

## Supporting Information

### Synthesis and anti-tubercular activity of *N*<sup>2</sup>-arylbenzo[*g*]isoquinolin-5,10-dione-3-iminium bromides

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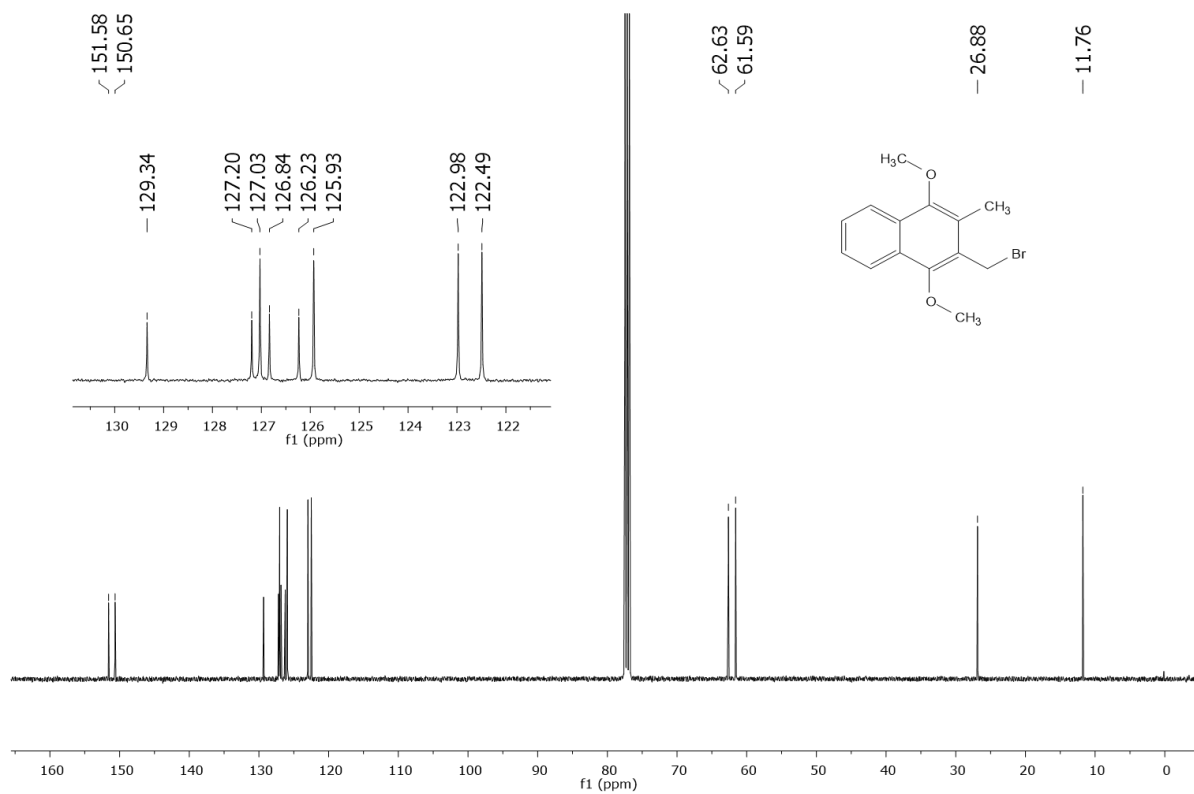
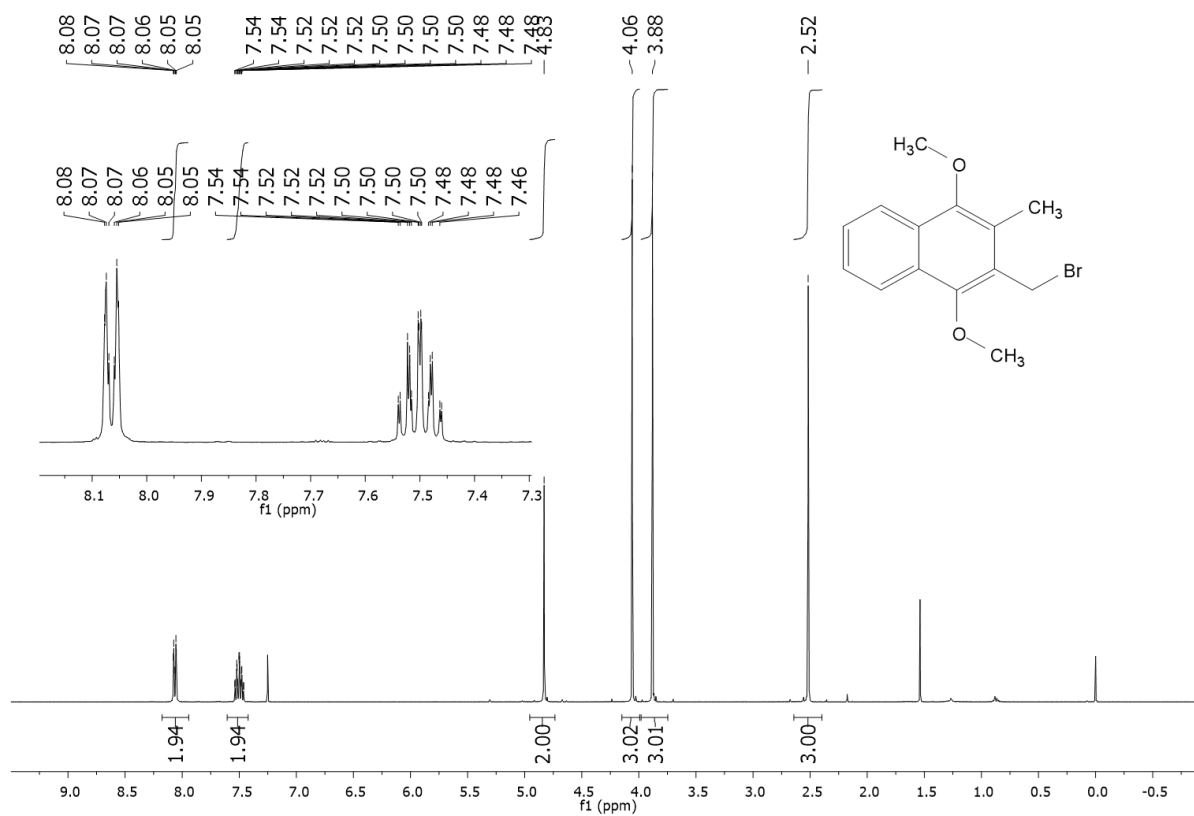
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### Table of Contents

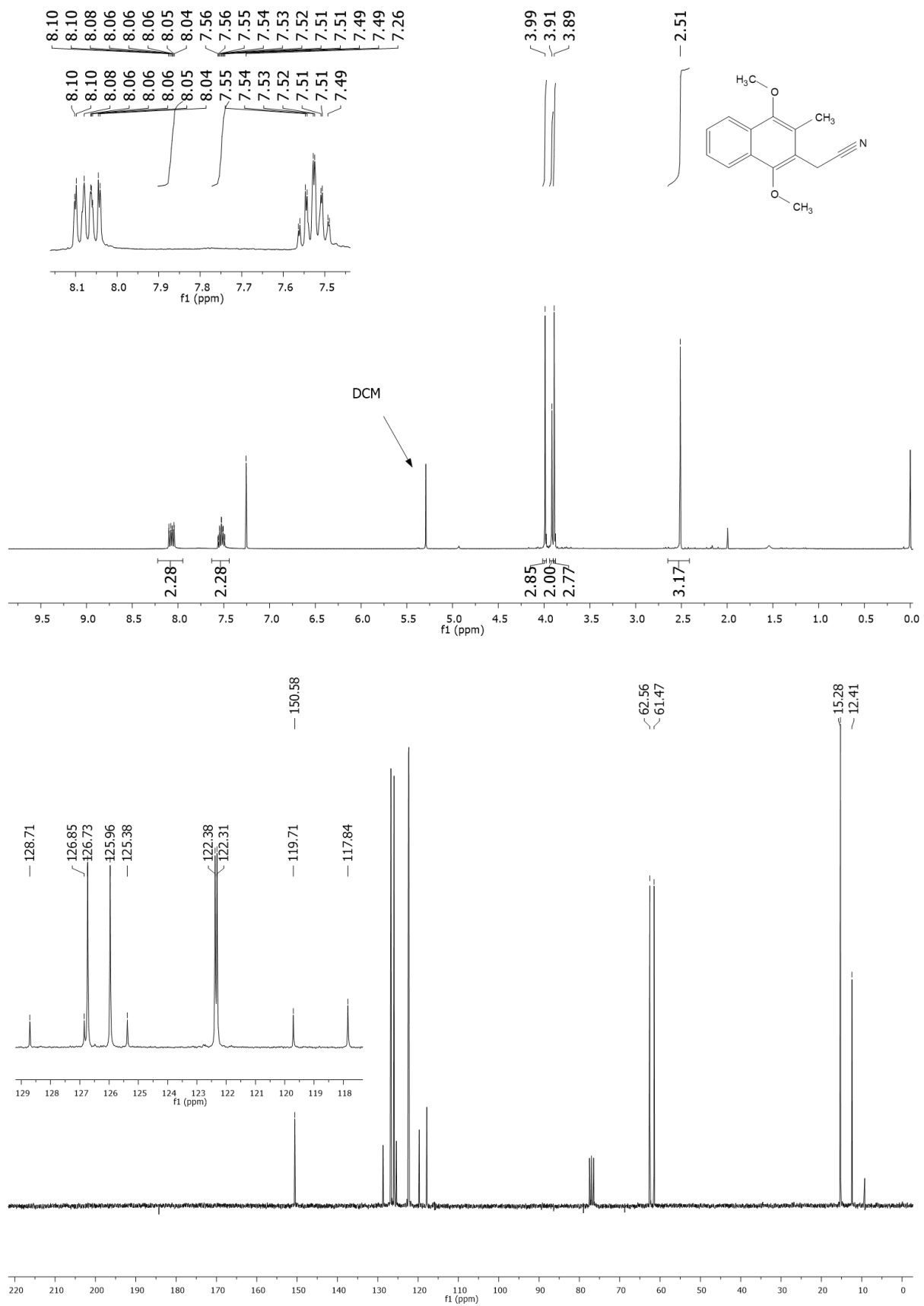
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		Page
1.	<sup>1</sup> H and <sup>13</sup> C spectra of compound <b>7</b>	S2
2.	<sup>1</sup> H and <sup>13</sup> C spectra of compound <b>8</b>	S3
3.	<sup>1</sup> H and <sup>13</sup> C spectra of compound <b>9</b>	S4
4.	<sup>1</sup> H and <sup>13</sup> C spectra of compounds <b>11a-k</b>	S5-S15
5.	<sup>1</sup> H and <sup>13</sup> C spectra of compounds <b>12a-j</b>	S16-S26
6.	<sup>1</sup> H and <sup>13</sup> C spectra of compounds <b>13i-j</b>	S27-S28
7.	<sup>1</sup> H and <sup>13</sup> C spectra of compound <b>14</b>	S29
8.	Biological evaluation of compounds <b>11a-k</b> and <b>12a-j</b>	S30-S31

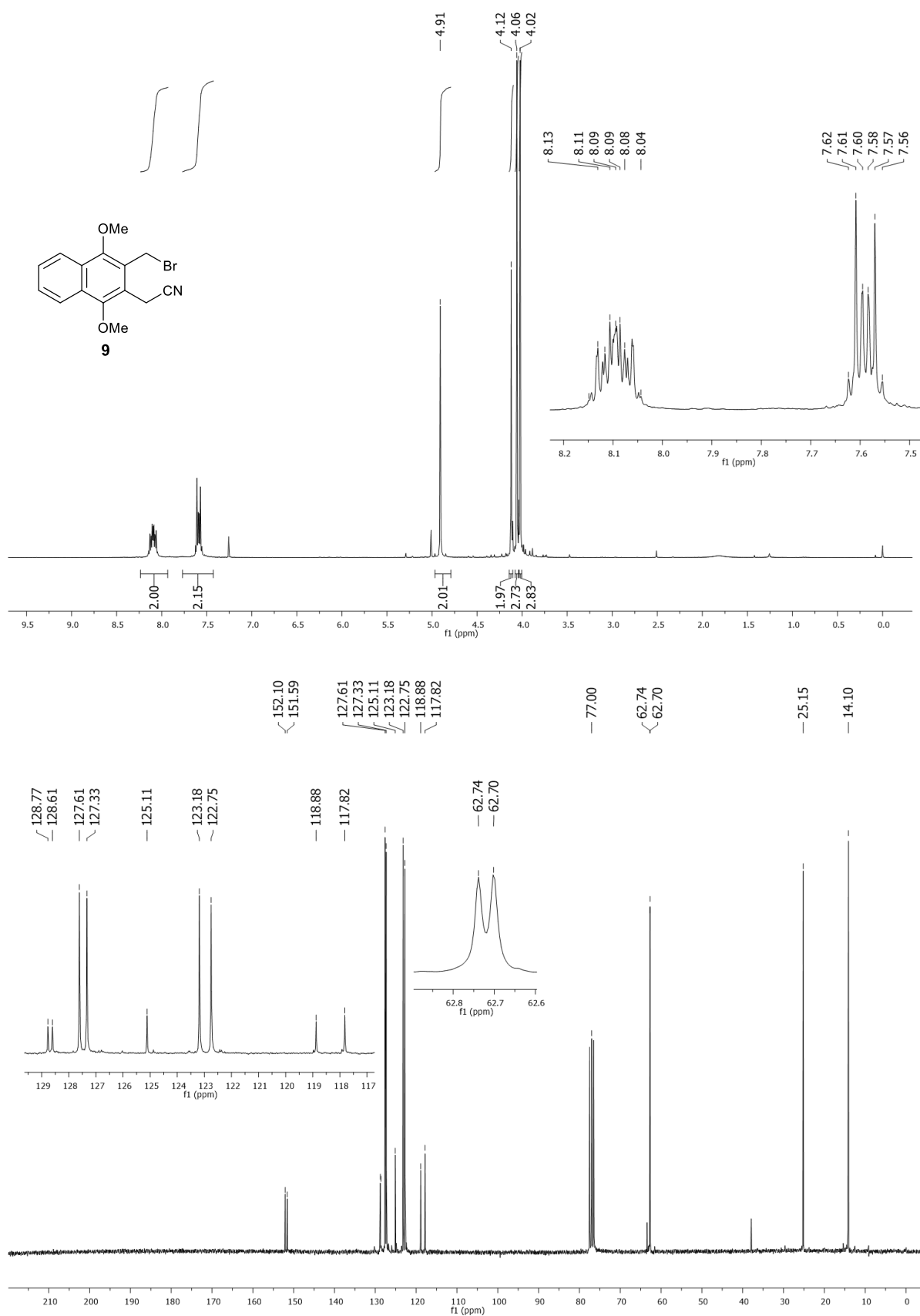
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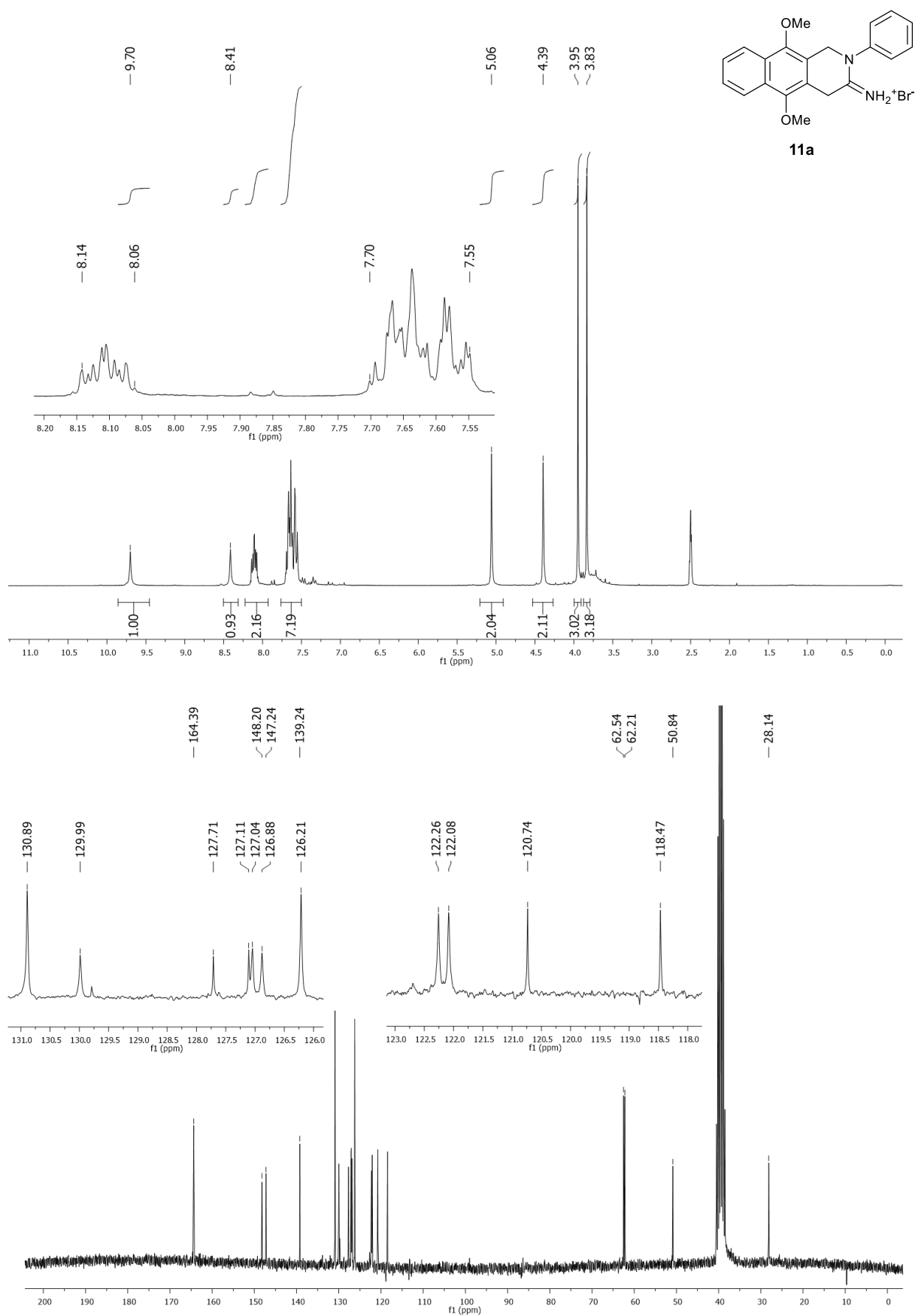
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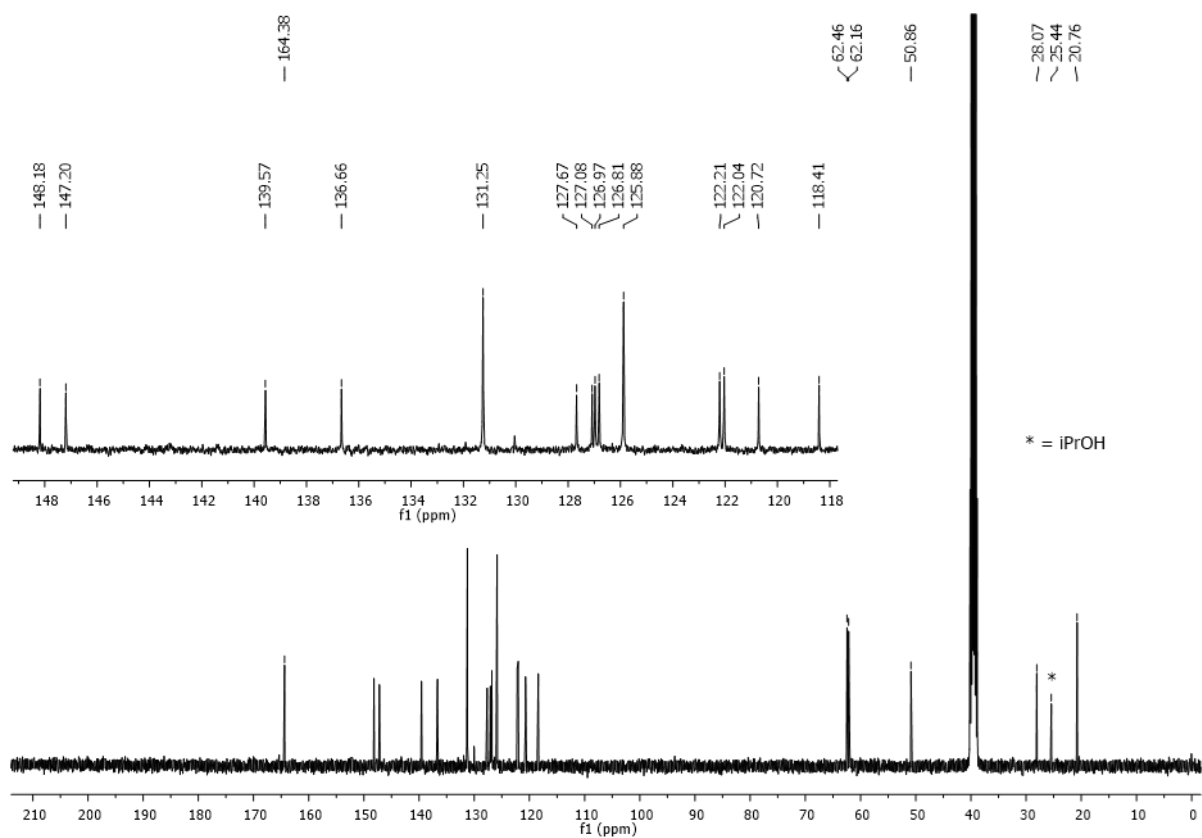
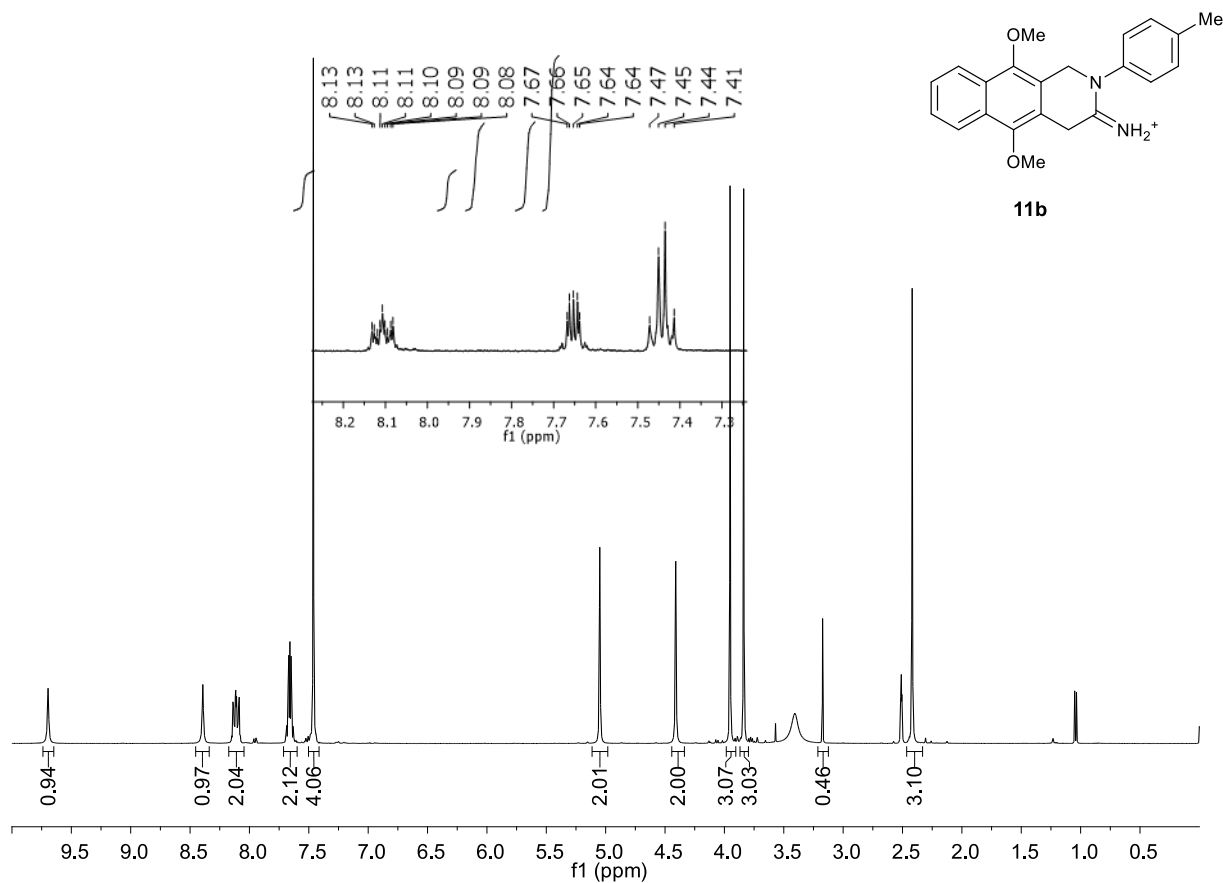


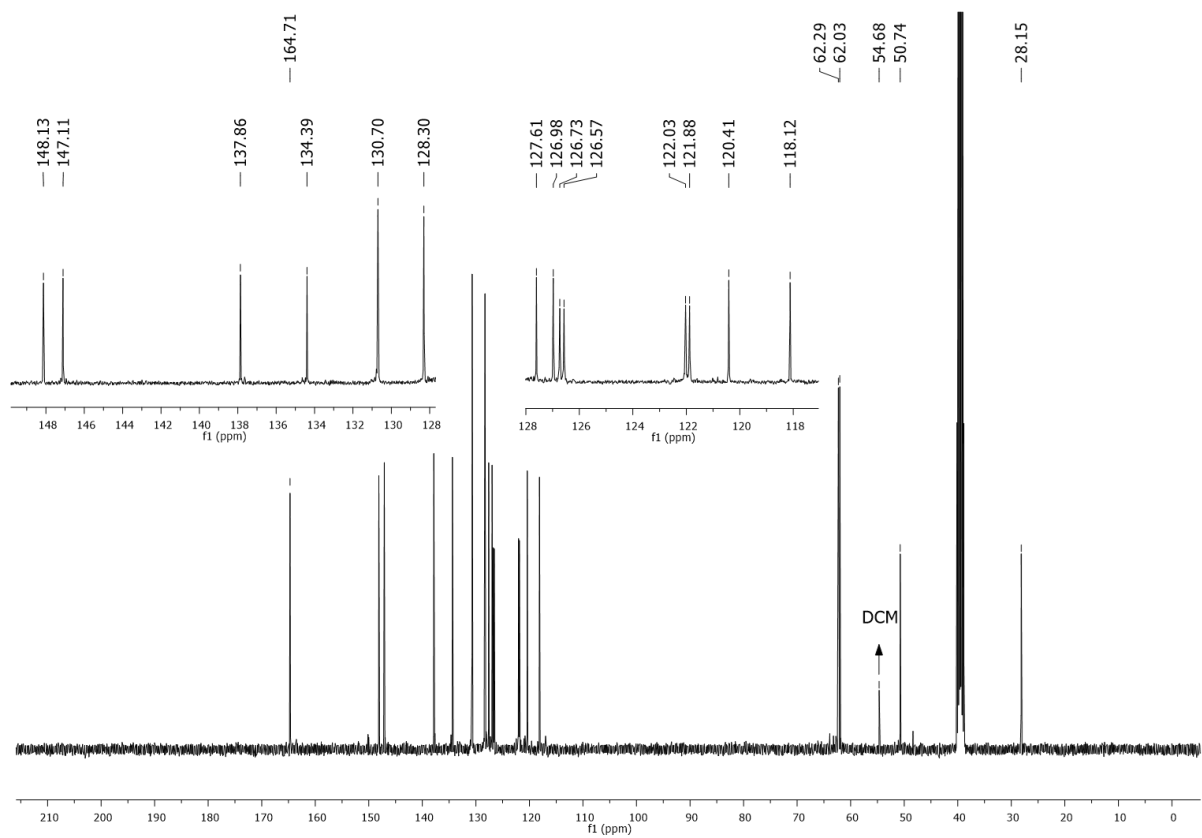
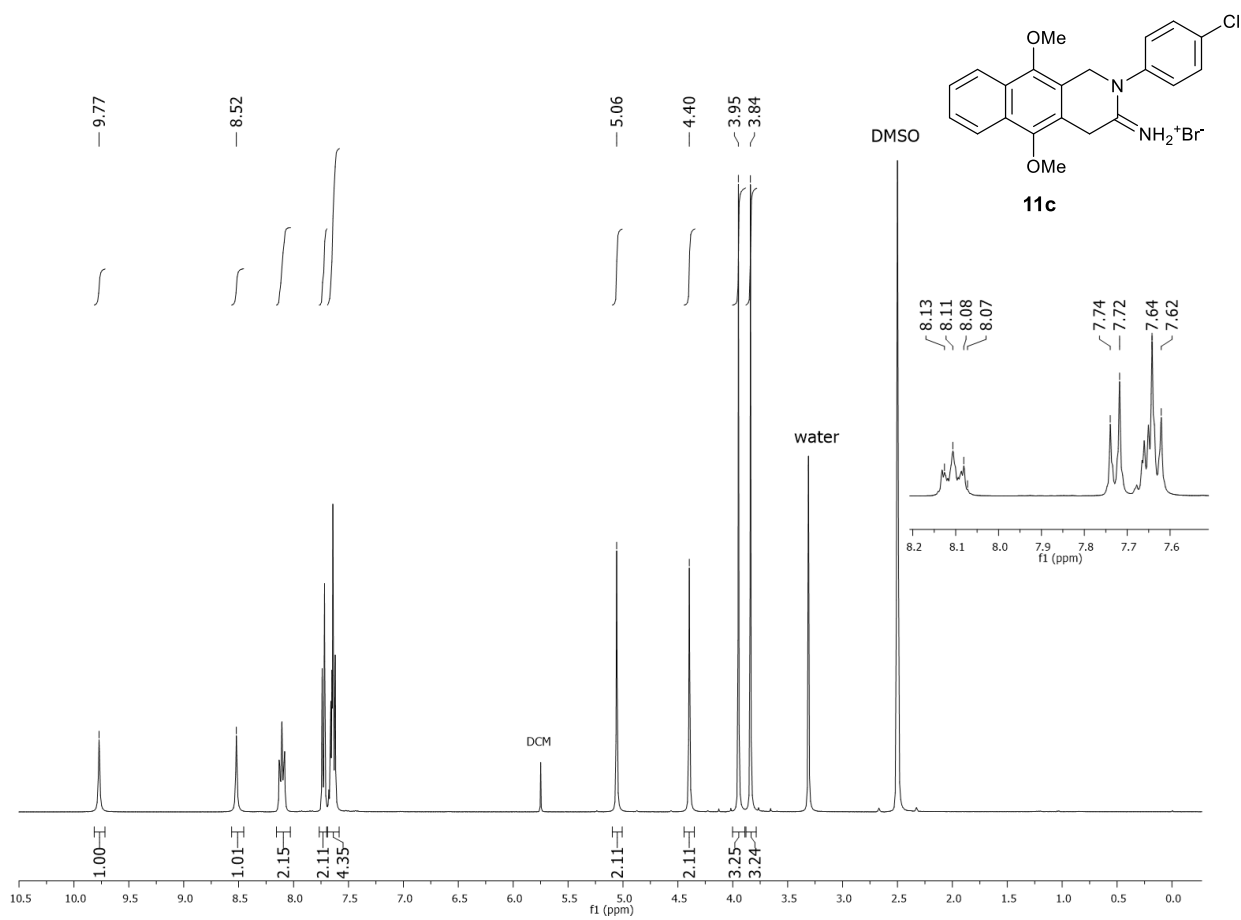
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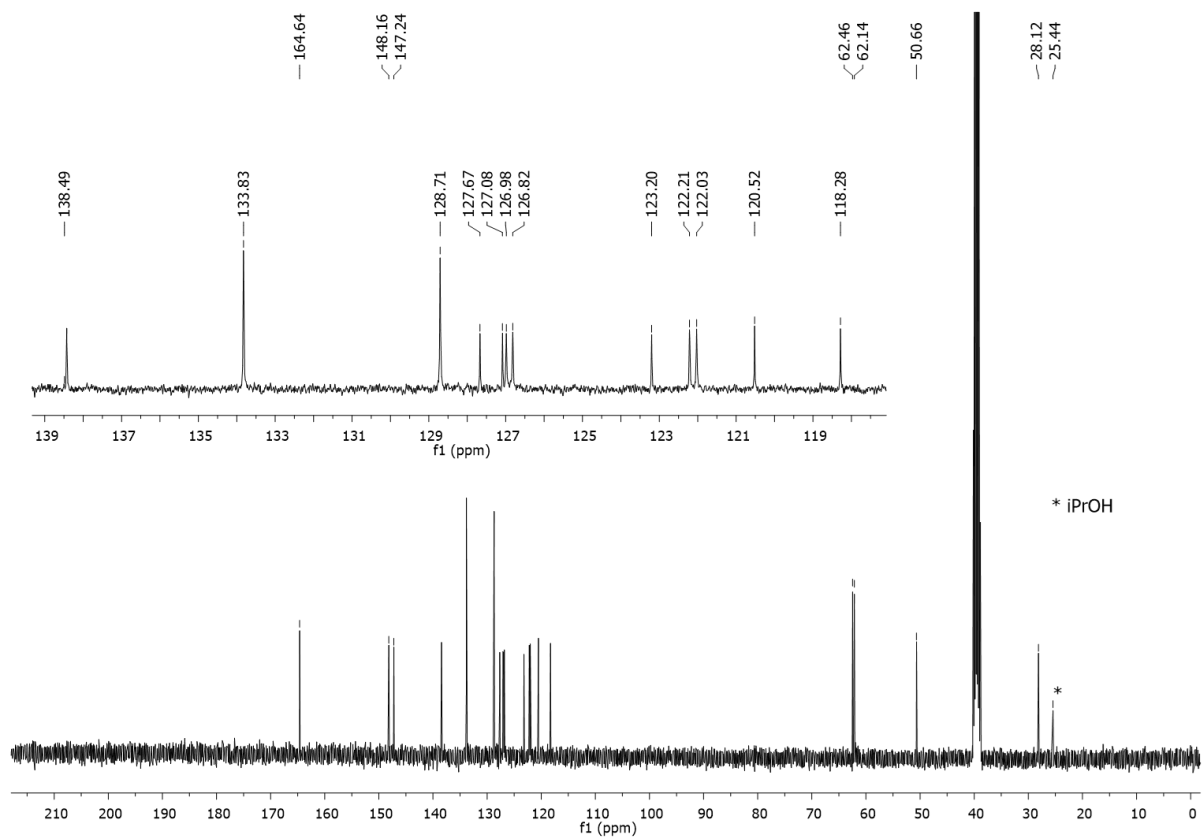
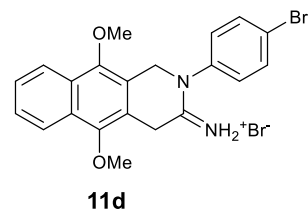
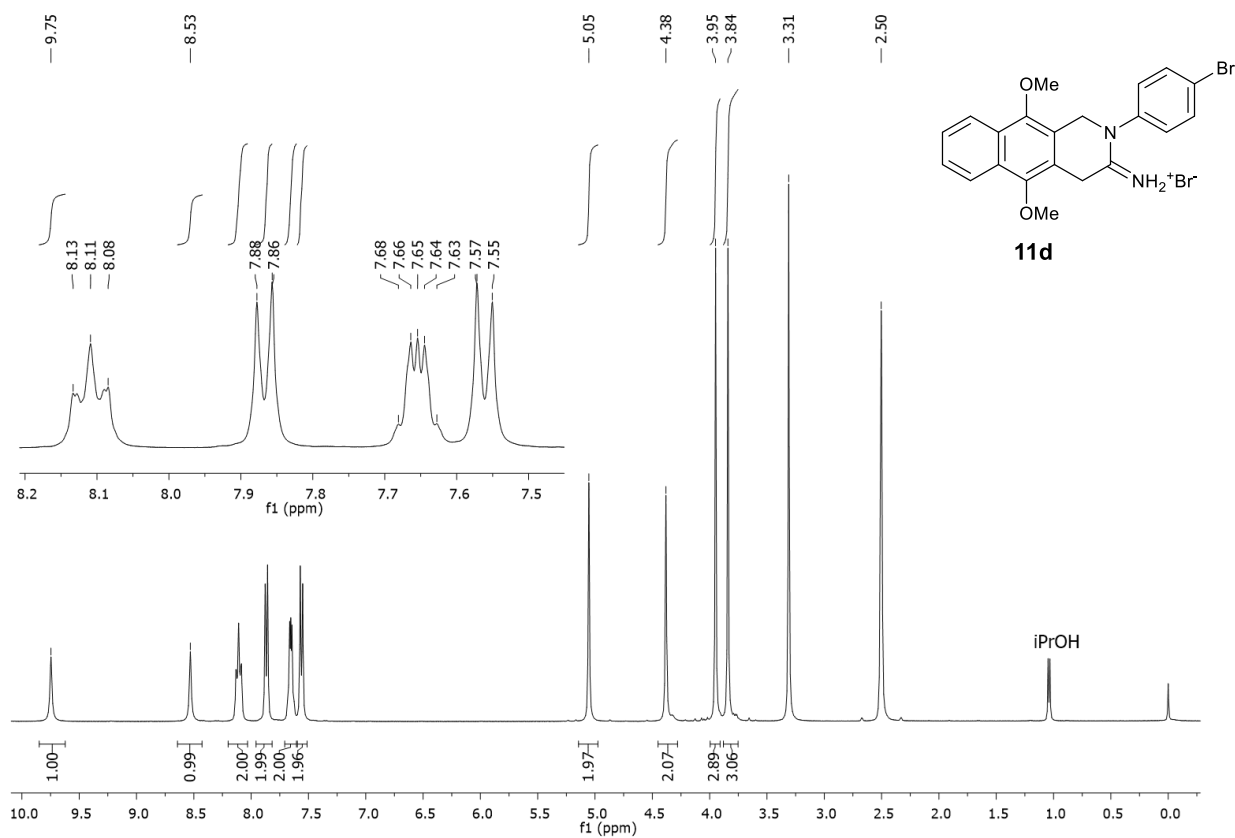


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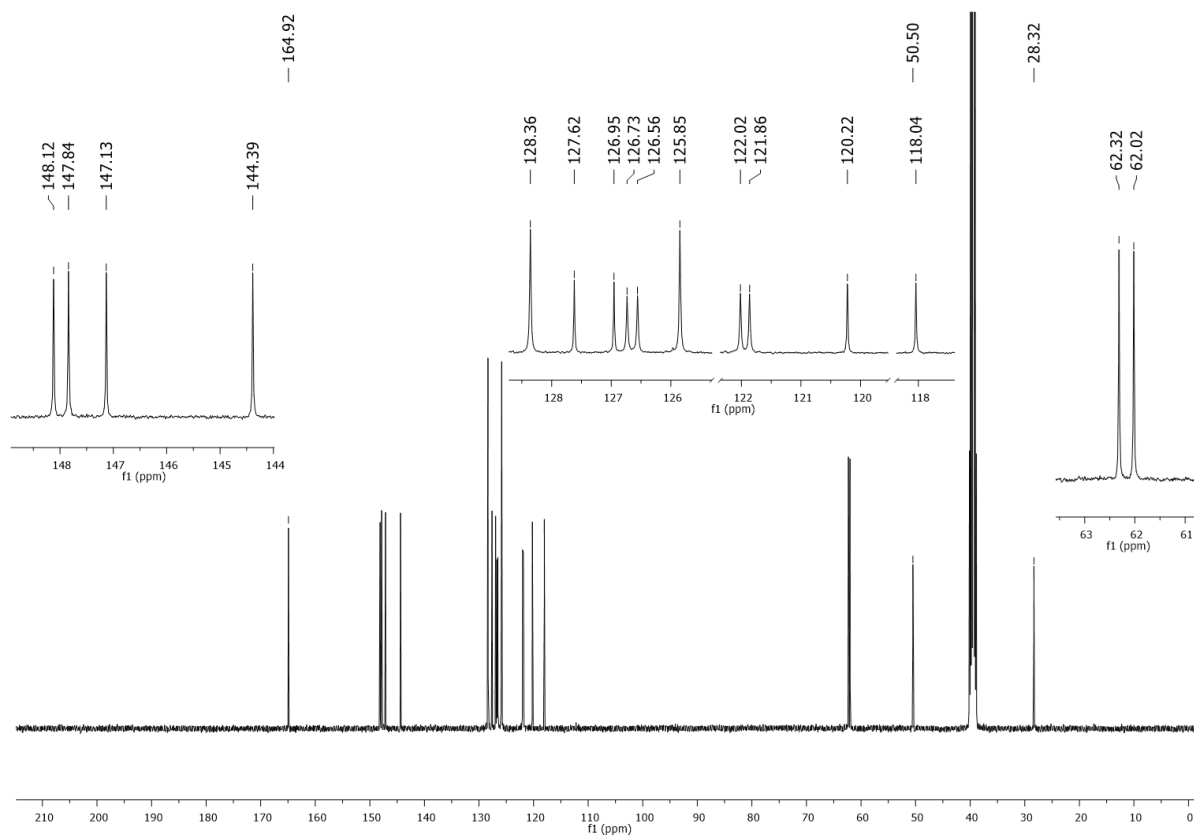
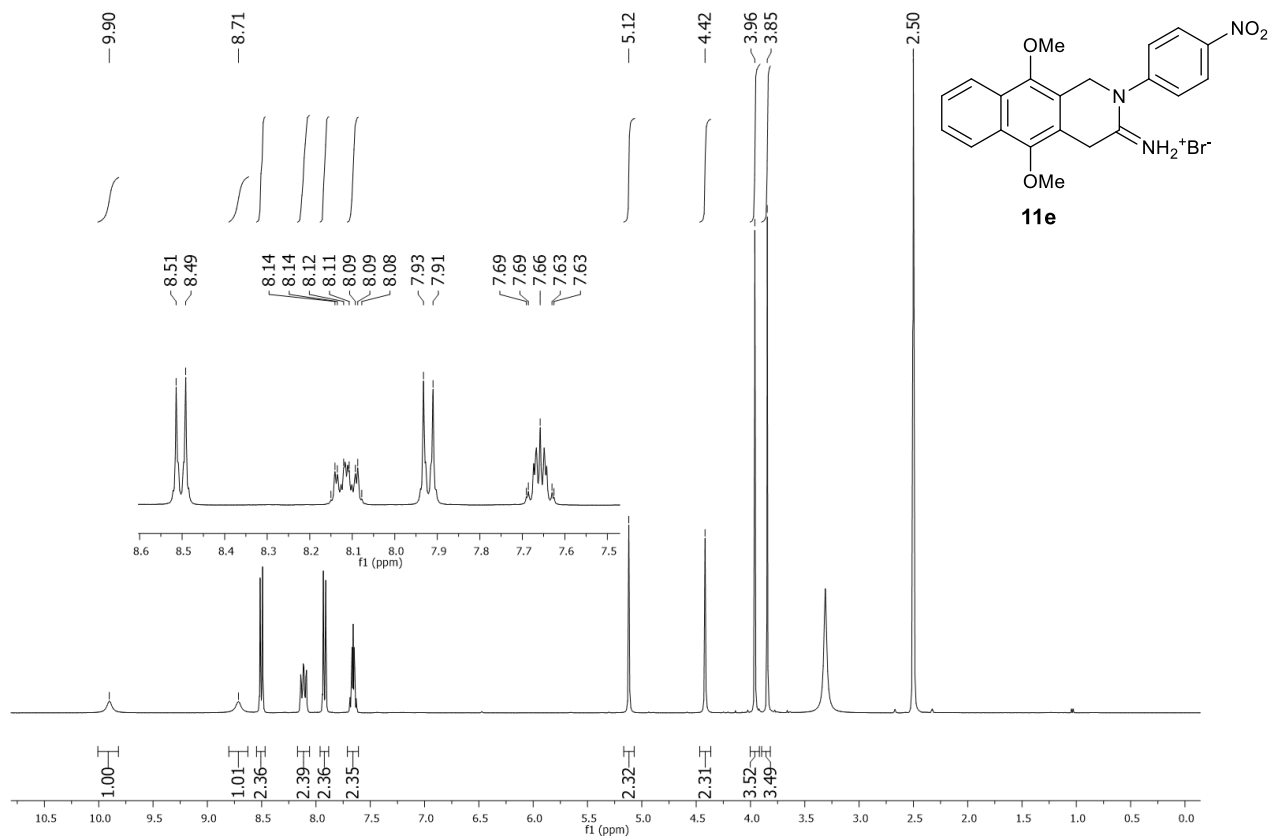


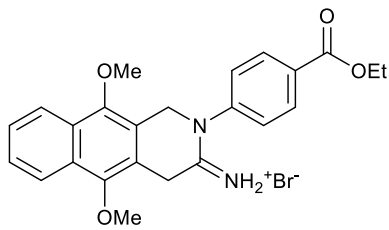
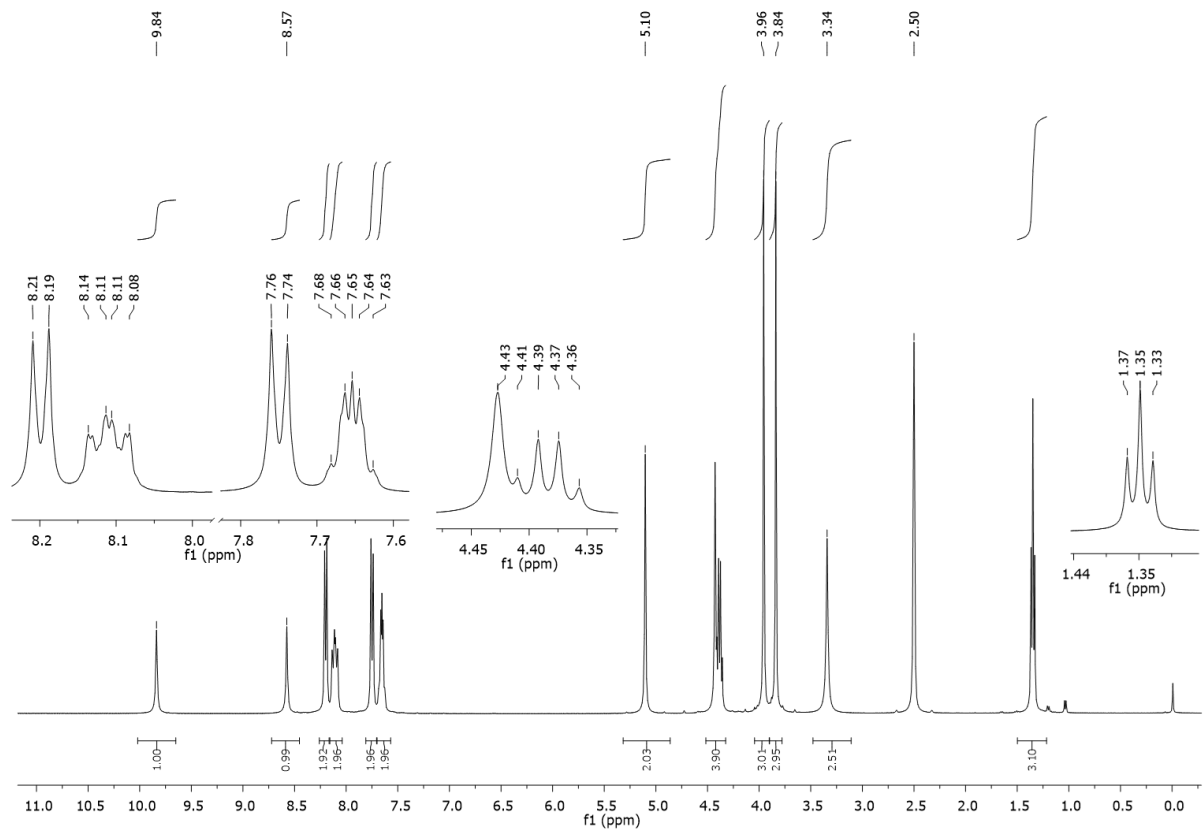




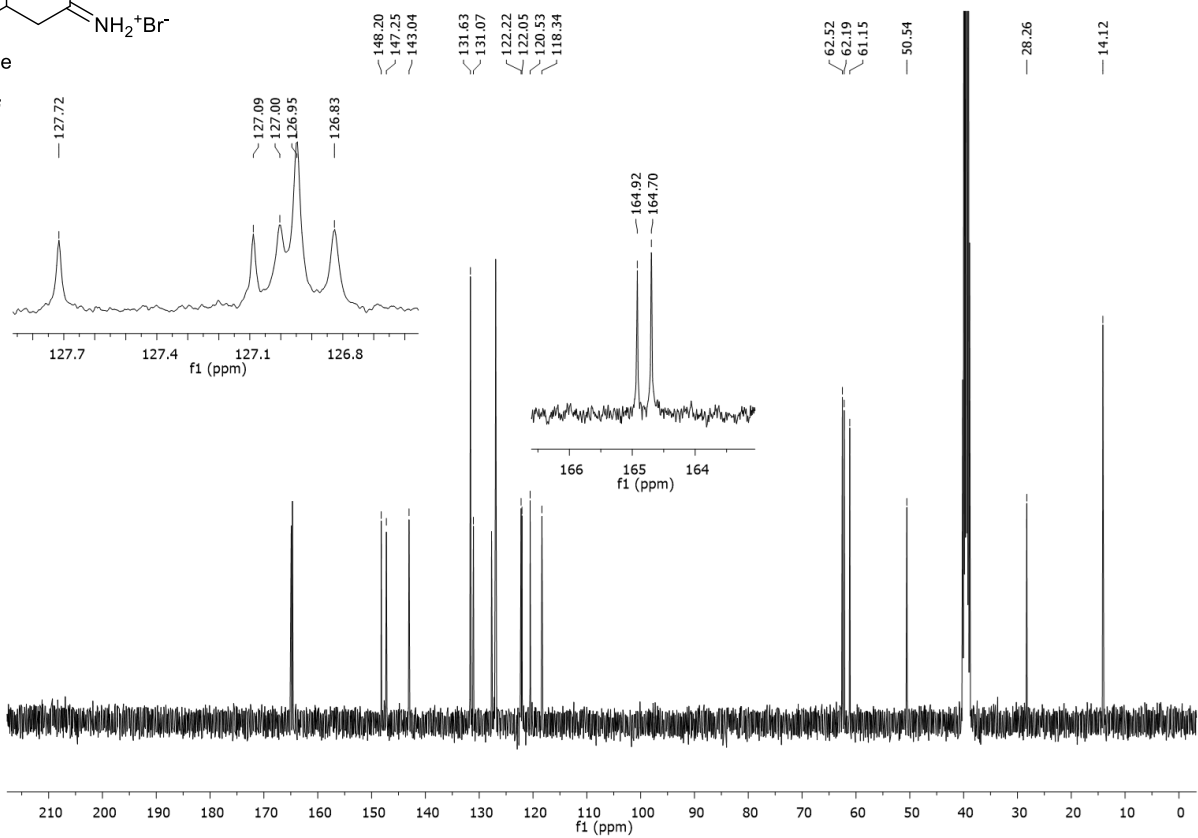


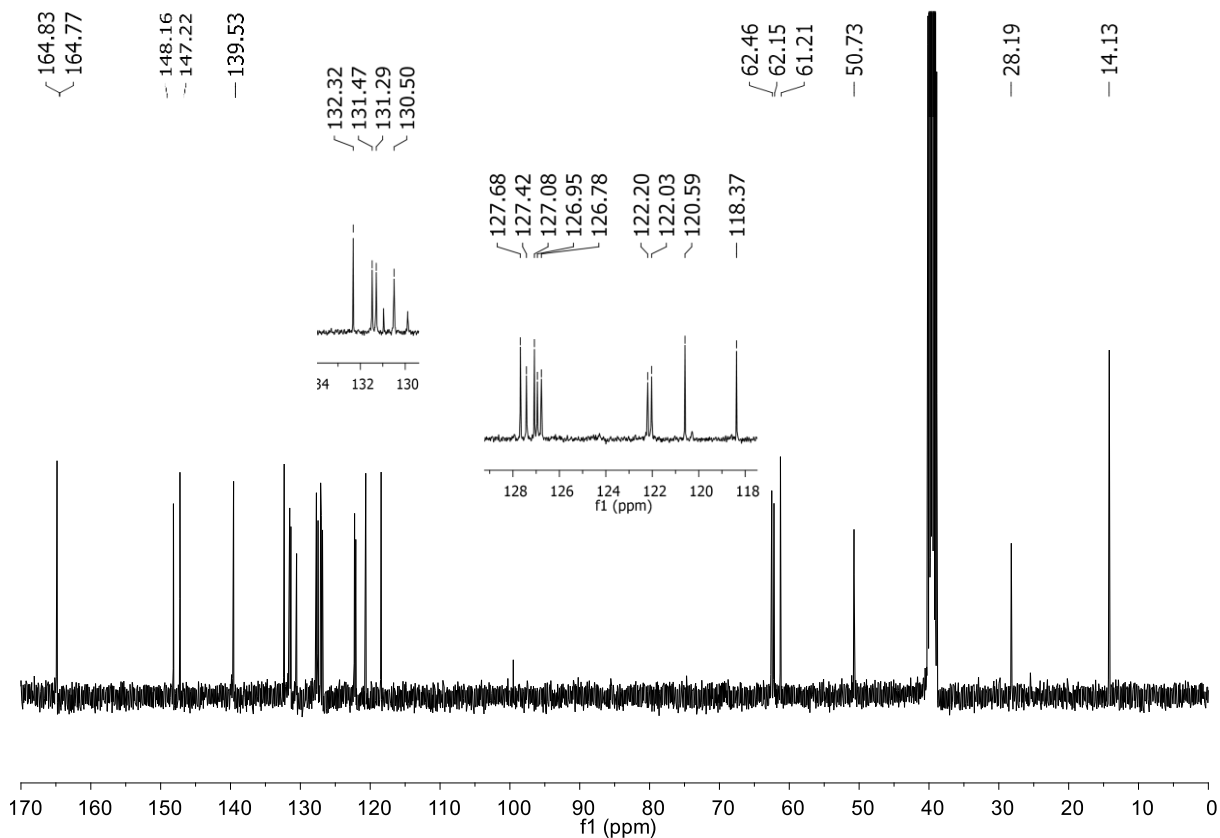
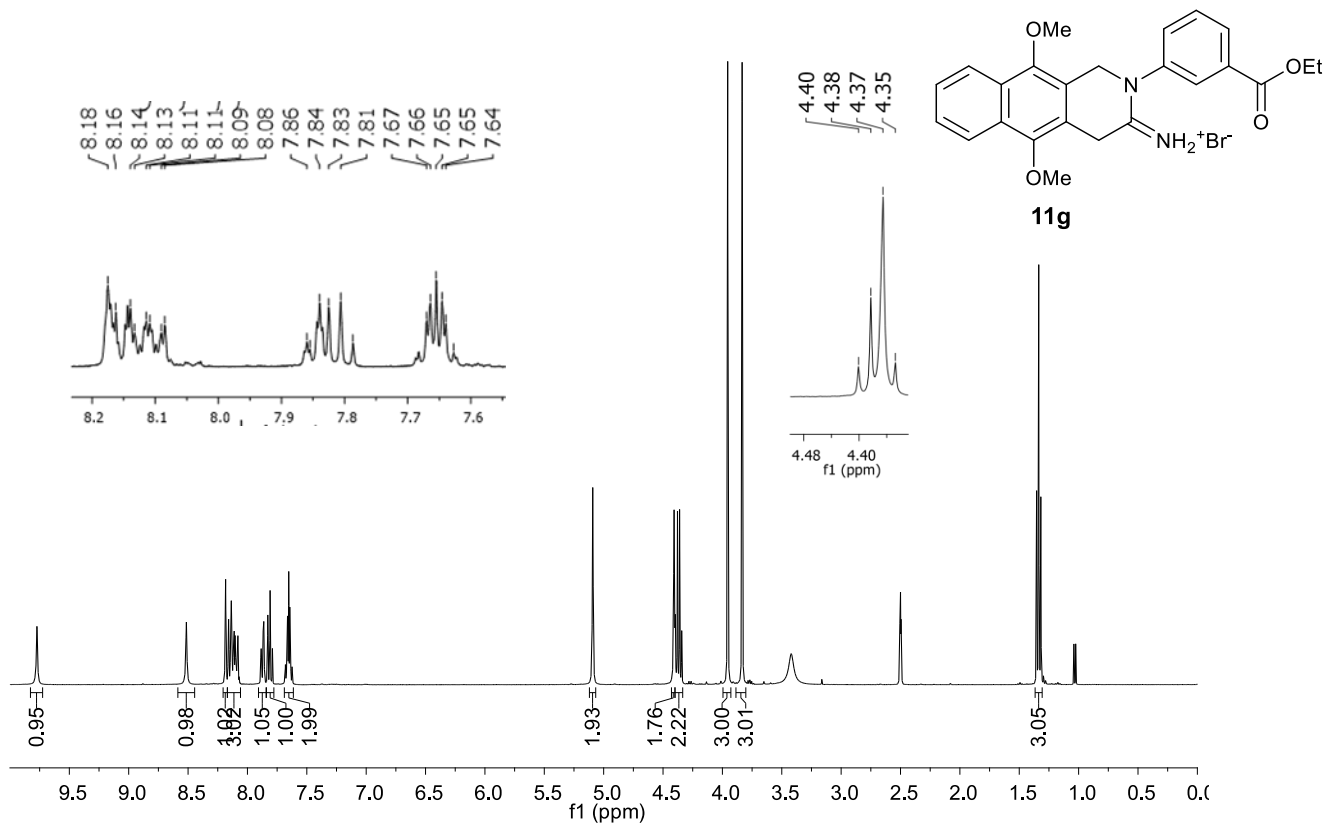


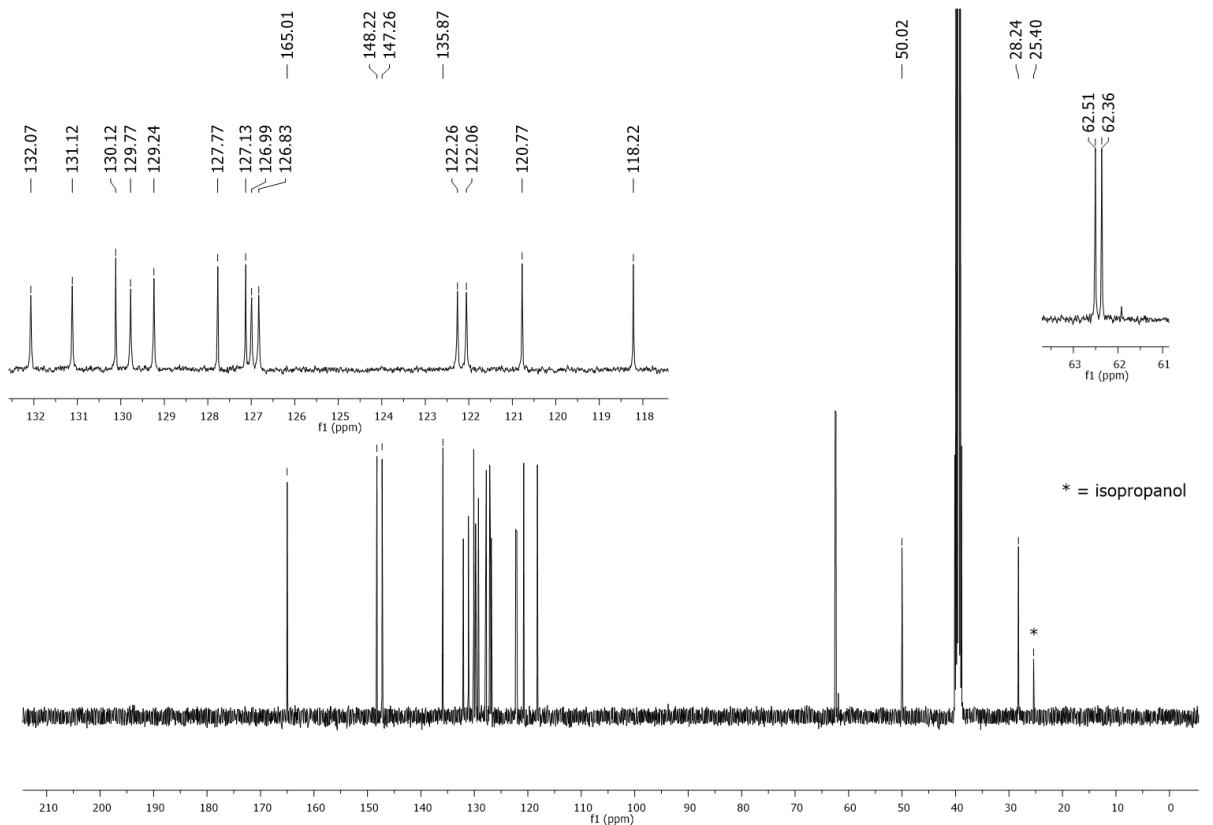
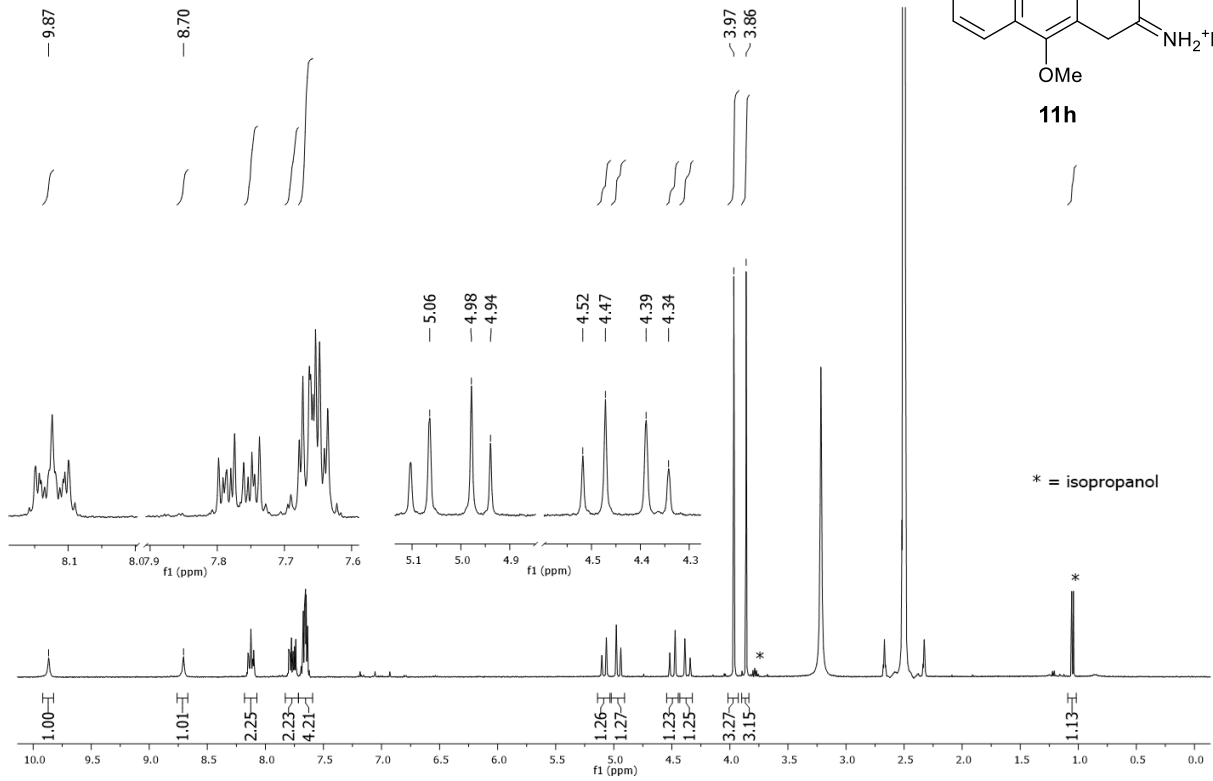
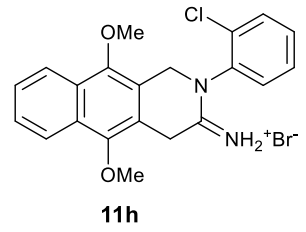


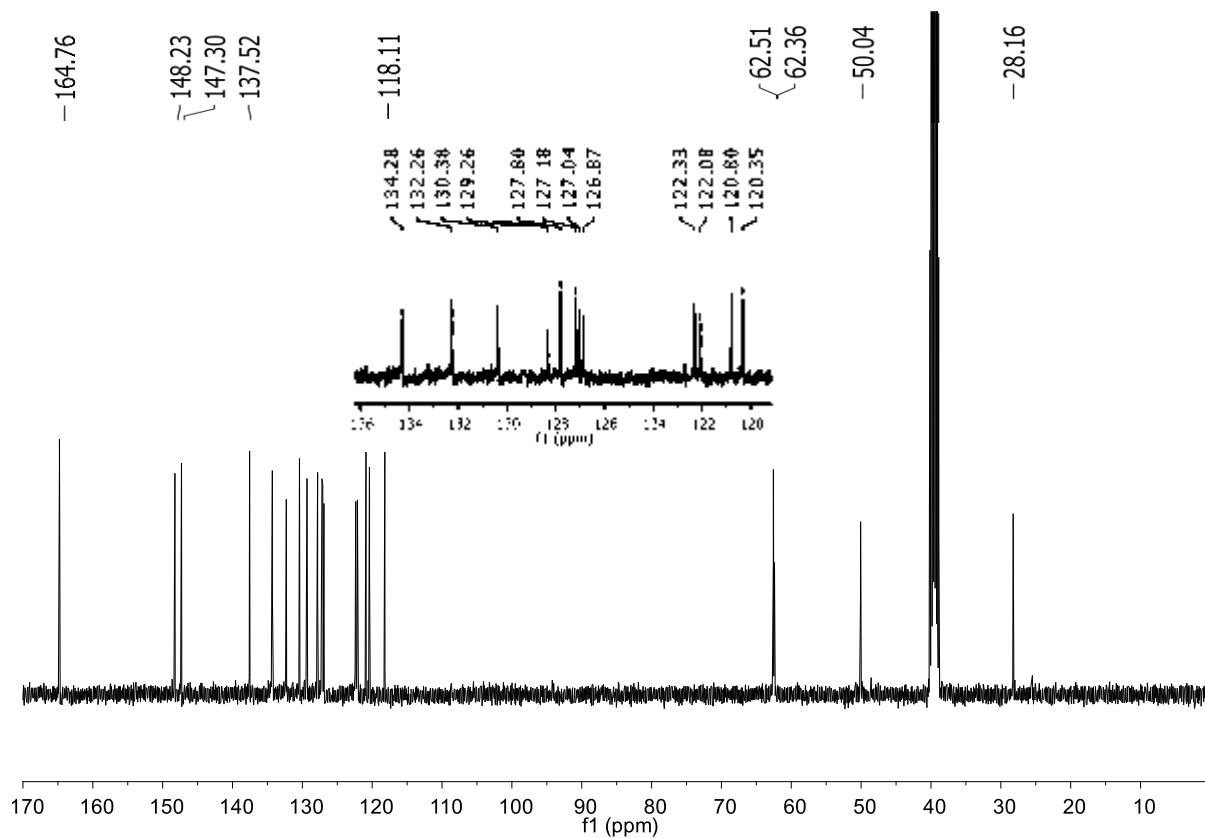
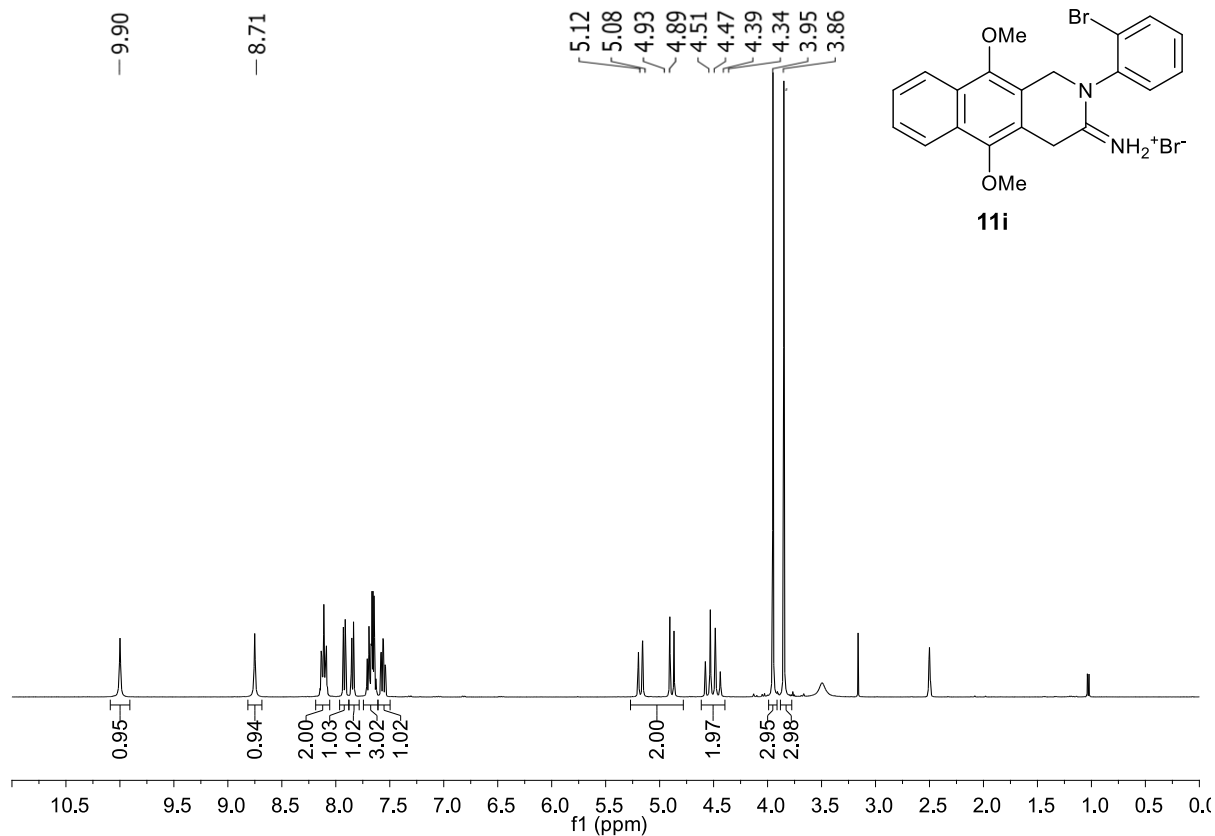


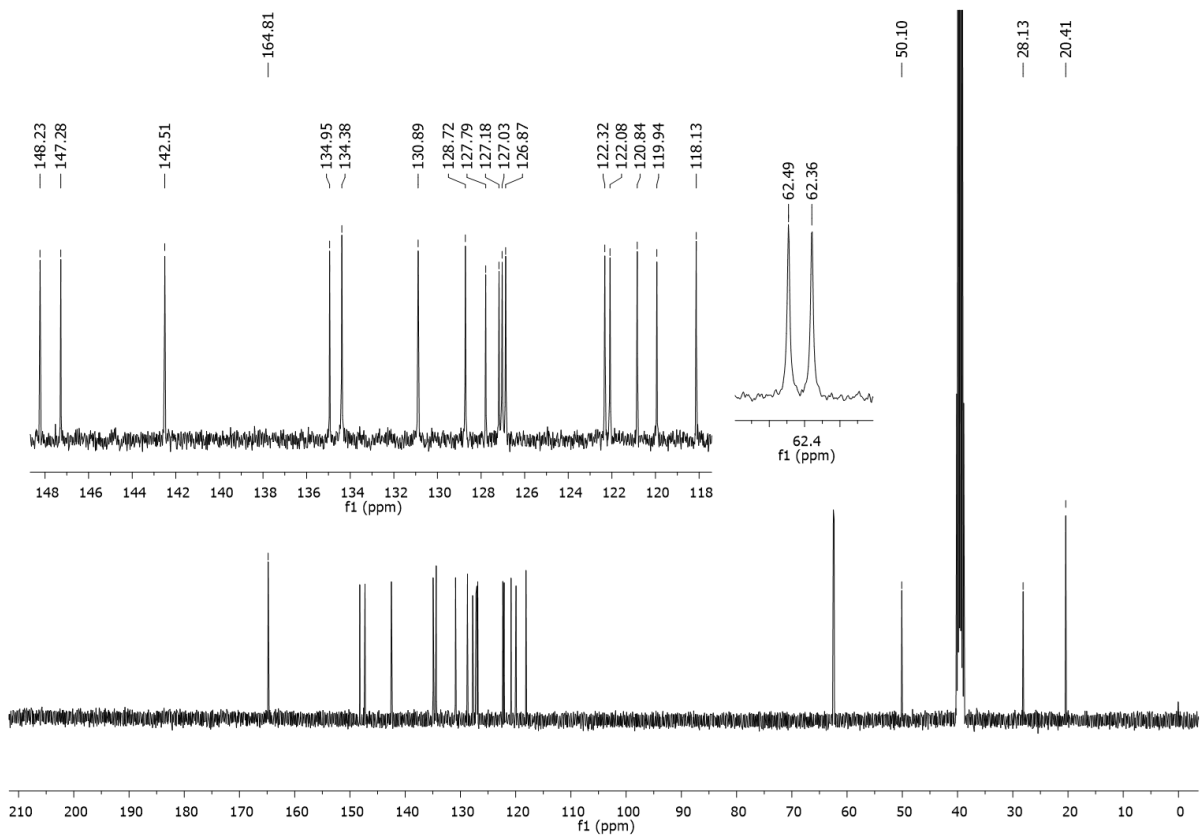
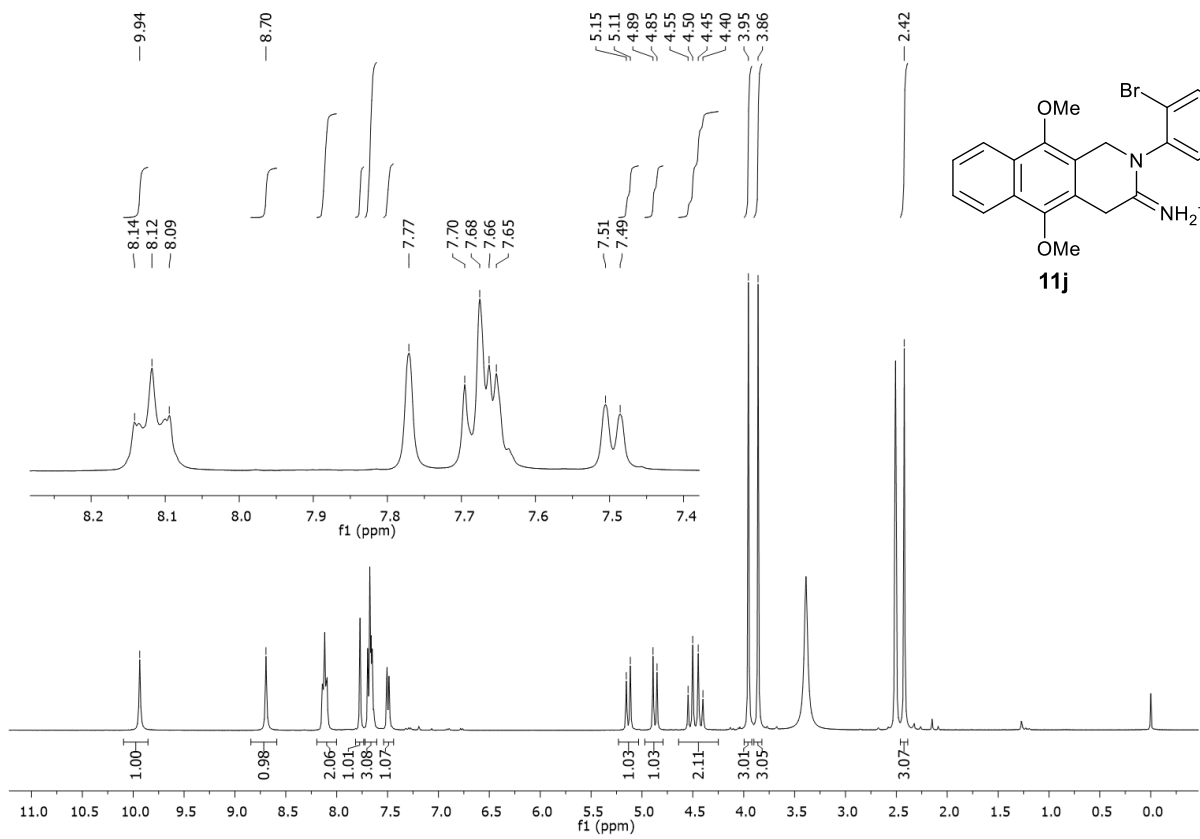
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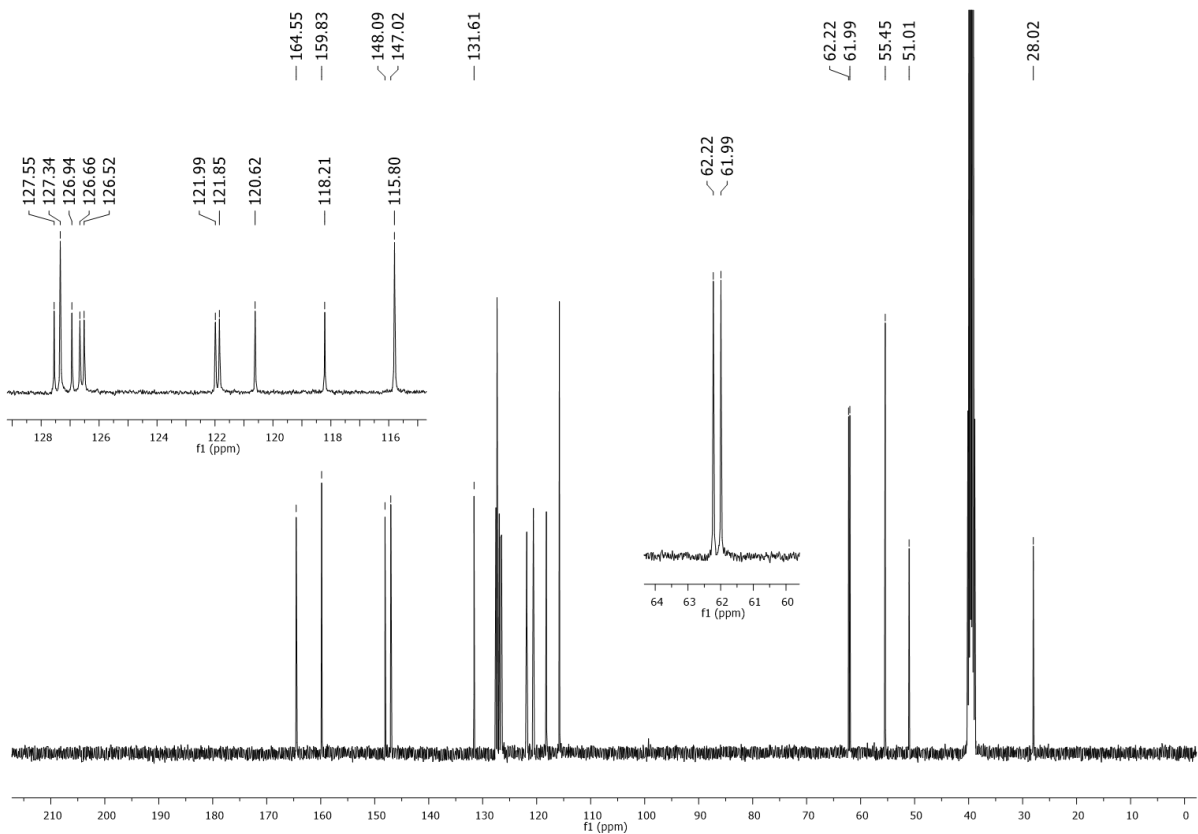
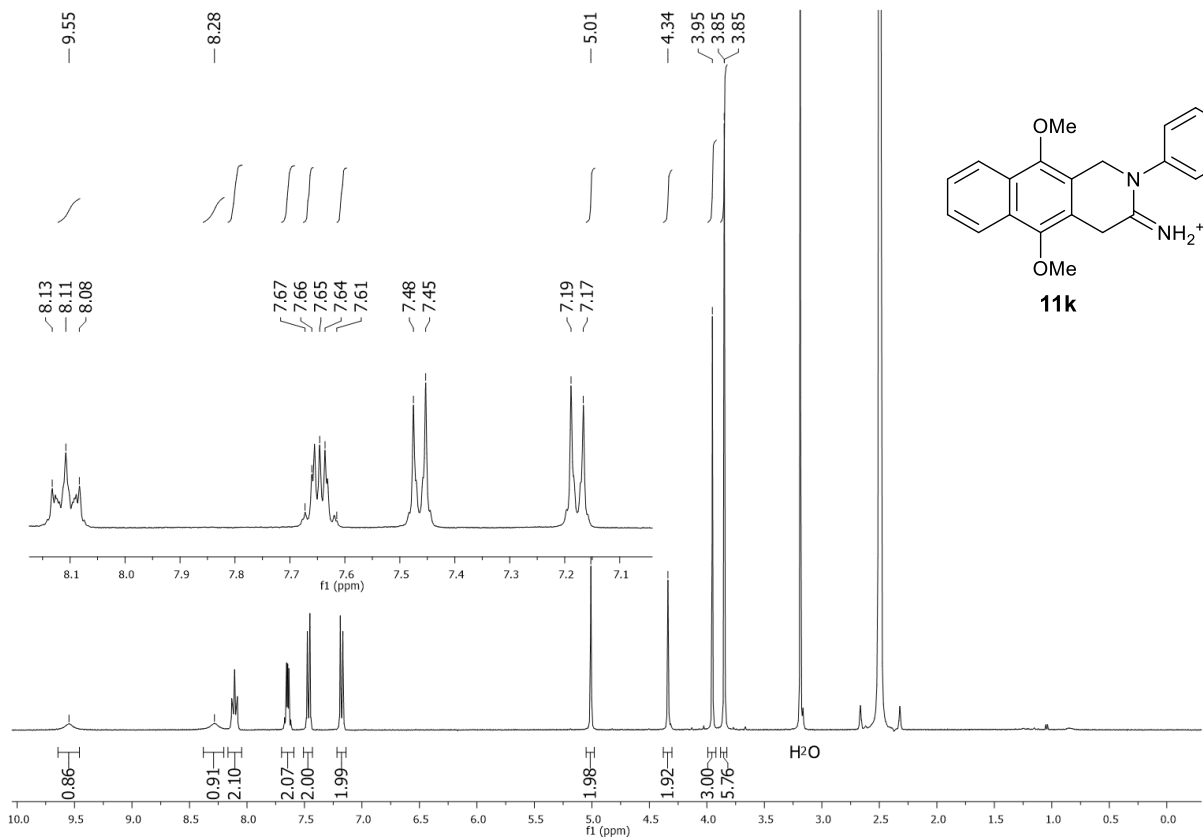




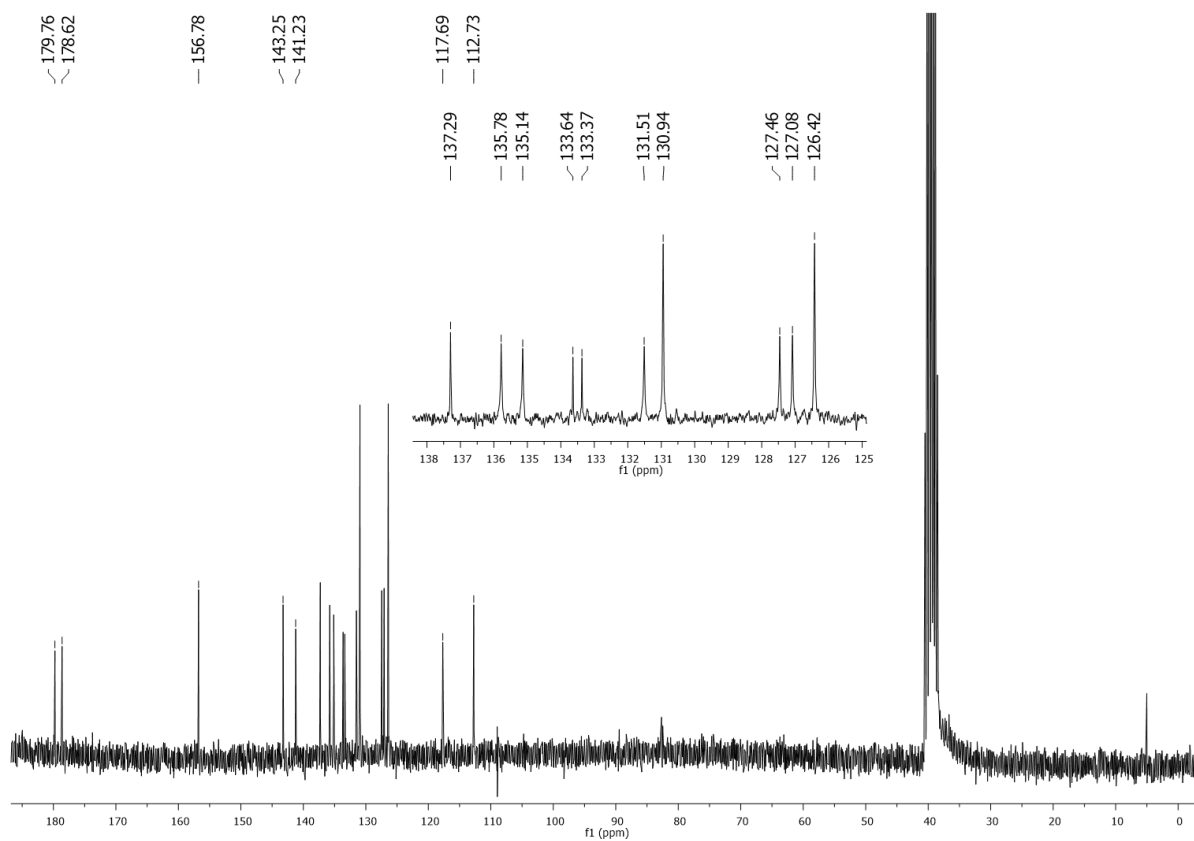
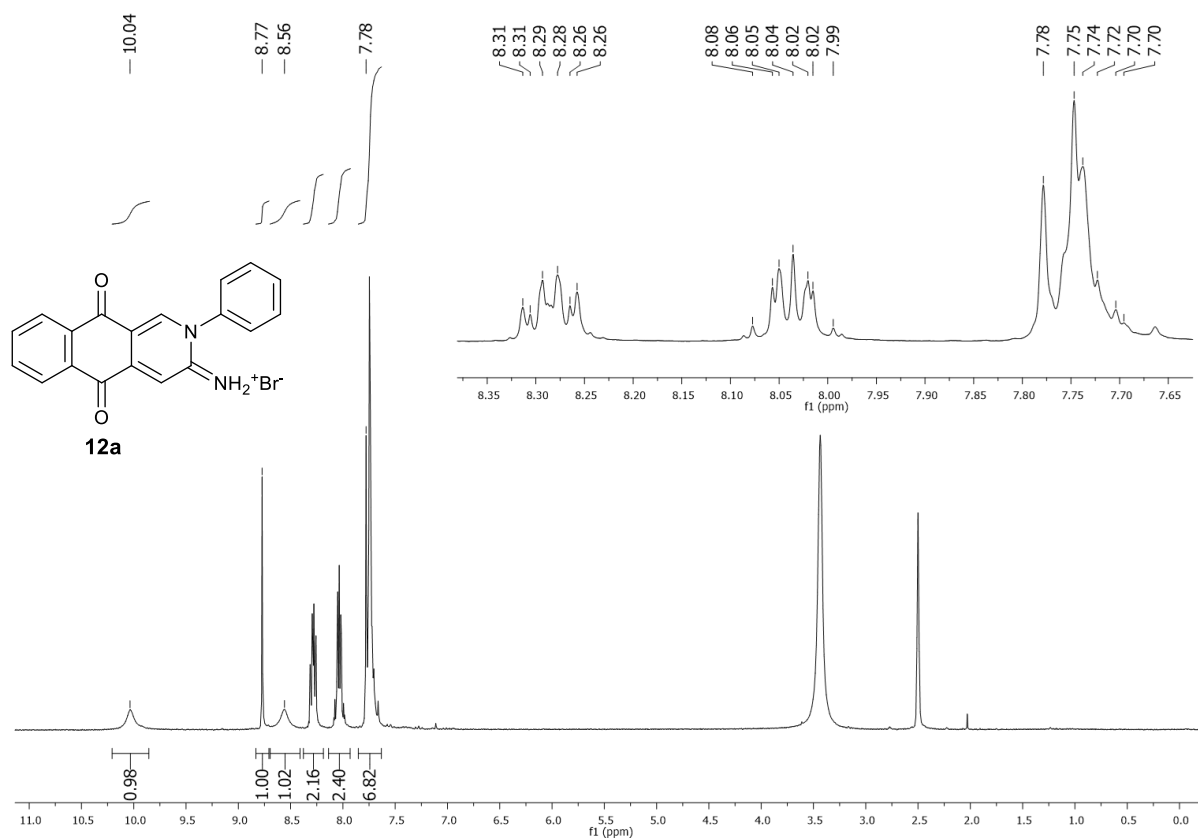




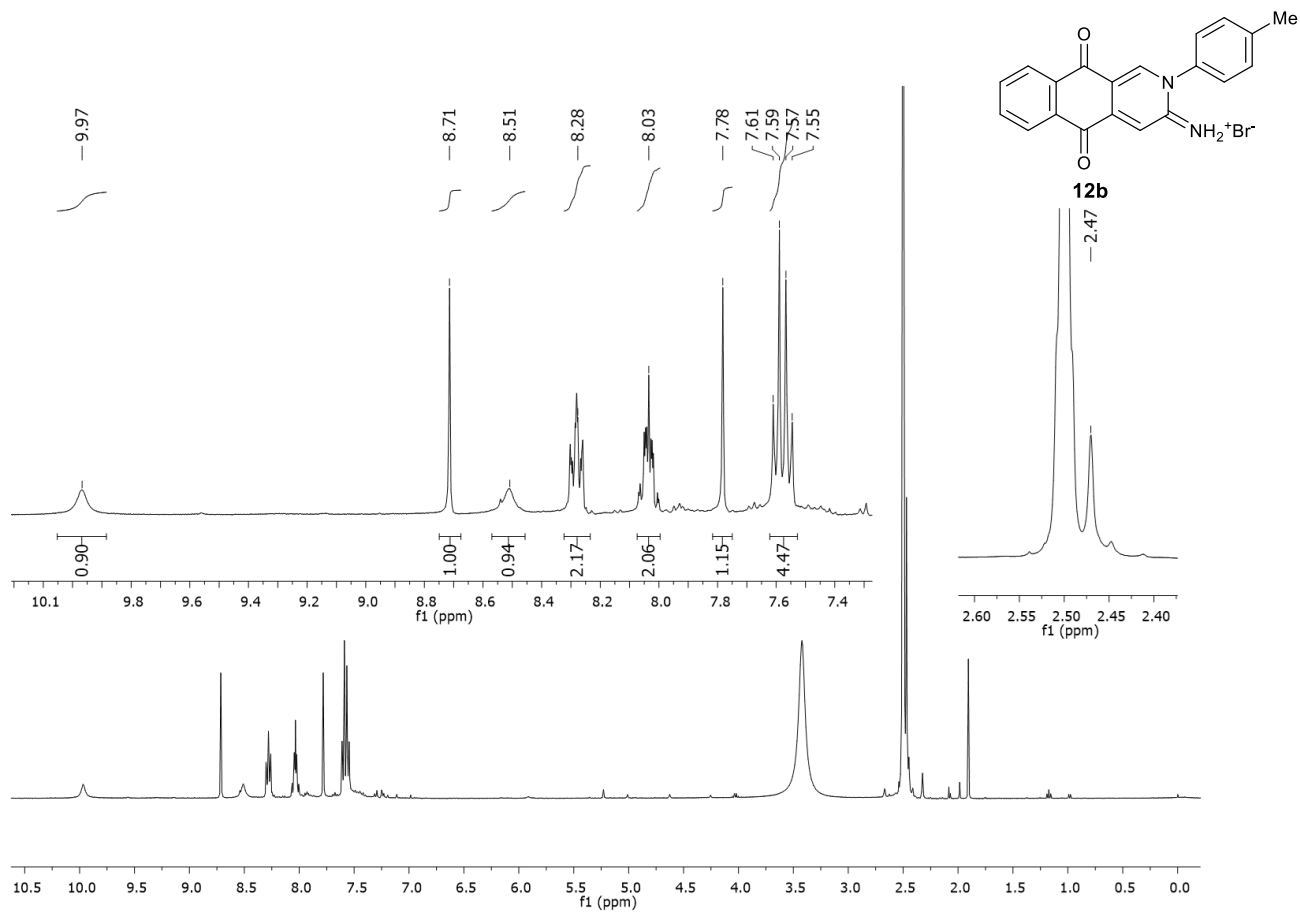




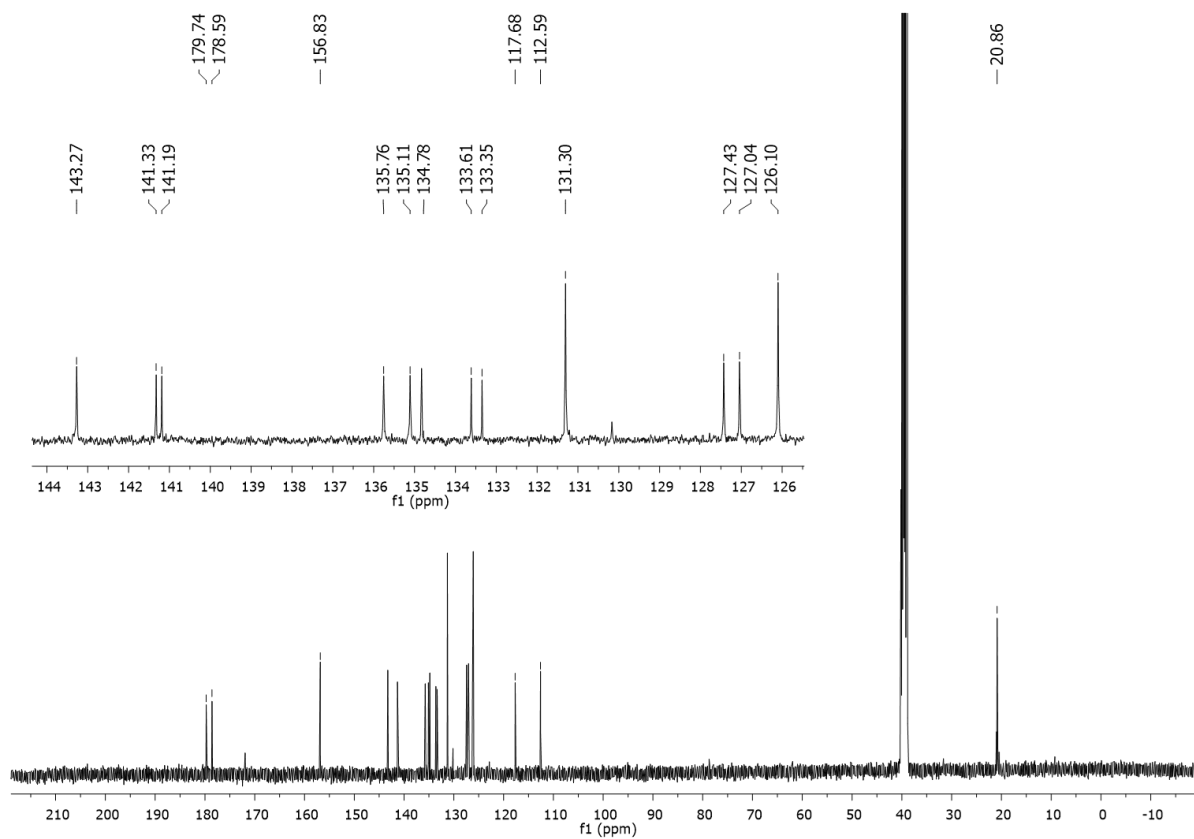
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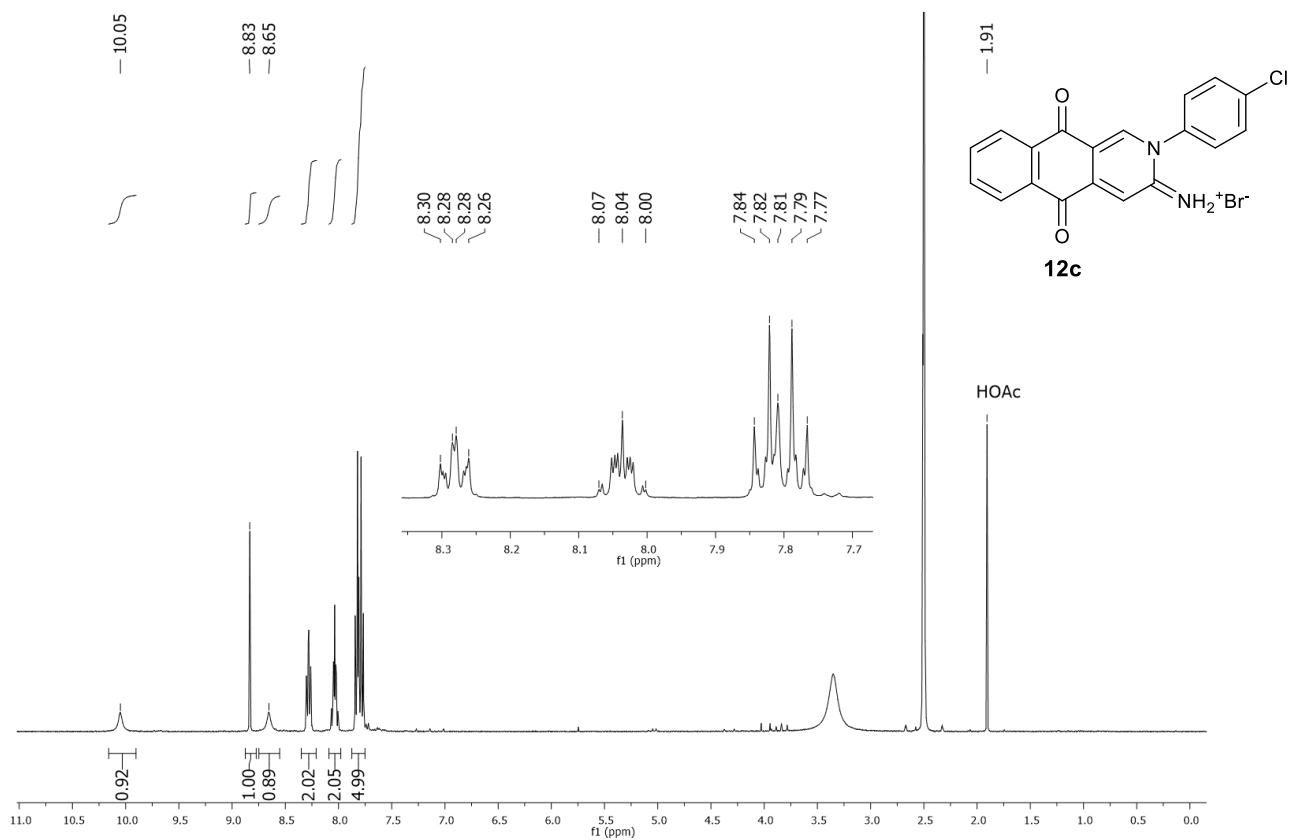




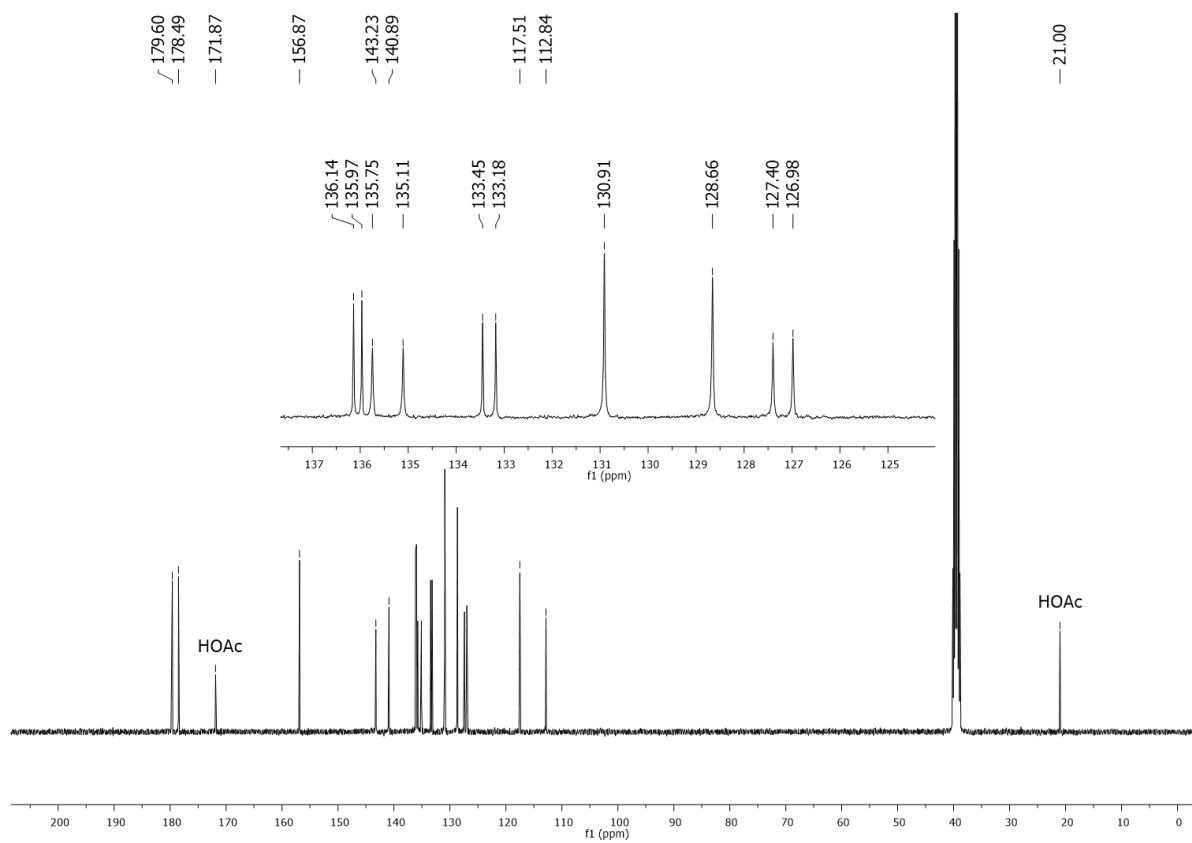


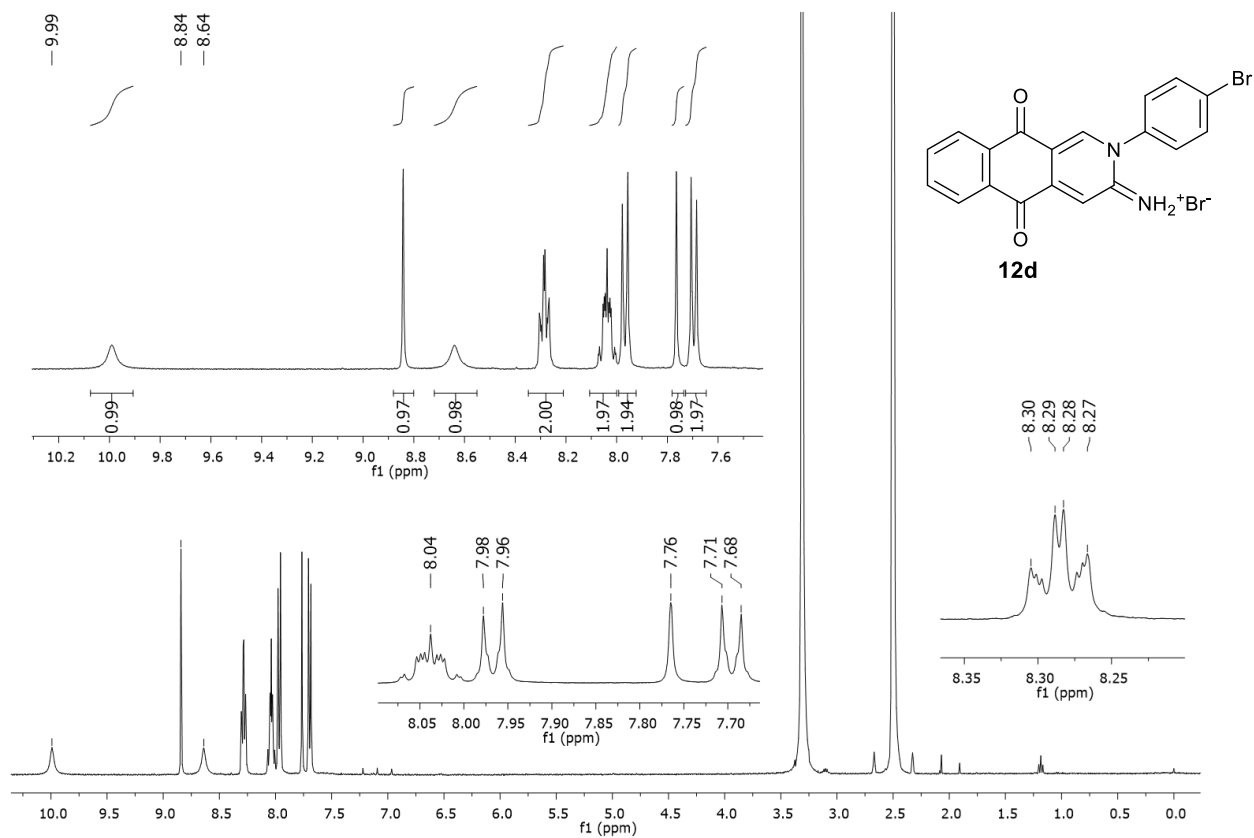
A triplet at 7.09 ppm ( $J = 51.1$  Hz) is observed in the <sup>1</sup>H NMR, which is typical for the NH<sub>4</sub><sup>+</sup> cation.



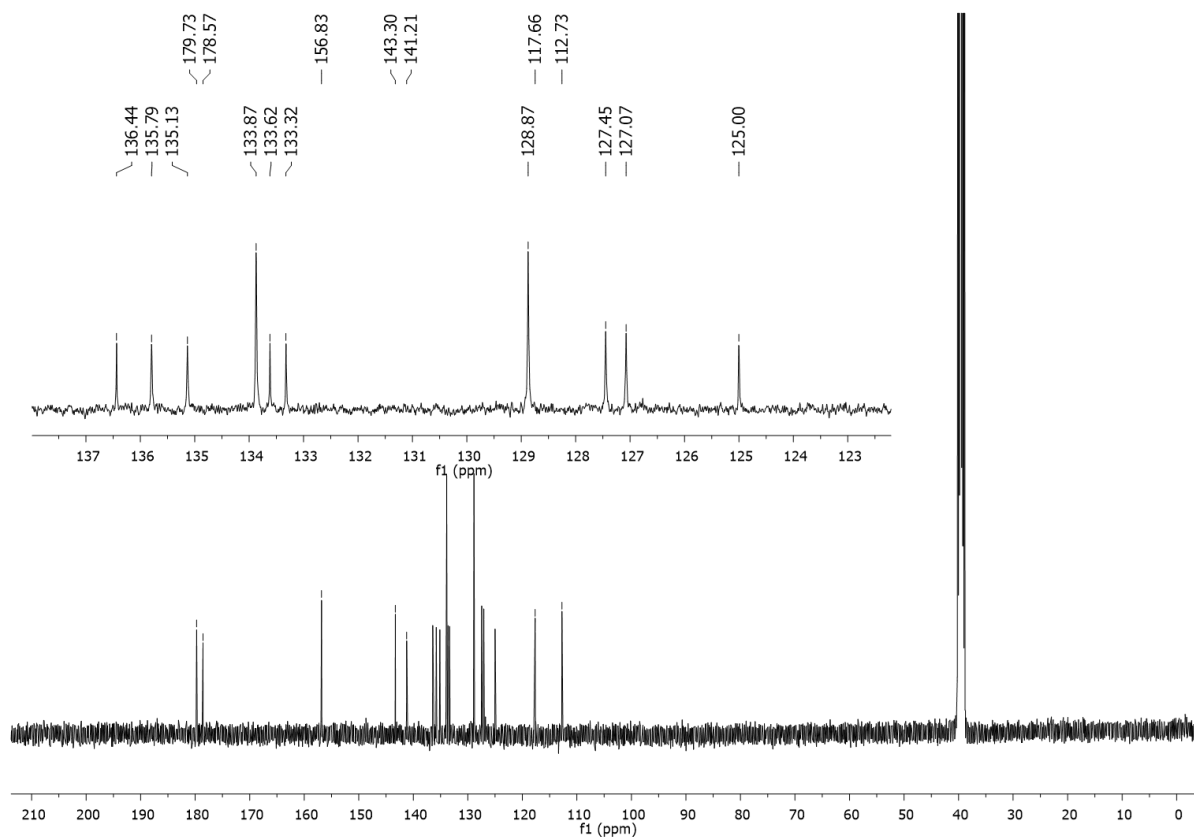


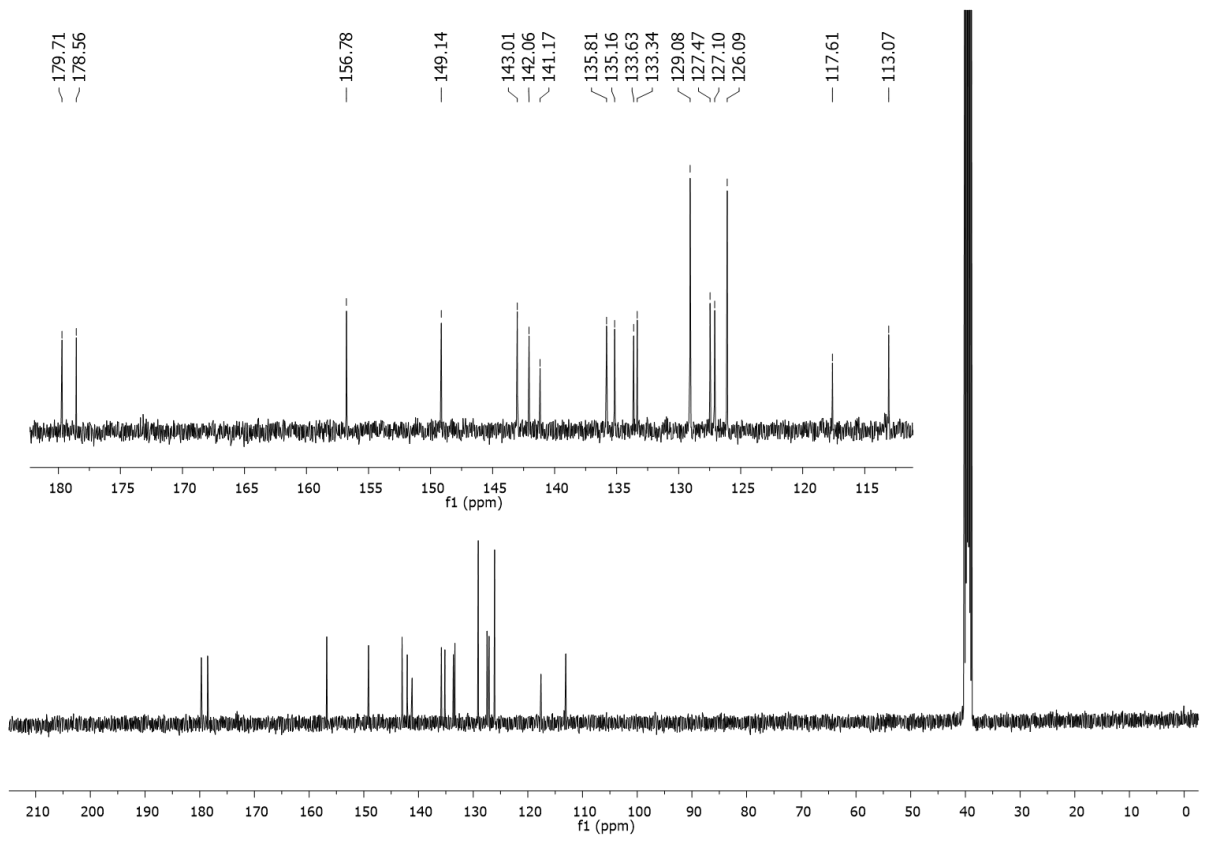
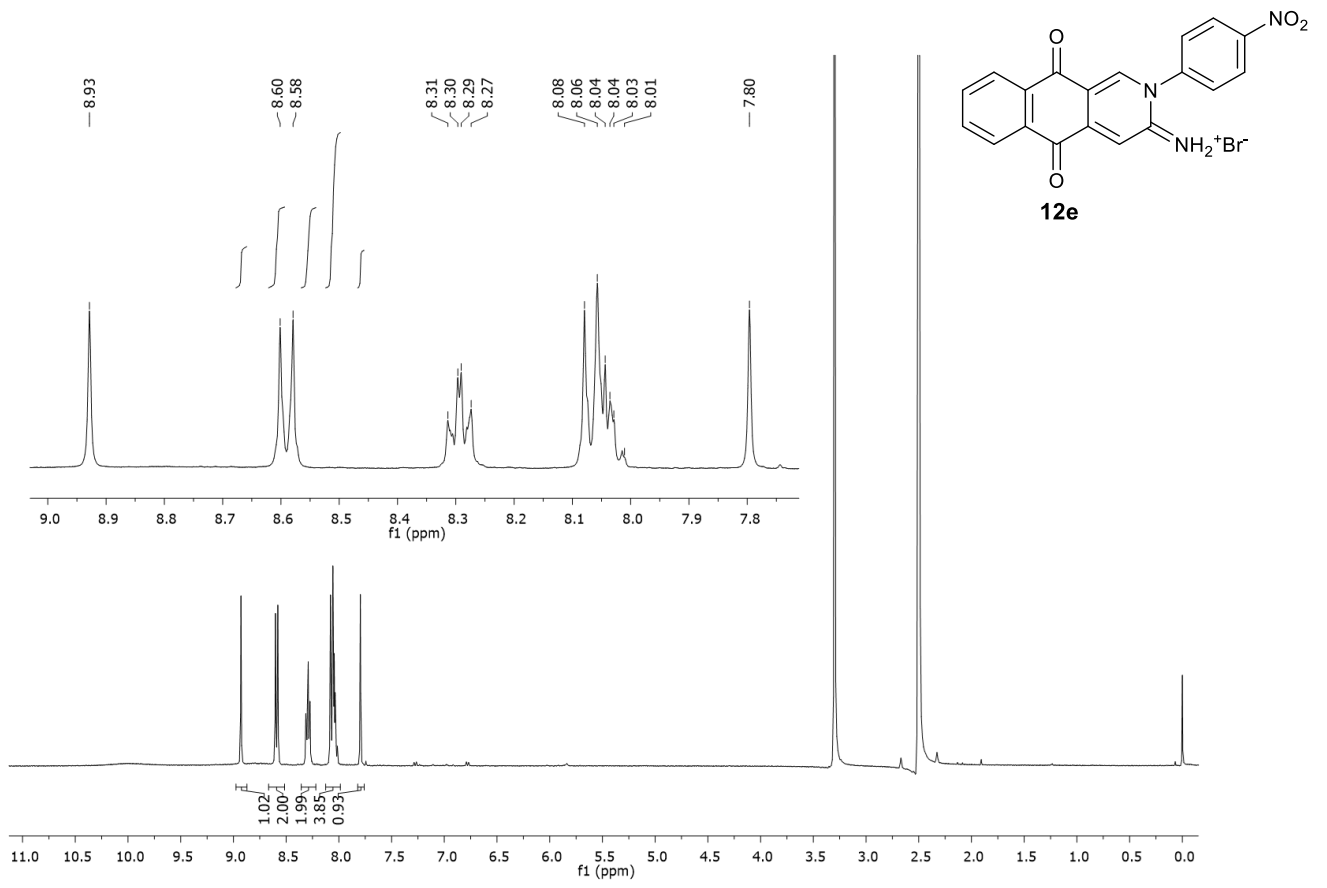
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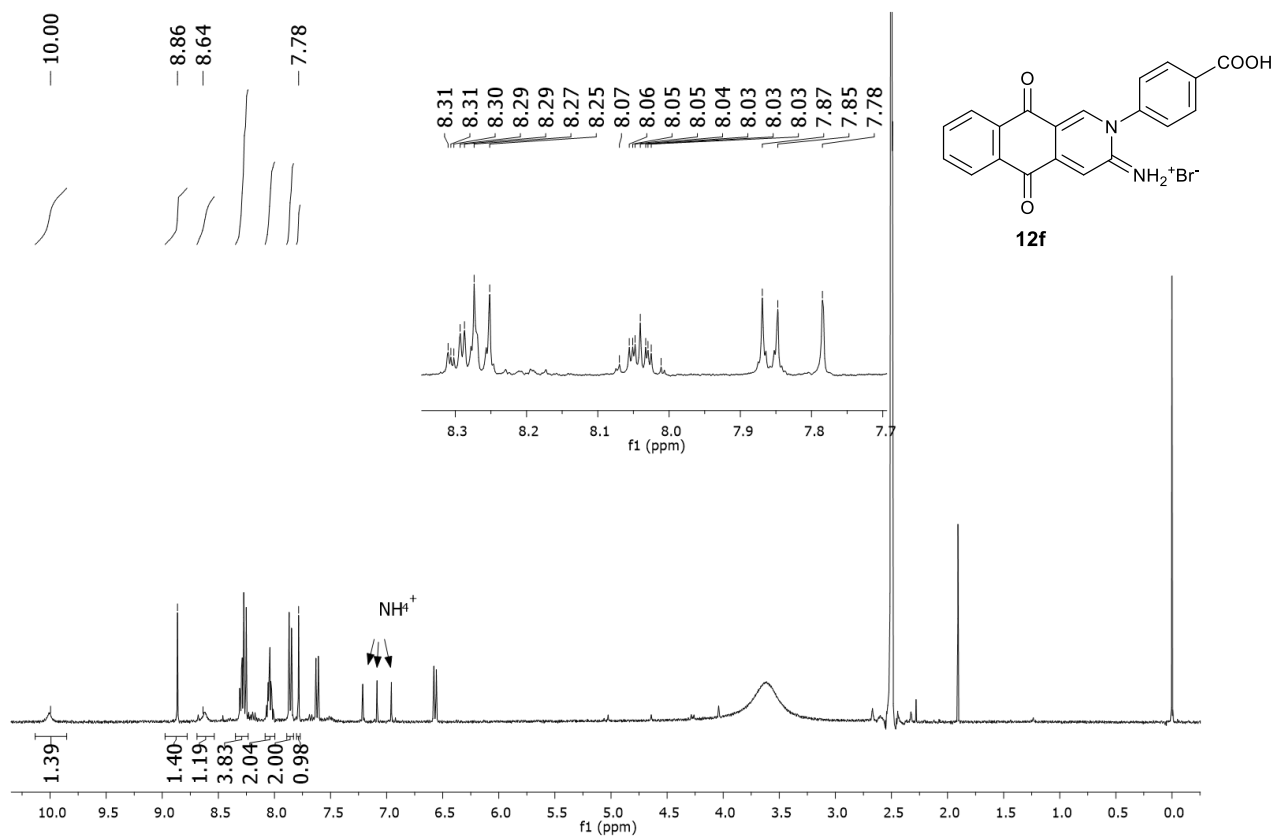




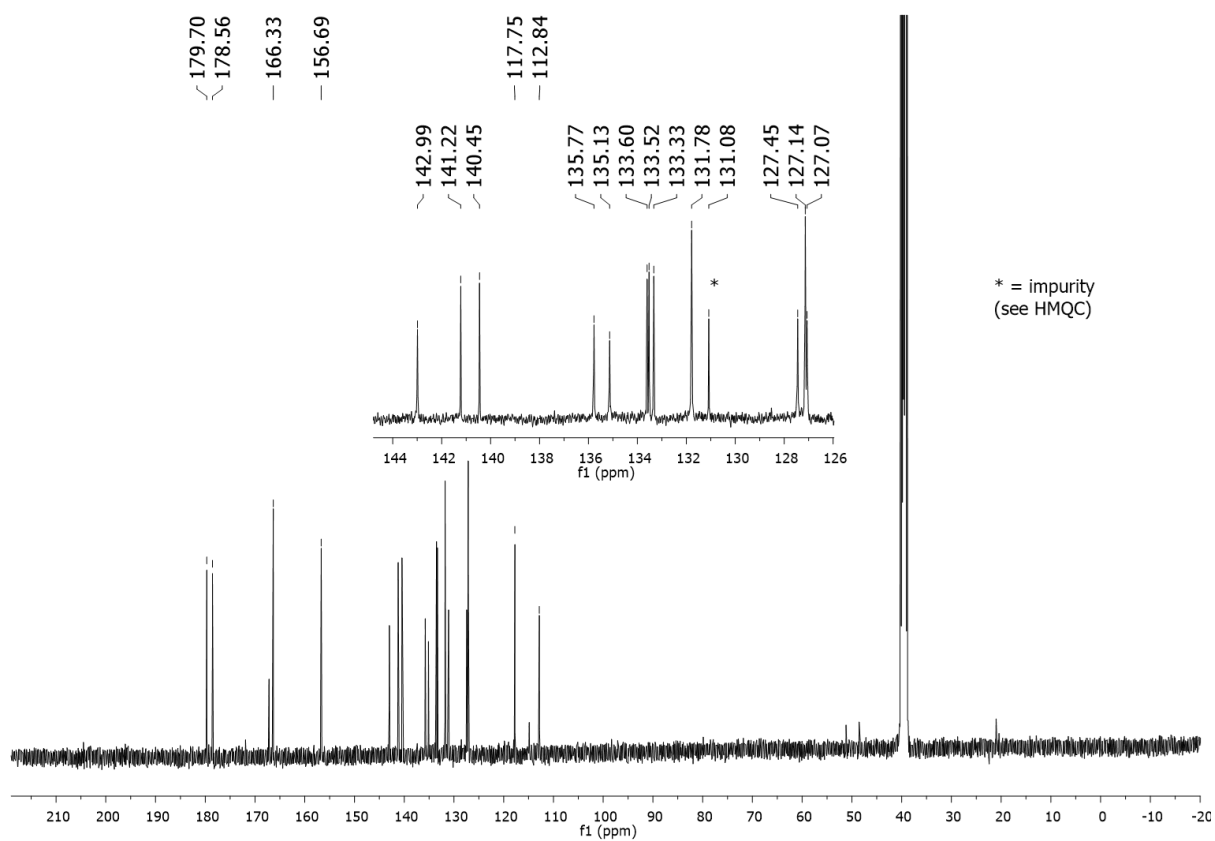
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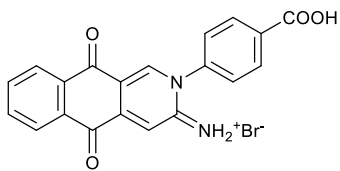




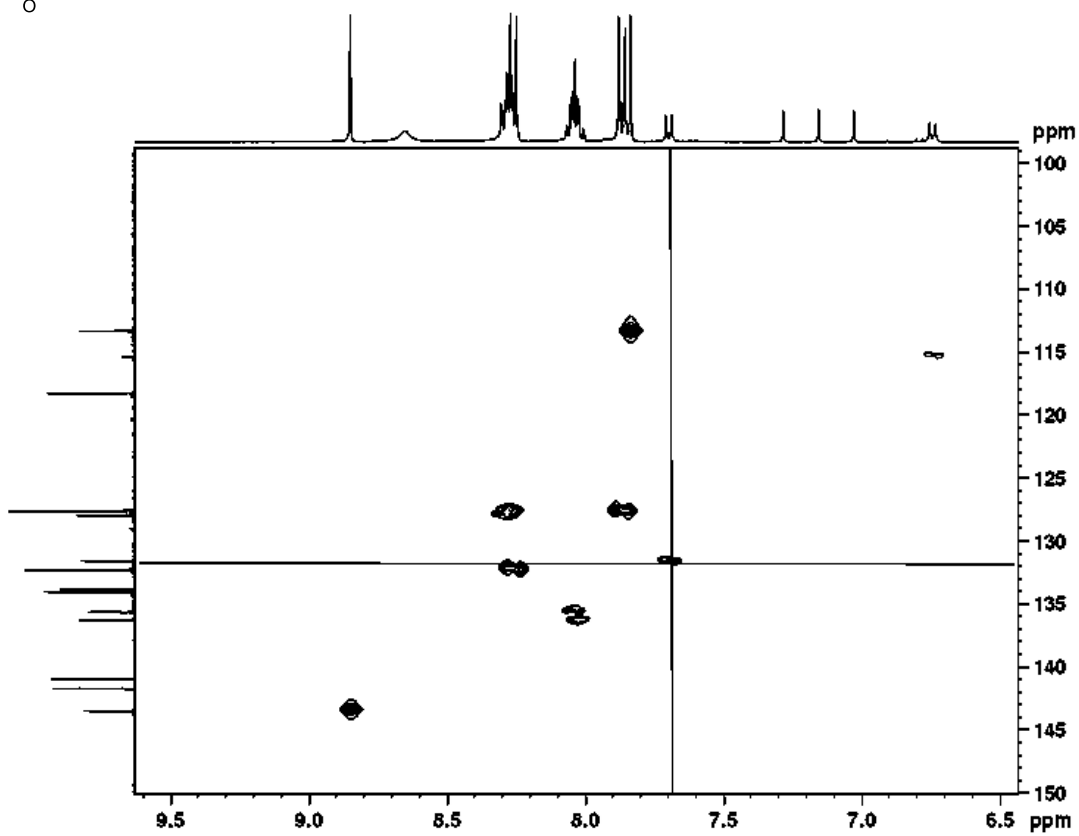


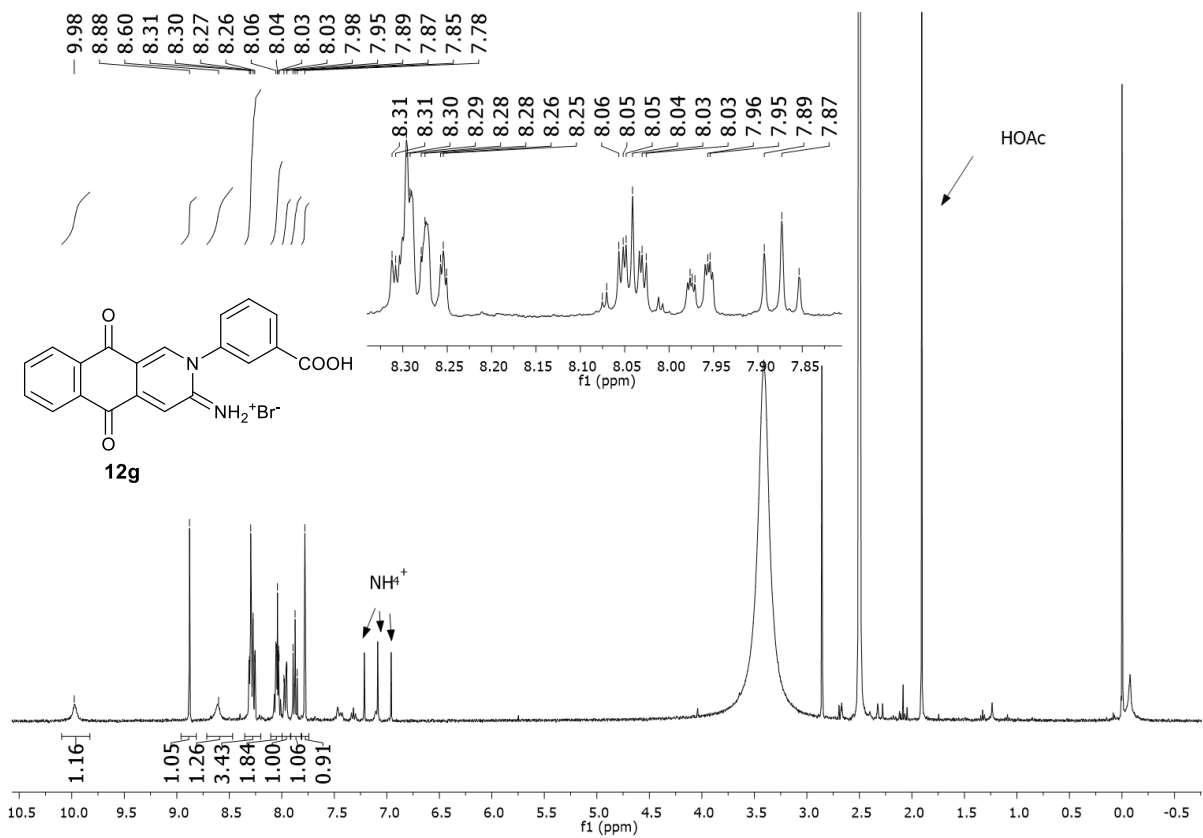
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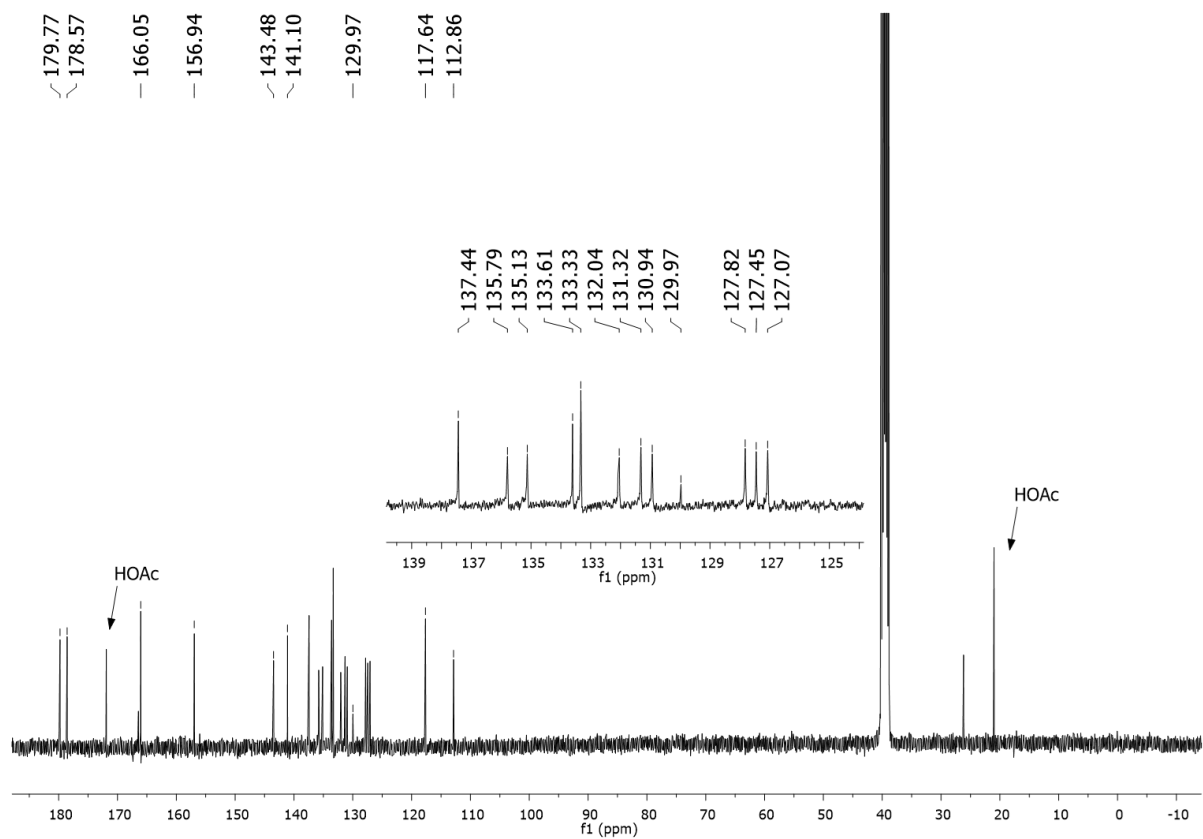


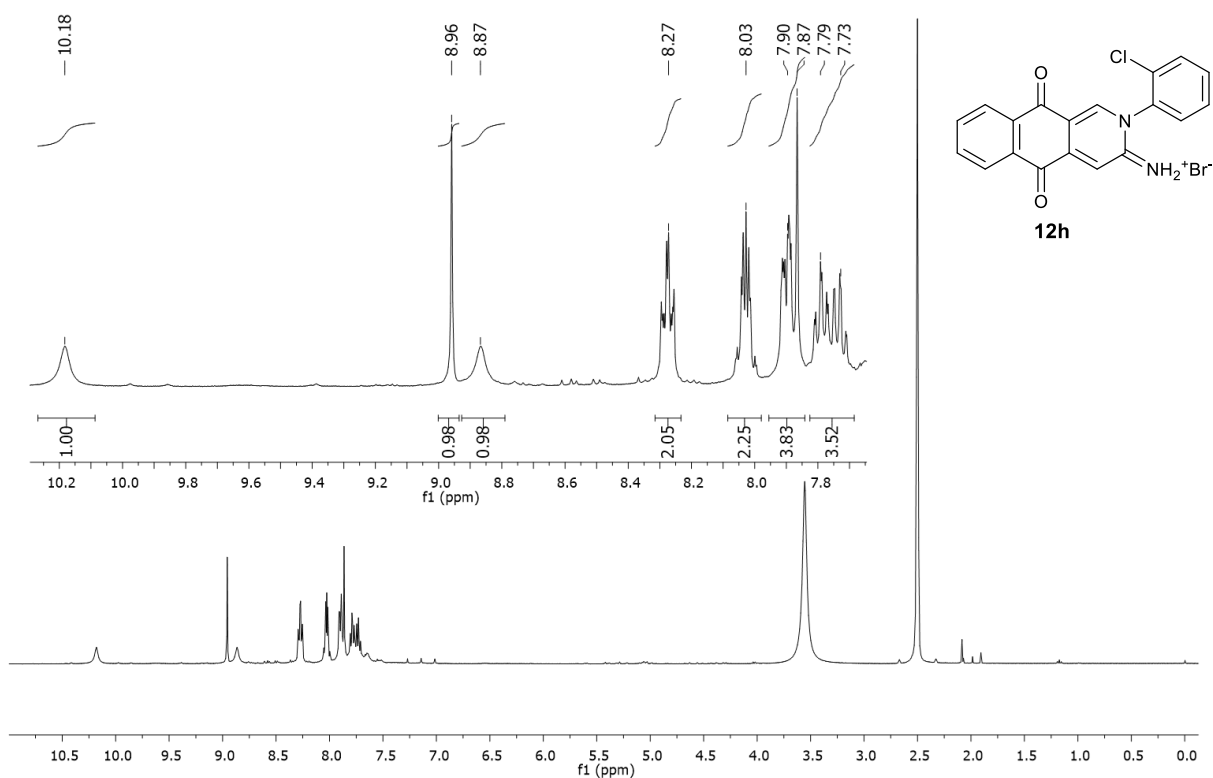
HMQC



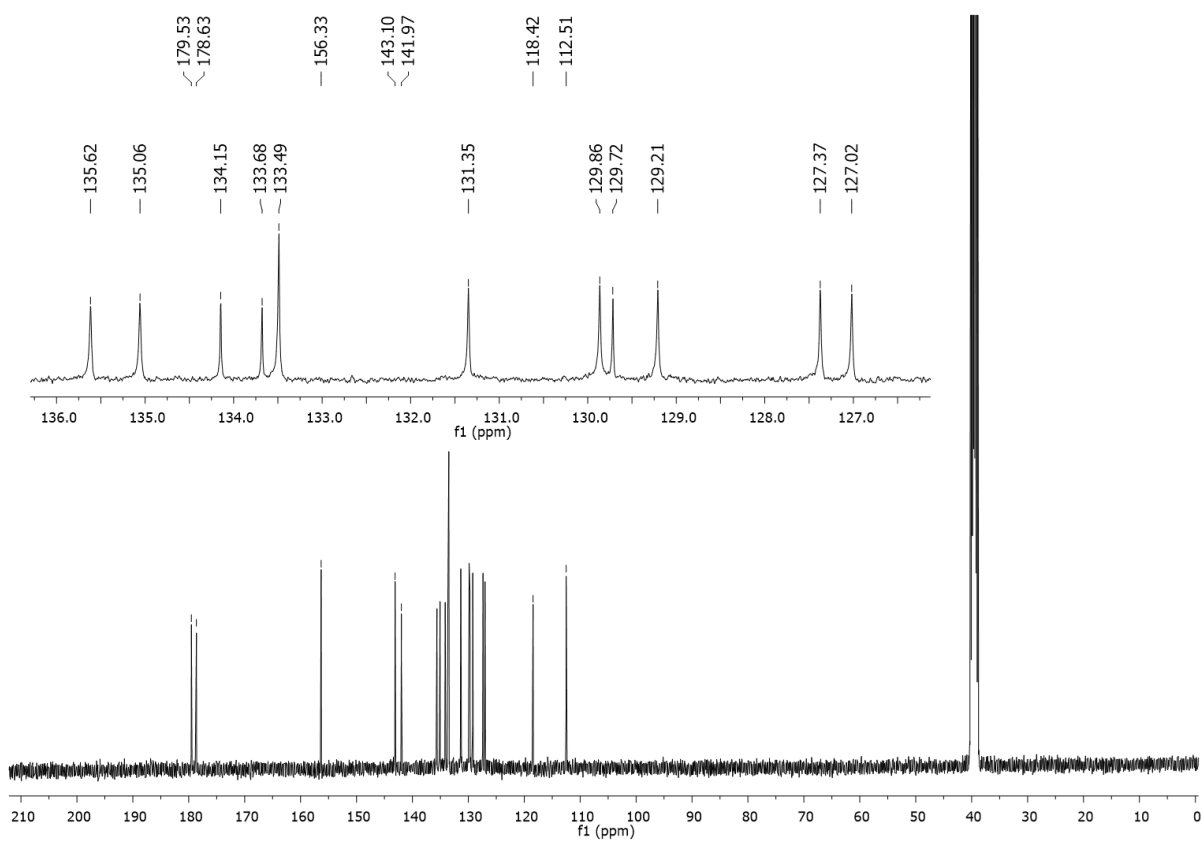


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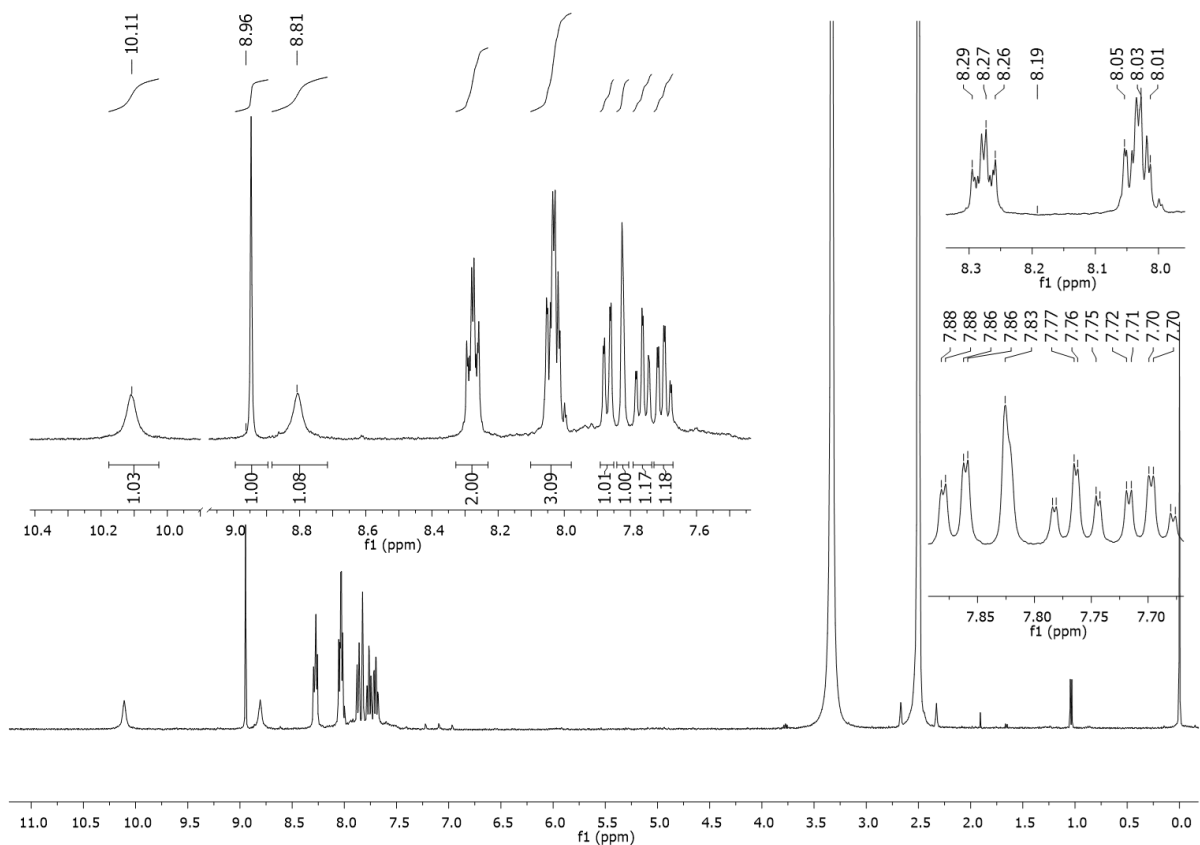




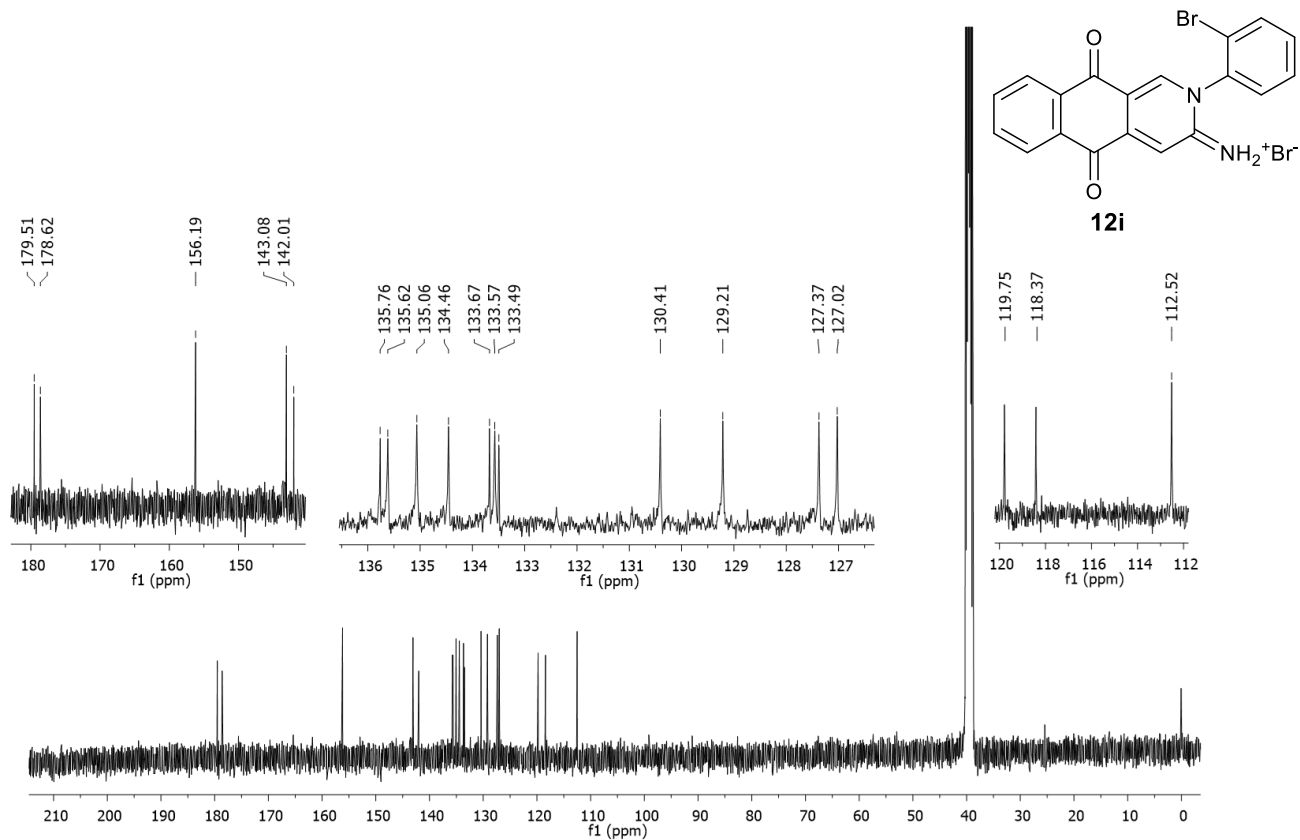
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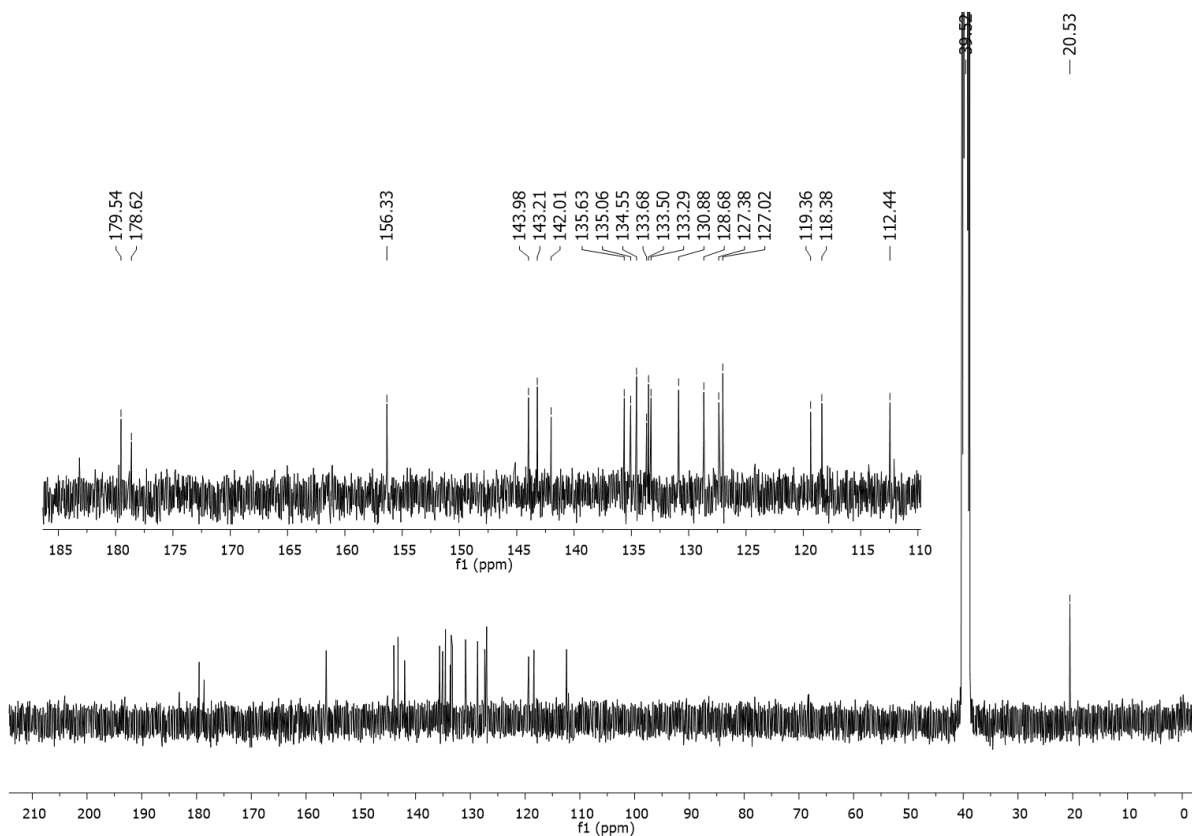
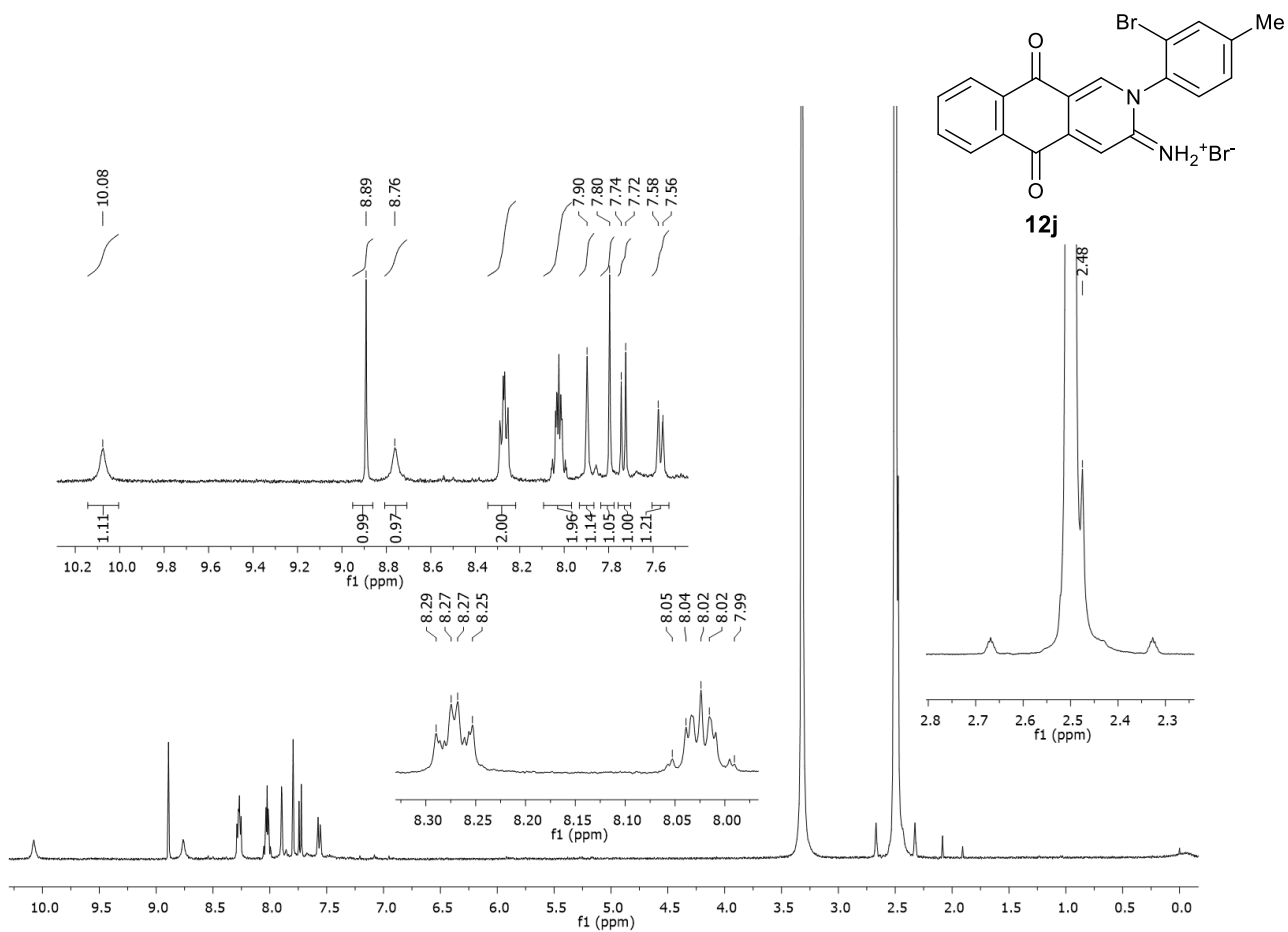




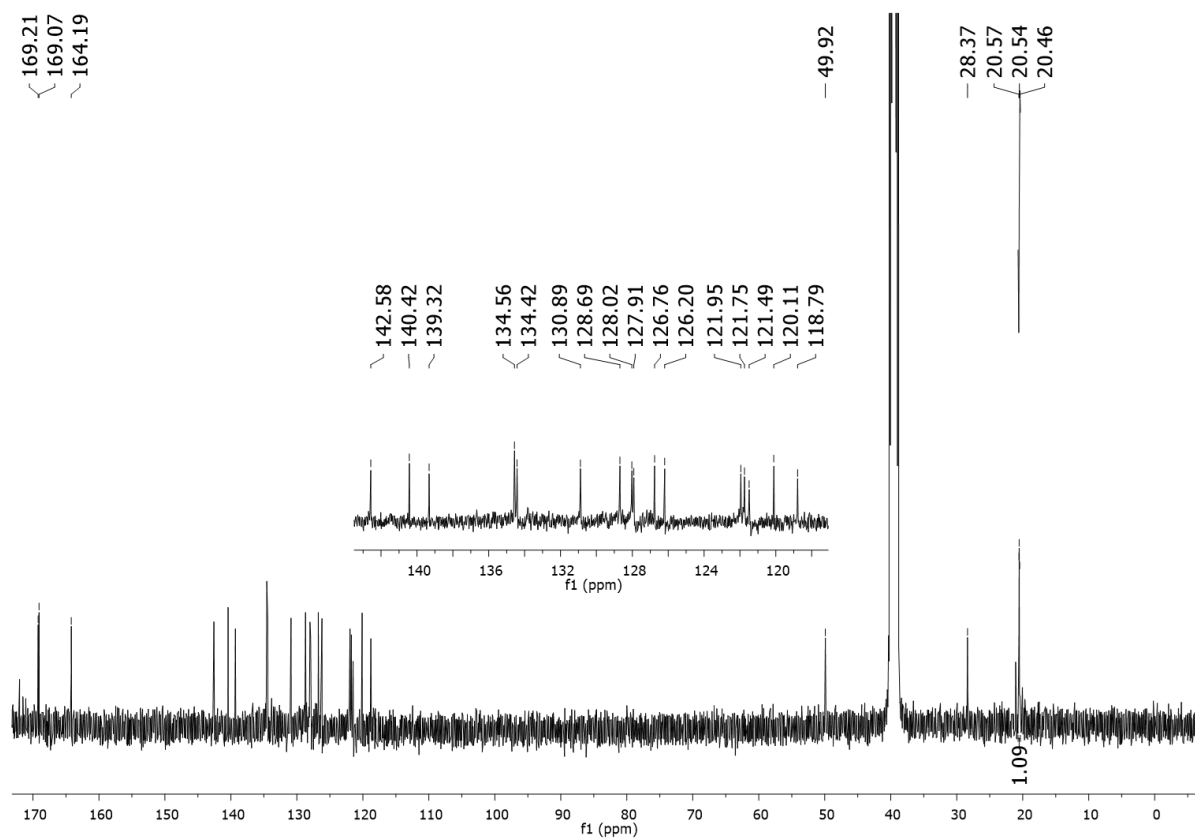
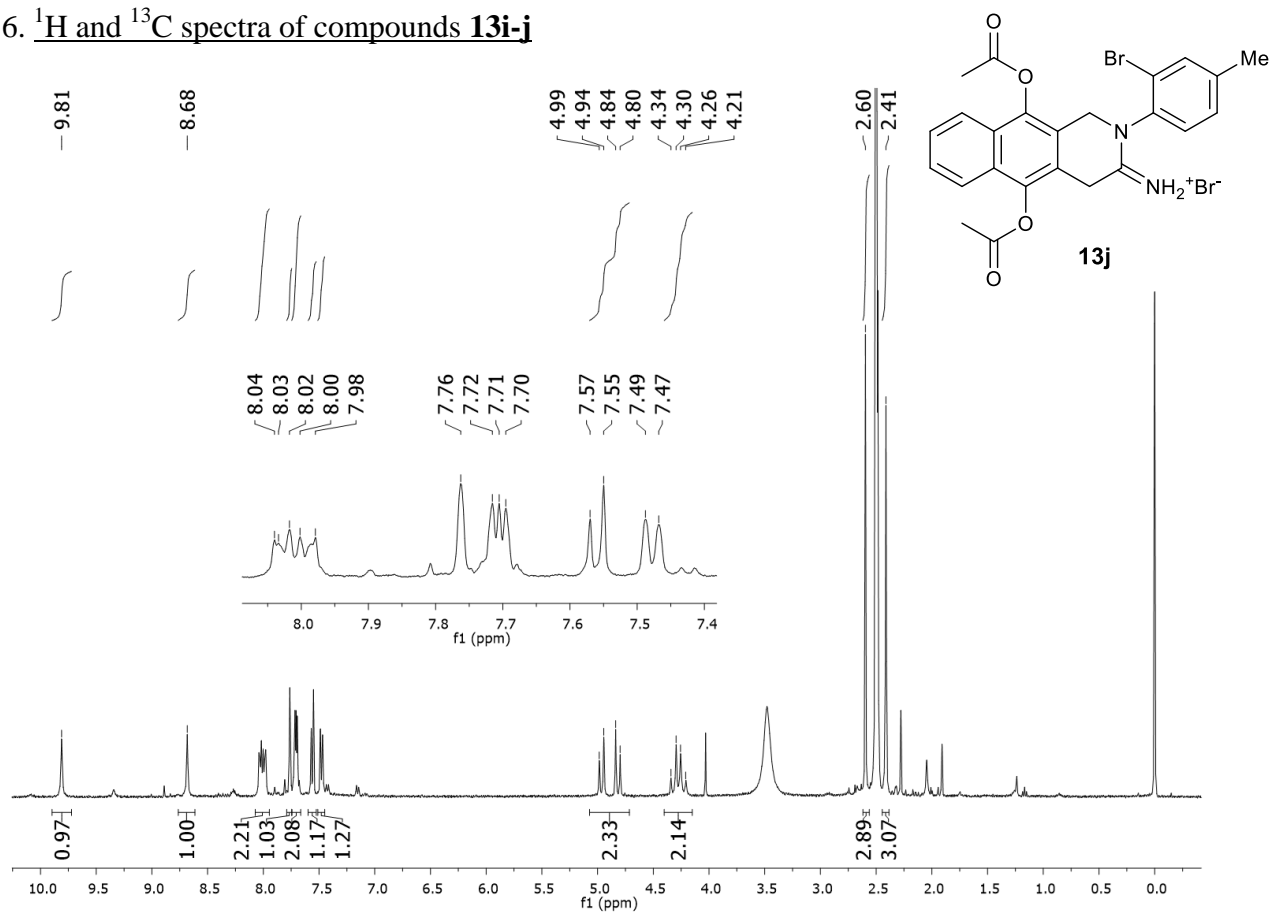


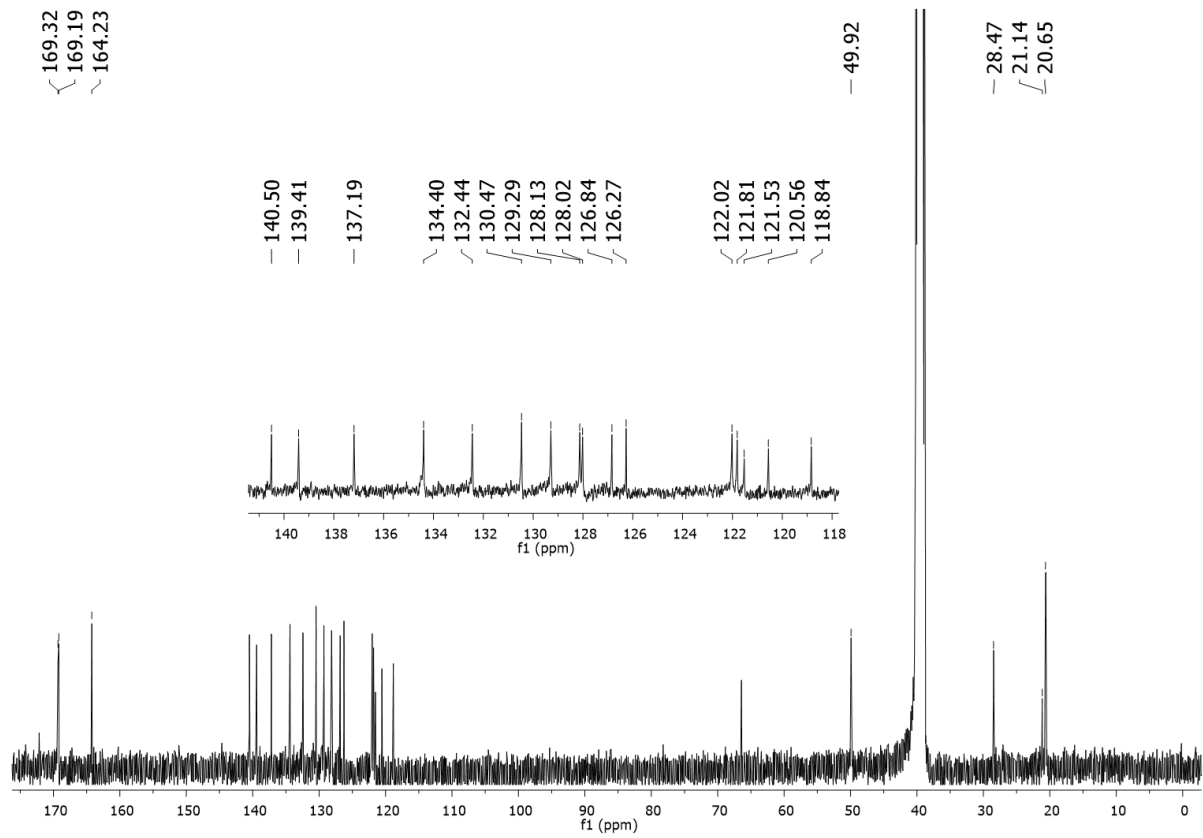
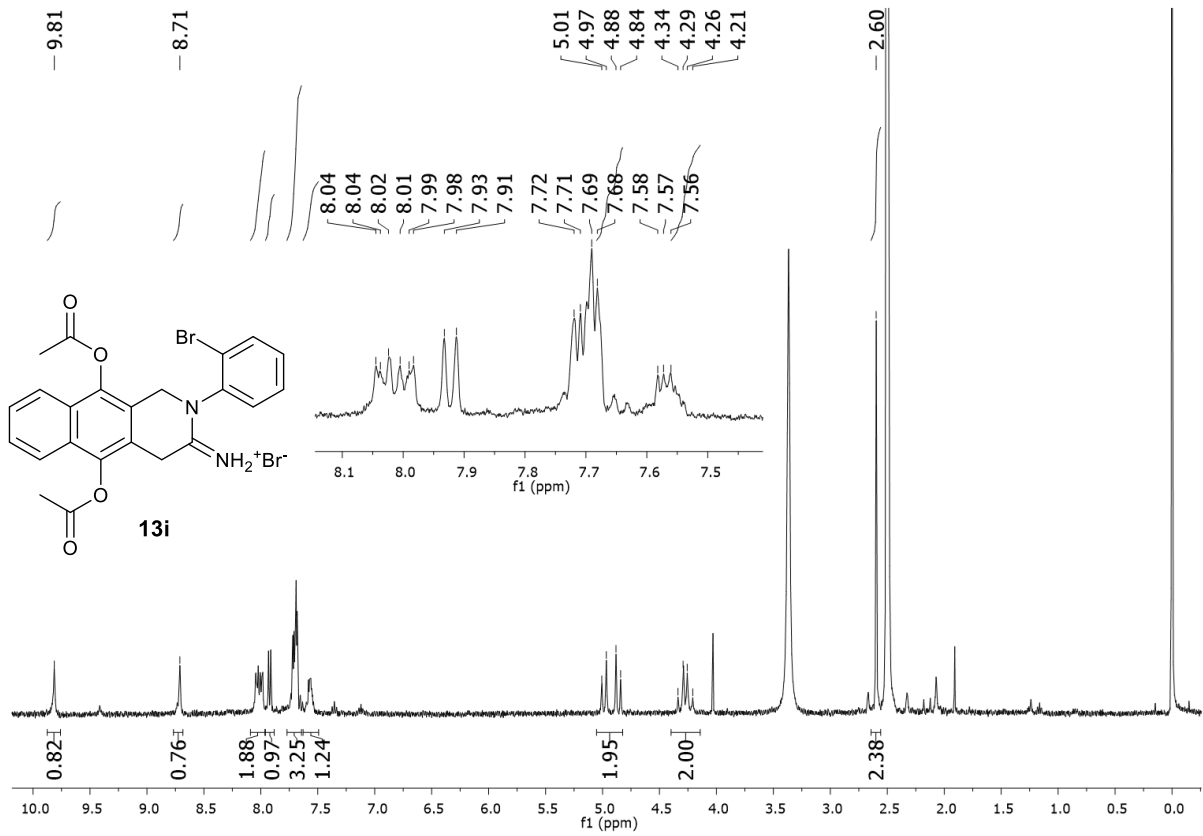
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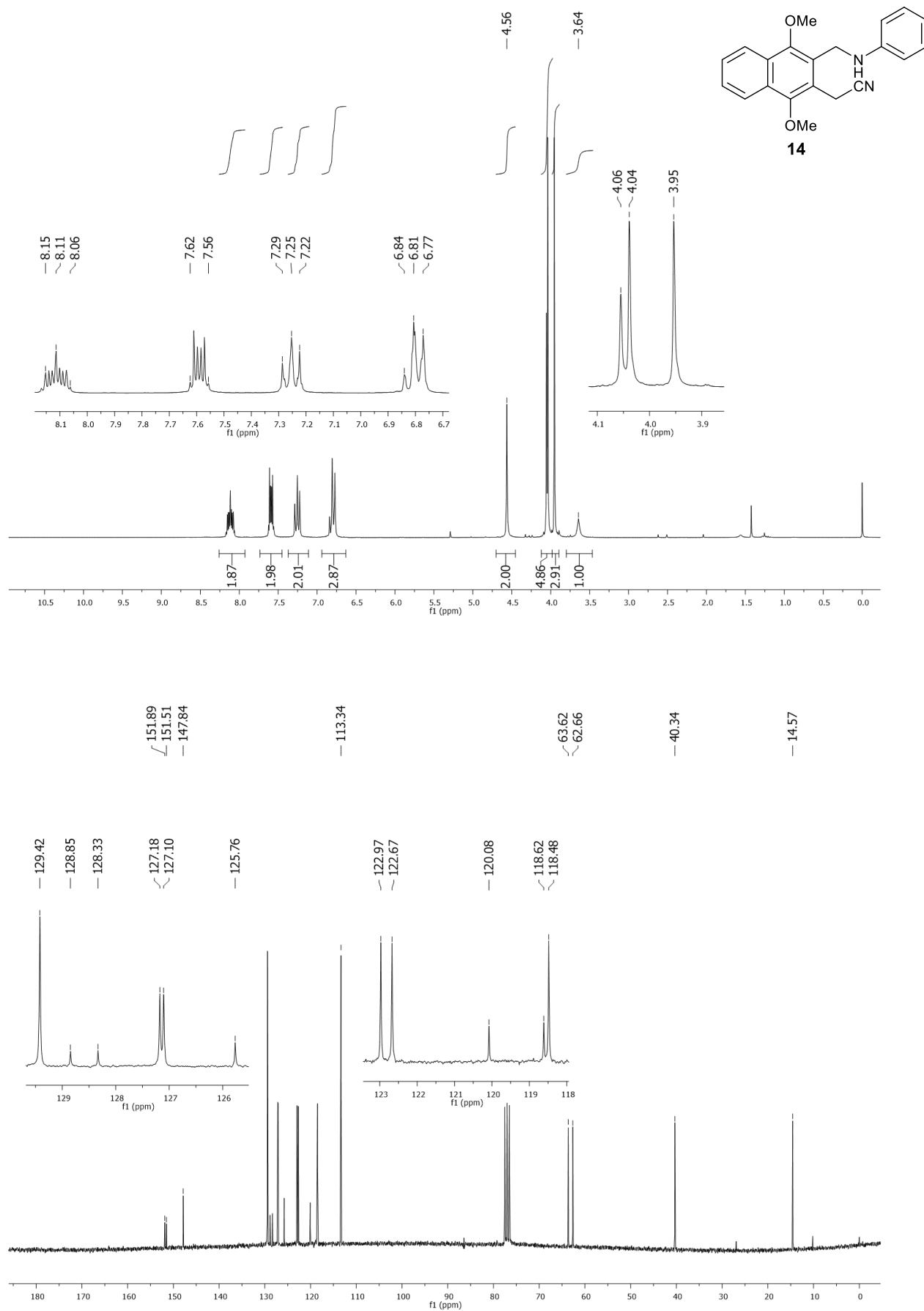


6.  $^1\text{H}$  and  $^{13}\text{C}$  spectra of compounds **13i-j**





7.  $^1\text{H}$  and  $^{13}\text{C}$  spectra of compound **14**



## 8. Biological evaluation of compounds 11a-k and 12a-j

*Monitoring mycobacterial growth by luminometry* – The minimal inhibitory concentration (MIC) against mycobacteria of all synthesized compounds was evaluated by testing serial dilutions. The *in vitro* assay was based on a method in which luminescent mycobacteria transformed with pSMT1 luciferase reporter plasmid is used. The tested compounds were solubilized in DMSO (Sigma-Aldrich) at stock concentrations of 10 mM. Serial dilutions of each compound were made in liquid 7H9 medium [Middlebrook 7H9 broth based (Difco)] + 10% FCS (Gibco). Volumes of 20  $\mu$ L of the serial dilutions were added in triplicate to 96 well, flat-bottomed micro well plates. The bacterial suspension was made by thawing and dissolving a frozen Mycobacteria pellet in 7H9-10 % FCS. The dissolved pellet was passed through a 5.0  $\mu$ M filter (Millipore) to eliminate clumps and left for 1 hour to recover at 37 °C, 5% CO<sub>2</sub>. Next, the bacterial suspension was diluted in 7H9-10% FCS to obtain 50,000 Relative Light Units (RLU)/mL and a volume of 180  $\mu$ L of bacteria was added to each well. A bacterial replication was analyzed by luminometry after 6 days of incubation. The bacterial suspension from each well was collected, and transferred to a black 96-well plate to evade cross luminescence between wells. The luminescent signal was evoked by addition of the substrate for the bacterial luciferase, 1% n-decanal in ethanol to each well by the multi plus reader from Promega and the light emission in each well was measured.

*Activity against multi-drug resistant M. tuberculosis* - Antimicrobial activity of the compounds was tested using the LAM-1 strain using the BACTEC™ MGIT™ 960 TB detection system. The compounds were solubilized in DMSO at stock concentrations of 1 mg/mL. Serial dilutions of each compound were made in 7H9 containing 10% OADC, at 83-fold the final concentrations. *Mtb* LAM-1 was pre-cultured in a 4 mL BACTEC vial to a growth index (*GI*) of 300. Then 100  $\mu$ L of this pre-culture was inoculated into a new 4 ml BACTEC vial together with 100  $\mu$ L of the serial dilutions of the compounds. As a positive control for the resistance, the MDR LAM-1 culture was inoculated with 0.1  $\mu$ M isoniazid. The *GI* was measured each day. To determine the IC<sub>99</sub>, the cultures, treated with the compounds were compared with an untreated culture diluted 100 times upon inoculation.

*Inhibition of intracellular Mtb growth* - The compounds were tested on the murine J774 A.1 macrophage cell line infected with *Mtb* H37Rv<sup>lux</sup>. The J774 macrophages were grown at 37°C, 5% CO<sub>2</sub> in complete DMEM medium until a semi confluent layer was formed. The macrophages were washed in fresh complete DMEM medium and seeded in a flat-bottomed 96-well microwell plate at a cell density of 40,000 cells per well. The cells were left to

recover overnight and were washed three times in complete DMEM medium. *Mtb* H37Rv<sup>lux</sup> was grown at 37 °C in 7H9 containing 10% FCS and 0.2% hygromycin to an OD<sub>580</sub> of 0.6–1.0. The fully-grown bacterial suspension was measured and brought into complete DMEM-Pen/Fung [DMEM medium containing 0.1% penicillin and 0.8% fungizone but without gentamicin]. The synthesized compounds were solubilized in DMSO at stock concentrations of 10 mM. Serial dilutions of the peptides were made in DMEM-Pen/Fung at two times the concentration of each compound to be tested. A volume of 100 µL of the bacterial suspension in DMEM-Pen/Fung containing 4000 RLU of bacteria (multiplicity of infection of 0.1) and 100 µL of the serial compound dilutions were added to the macrophage cultures. To measure the effects of the compounds on intracellular growth of *Mtb*, the infected macrophages were washed three times on day 5 to remove all extracellular bacteria, incubated 1 h with 1% gentamicin to kill the residual extracellular bacteria, lysed with 200 µL 1% Triton X-100 (Sigma) and the wells washed four times with 200 µL PBS. The lysate was transferred in a 2.5 mL tube together with the 4 PBS washings. One hundred µL of 1% n-decanal in ethanol was added to the tube and the luminescence was measured. RLU values shown were obtained from six replicate cultures. Cell viability of the macrophage culture was observed by Trypan blue with a microscope.