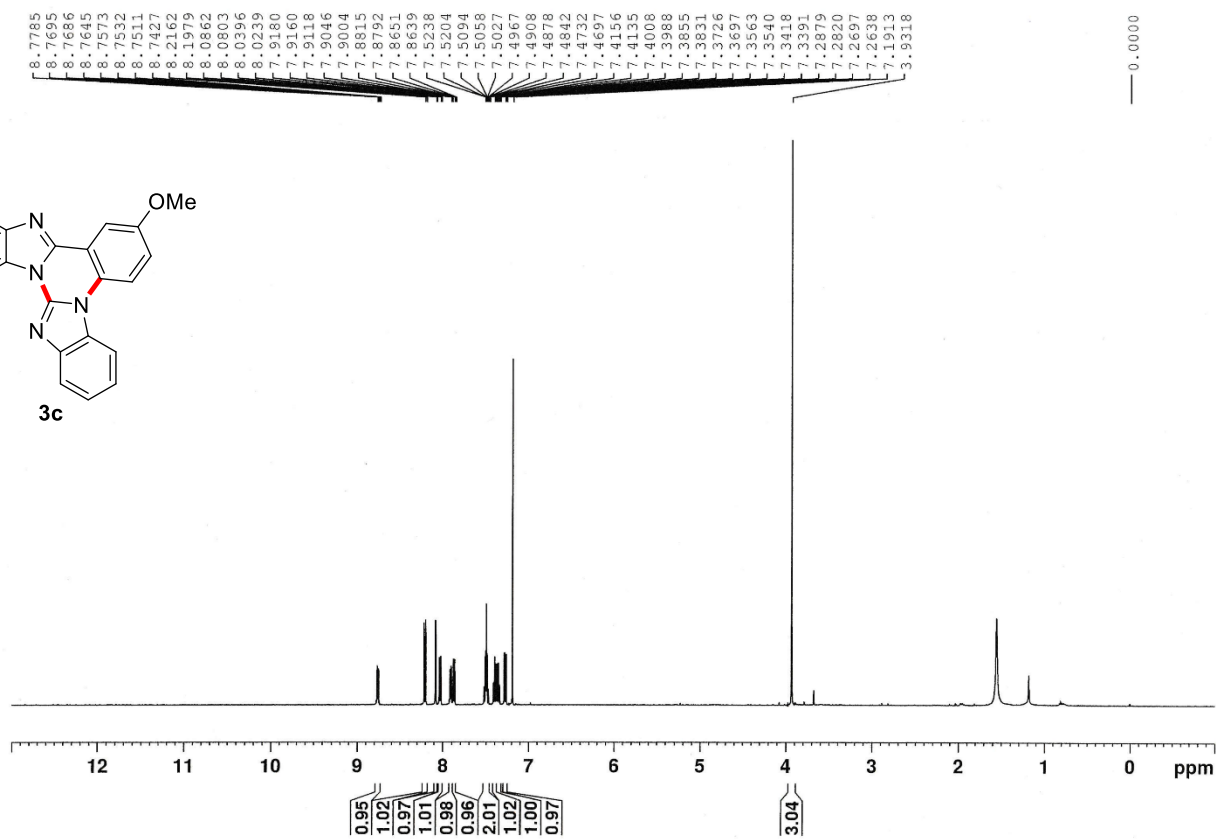
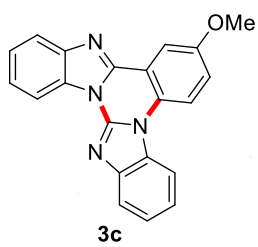
References

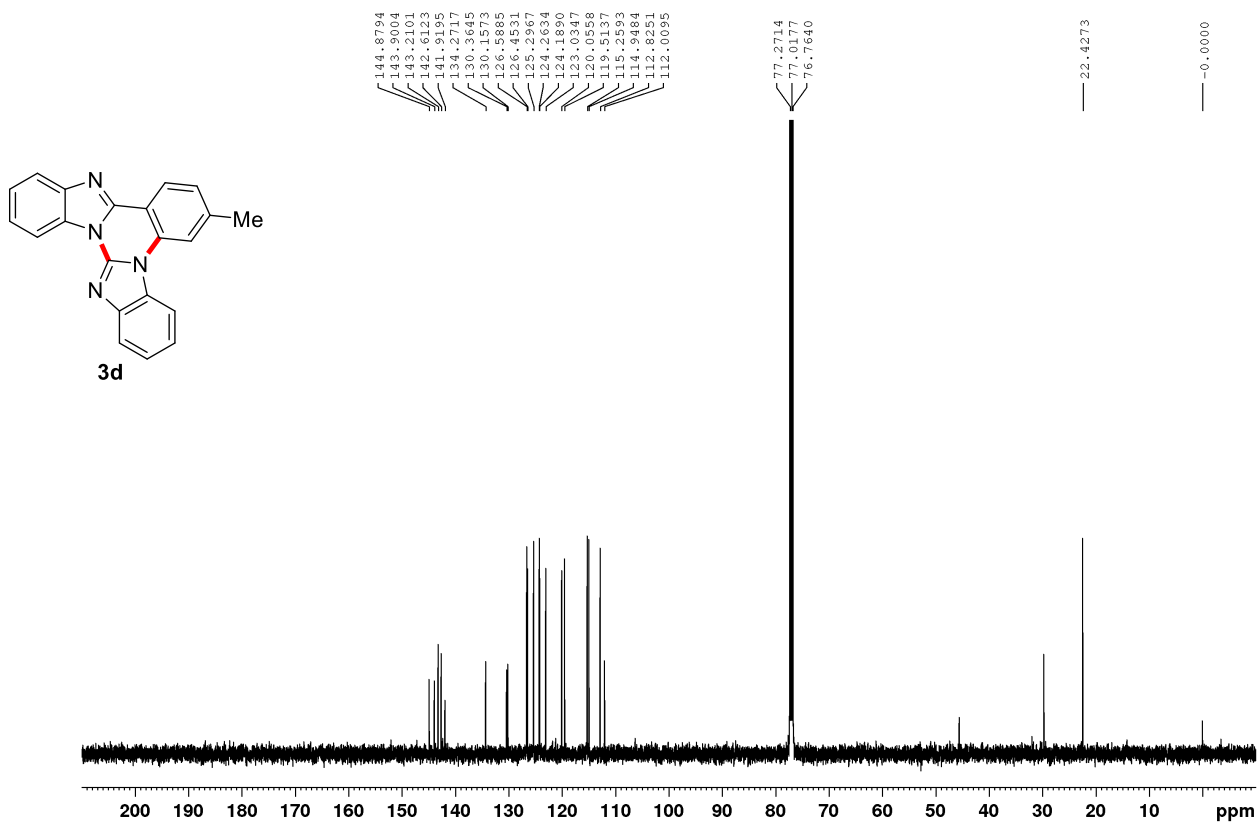
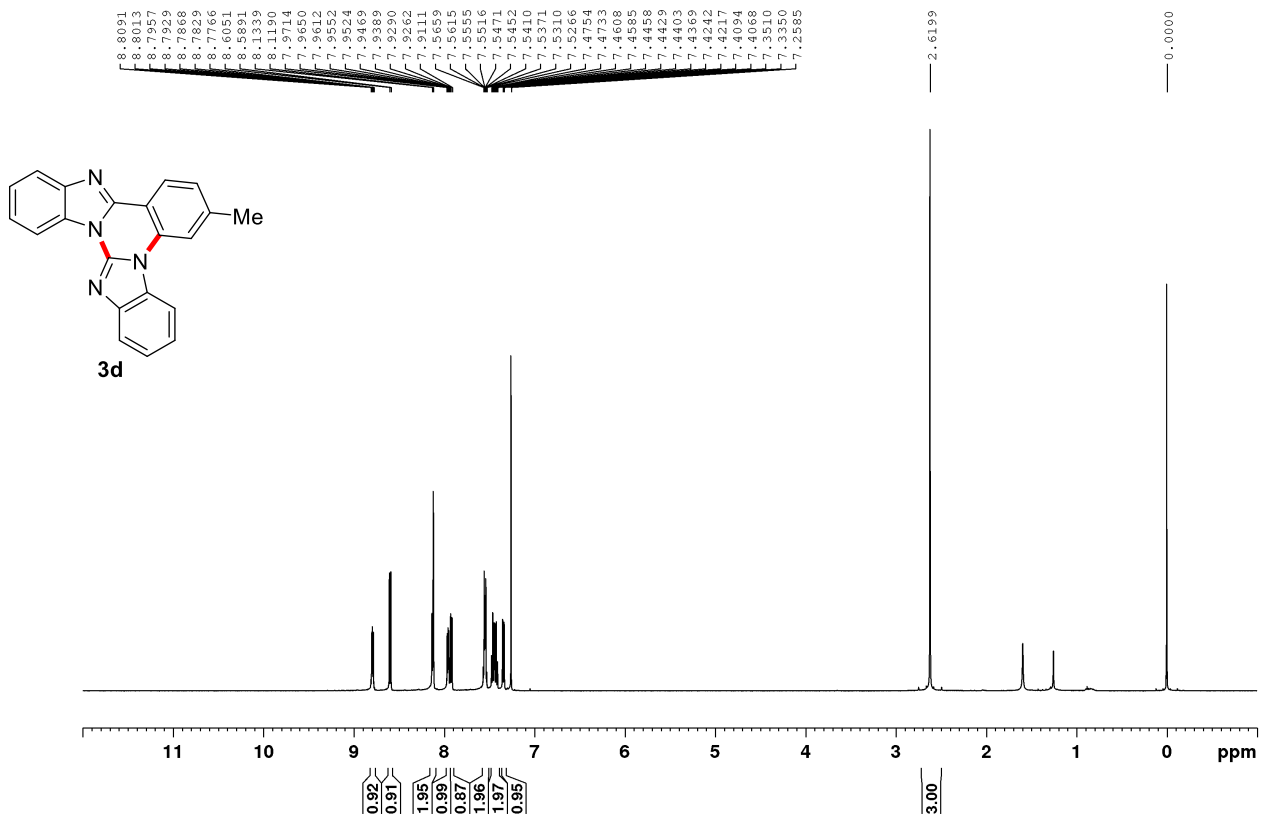
- 1 Y.-Q. Jiang, S.-H. Jia, X.-Y. Li, Y.-M. Sun, W. Li, W.-W. Zhang, G.-Q. Xu, *Chem. Pap.* 2018, **72**, 1265.
- 2 T. D. Diep, P. D. Q. Dao, C. S. Cho, *Eur. J. Org. Chem.* 2019, **2019**, 4071.
- 3 (a) G. Yuan, H. Liu, J. Gao, K. Yang, Q. Niu, H. Mao, X. Wang, X. Lv, *J. Org. Chem.* 2014, **79**, 1749; (b) N. K. Nandwana, K. Pericherla, P. Kaswan, A. Kumar, *Org. Biomol. Chem.* 2015, **13**, 2947.
- 4 W. M. Haynes, *CRC Handbook of Chemistry and Physics*, 97th ed., CRC Press, Boca Ration, FL, 2017, Section 8, P 91.

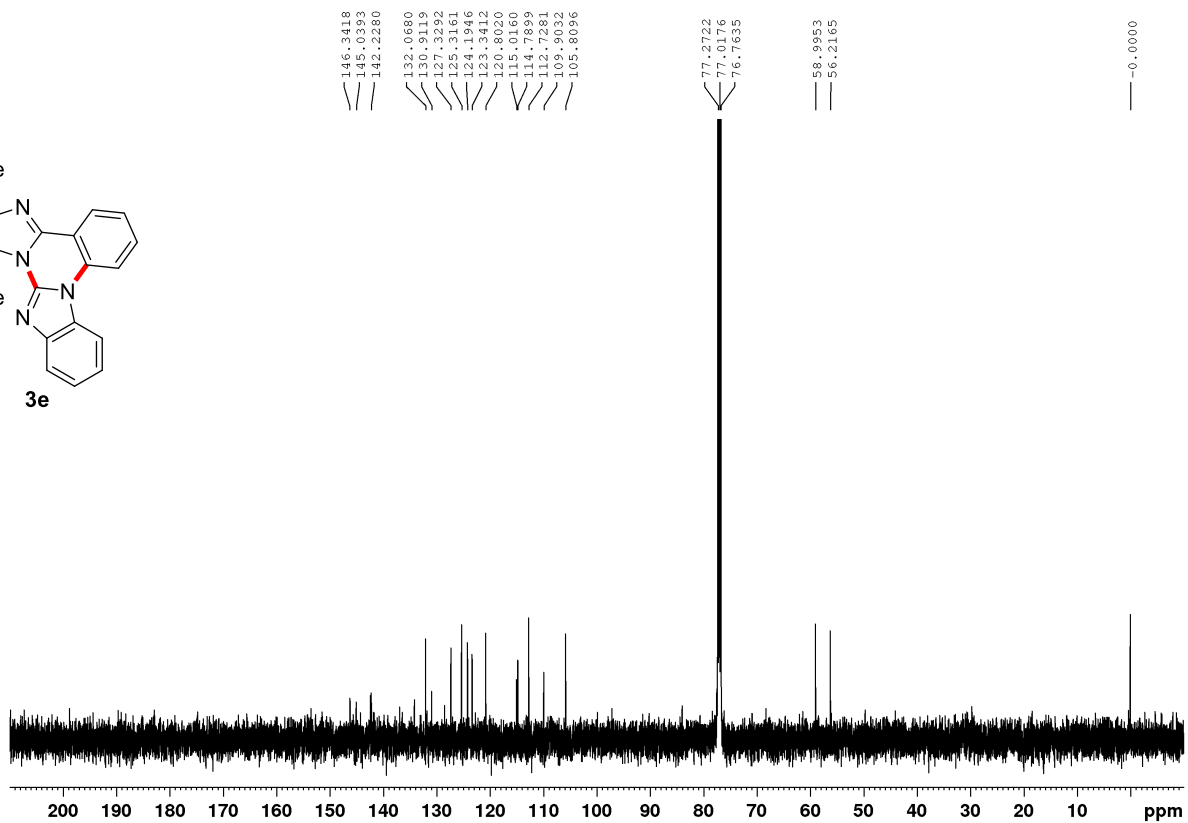
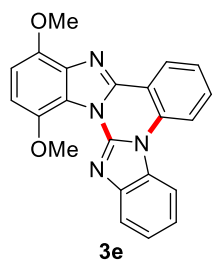
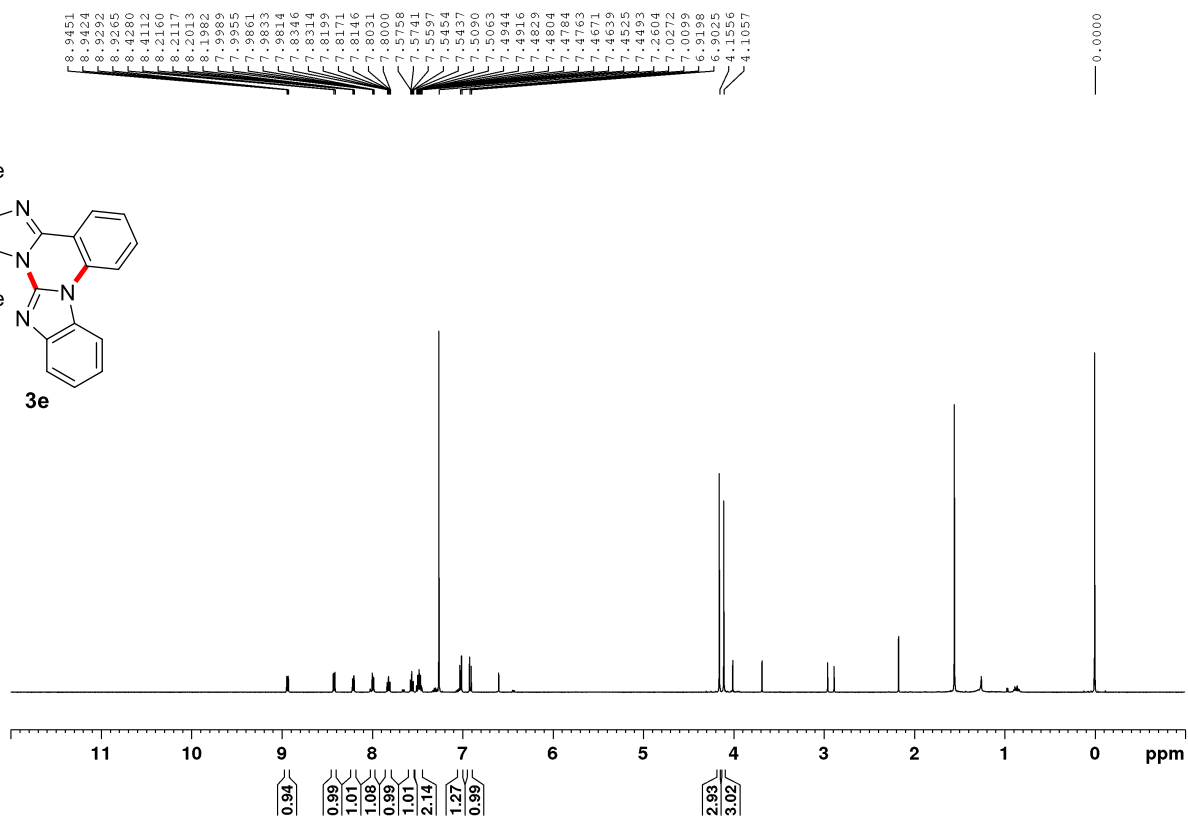
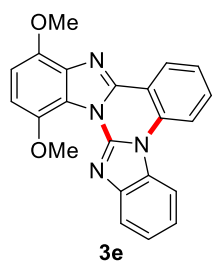
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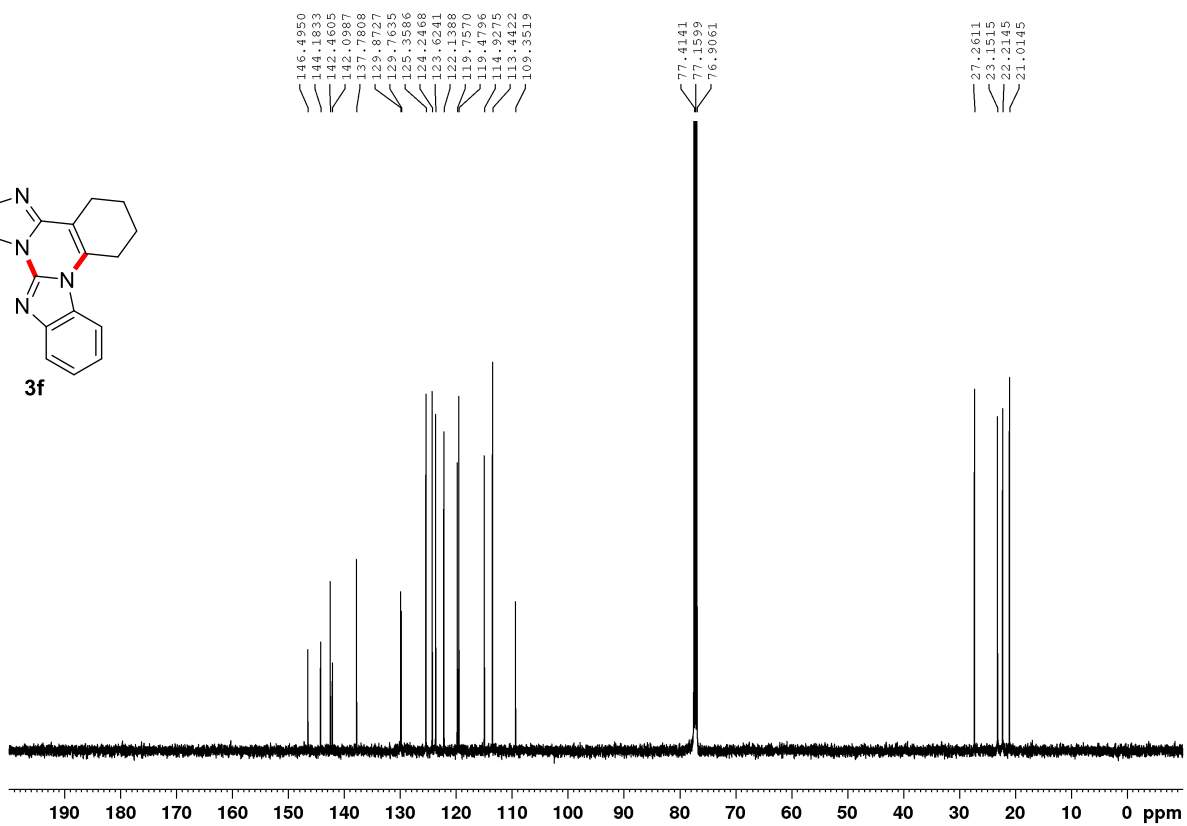
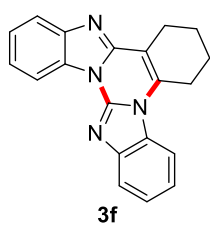
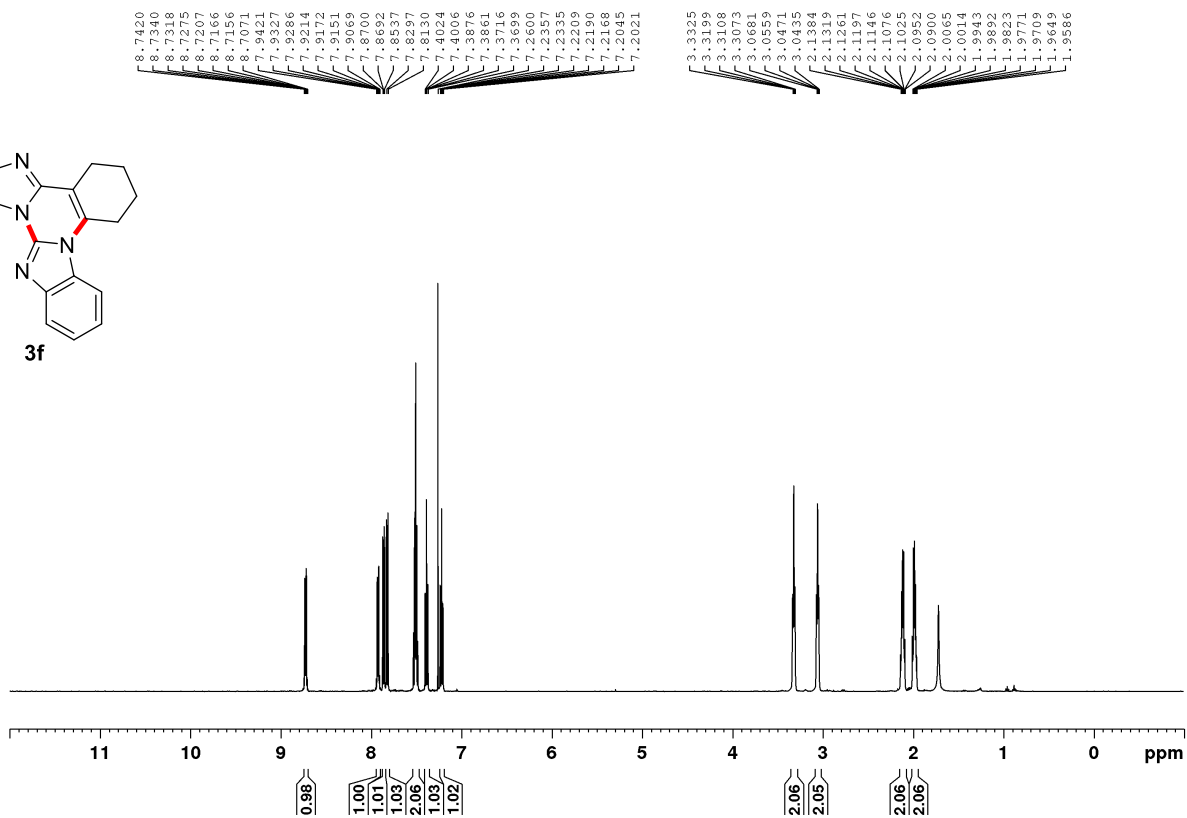
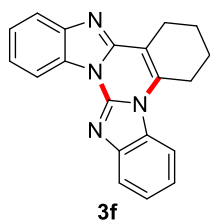


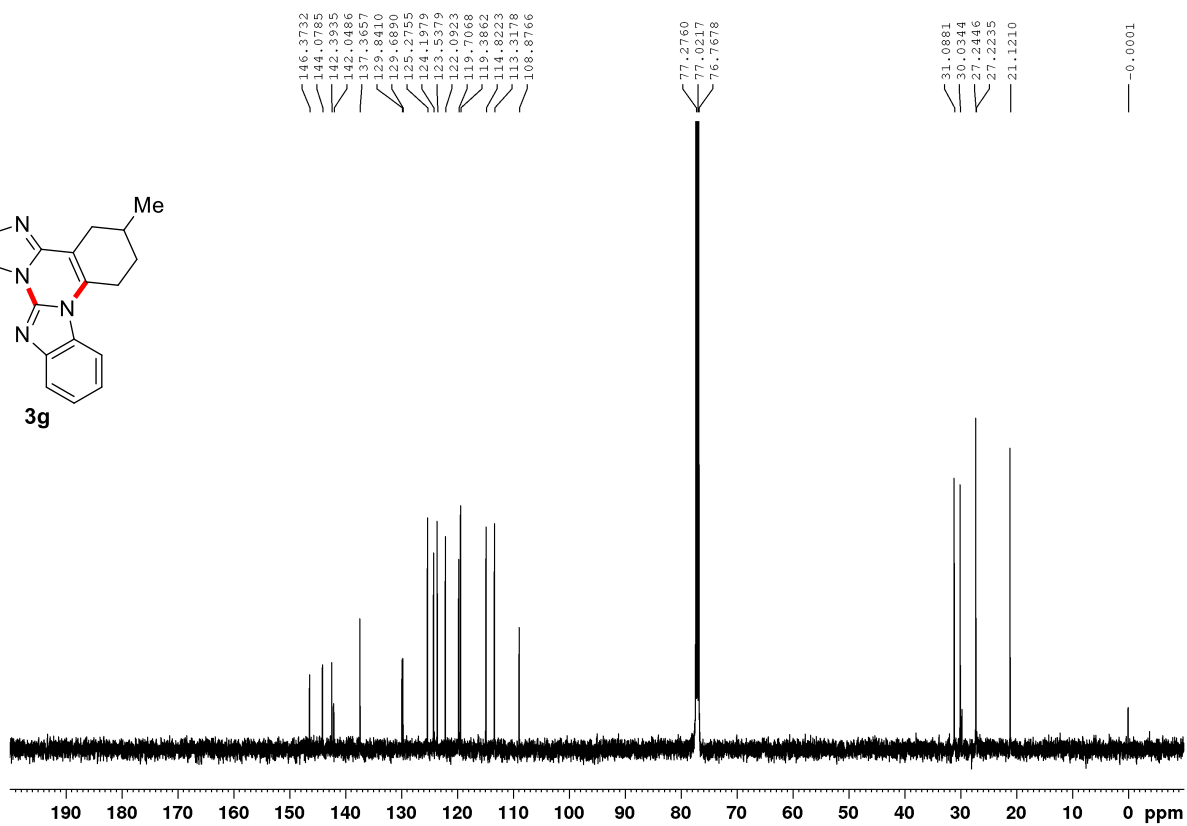
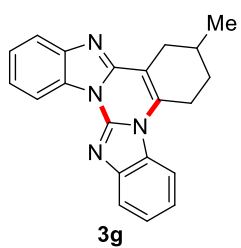
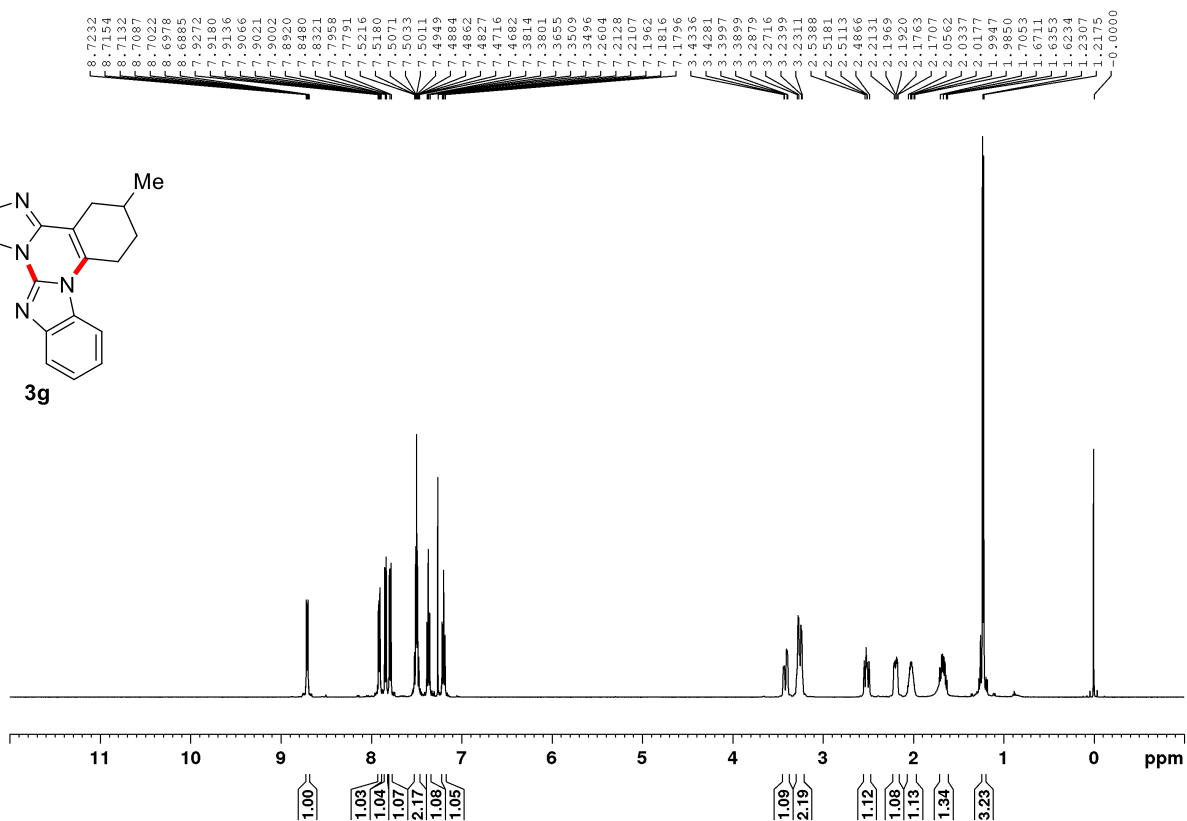
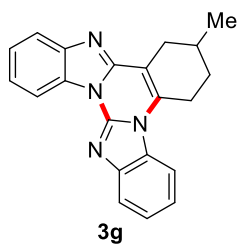


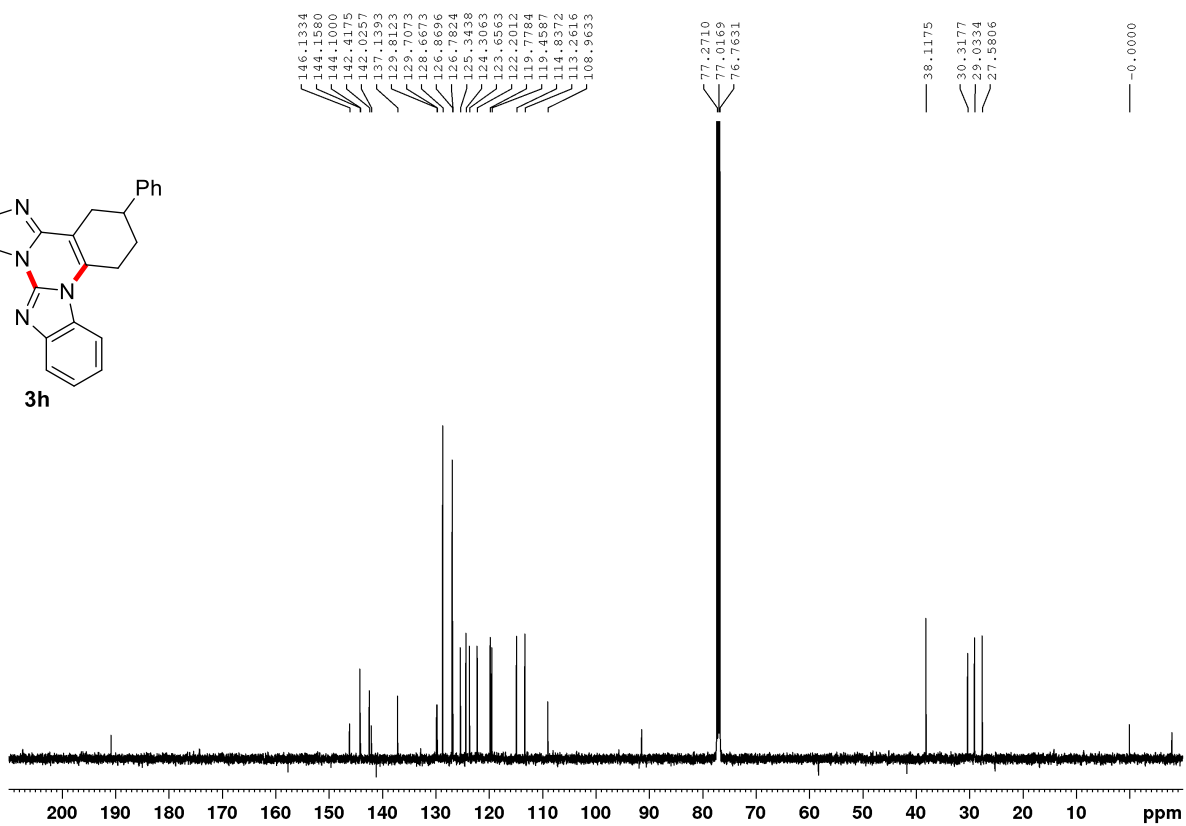
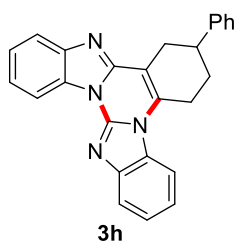
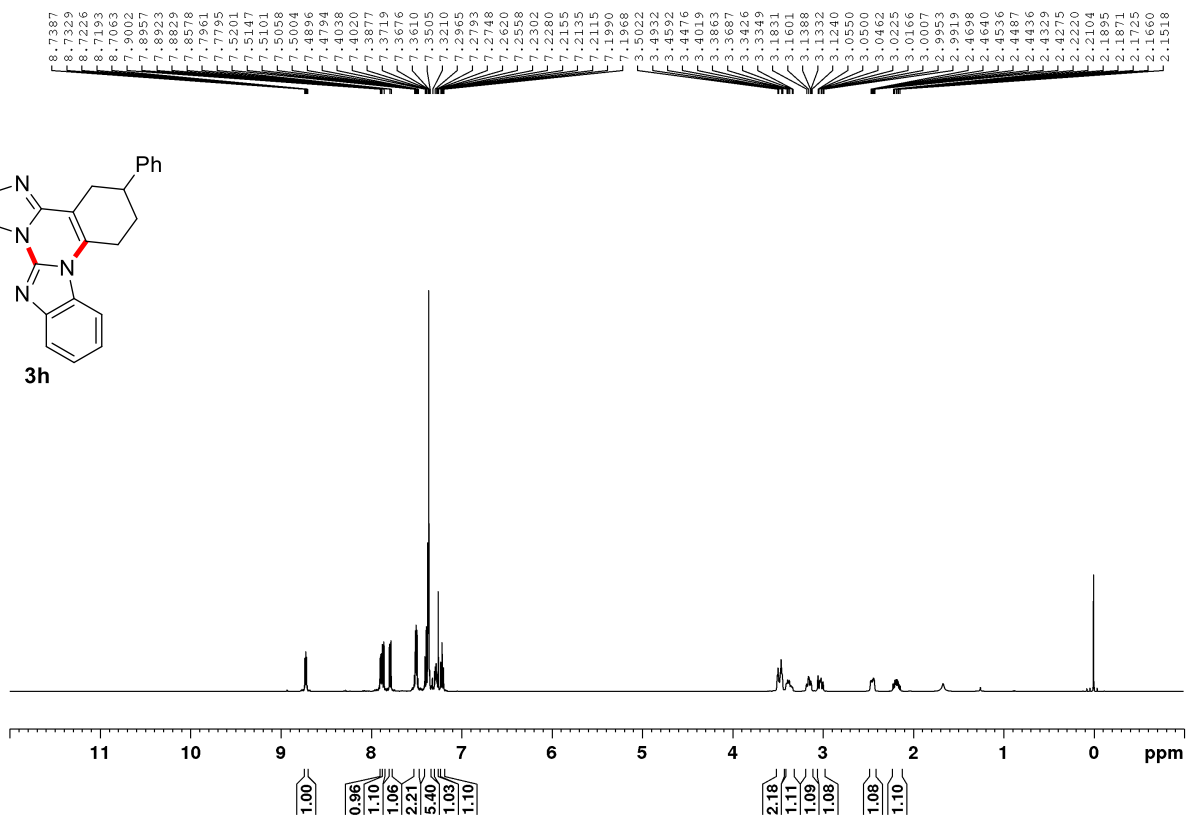
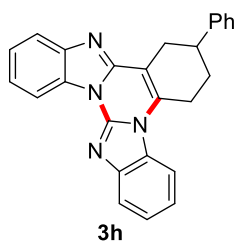


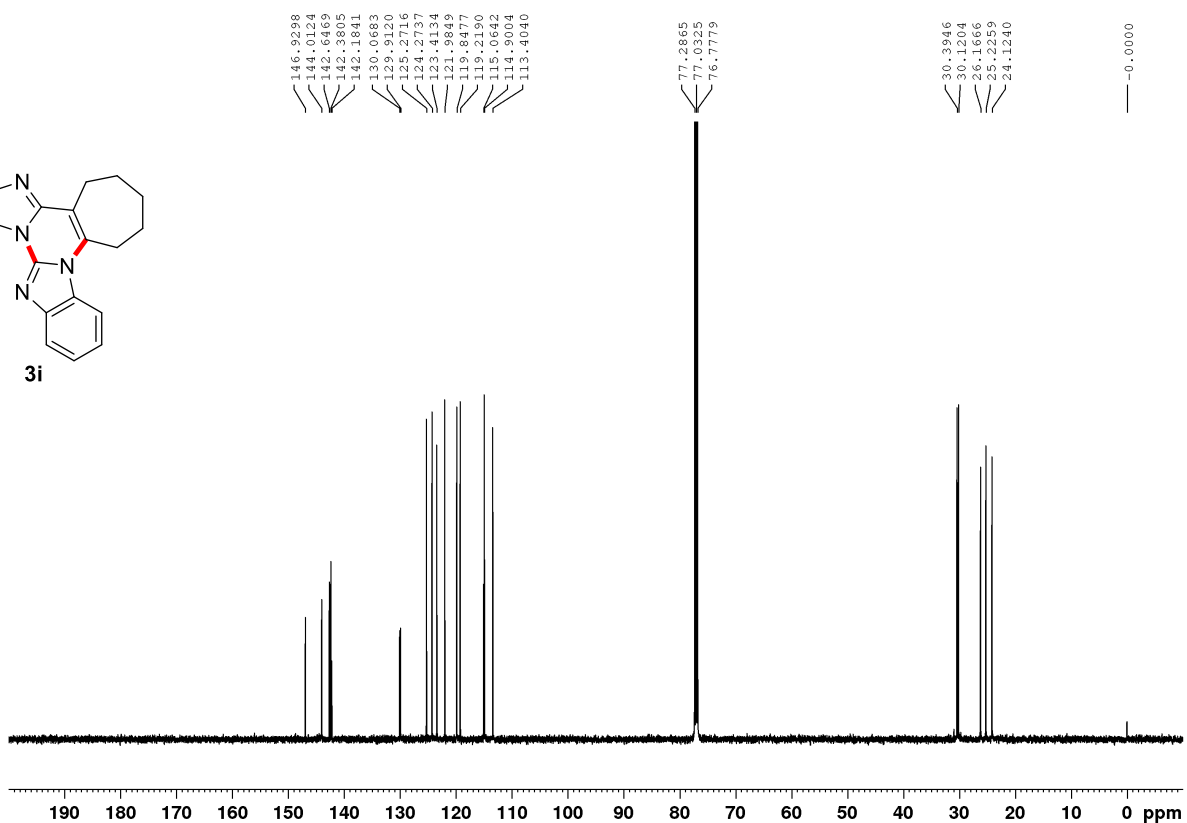
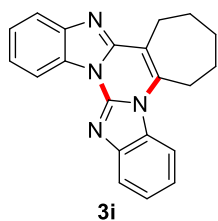
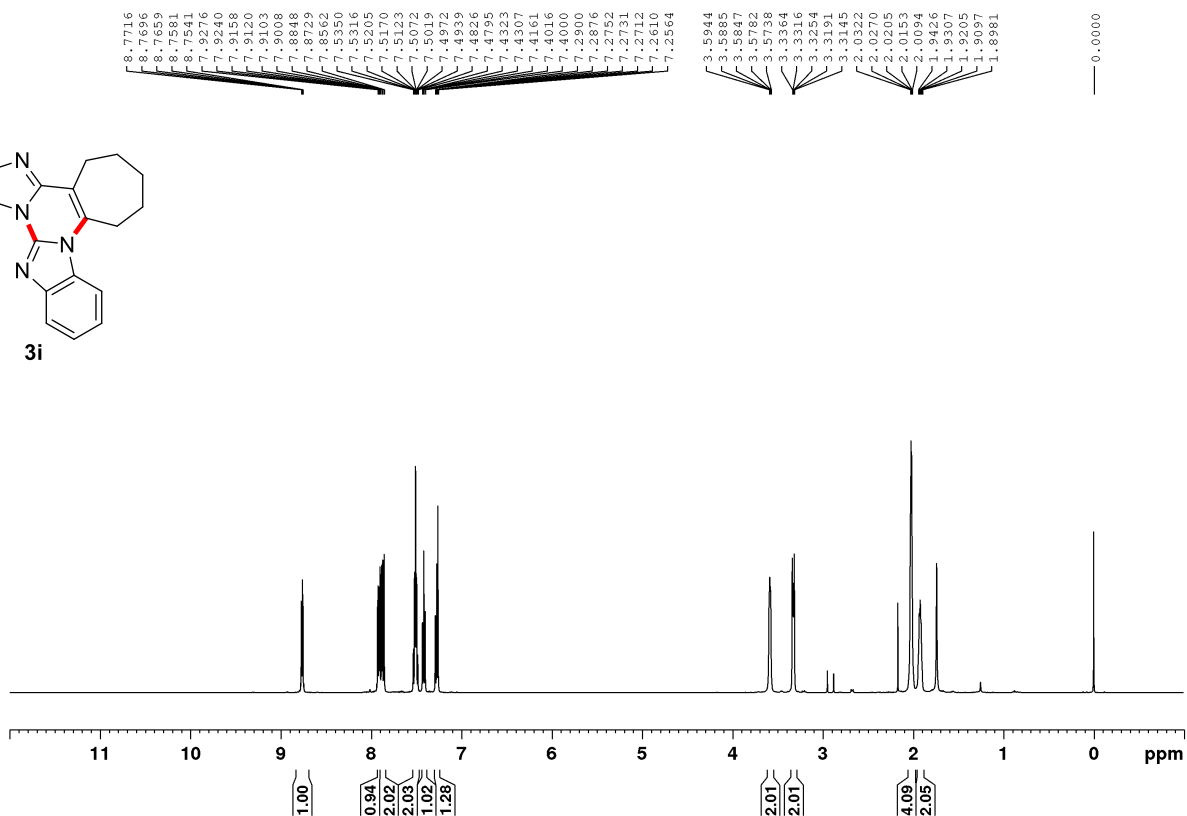
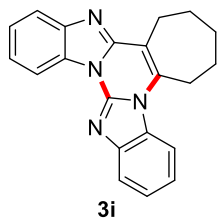


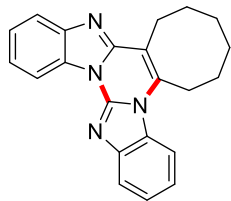




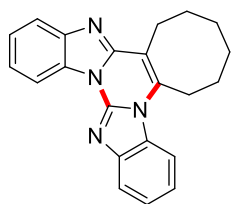
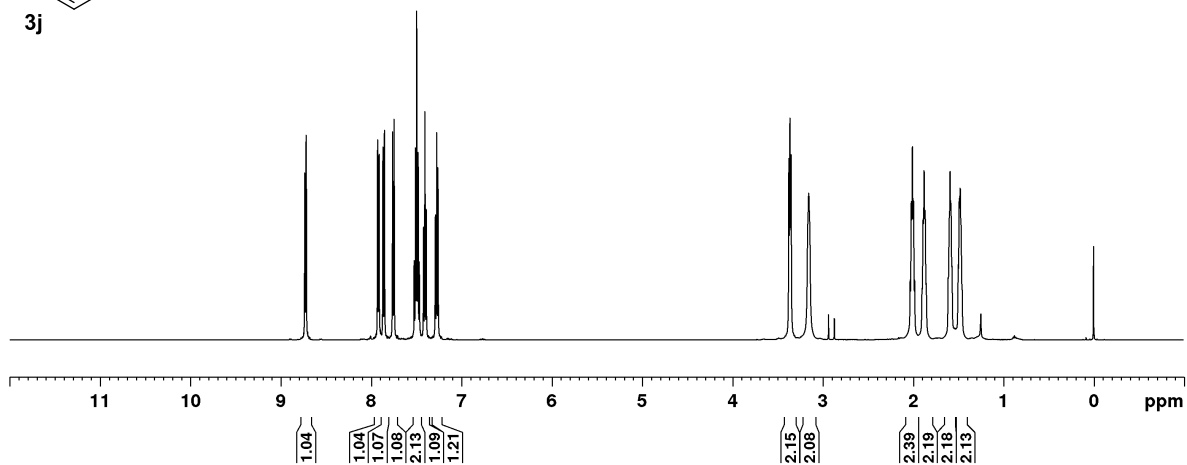




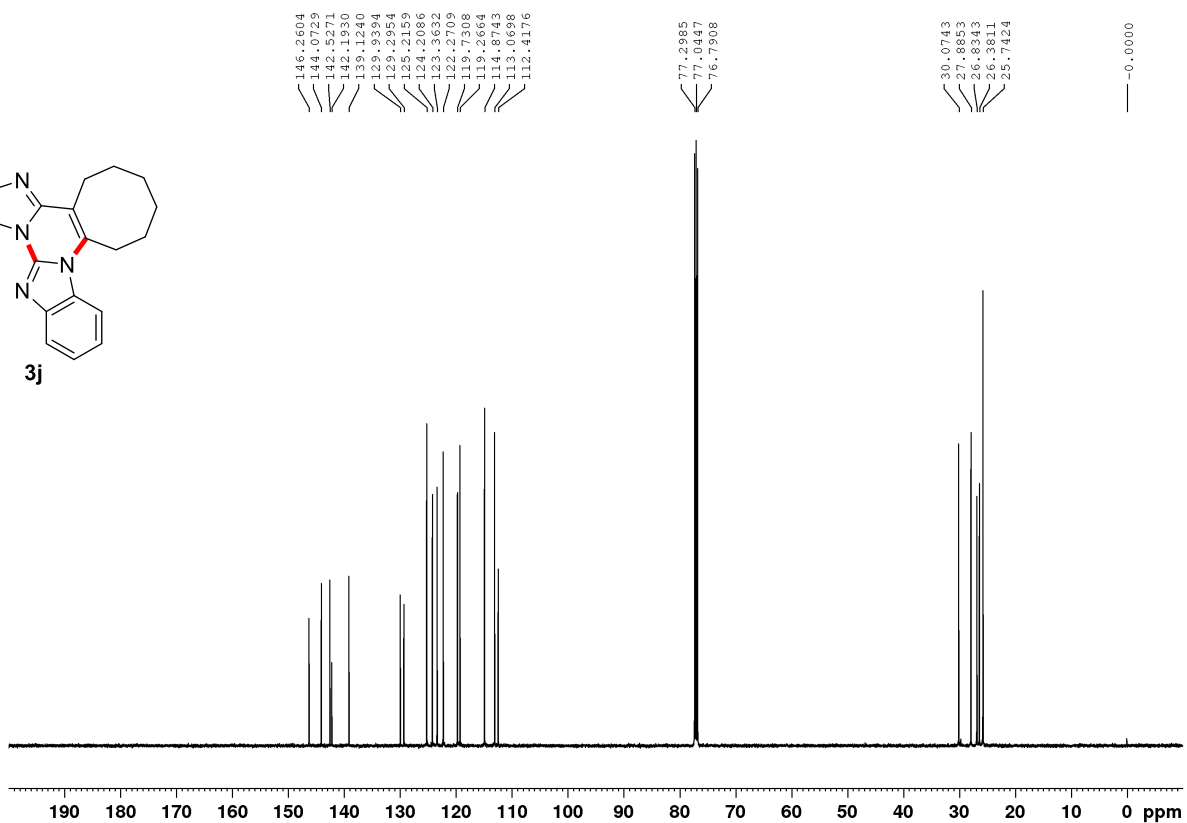


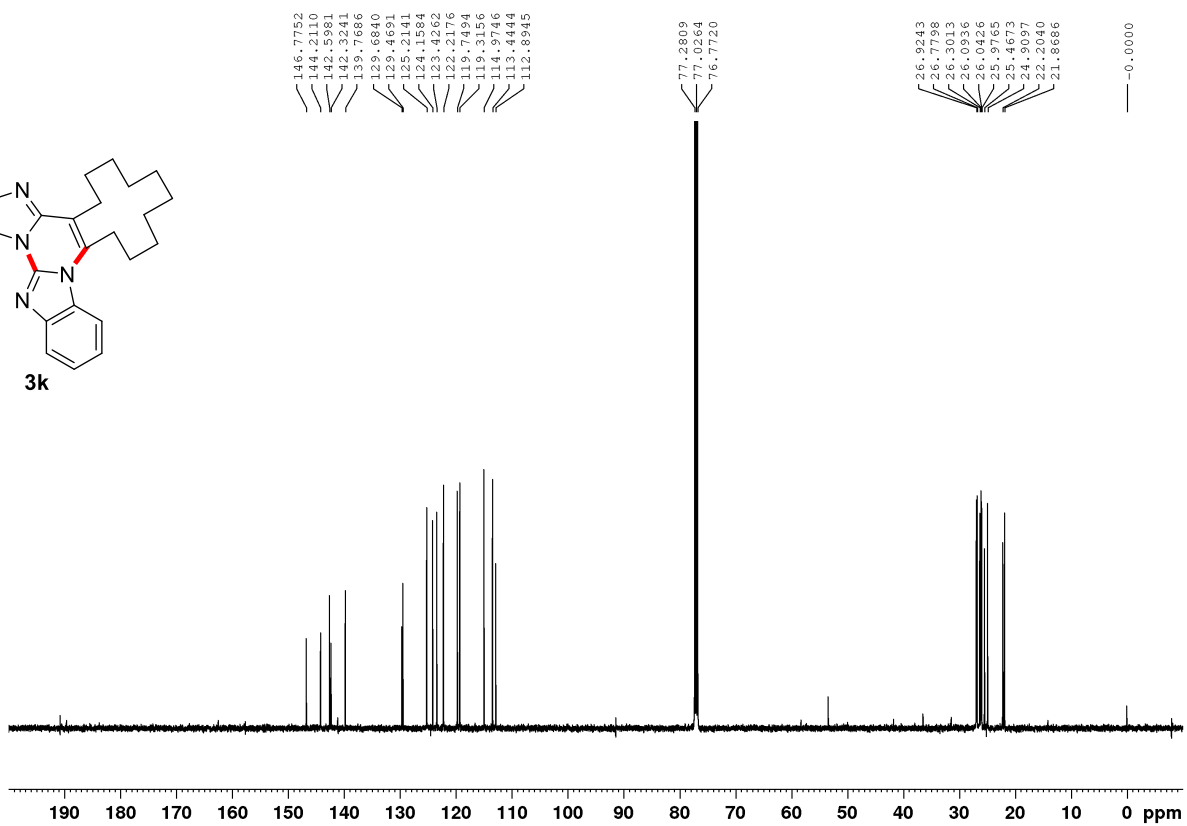
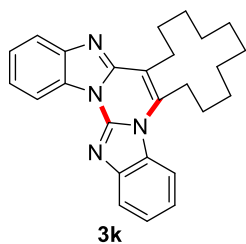
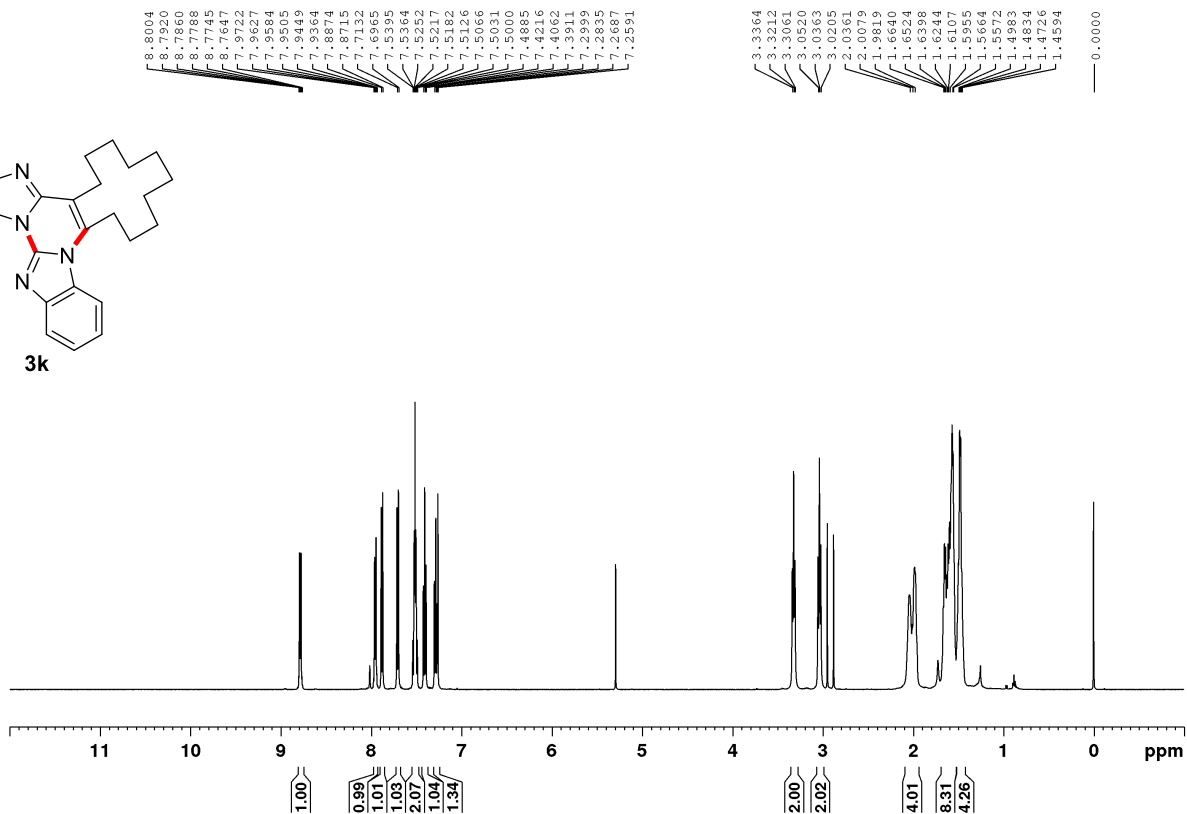
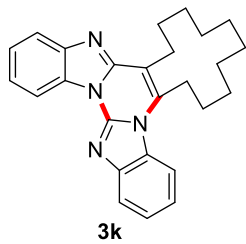


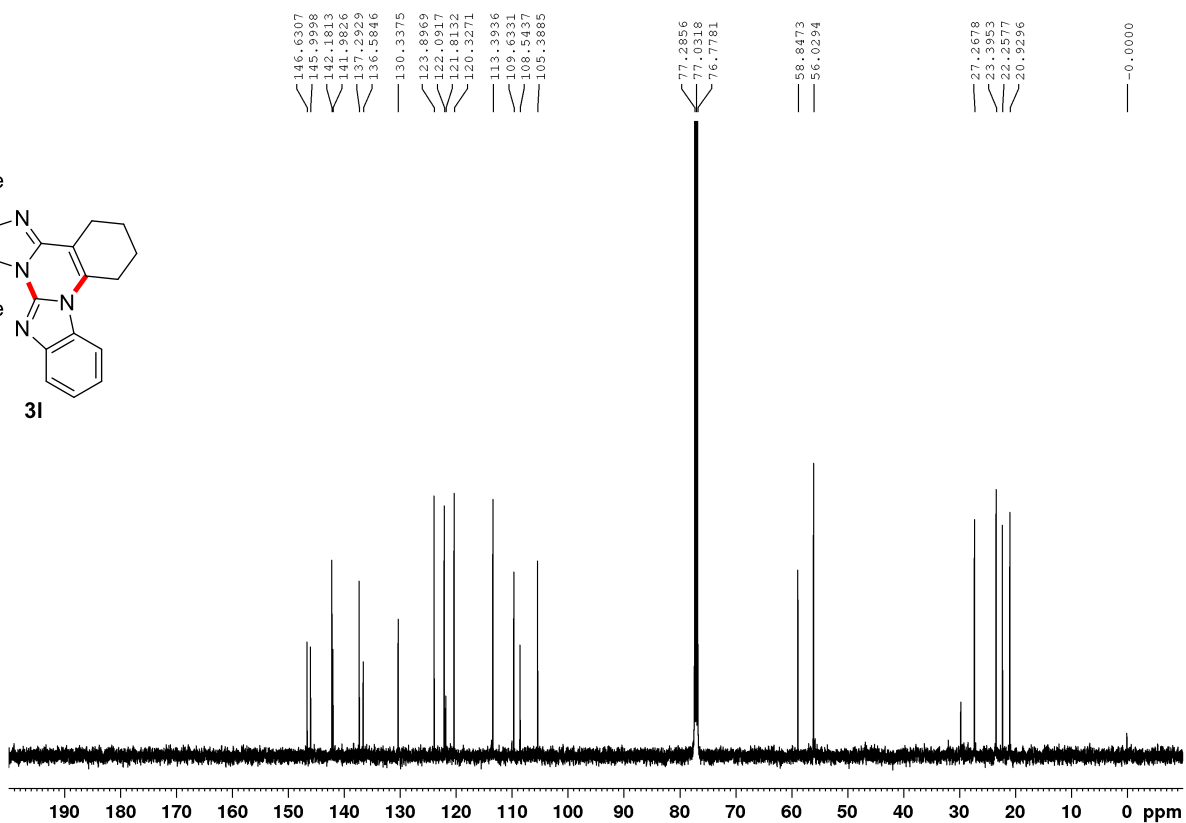
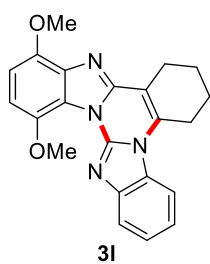
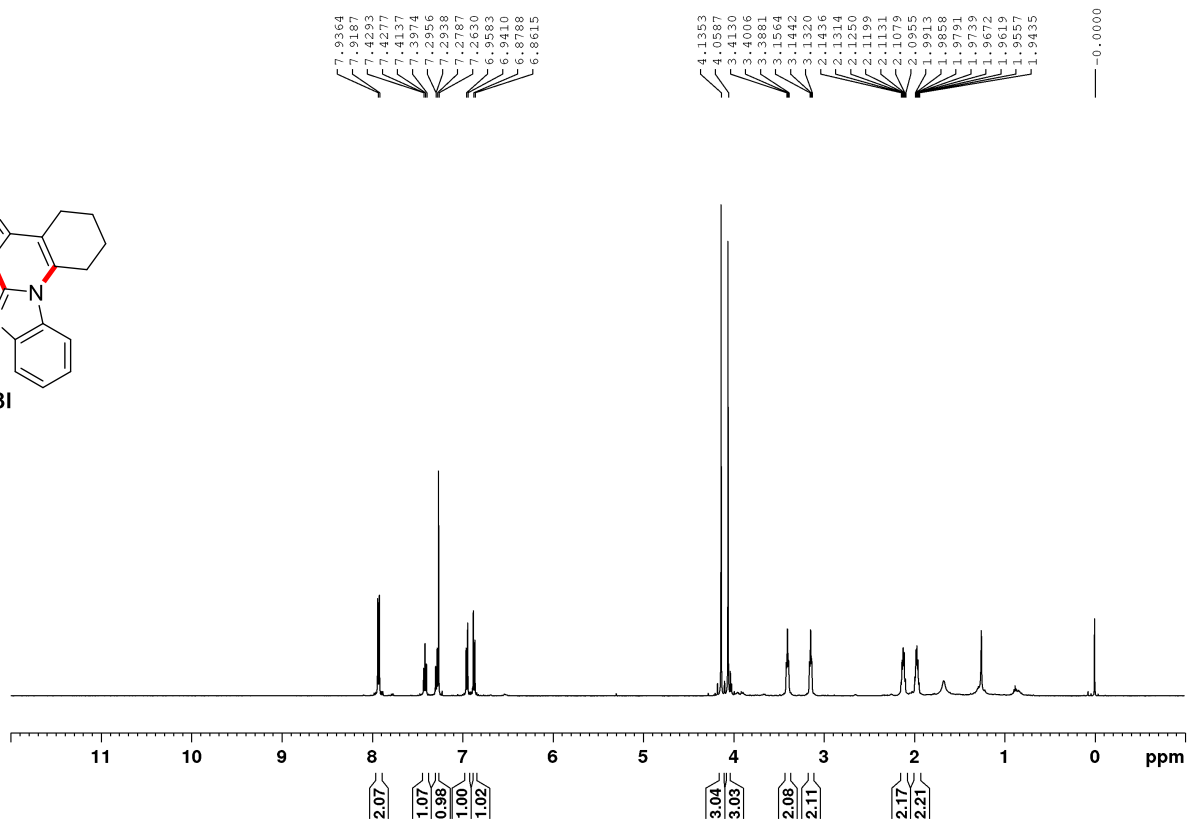
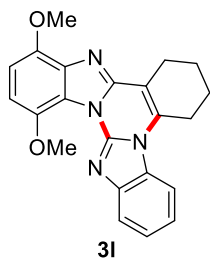
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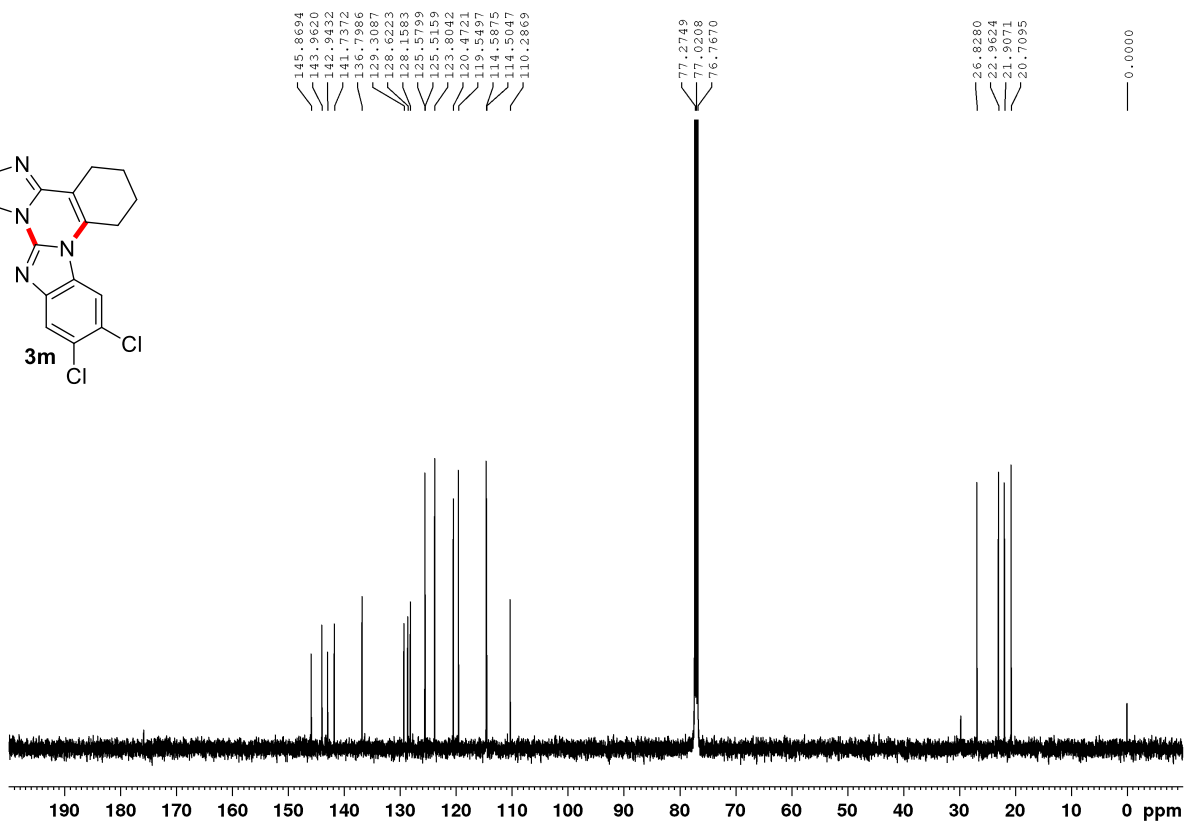
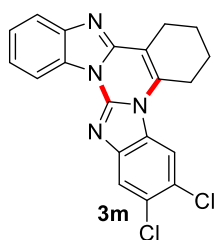
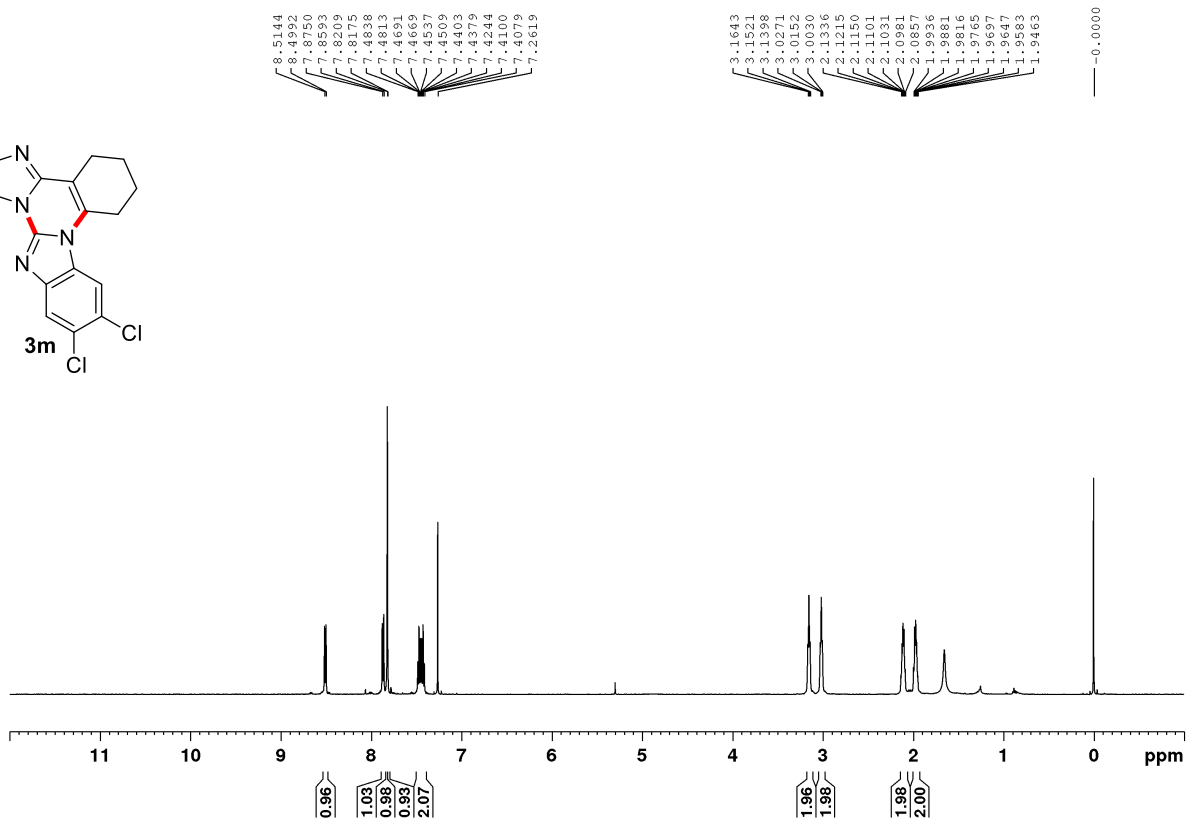
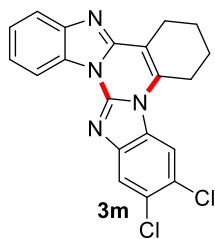


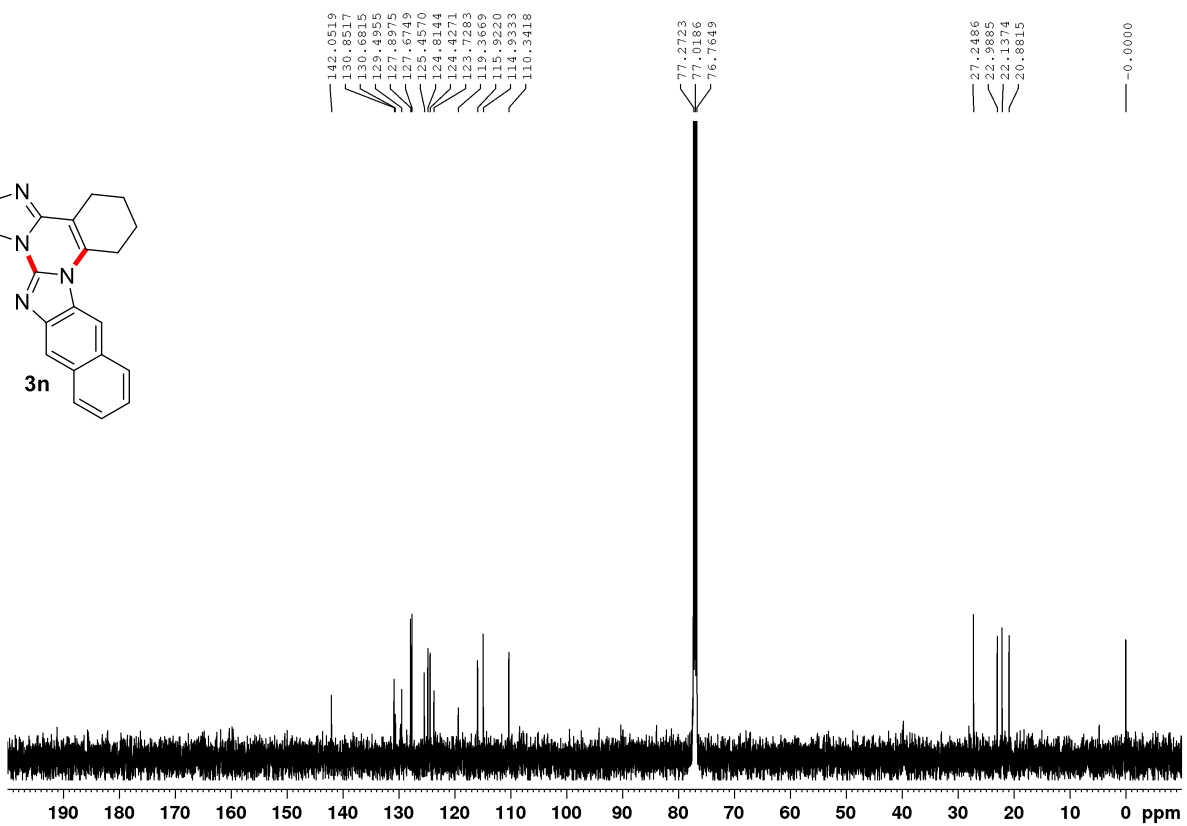
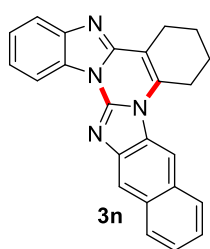
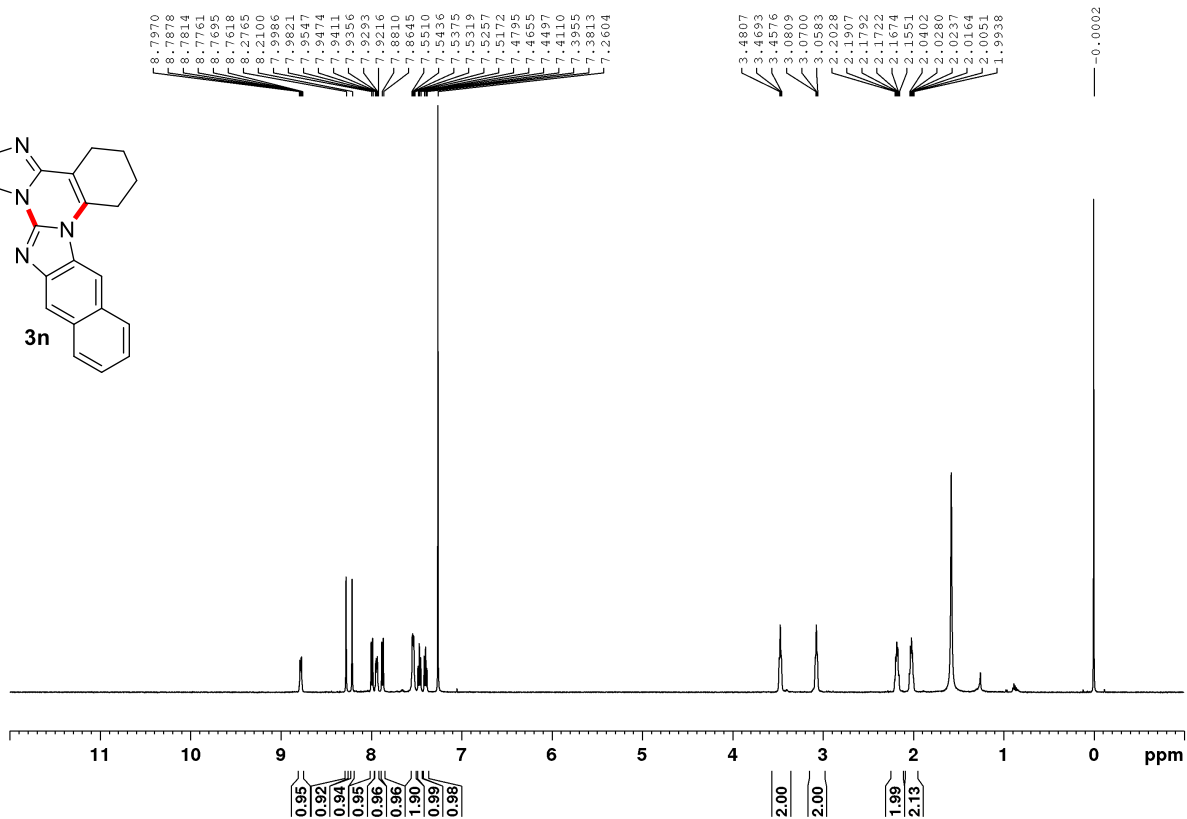
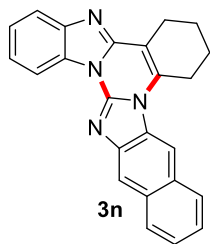
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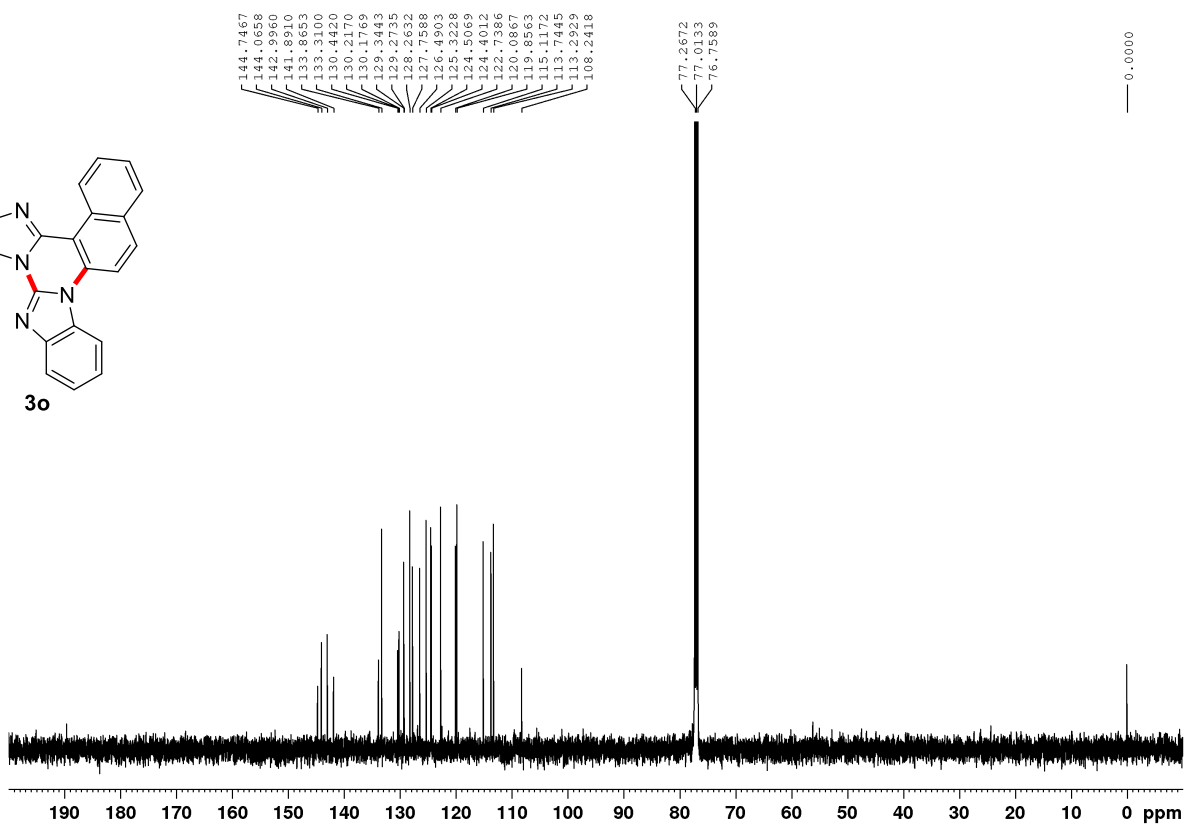
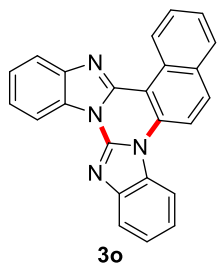
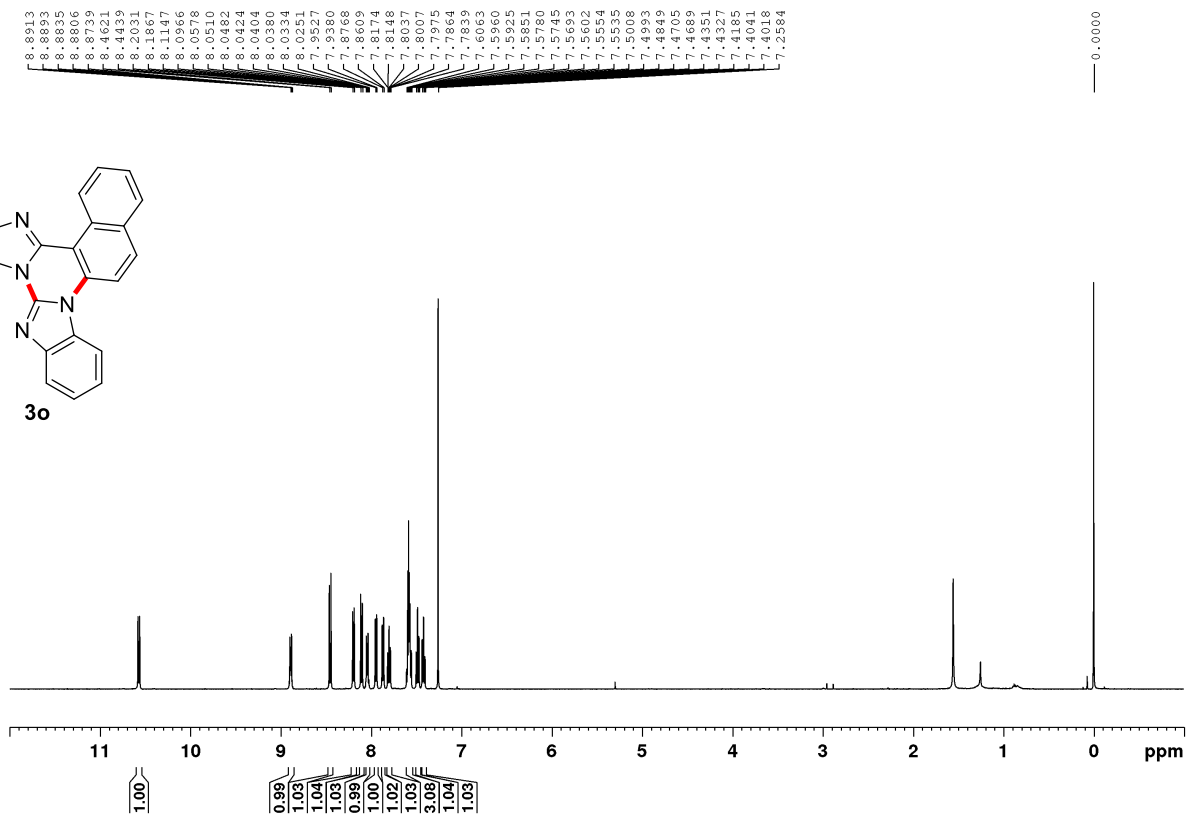
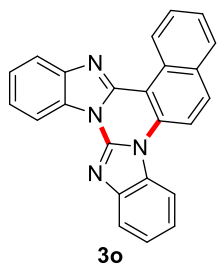


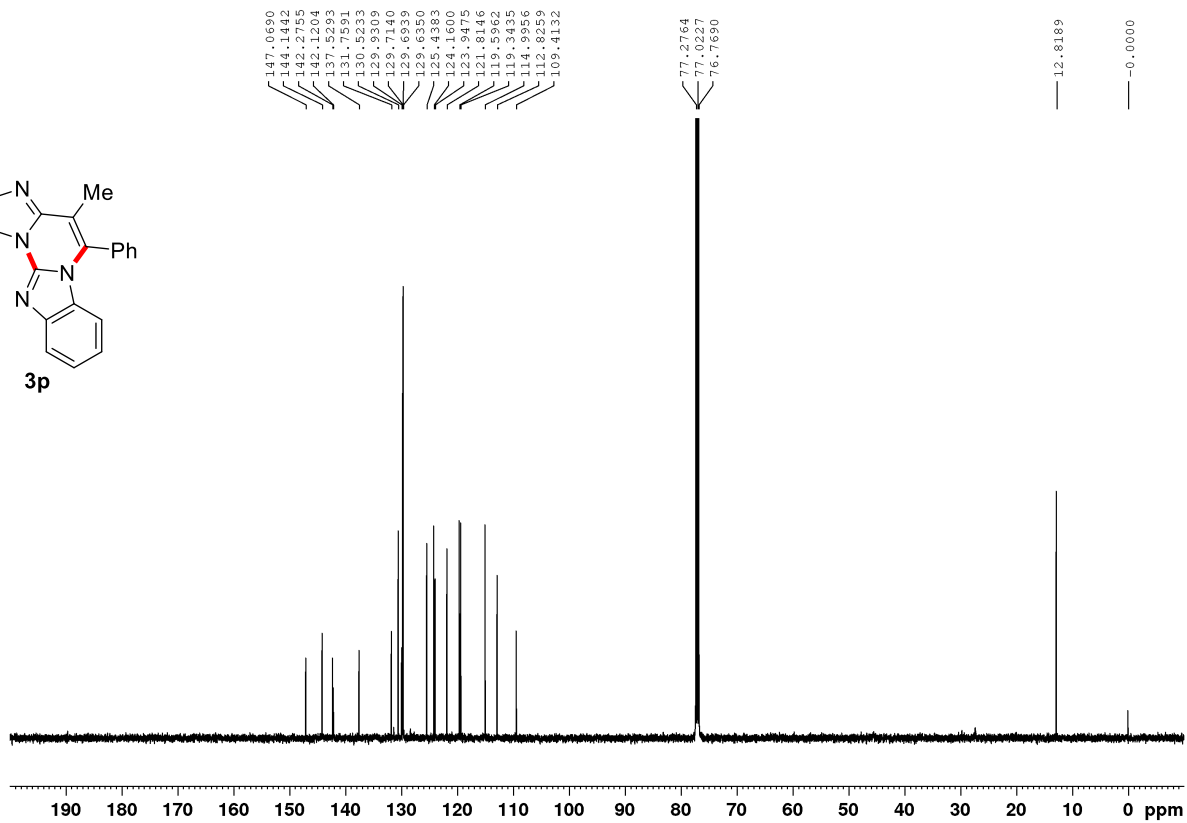
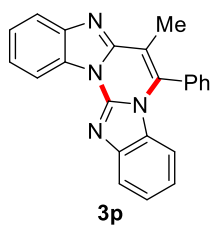
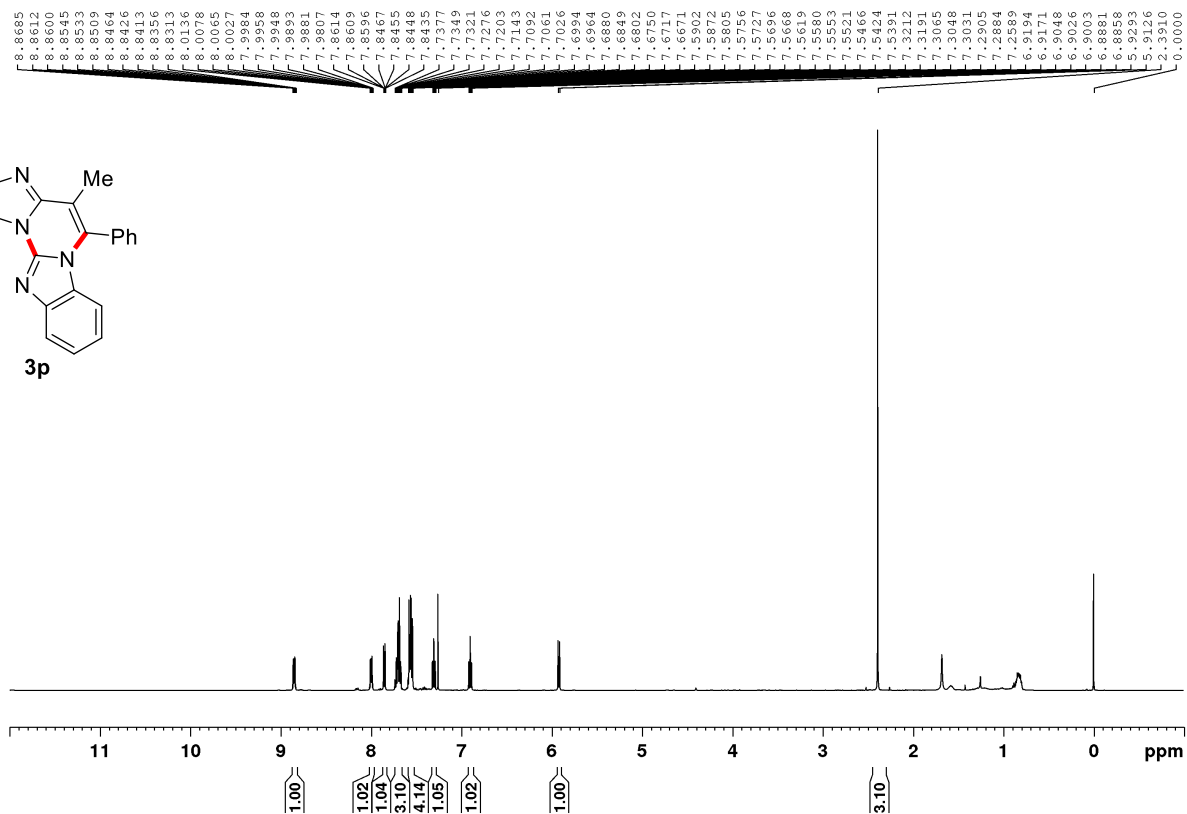
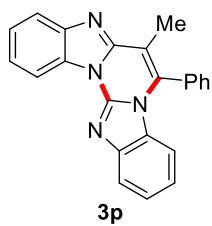


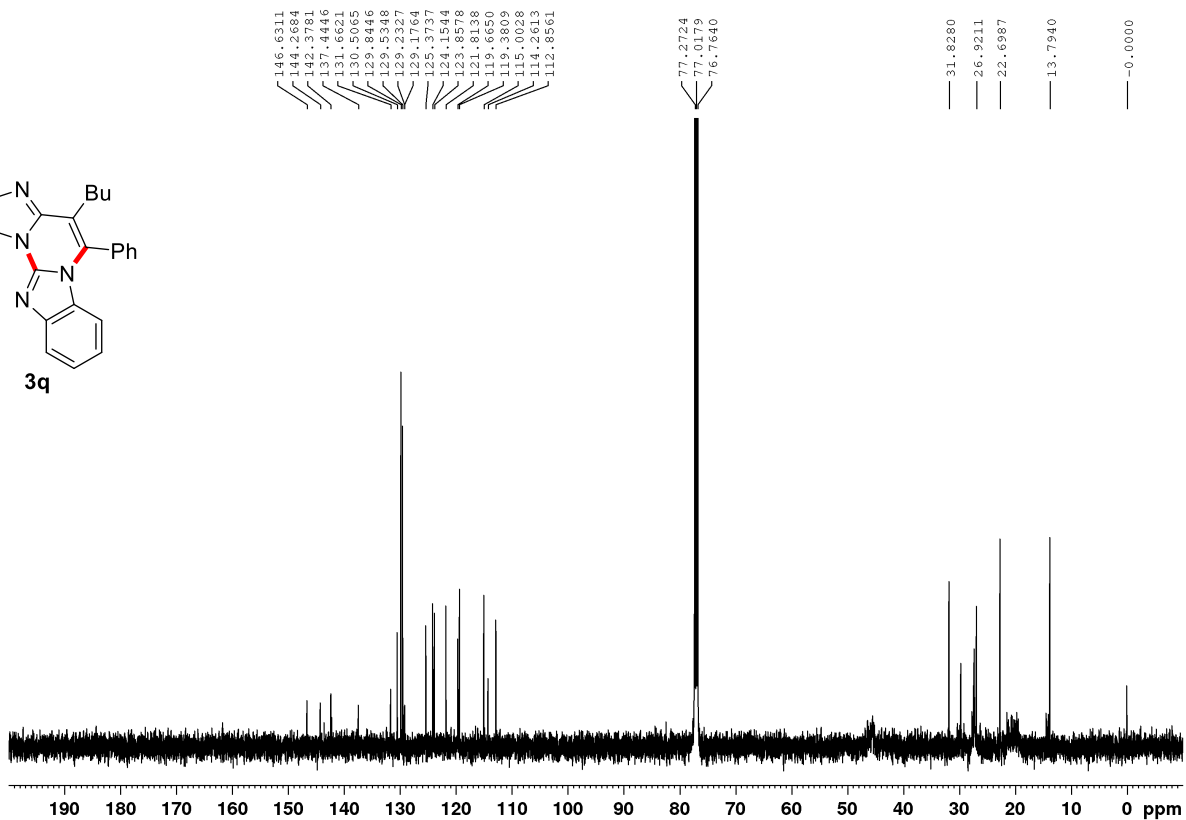
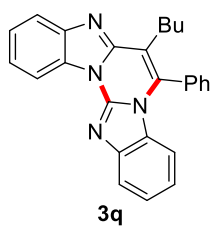
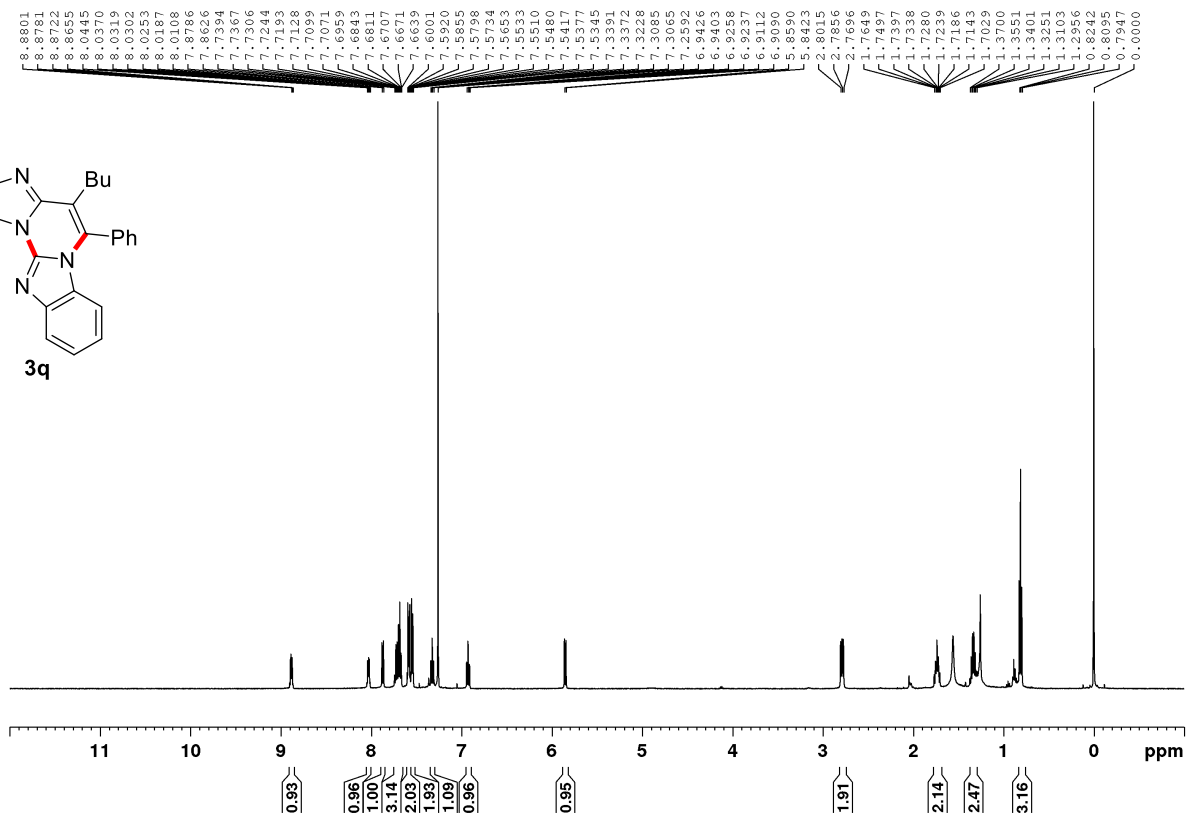
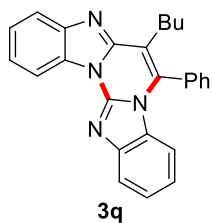


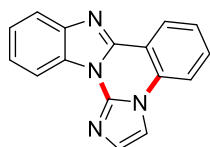




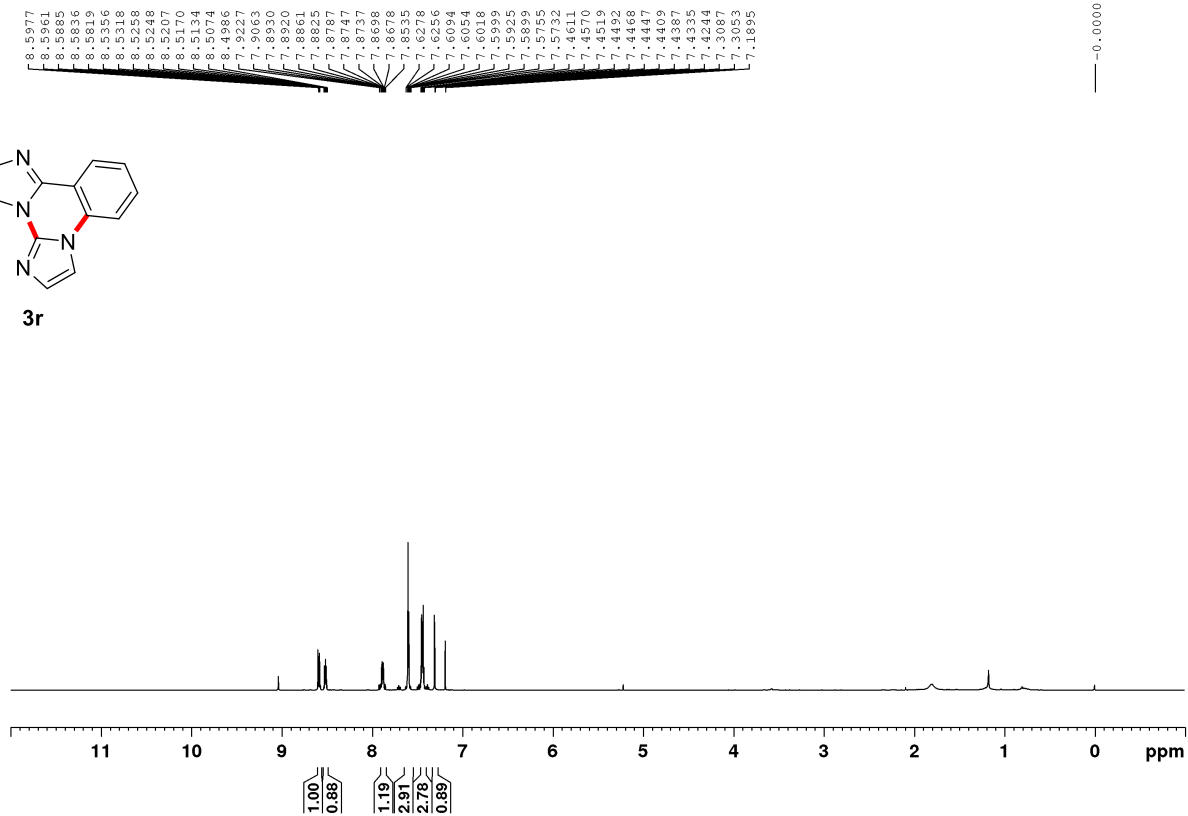




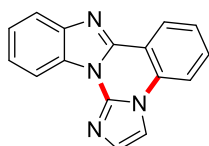




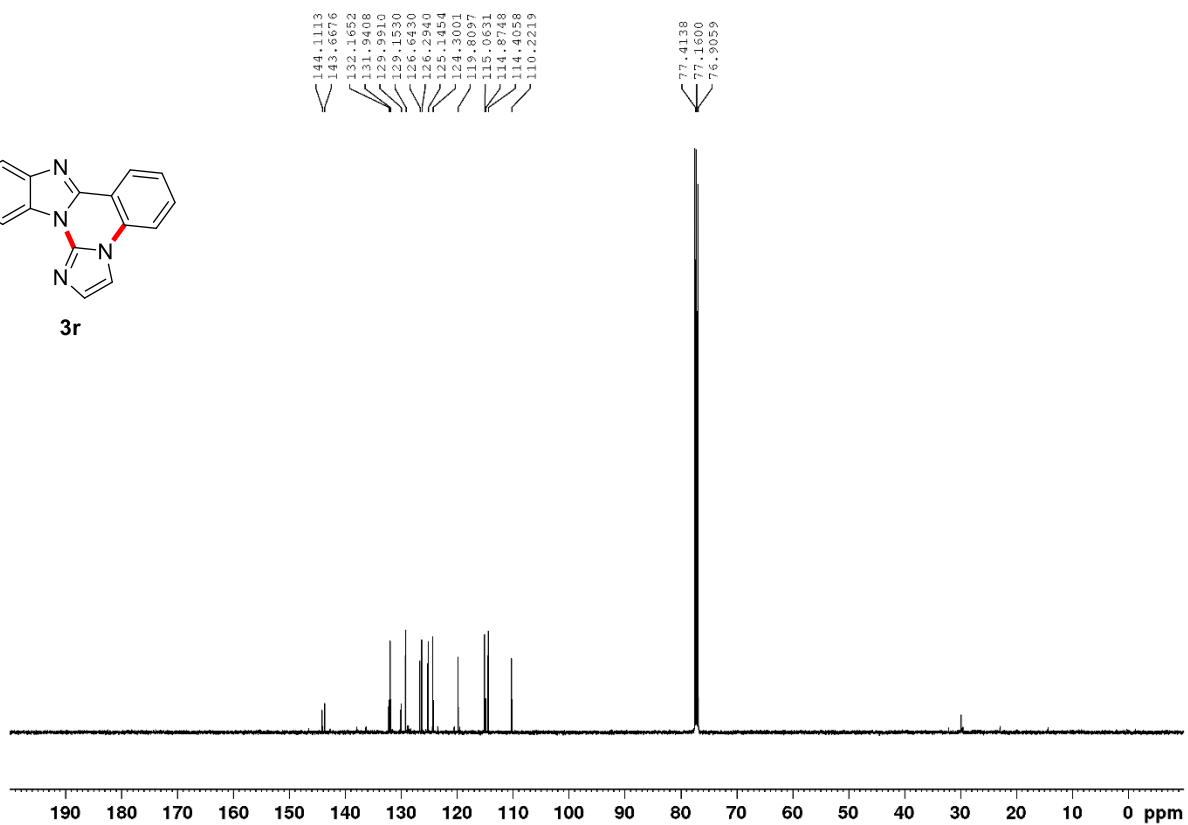
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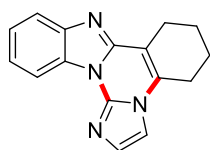


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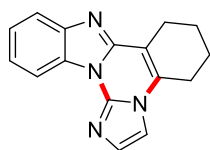
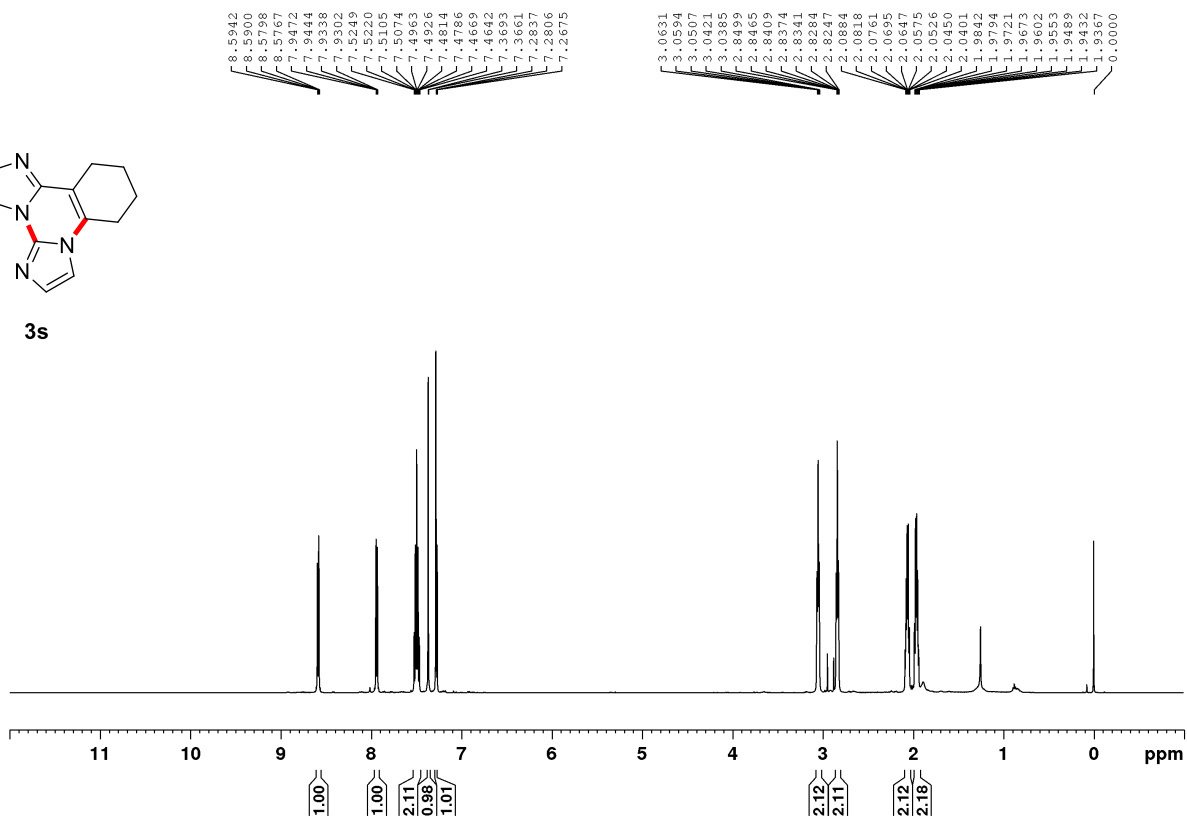


3r





3s



3s

