

One-pot regioselective C-H activation iodination - cyanonation of 2,4-diarylquinazolines using malononitrile as a cyano source

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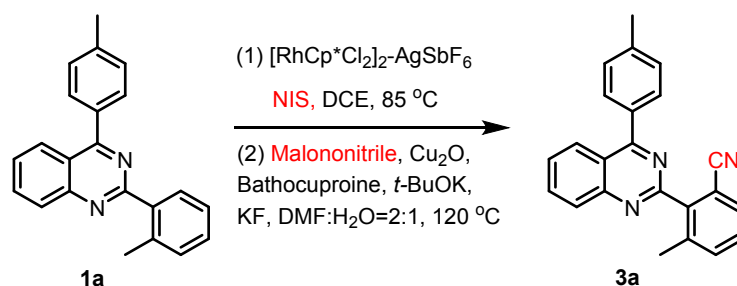
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2. General procedure for the preparation of substrate **3** and **4**... (1-2)
3. ¹H and ¹³C NMR spectra of compounds **3** and **4**(3-32)

Experimental section.

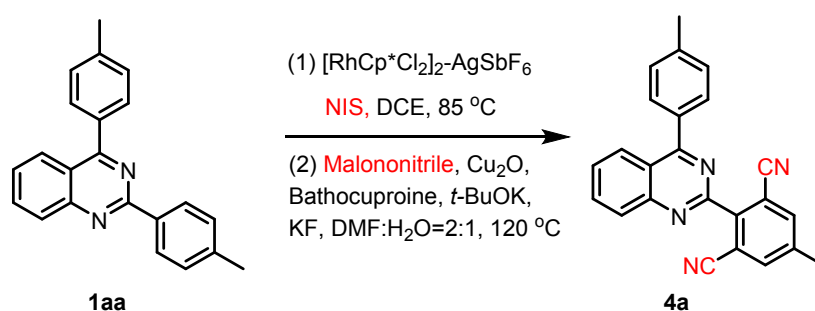
General experimental methods: Unless otherwise noted, commercial reagents were purchased from Aldrich, Alfa Aesar, or other commercial suppliers, and were used as received. All solvents were dried and distilled according to standard procedures before use. Reactions were conducted in standard schlenk techniques on vacuum line. Analytical thin-layer chromatography (TLC) was performed using glass plates pre-coated with 0.25 mm 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Flash column chromatography was performed using silica gel (60-Å pore size, 32-63 μm, standard grade). Organic solutions were concentrated on rotary evaporators at ~20 Torr (house vacuum) at 25-35 °C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million (ppm) from internal standard tetramethylsilane (TMS) on the δ scale.

General procedure for the preparation of substrate **3**



A mixture of 2,4-phenylquinazolines **1a** (0.2 mmol, 1.0 equiv), NIS (0.3mmol. 1.5eq), [RhCp*Cl₂]₂ (1mol%), AgSbF₆(8 mol%) and in DCE (2.0 mL) was stirred at 85°C under for 0.5 h, until **1a** was completed consumed. The solvent was removed under reduced pressure. A mixture of malononitrile (2.0 eq), Cu₂O (10 mol%), Bathocuproine (20 mol%), t-BuOK(2.0 eq), KF (2.0 eq) in DMF and water (3mL, 2:1) was stirred at 120°C. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature. The solvent was evaporated, residue was diluted with EtOAc (10 mL), washed with H₂O (10 mL), dried by anhydrous Na₂SO₄. Evaporation of the solvent followed purification by column chromatograph over silica gel provided the corresponding product **3a**.

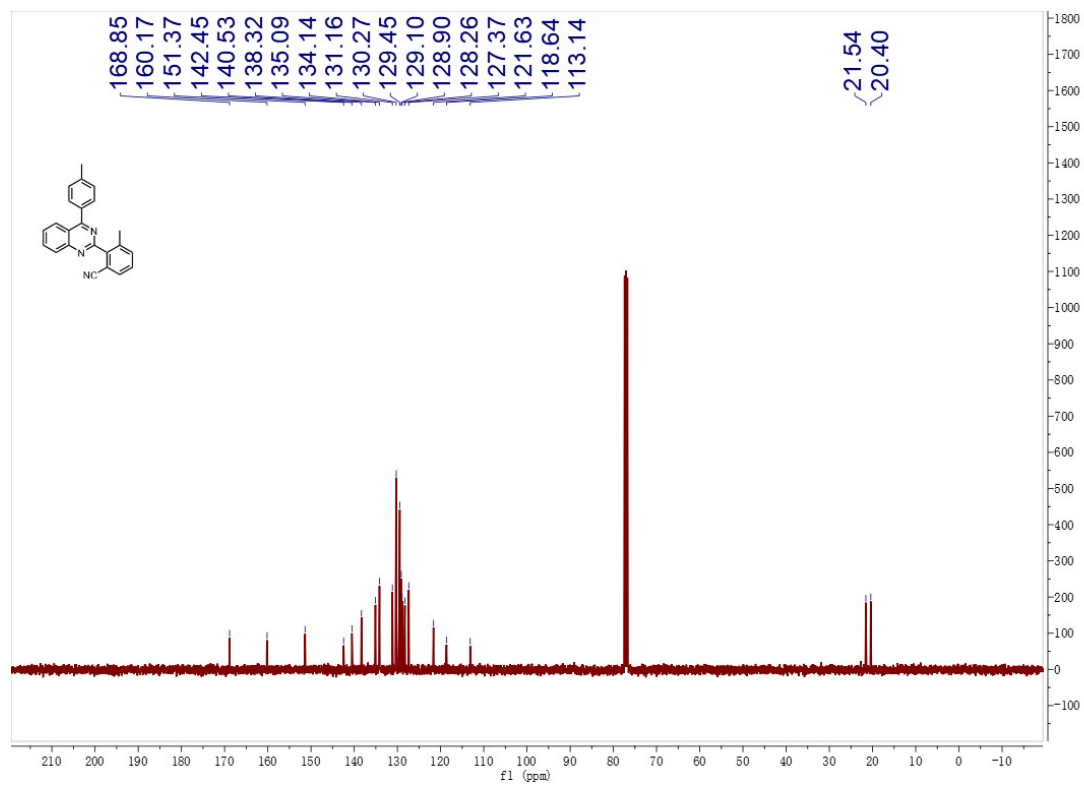
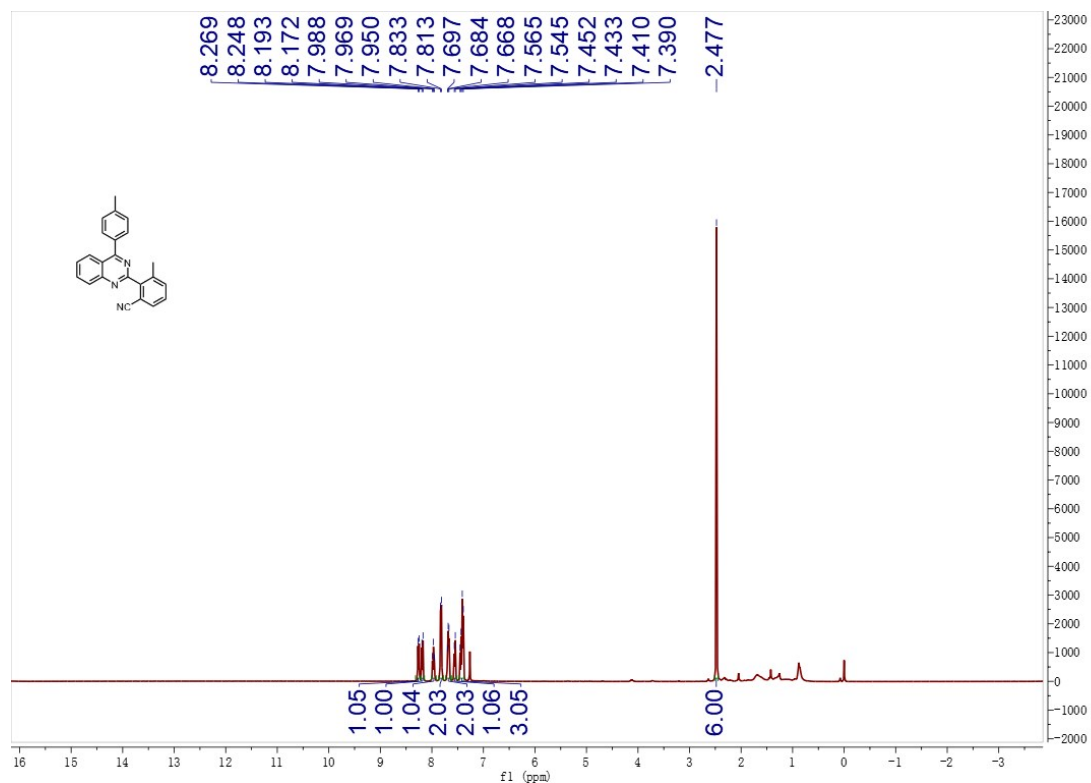
General procedure for the preparation of substrate 4



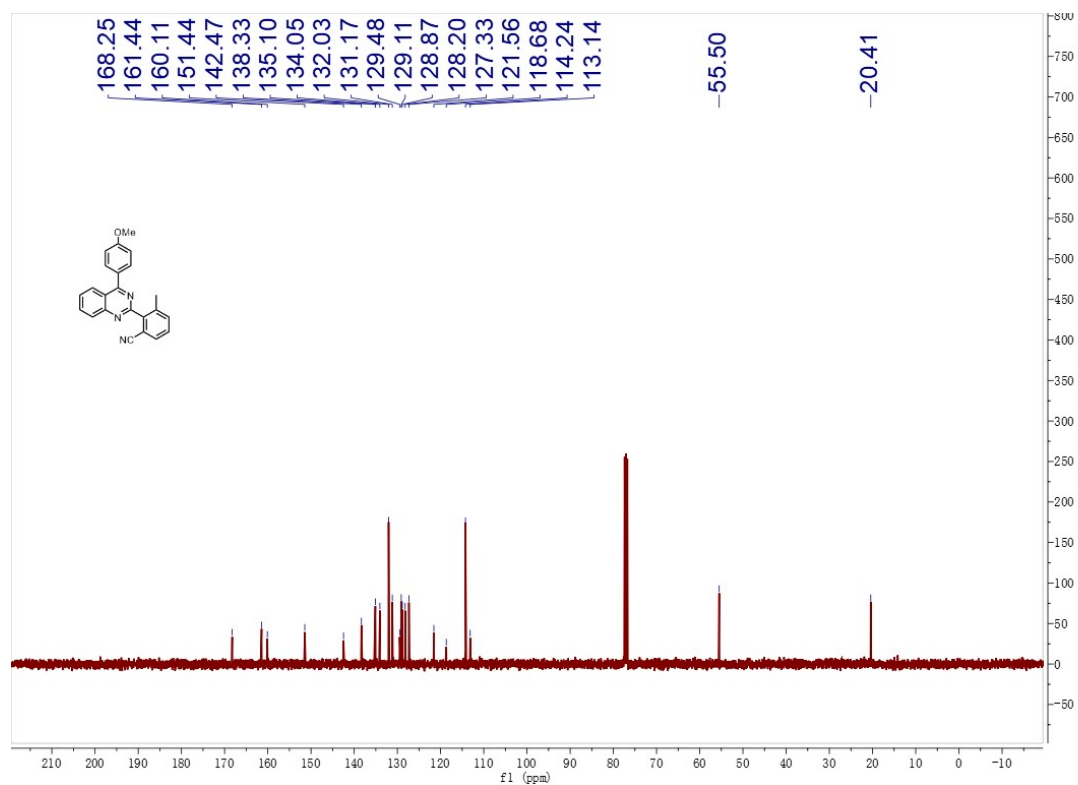
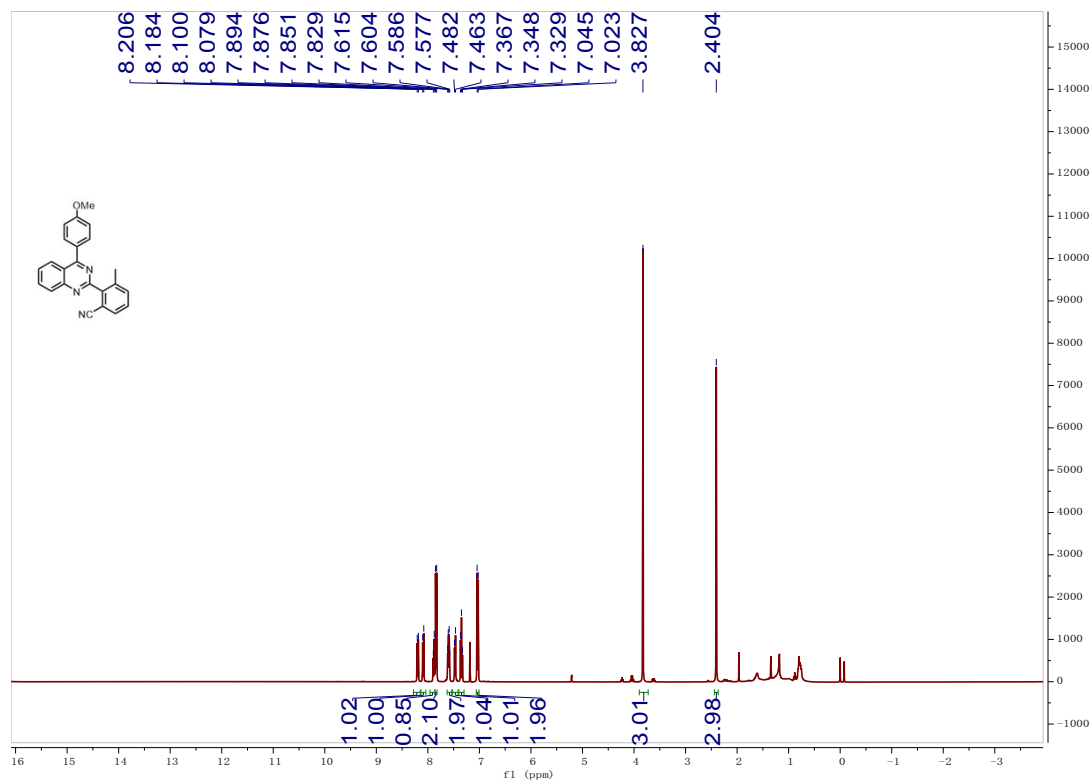
A mixture of 2,4-phenylquinazolines **1aa** (0.2 mmol, 1.0 eq.), NIS (0.6 mmol. 3.0 eq.), [RhCp*Cl₂]₂ (2.0 mol%), AgSbF₆(16 mol%) and in DCE (2.0 mL) was stirred at 85°C under for 0.5 h, until **1aa** was completed consumed. The solvent was removed under reduced pressure. A mixture of malononitrile (4.0 eq.), Cu₂O (20 mol%), Bathocuproine (40 mol%), t-BuOK (4.0 eq.), KF (4.0 eq.) in DMF and water (3.0 mL, 2:1) was stirred at 120°C. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature. The solvent was evaporated, residue was diluted with EtOAc (10 mL), washed with H₂O (10 mL), dried by anhydrous Na₂SO₄. Evaporation of the solvent followed purification by column chromatograph over silica gel provided the corresponding product **4a**.

^1H and ^{13}C NMR spectra of the products

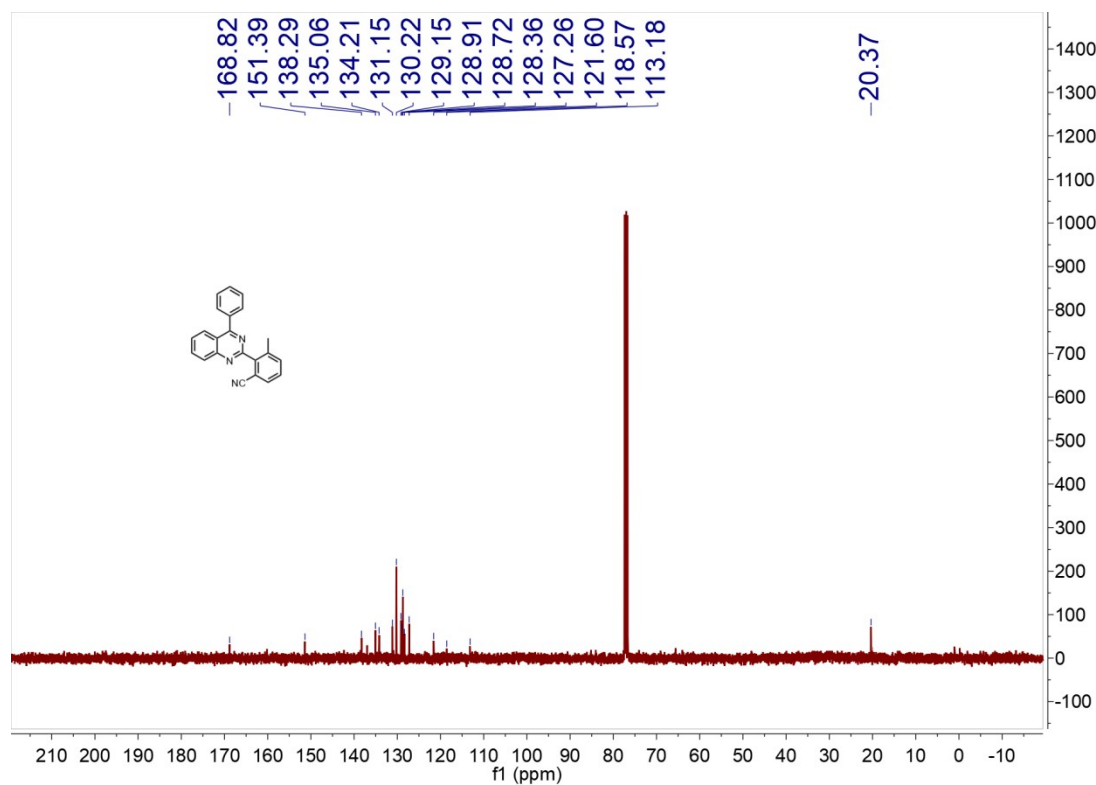
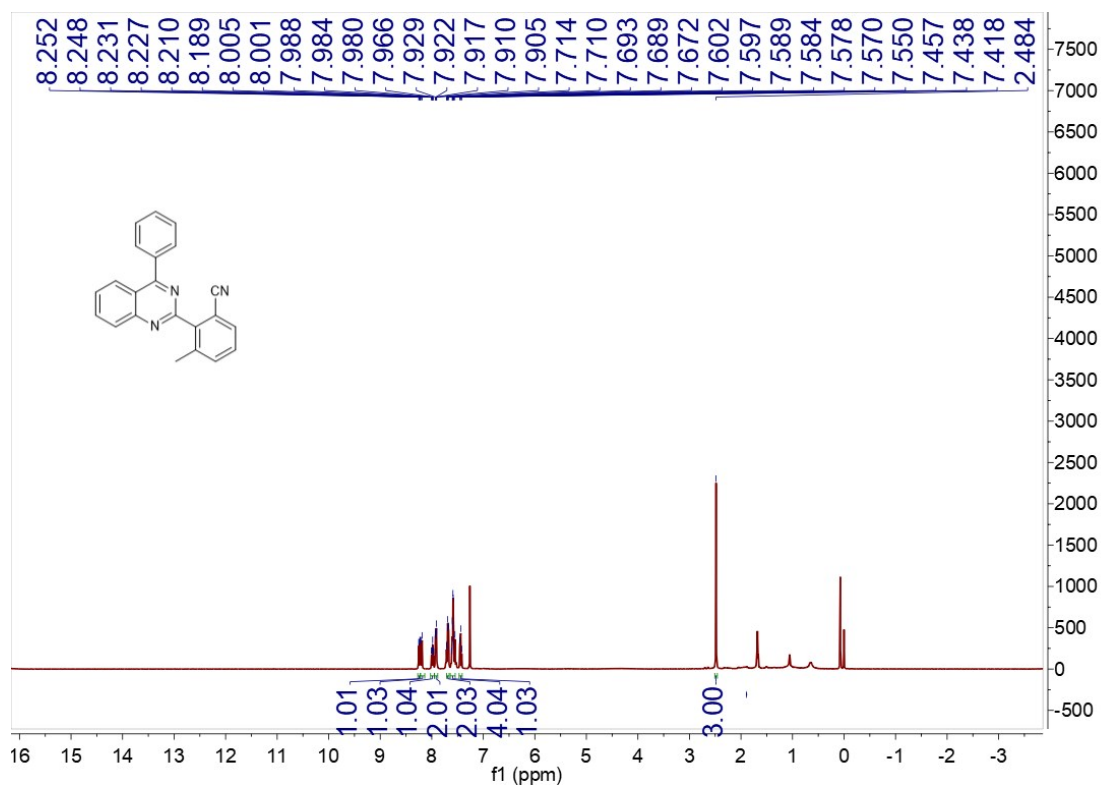
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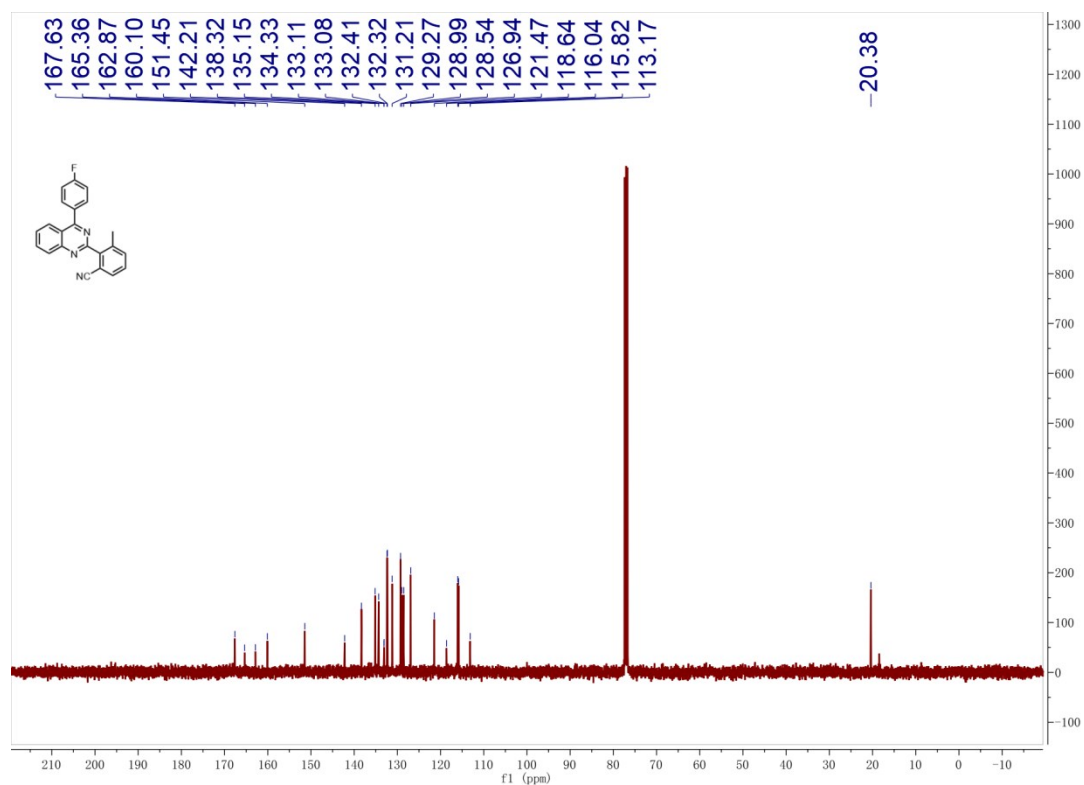
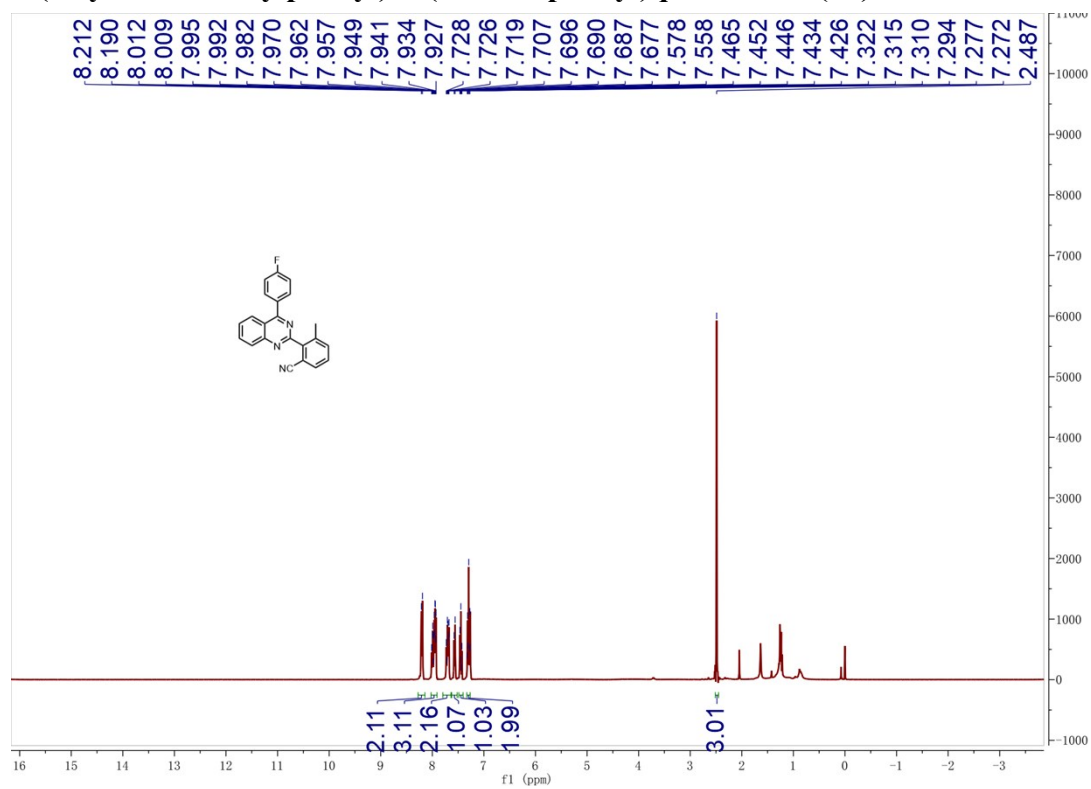
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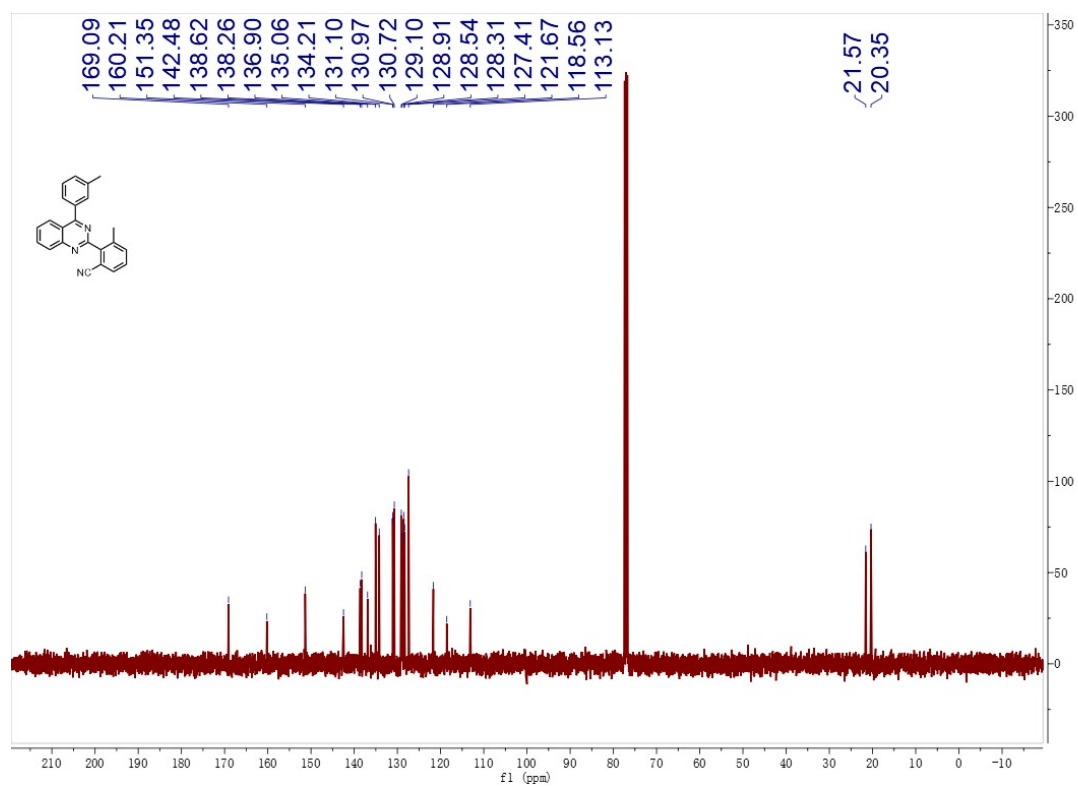
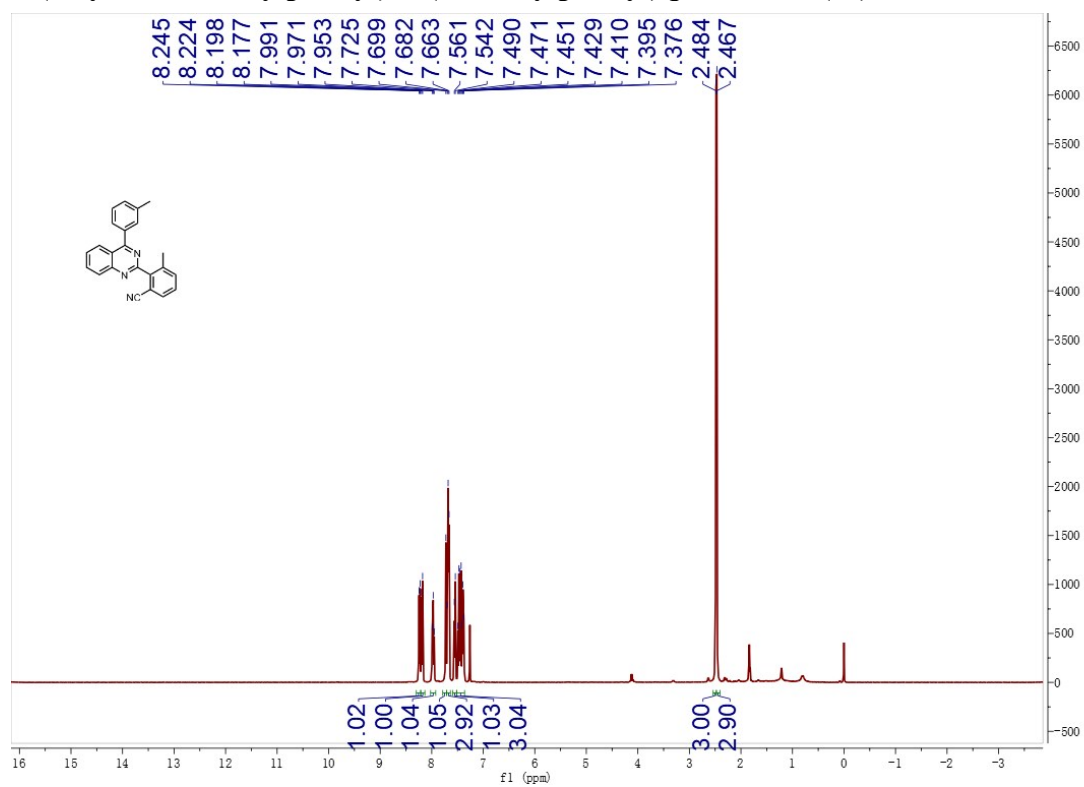
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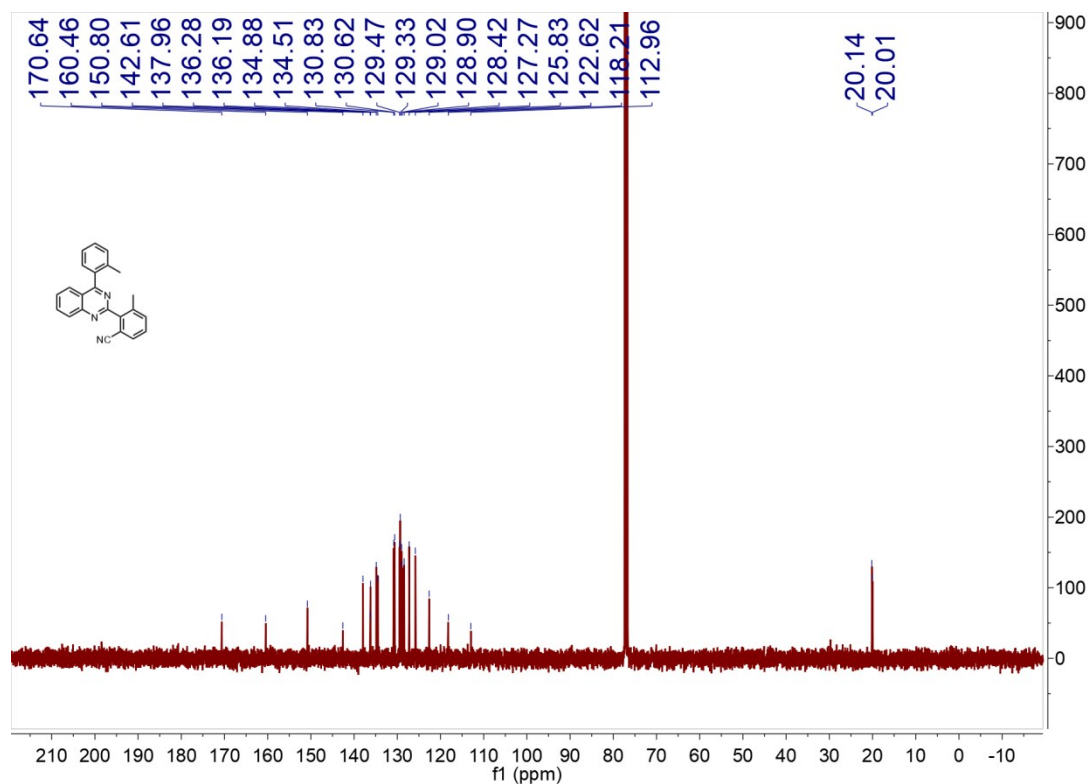
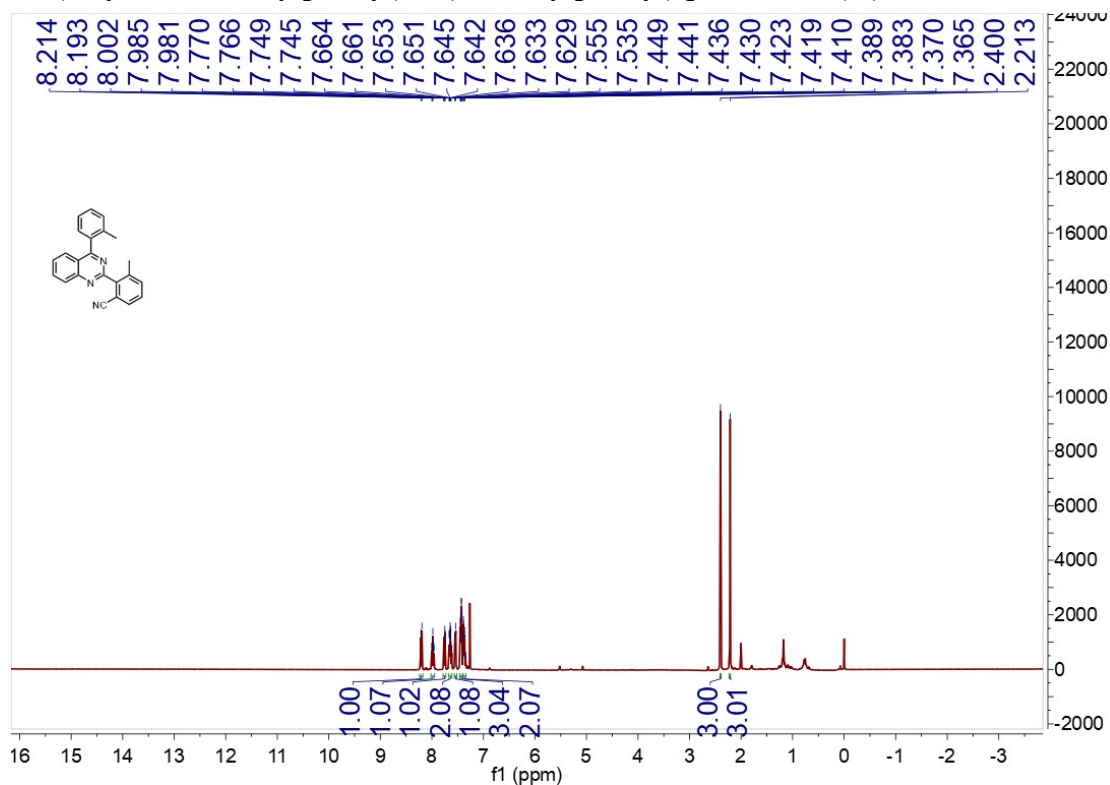
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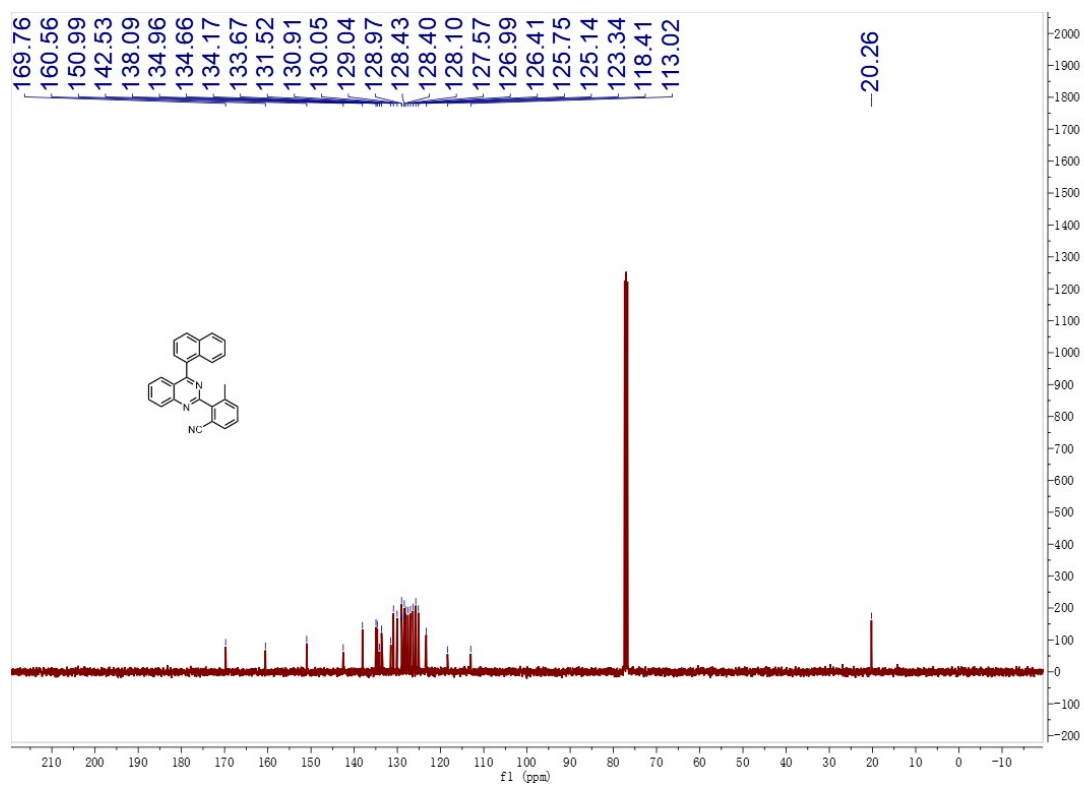
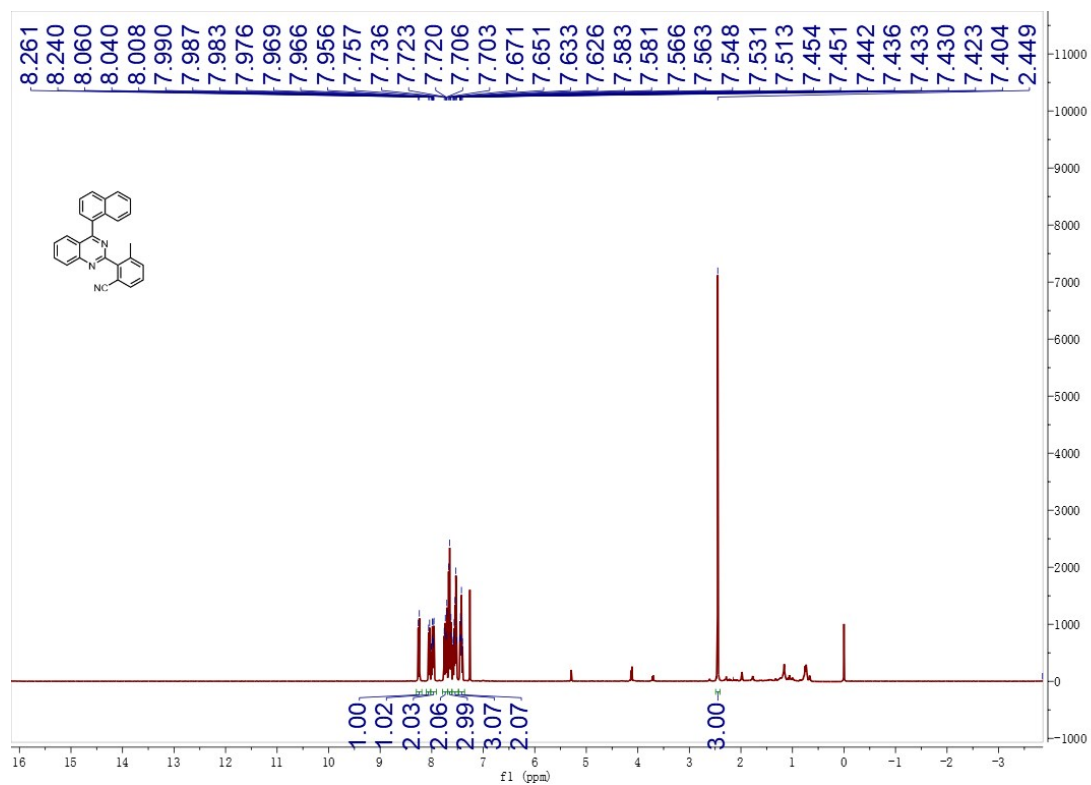
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2-(2-cyano-6-methylphenyl)-4-(2-methylphenyl)quinazoline(3f)

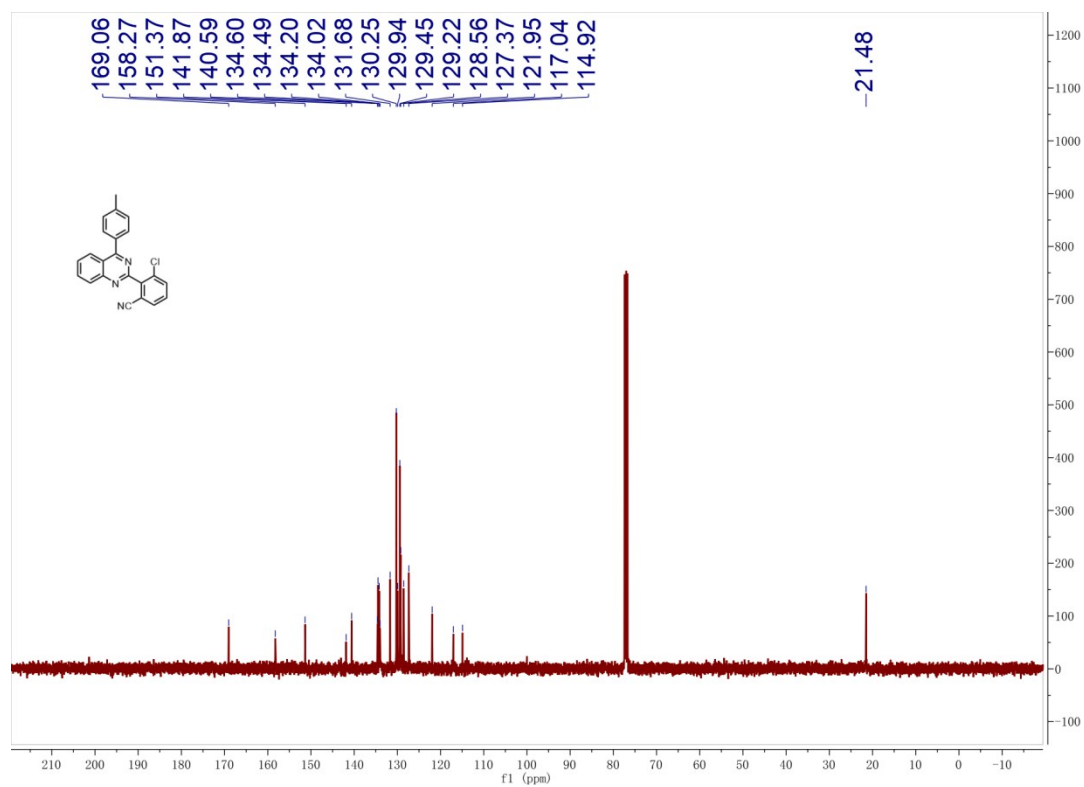
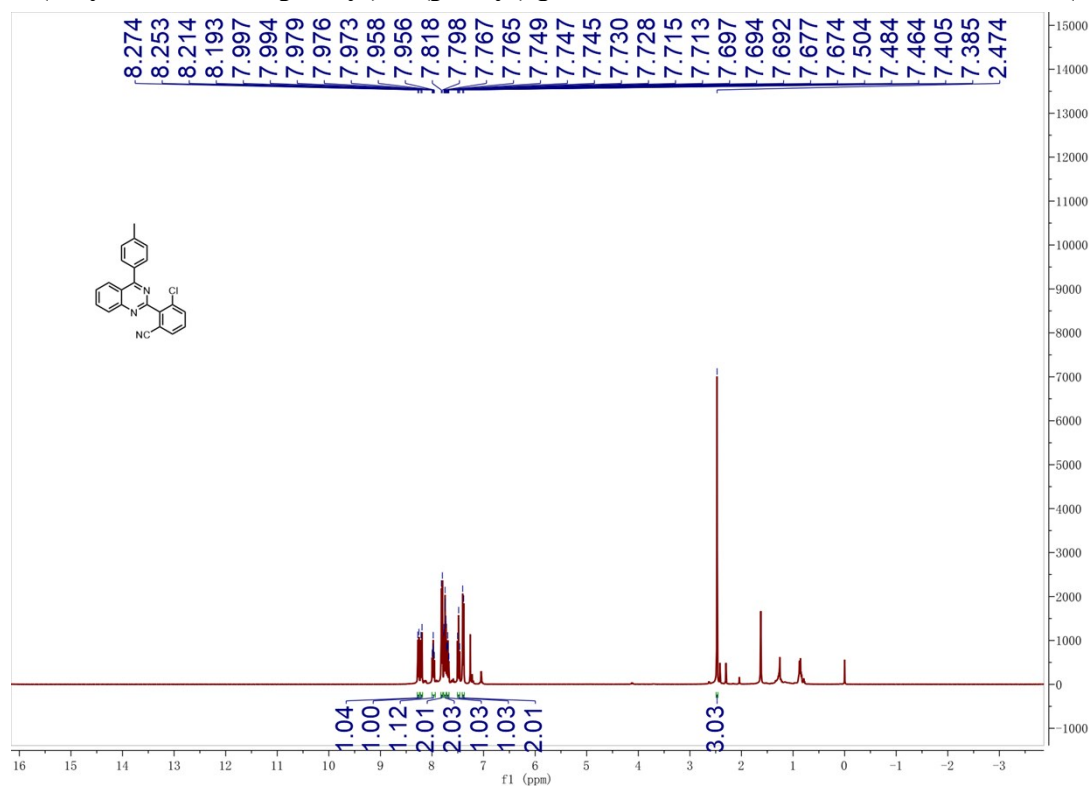


2-(2-cyano-6-methylphenyl)-4-(naphthalen-1-yl)quinazoline (3g)

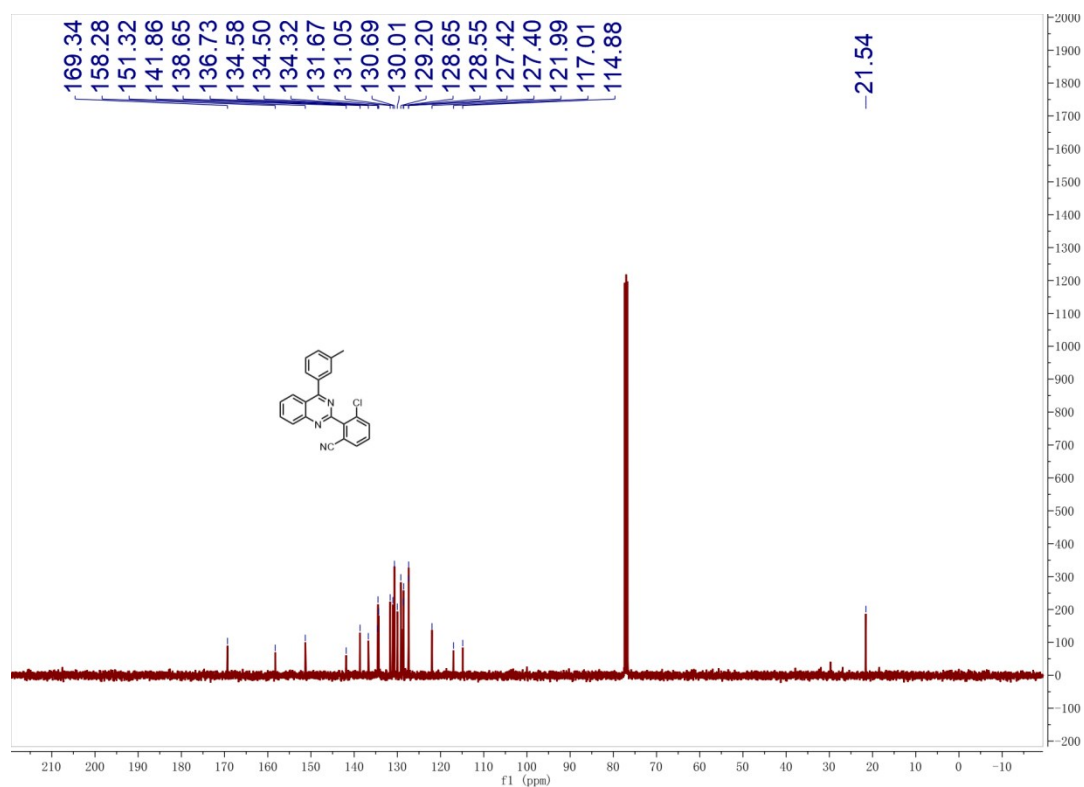
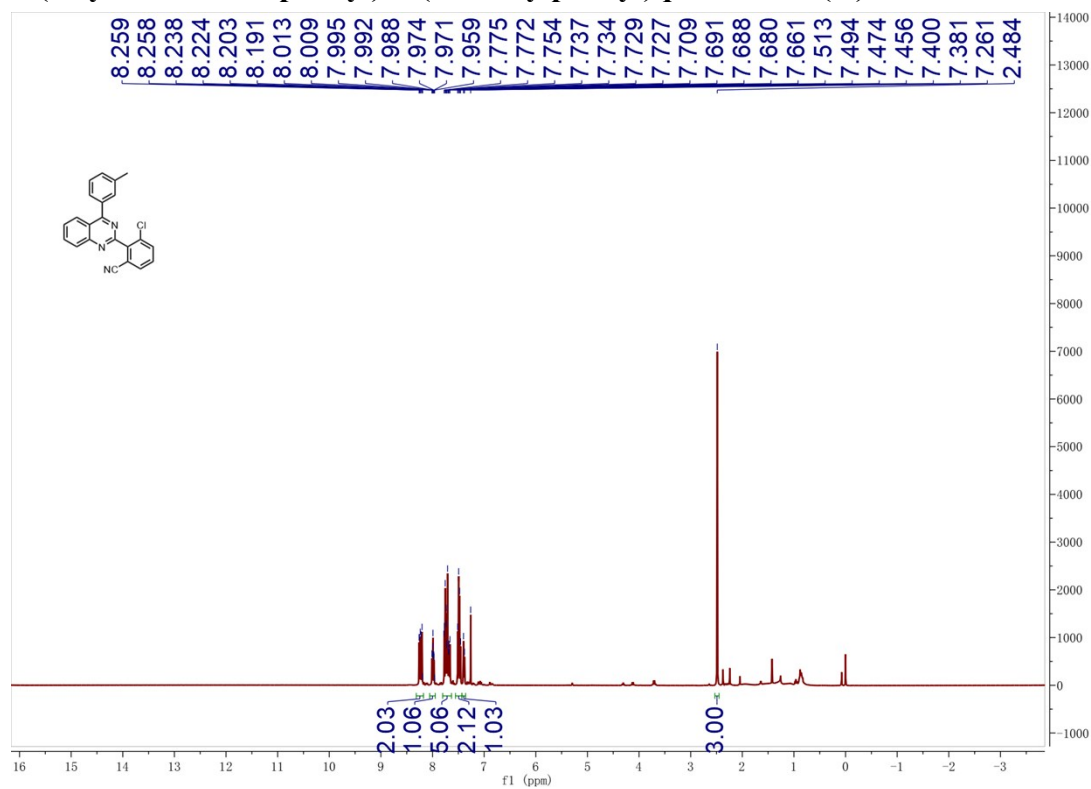


2-(2-cyano-6-chlorophenyl)-4-(p-tolyl)quinazoline

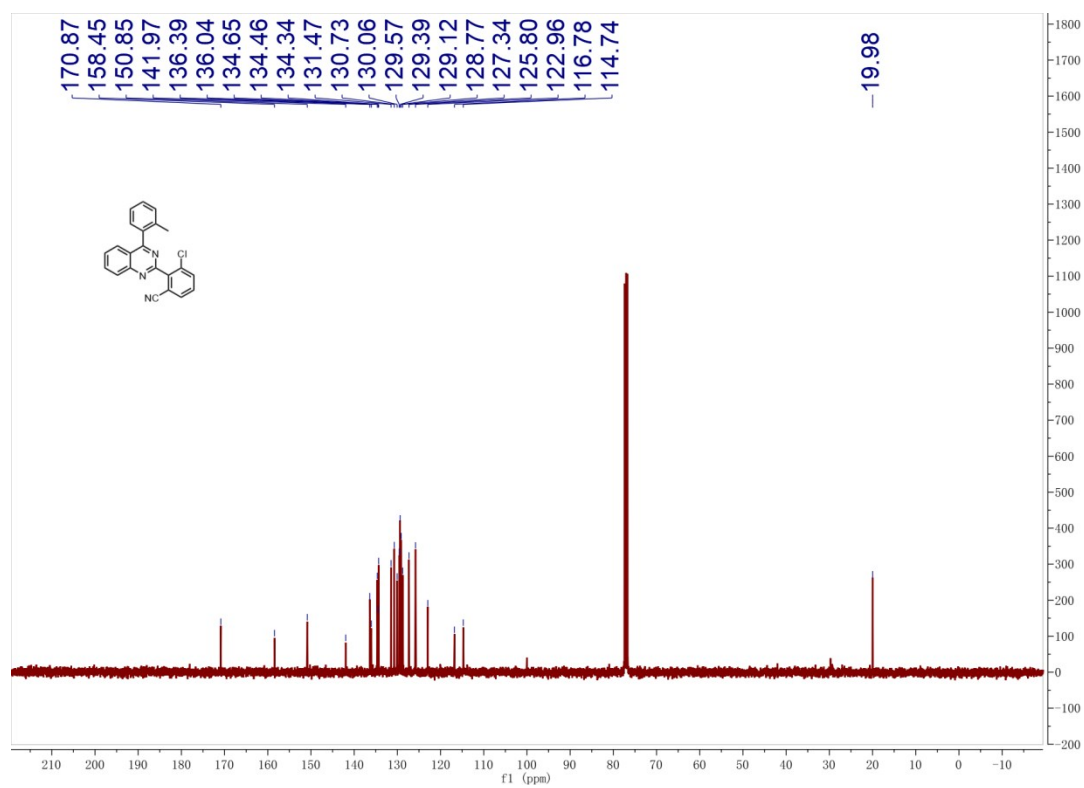
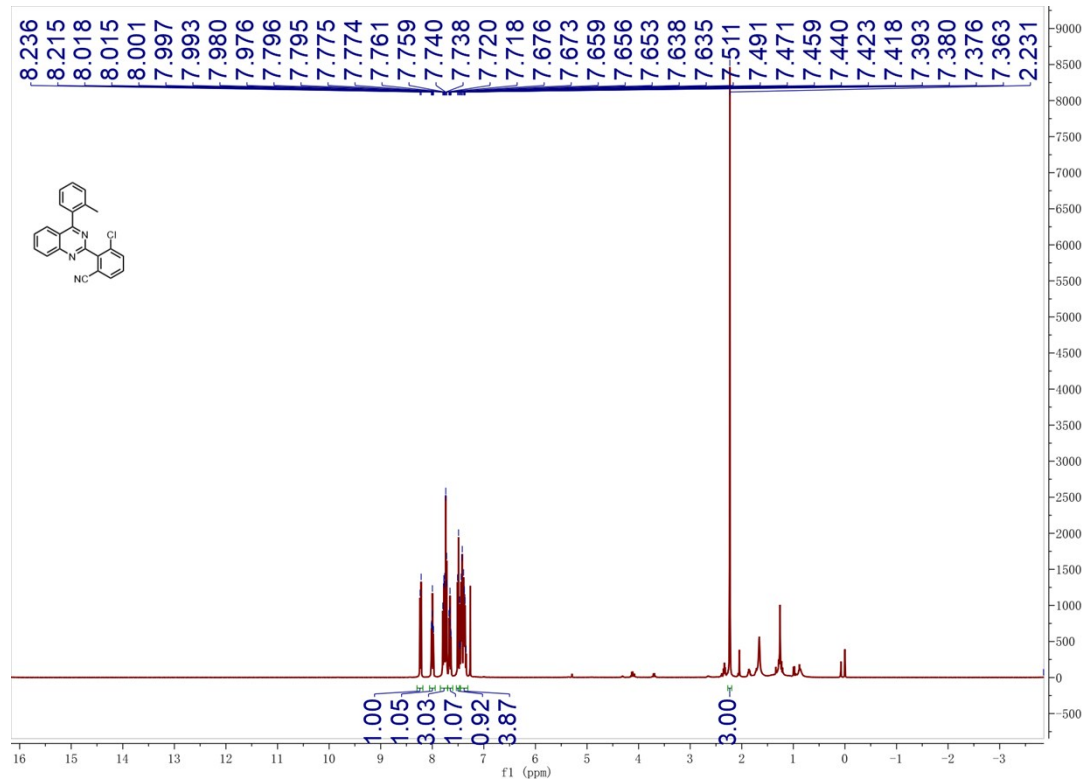
(3h)



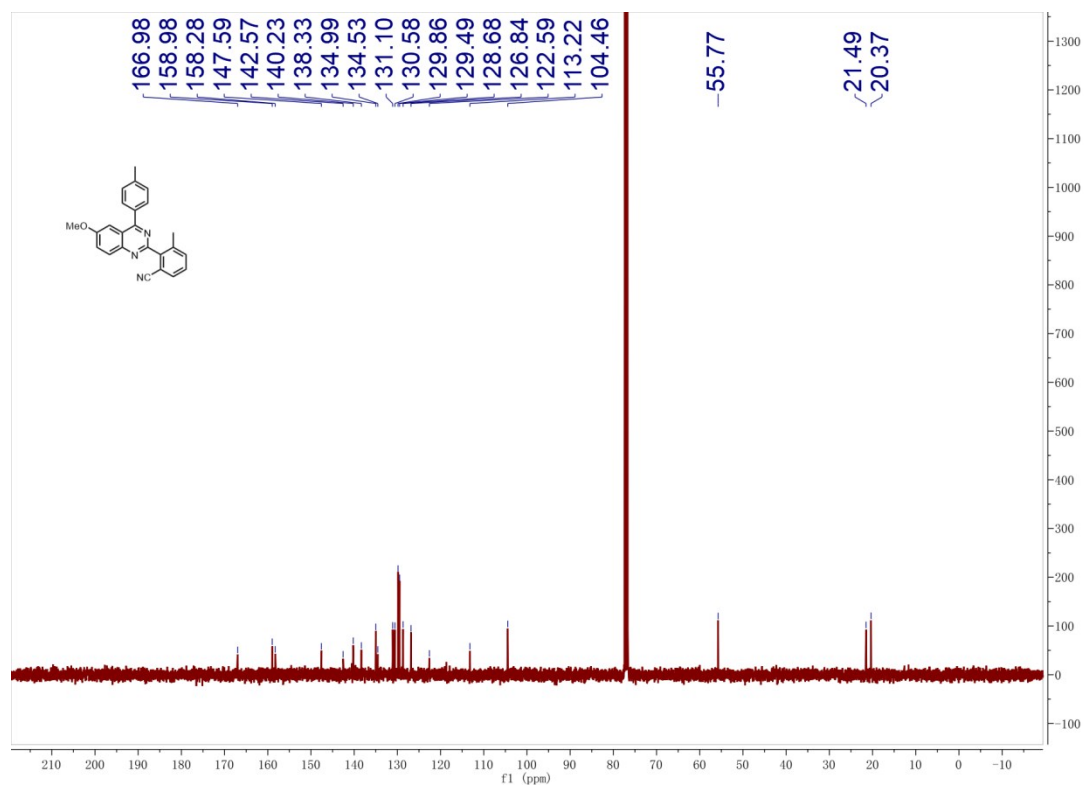
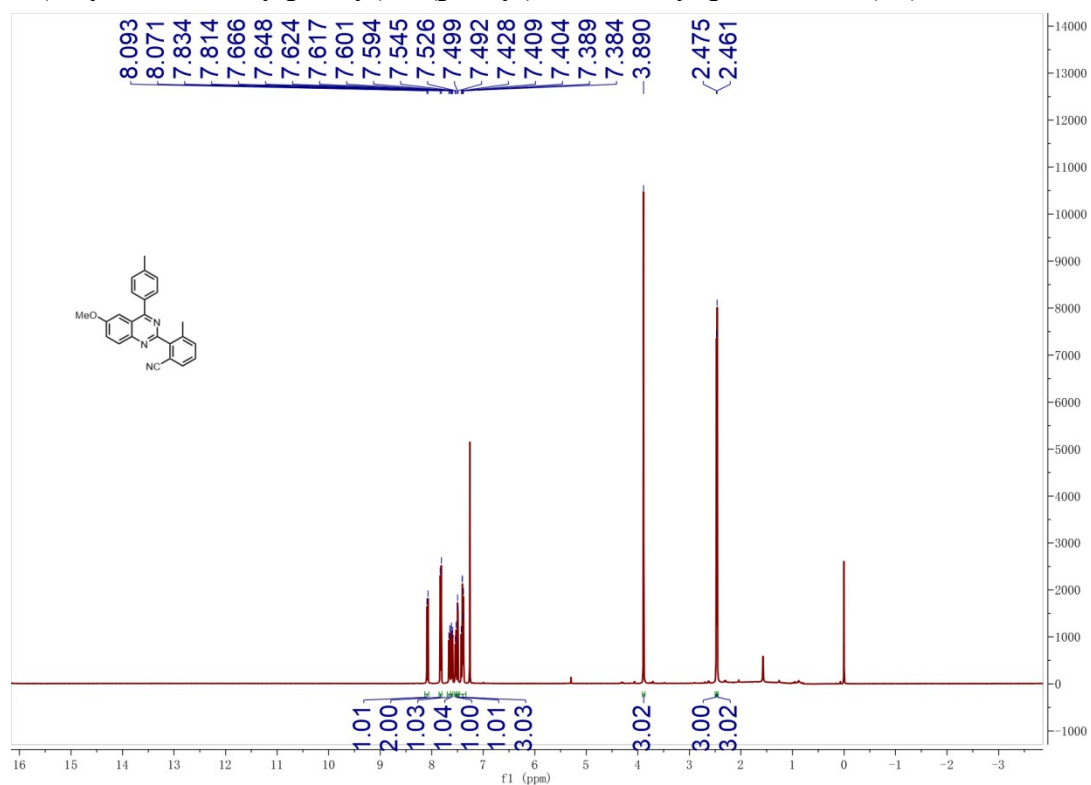
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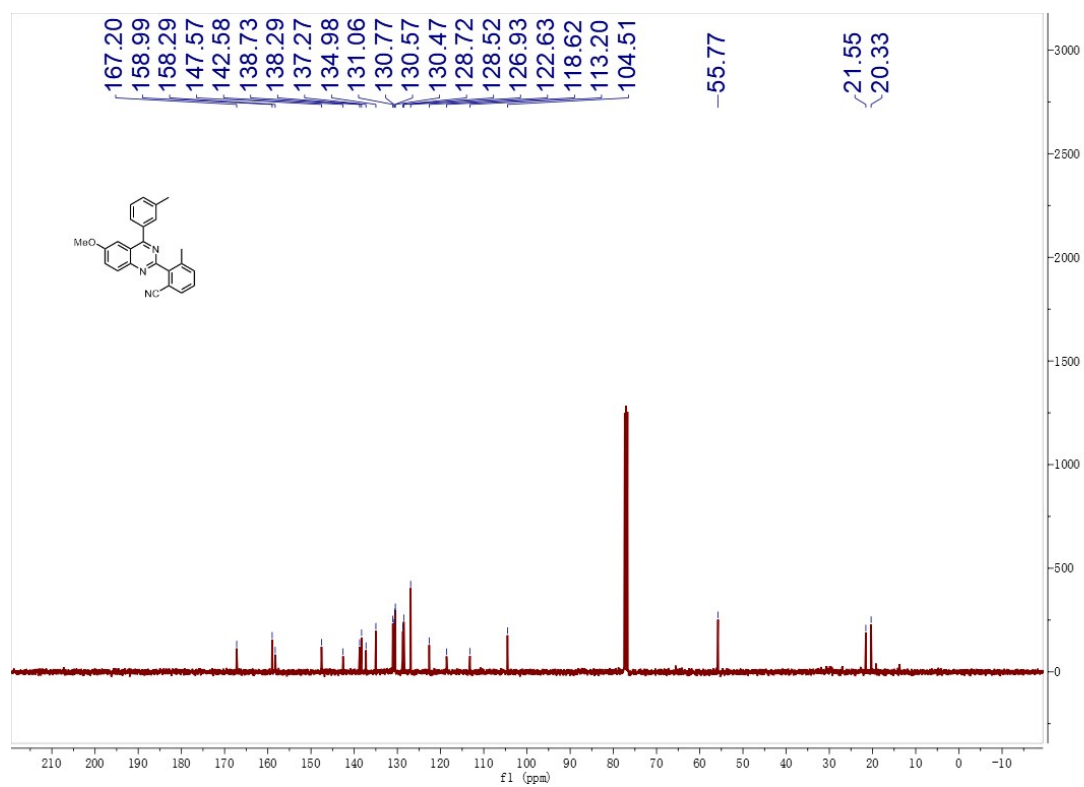
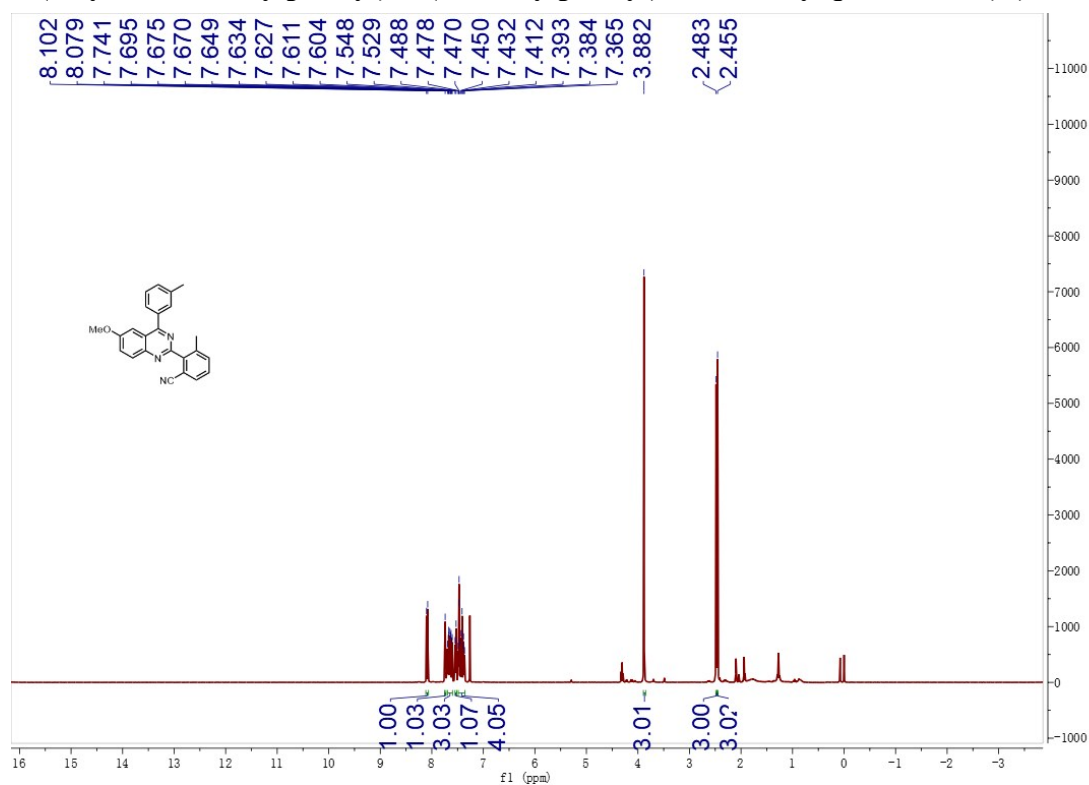
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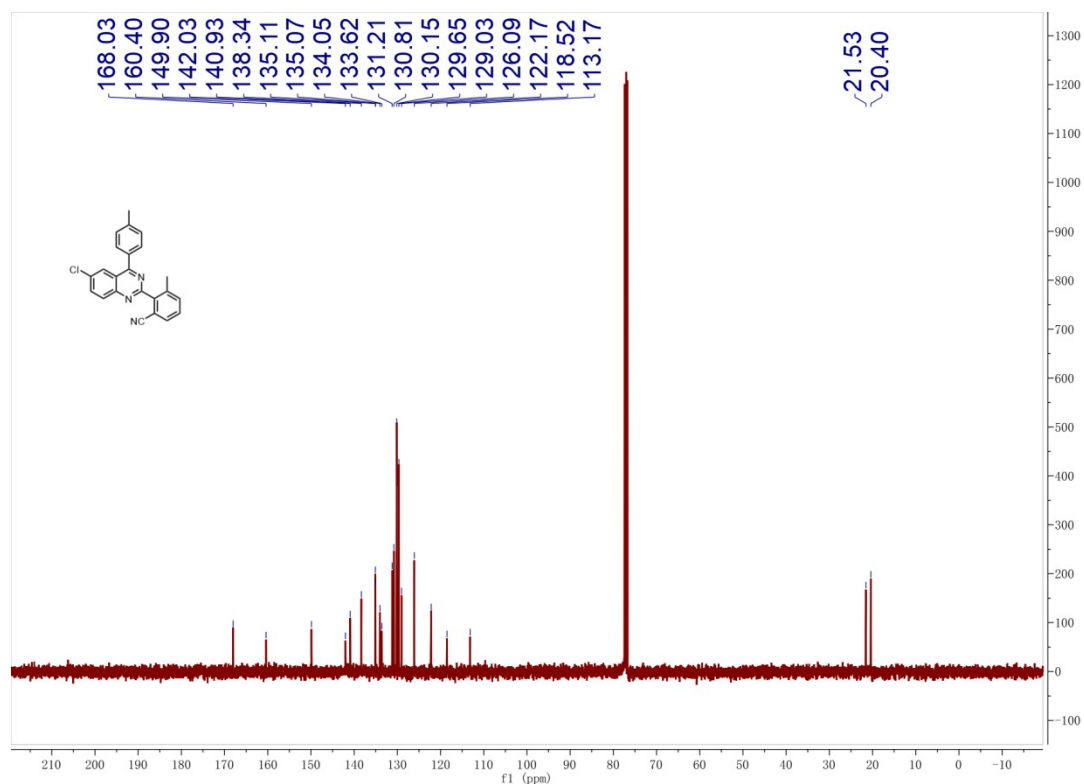
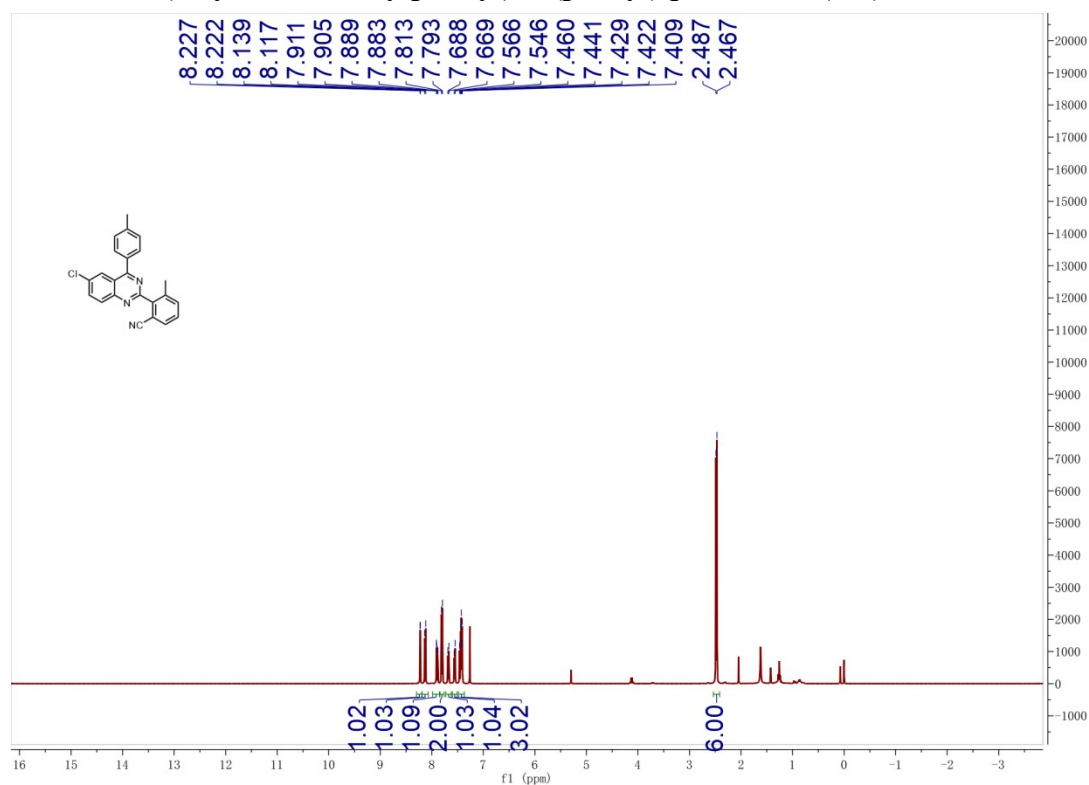
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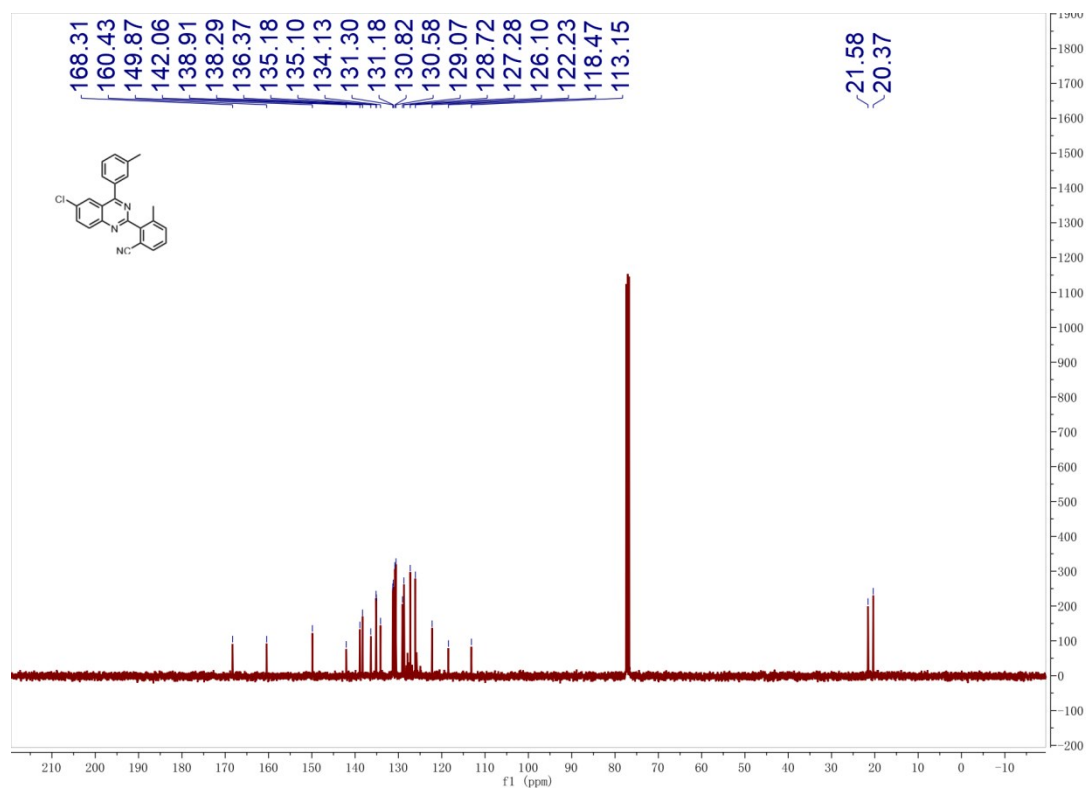
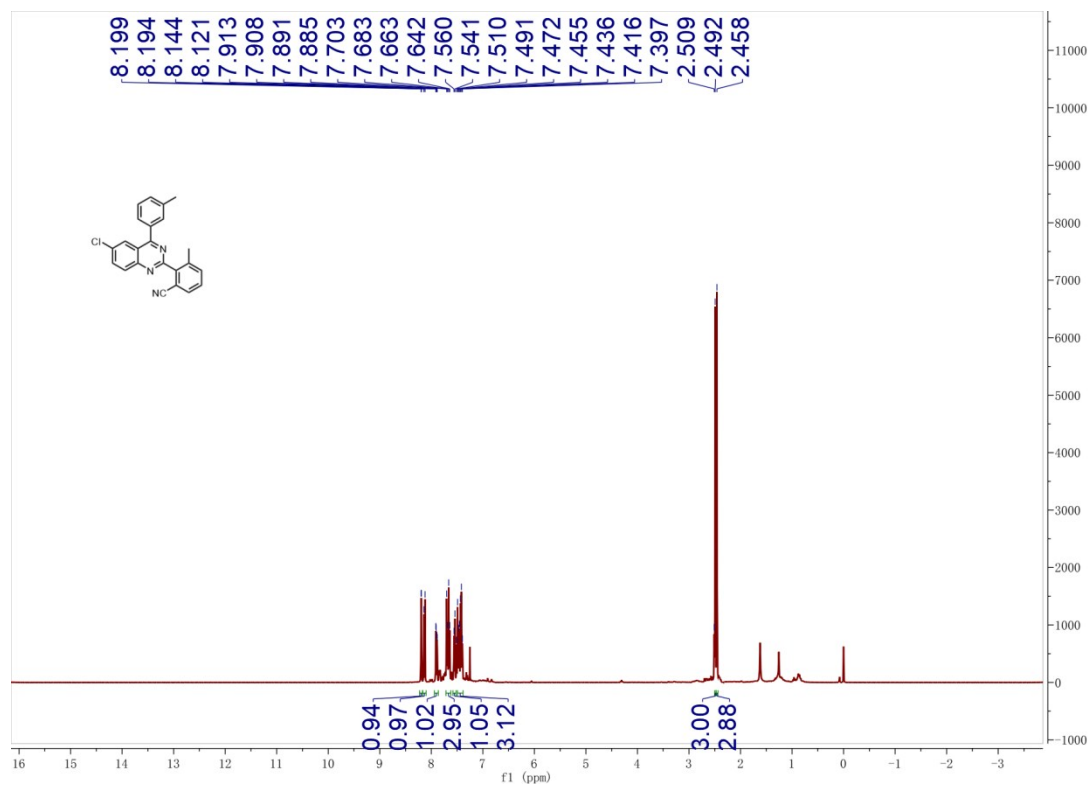
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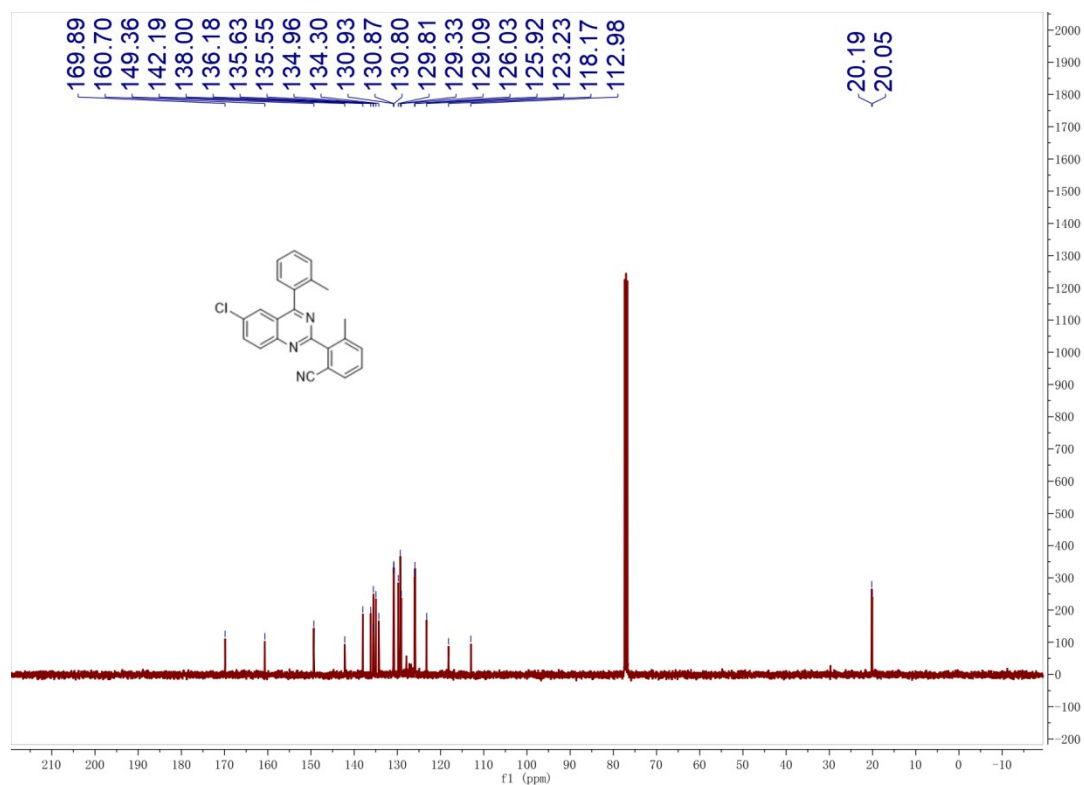
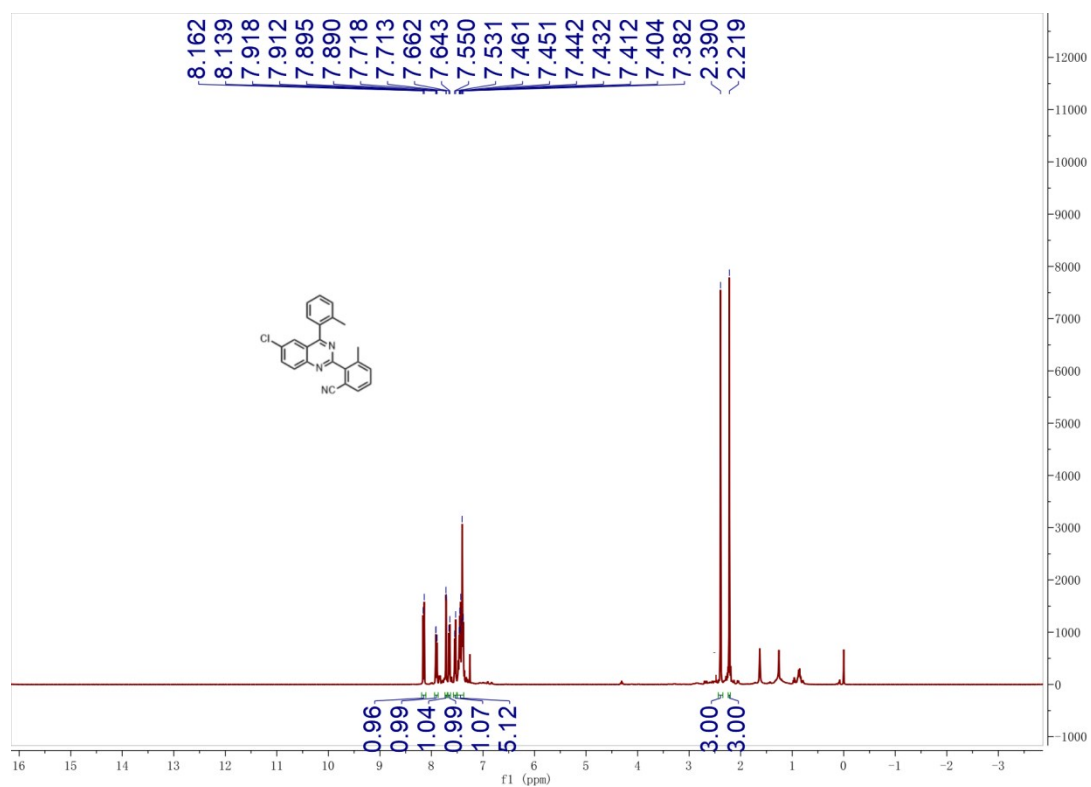
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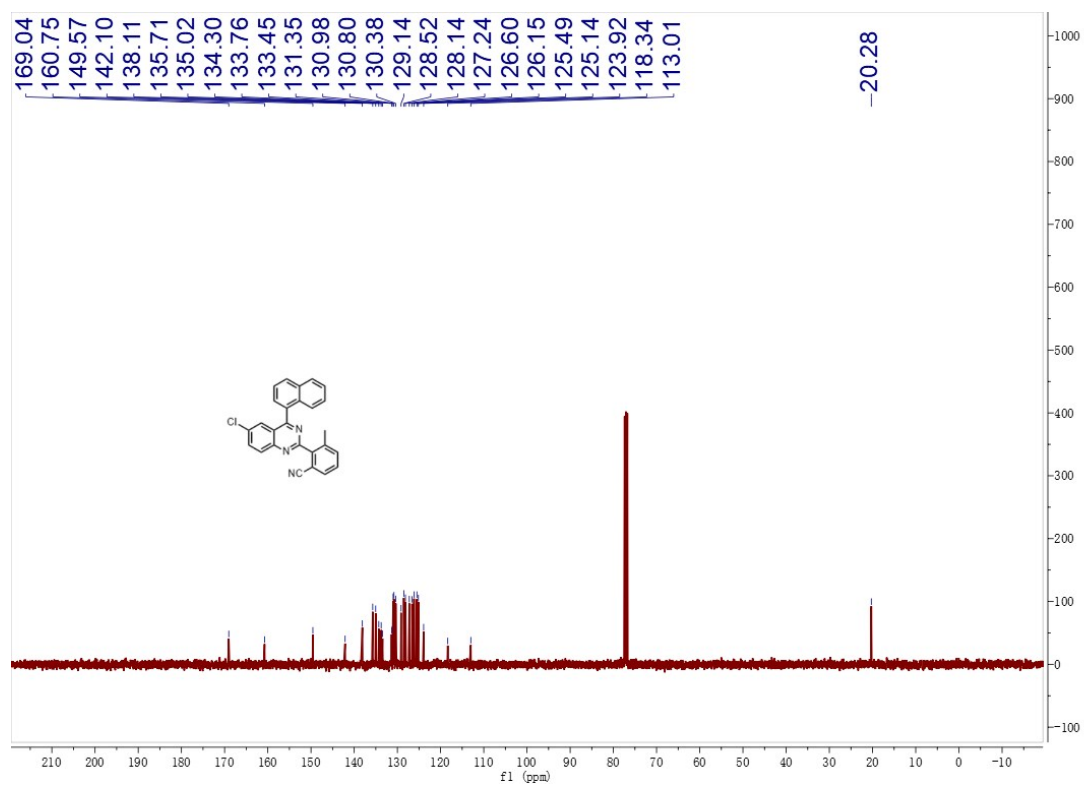
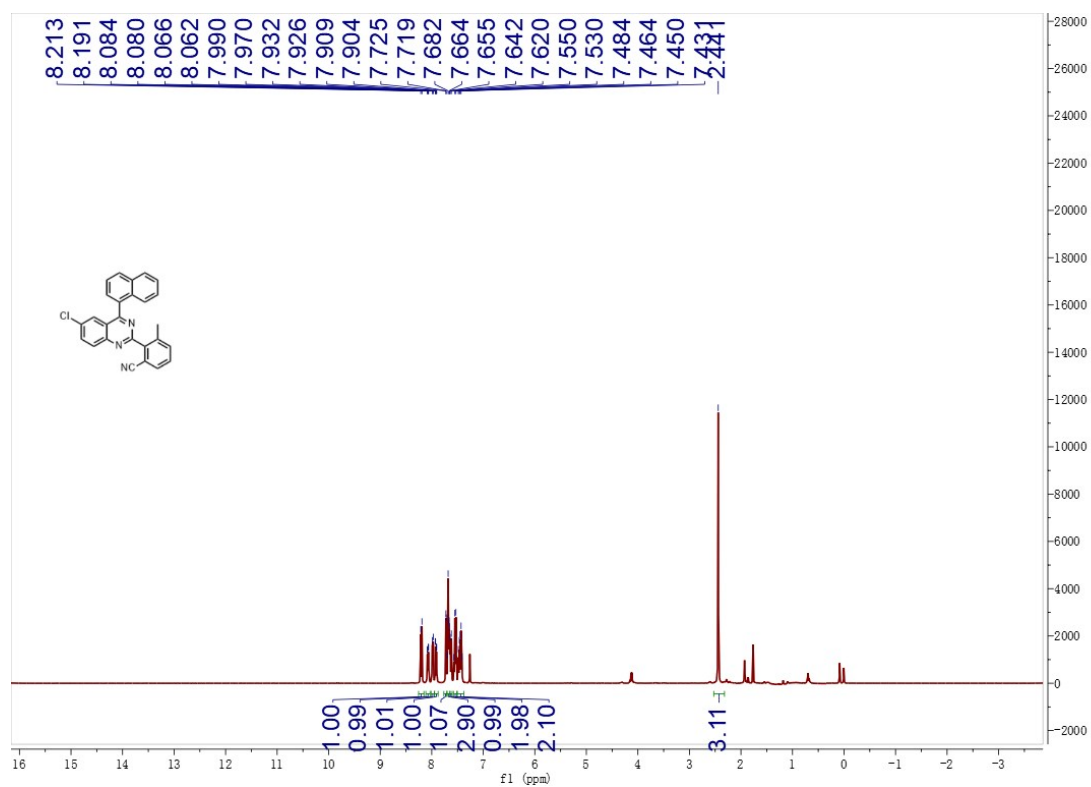
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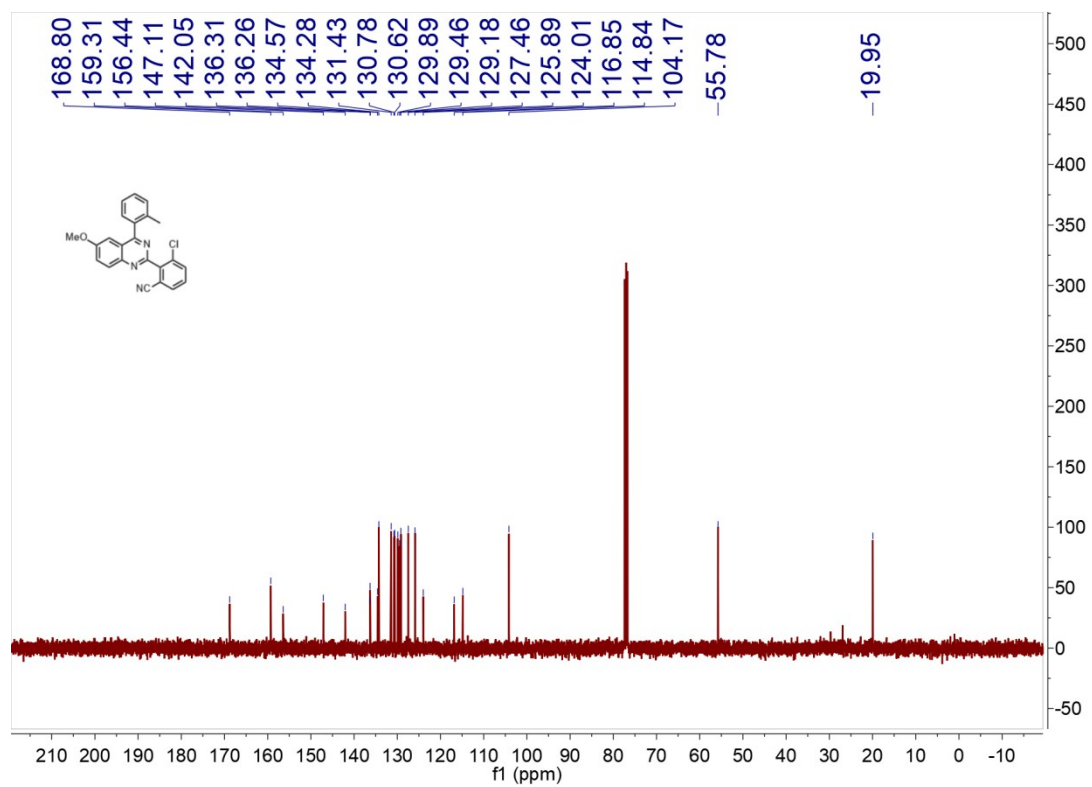
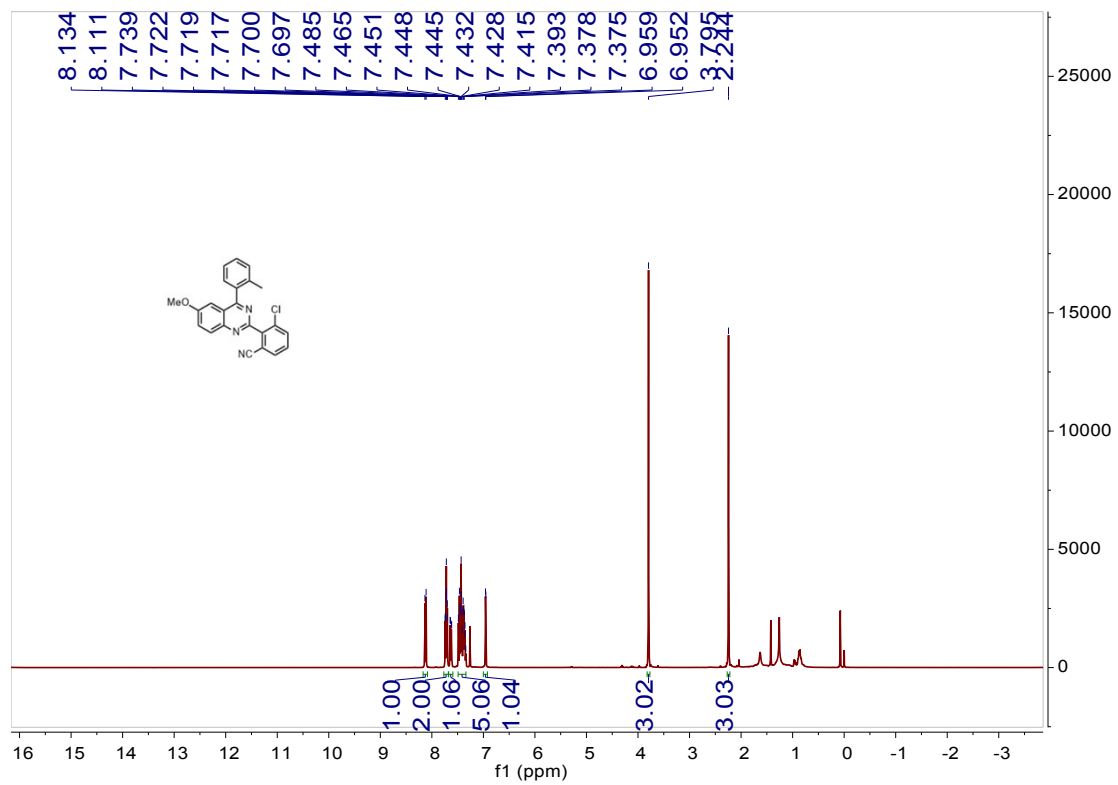
6-chloro-2-(2-cyano-6-methylphenyl)-4-(2-methylphenyl)quinazoline (30)



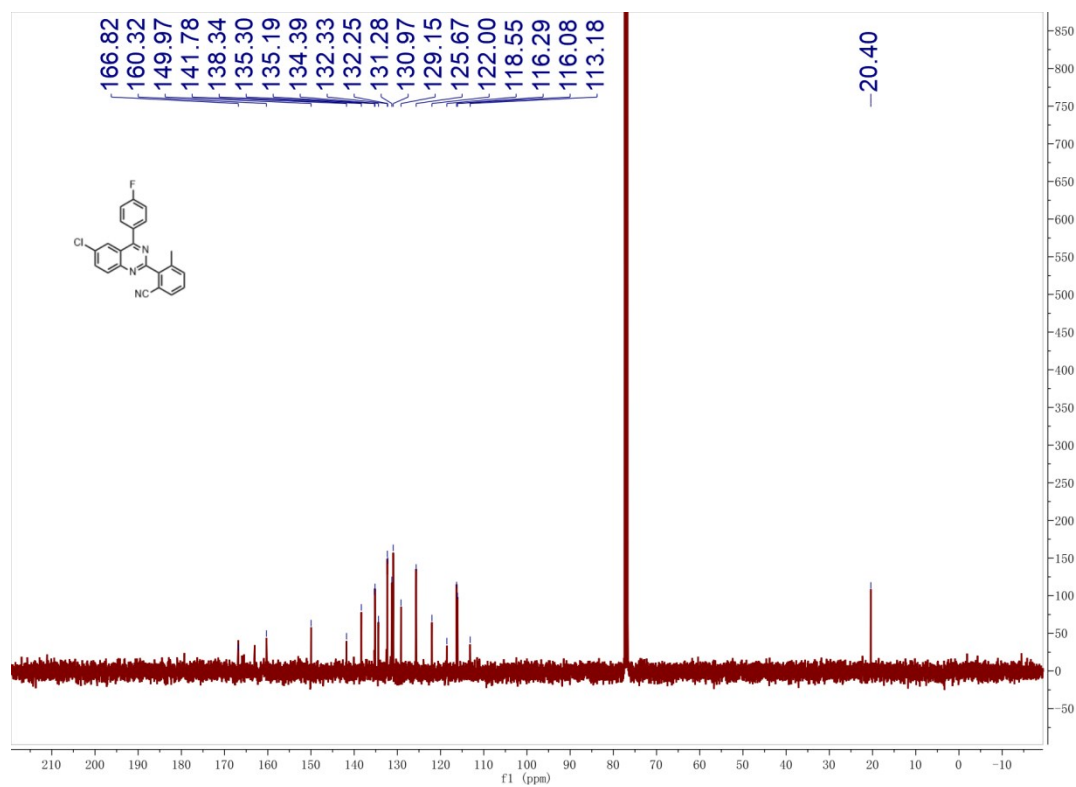
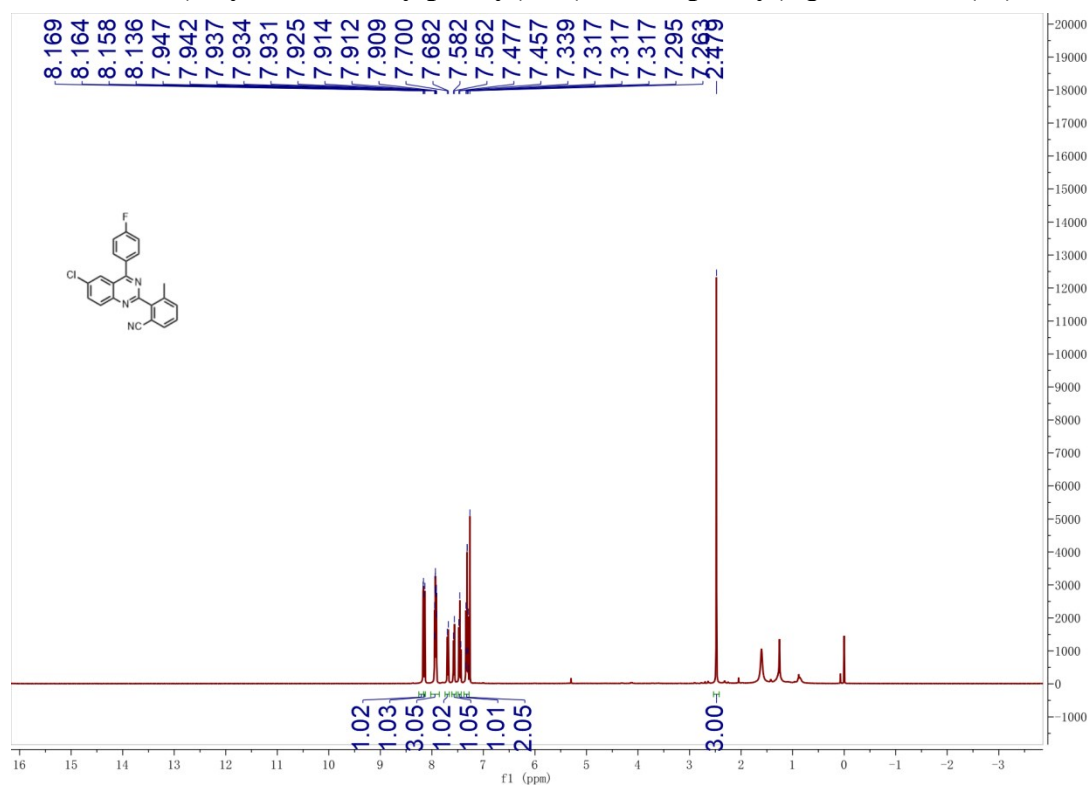
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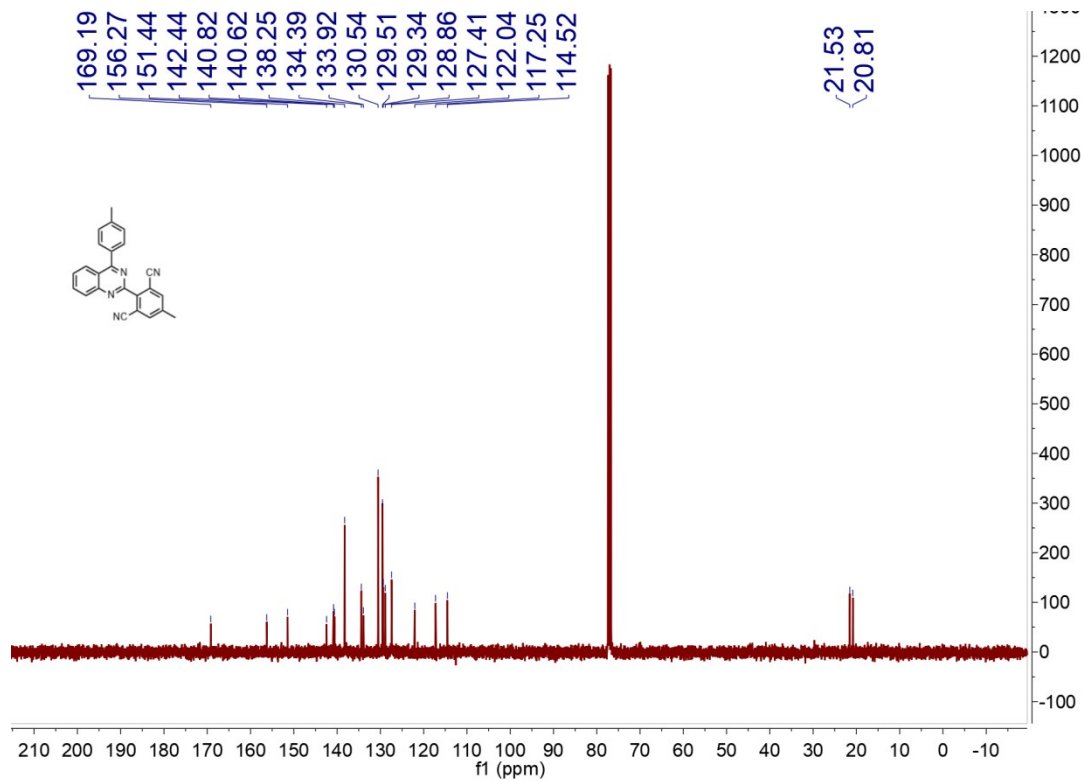
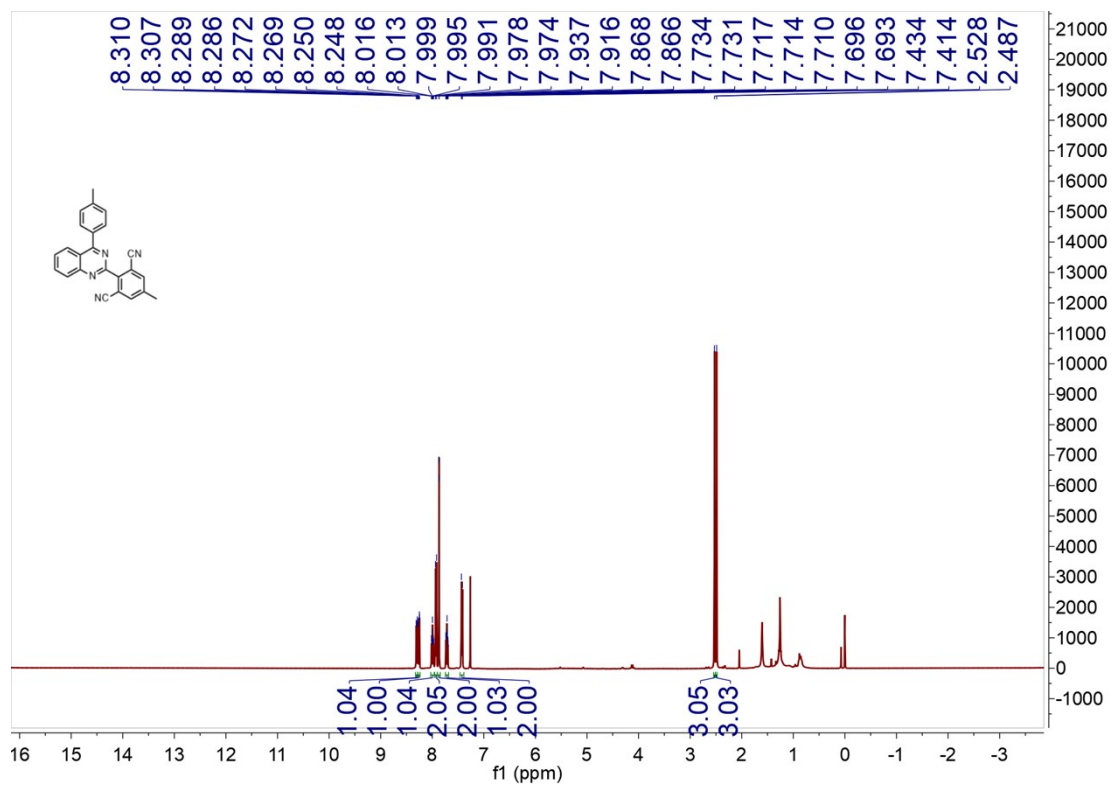
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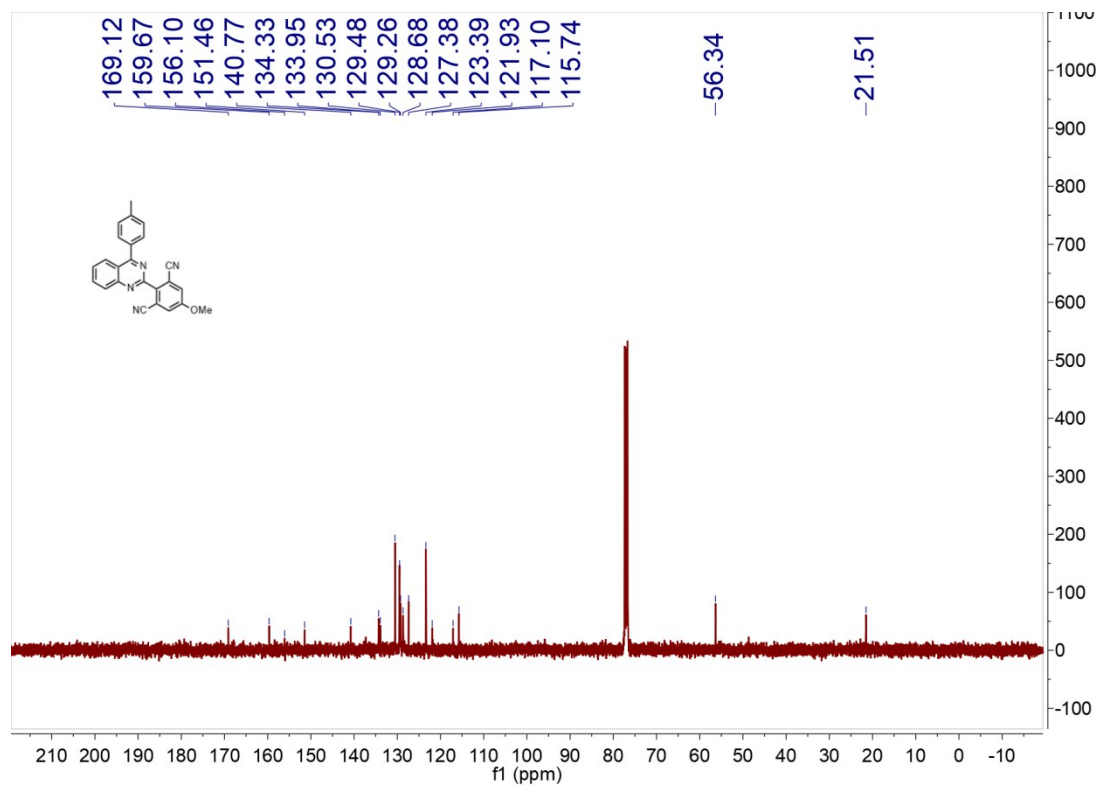
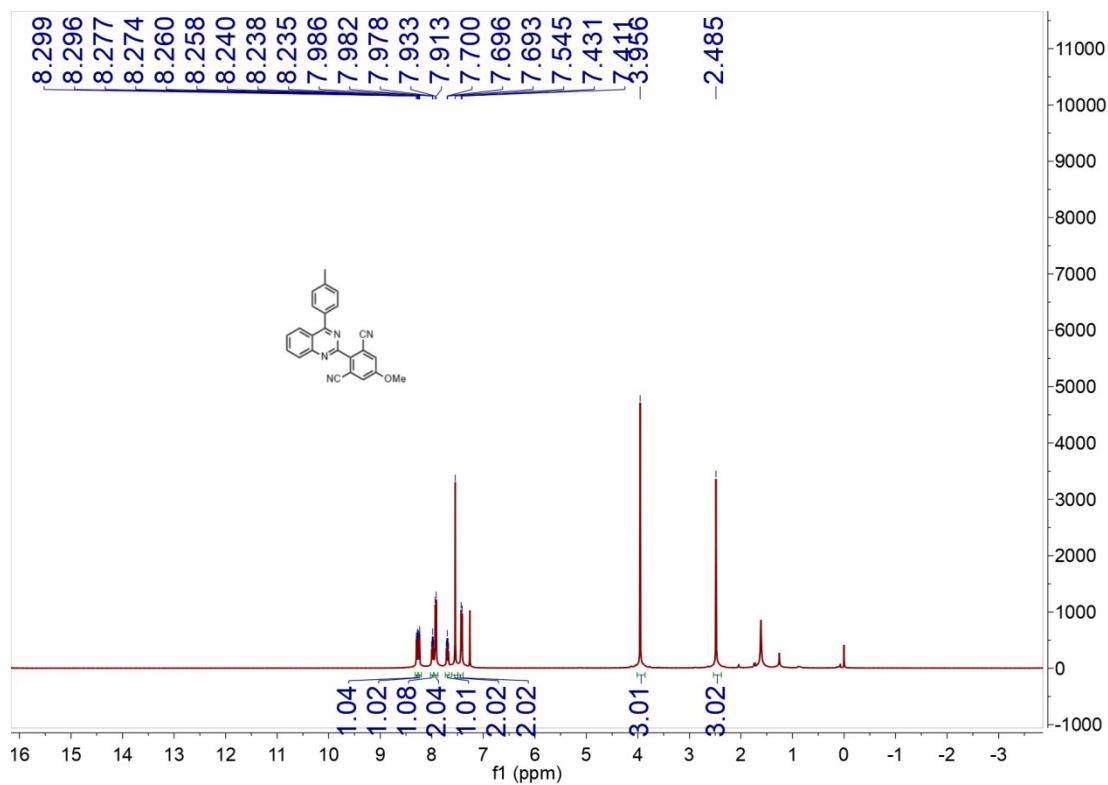
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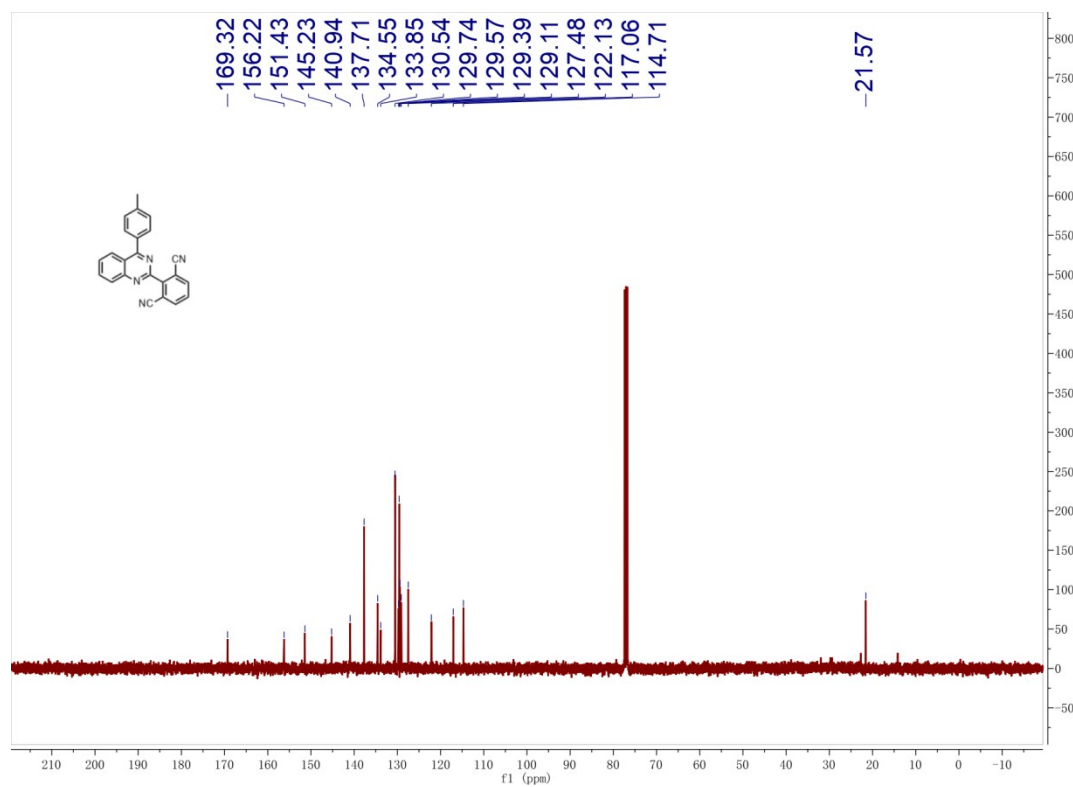
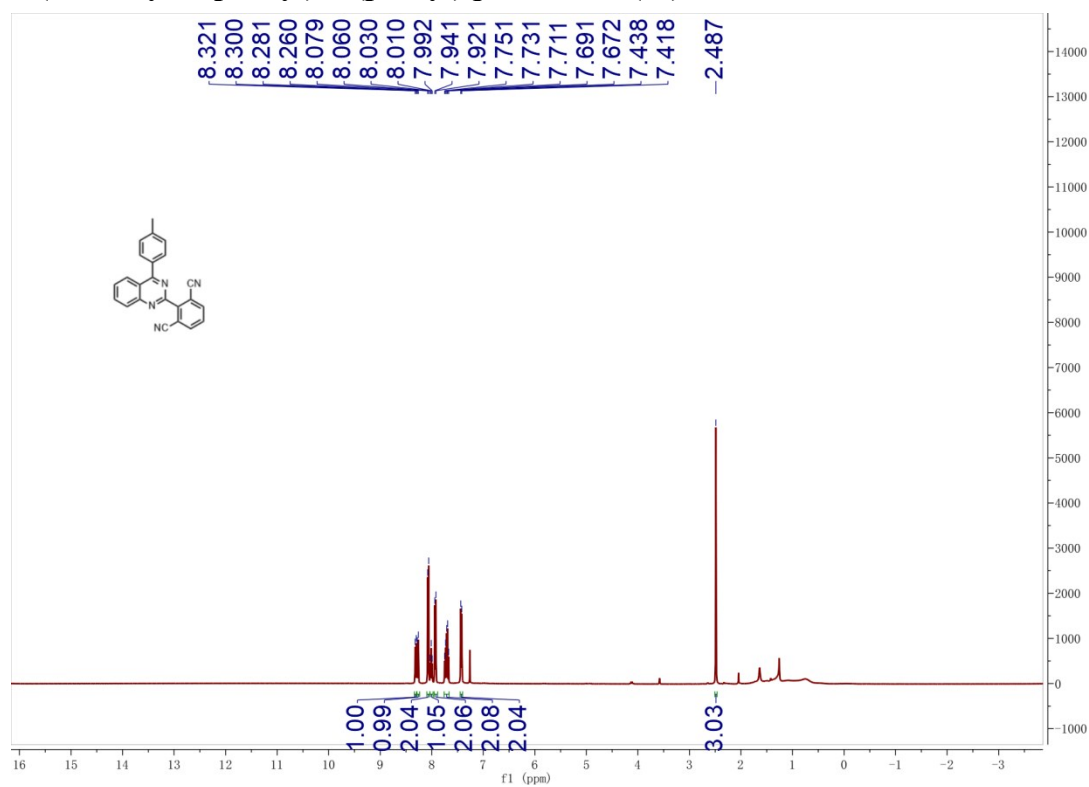
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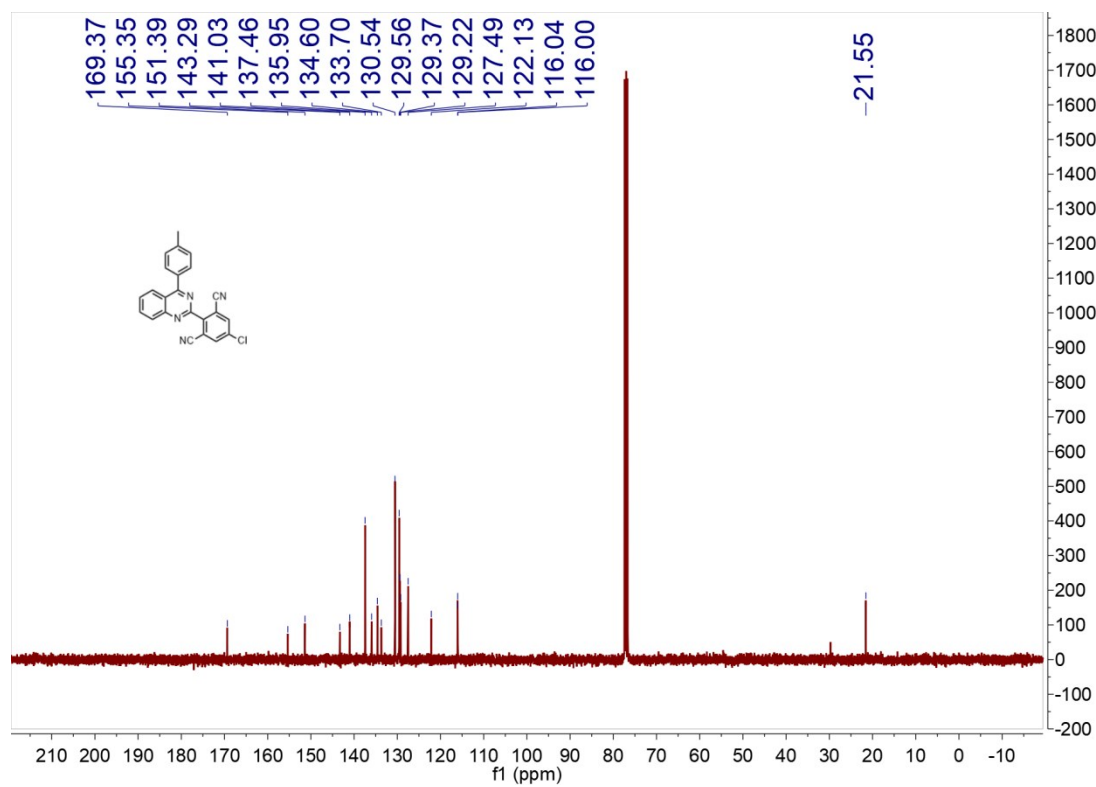
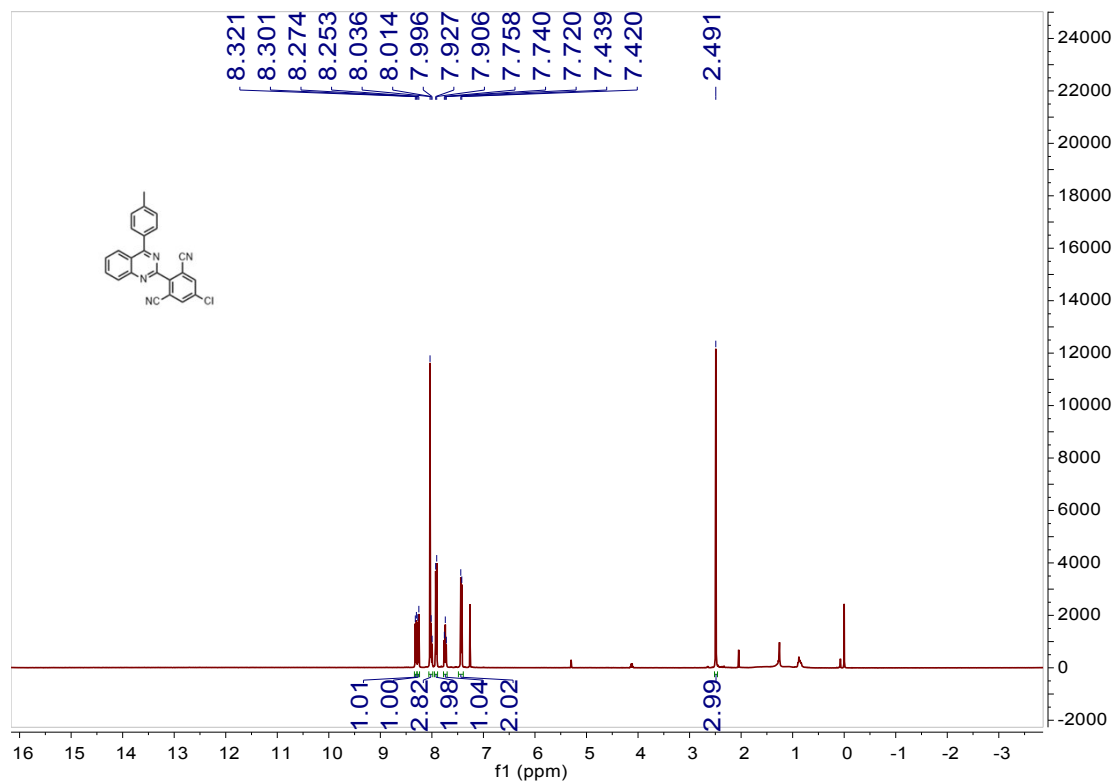
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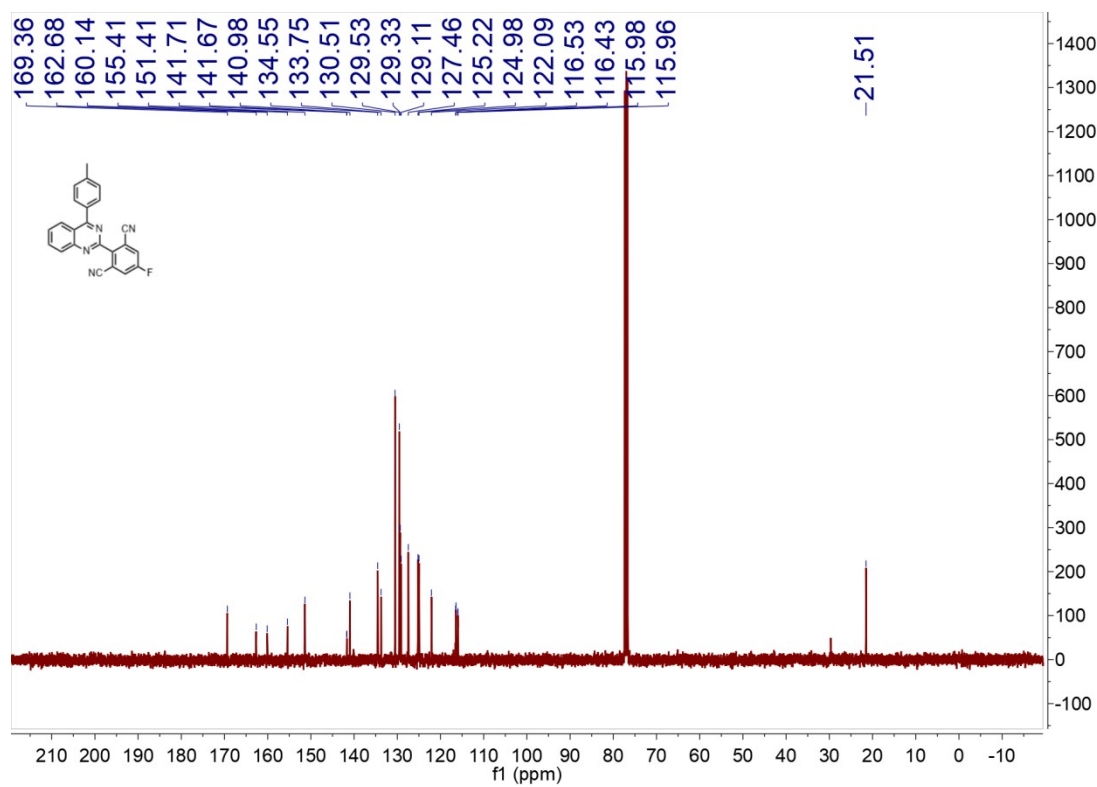
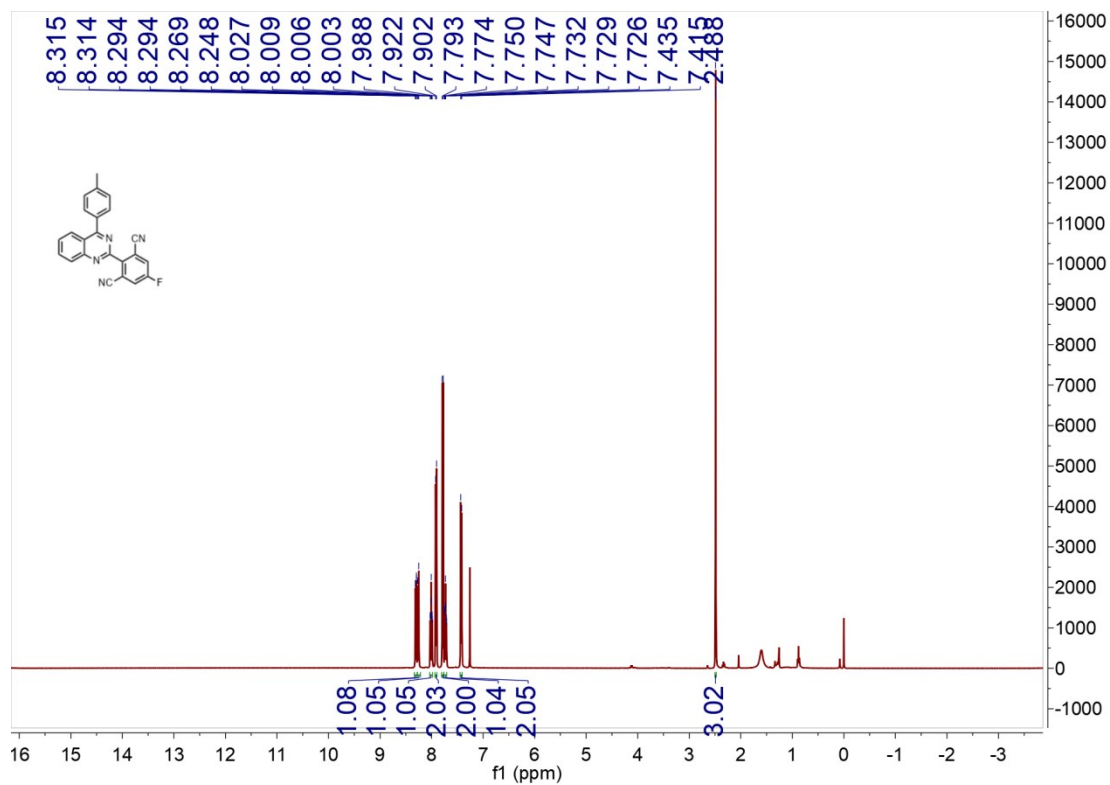
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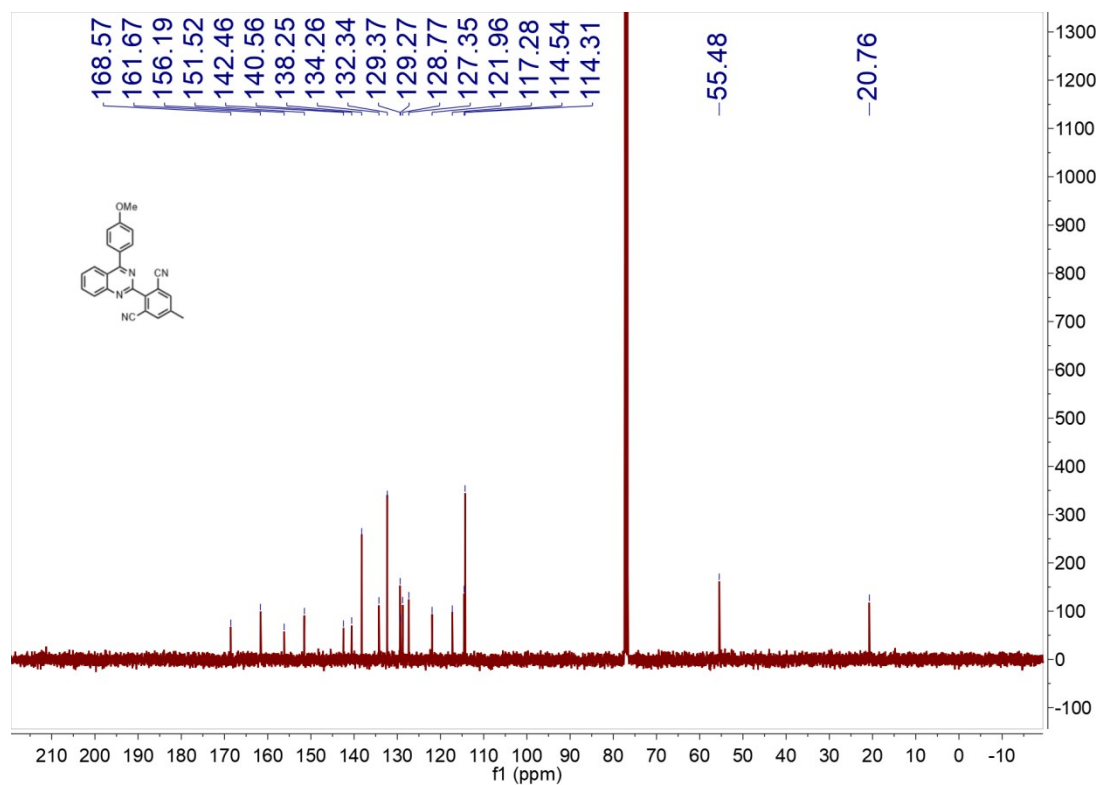
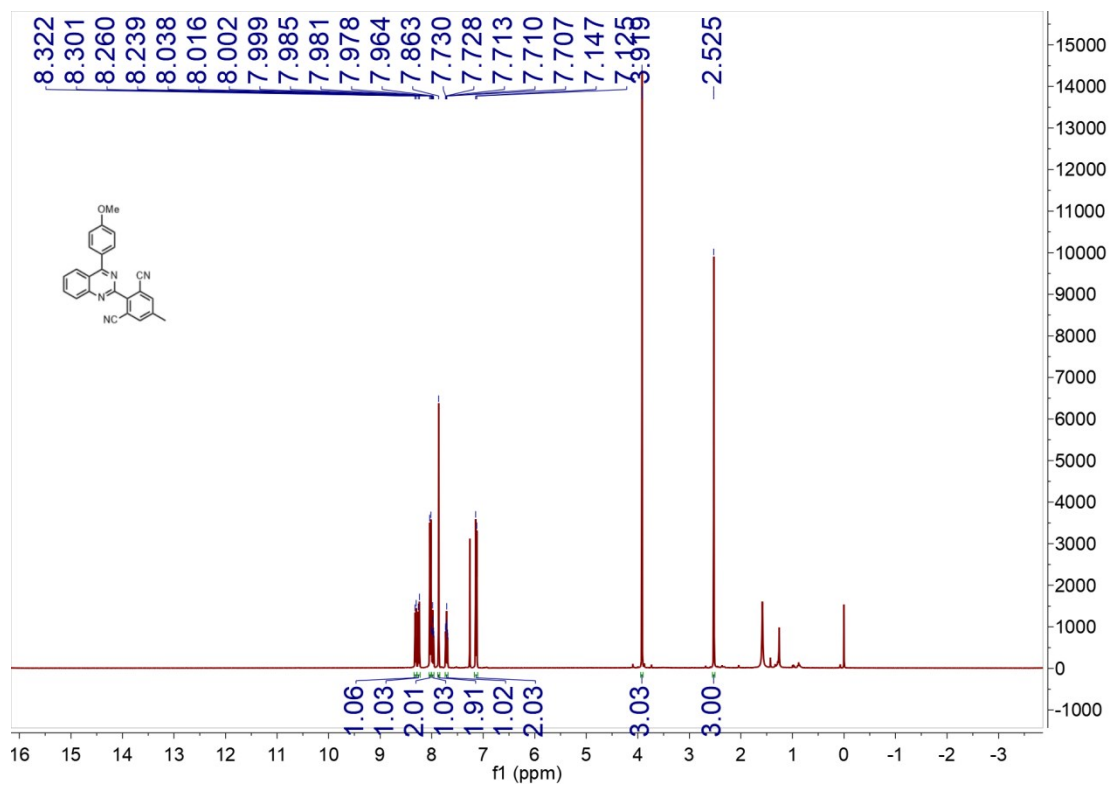
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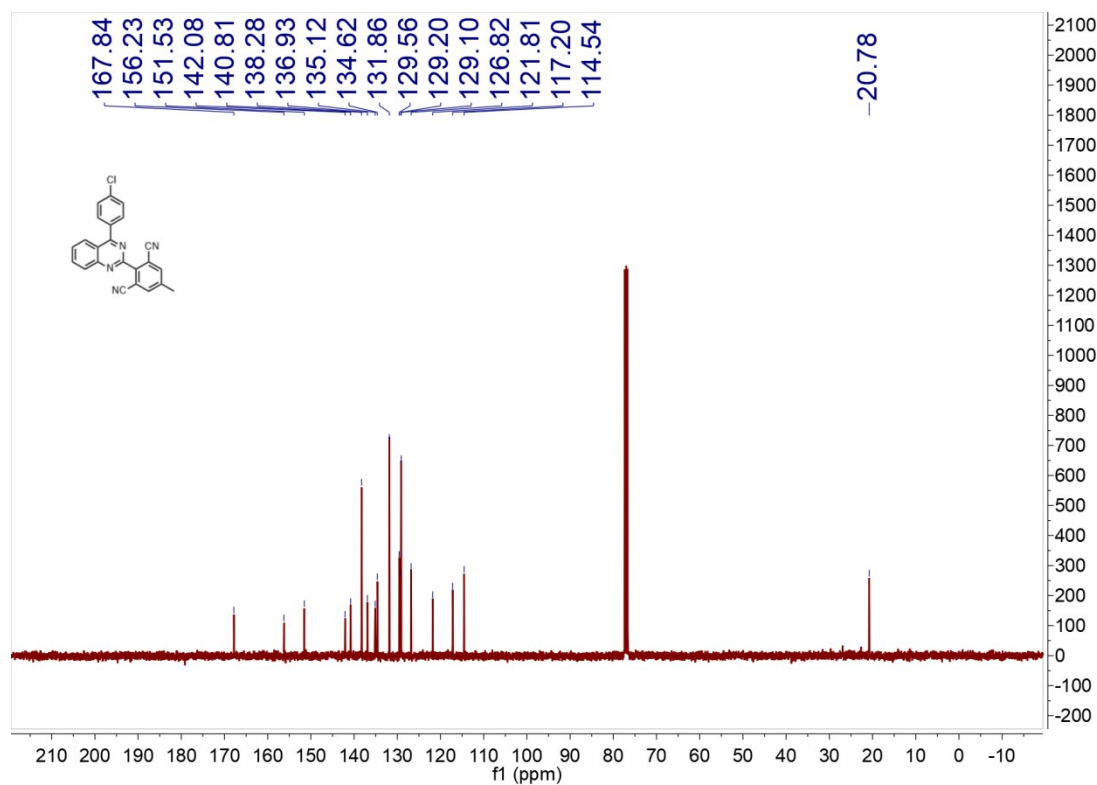
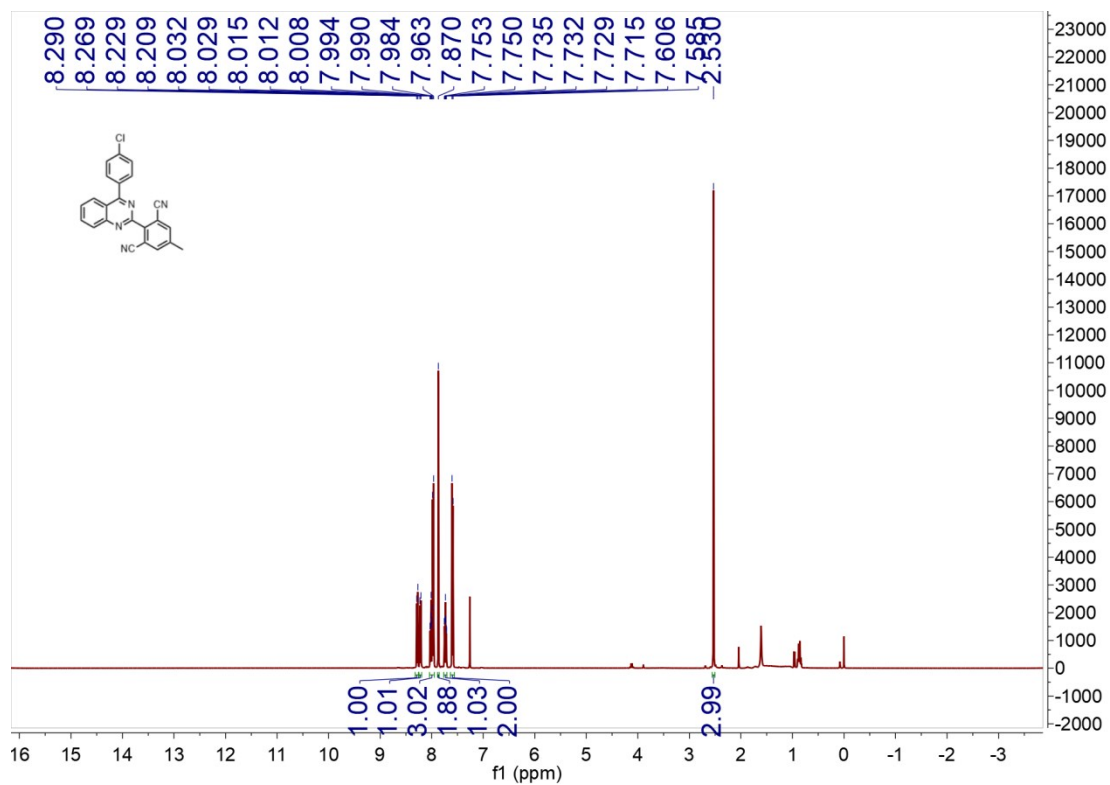
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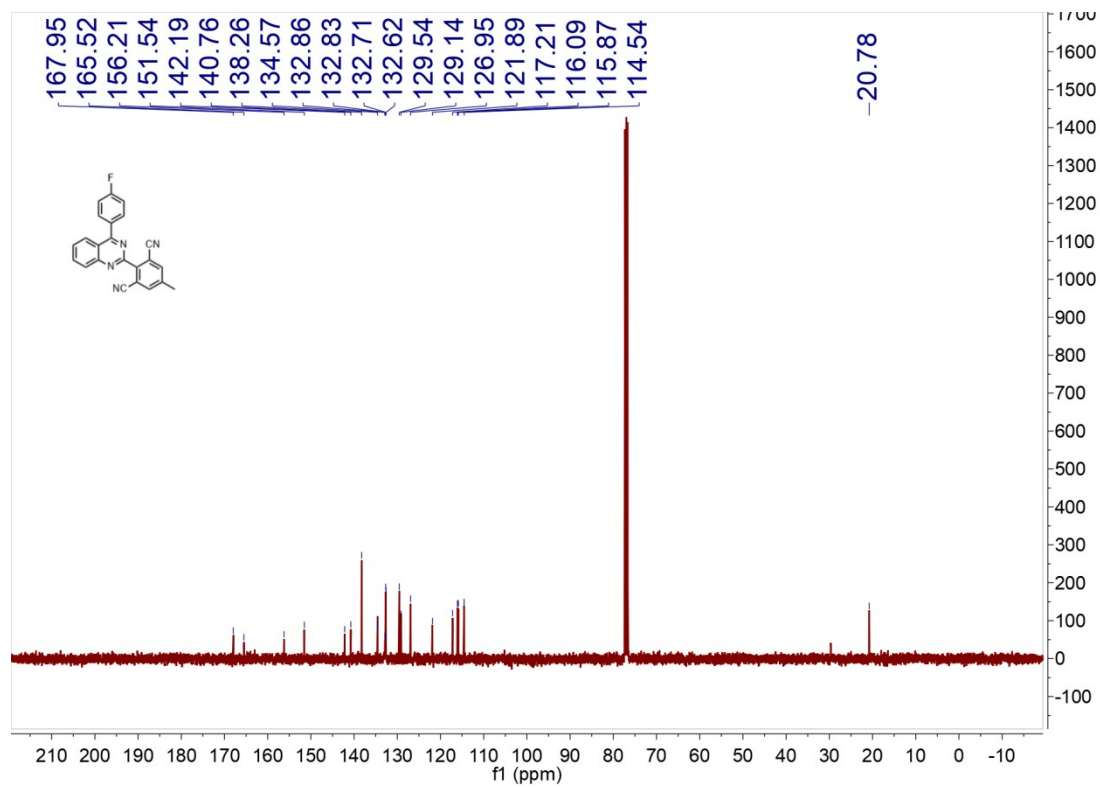
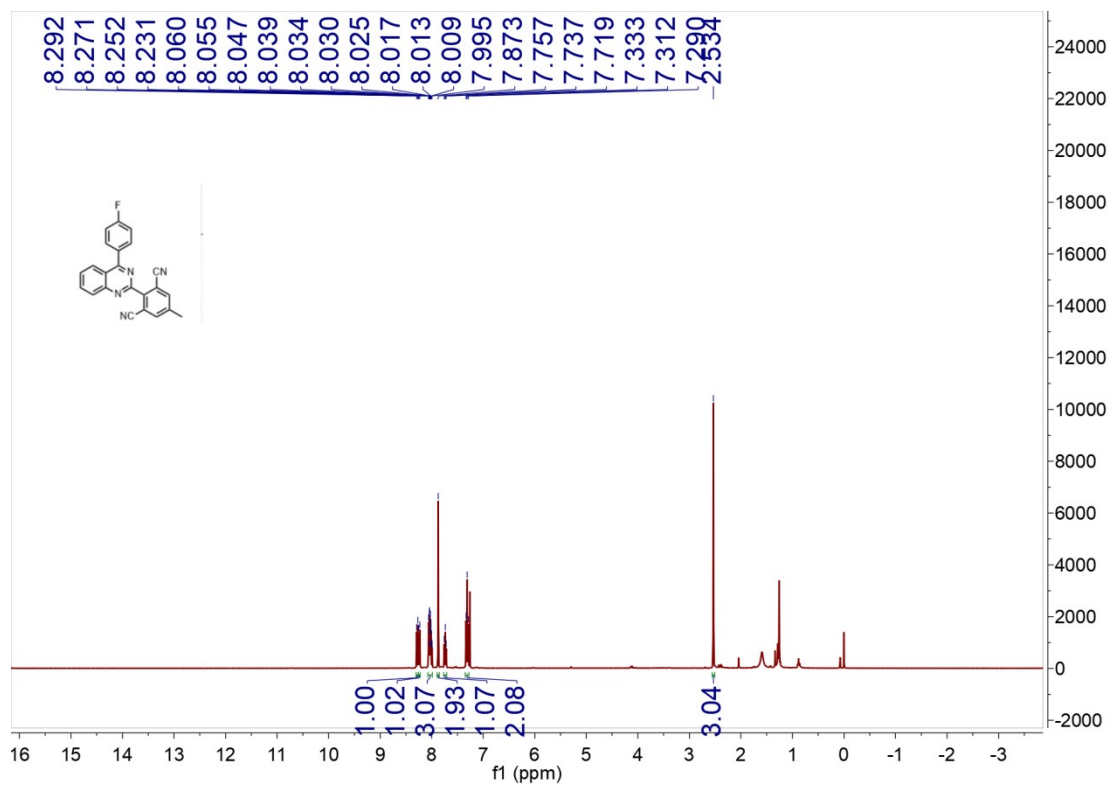
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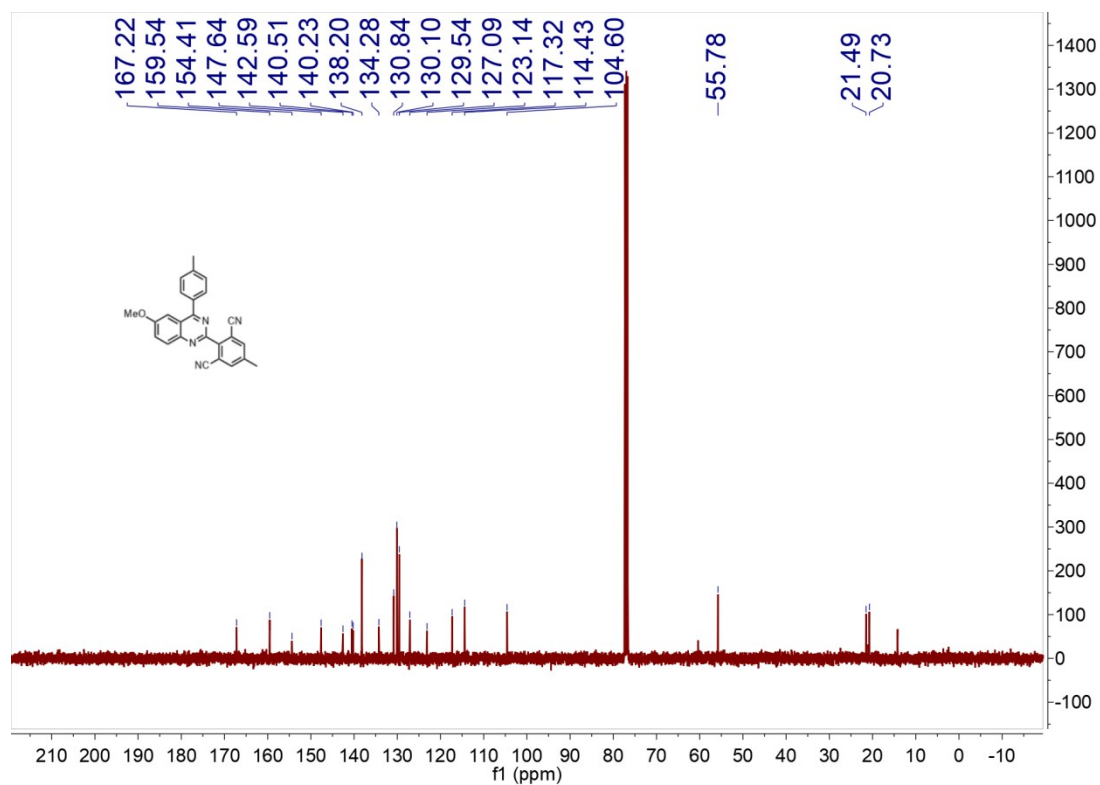
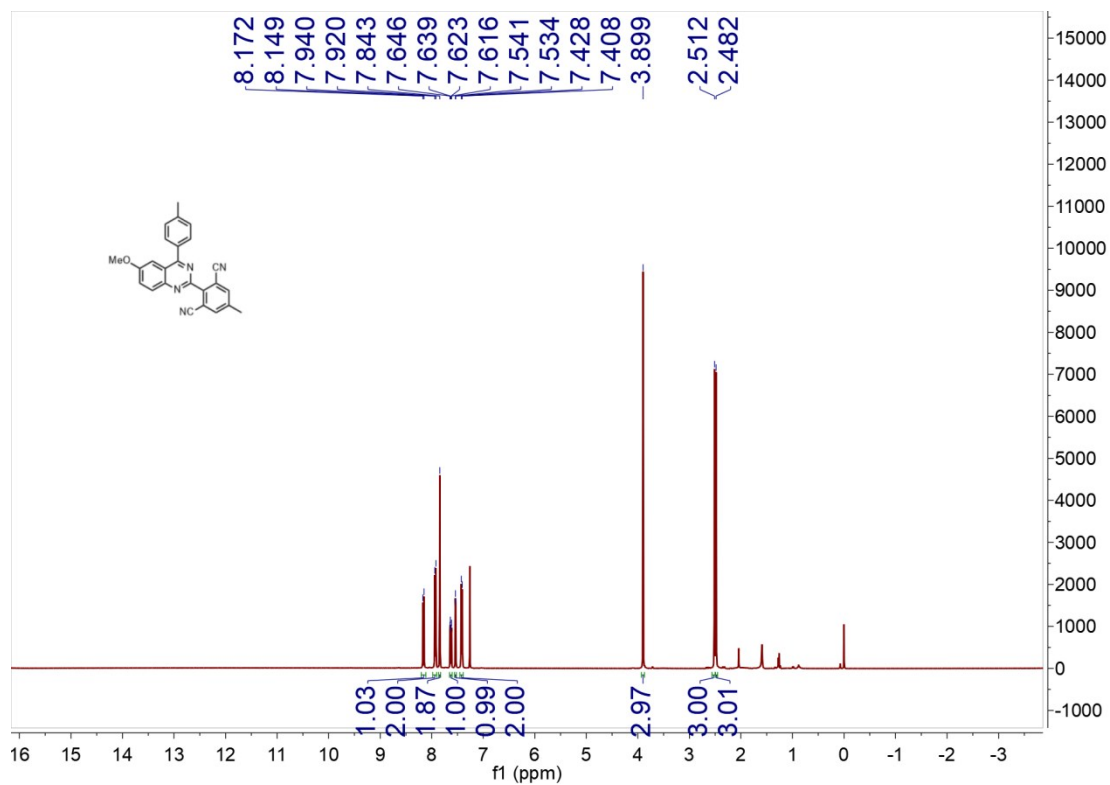
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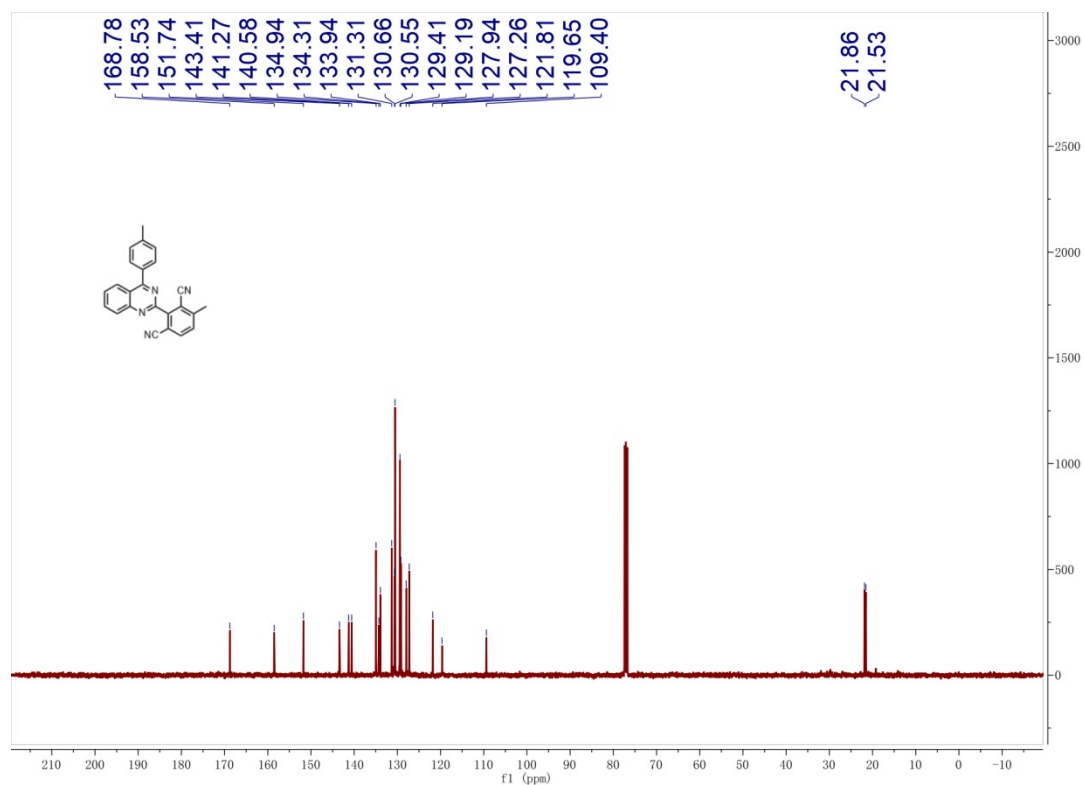
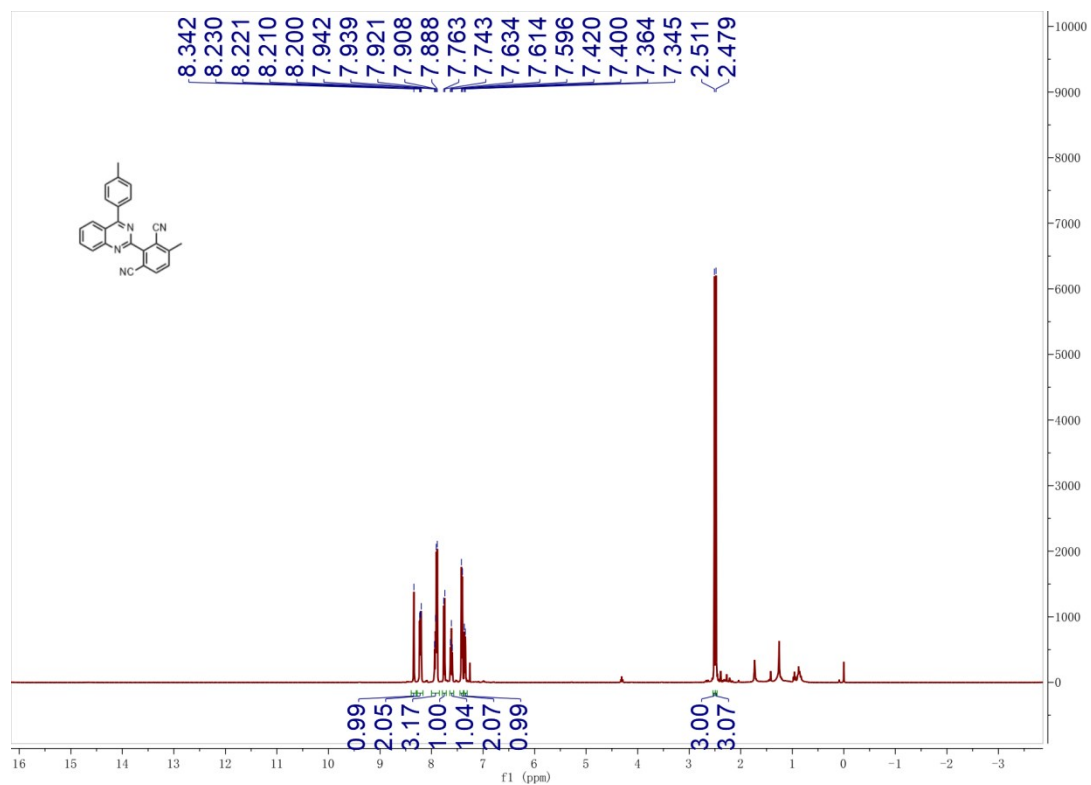
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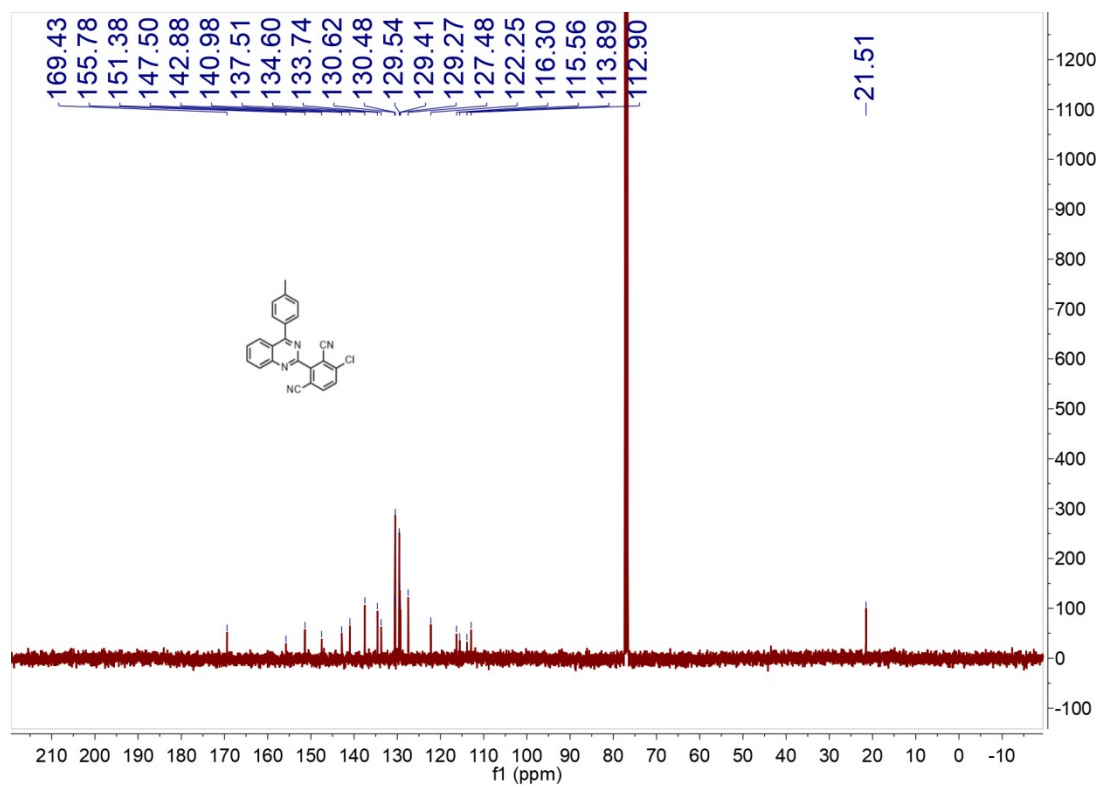
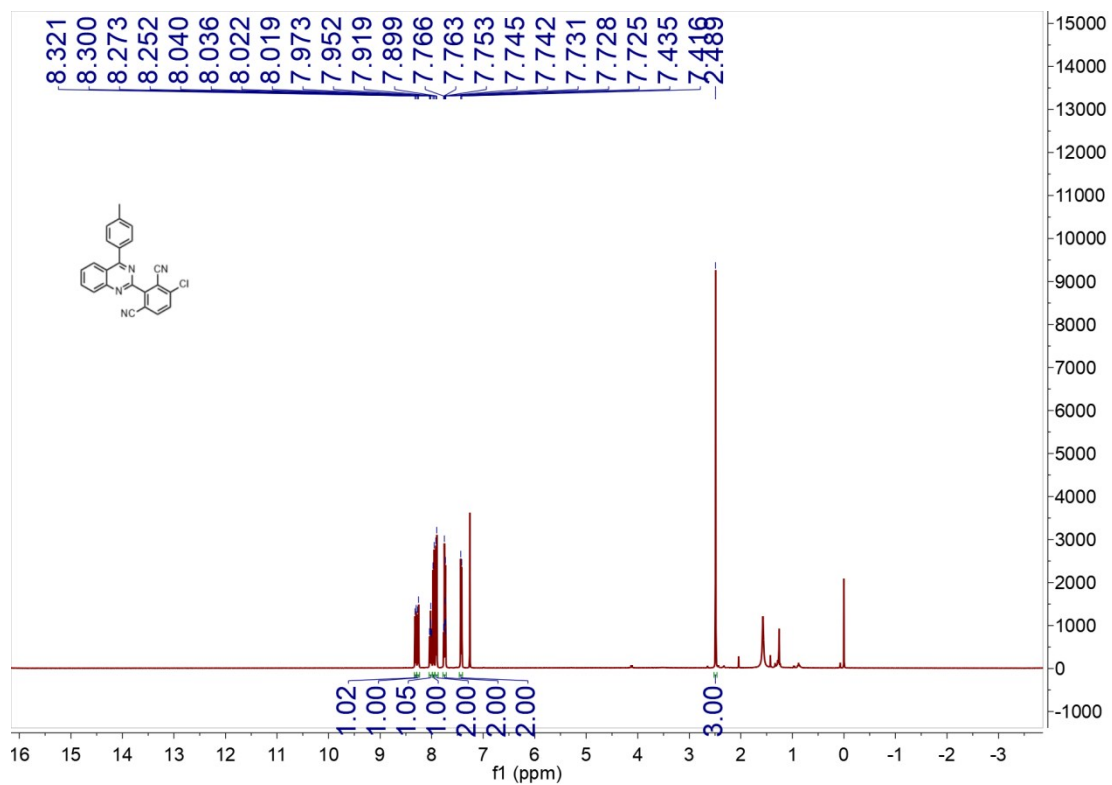
2-(2,6-dicyano-4-methylphenyl)-4-(p-tolyl)-6-methoxyquinazoline(4i)



2-(2, 6-dicyano-3-methylphenyl)-4-(p-tolyl)quinazoline (4j)



2-(2, 6-dicyano-3-chlorophenyl)-4-(p-tolyl)quinazoline (4k)



2-(Pyridin-2-yl)isophthalonitrile (4l)

