

**SUPPORTING INFORMATION**

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**Title:** Convenient Access to Di- and Trifluoroethylamines for Lead Structure Research

**Author(s):** Amrei Deutsch, Christian Wagner, Carl Deutsch,\* Anja Hoffmann-Röder\*

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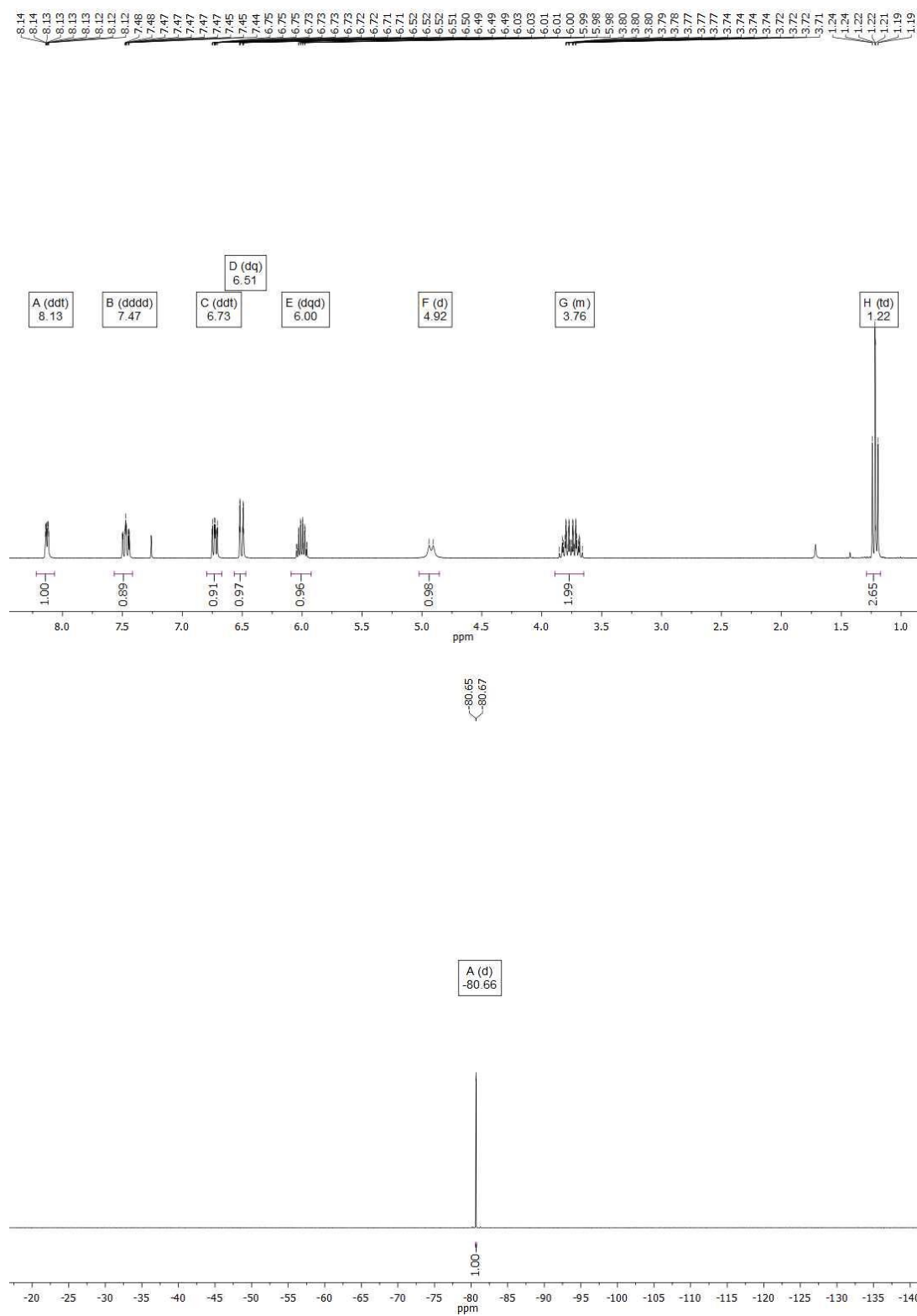
## 1. Materials and methods

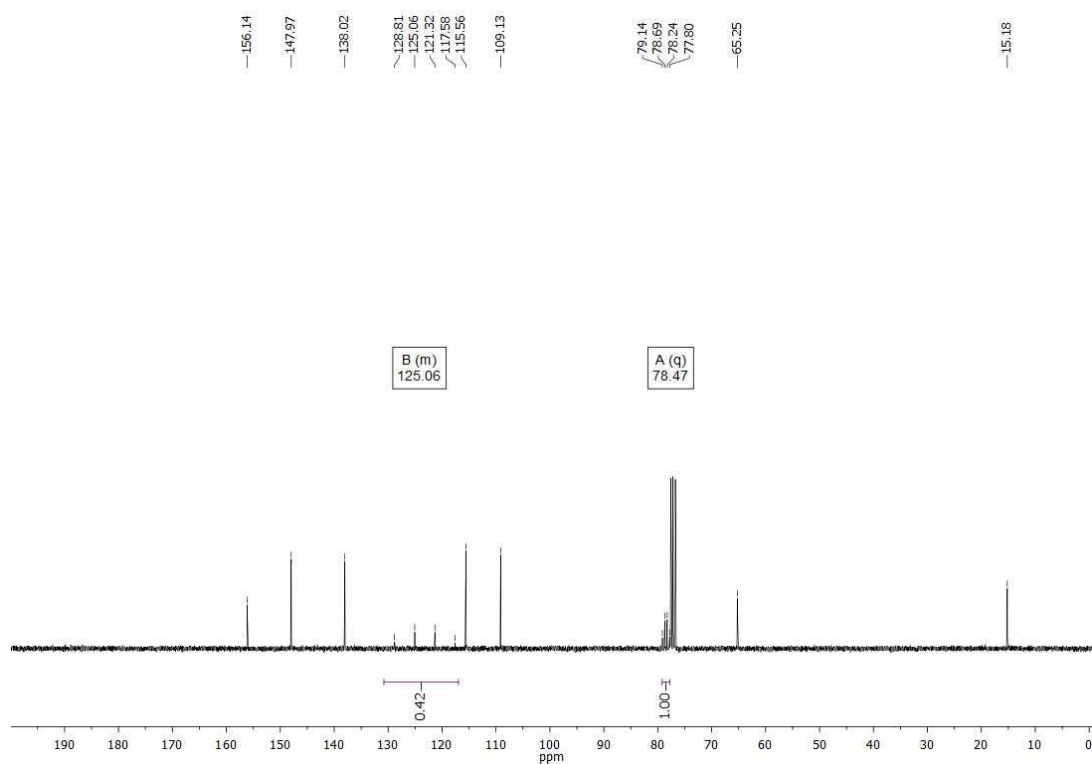
All reactions were carried out under argon atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with argon prior to use. Dry THF was freshly distilled from sodium and benzophenone under argon. Commercially available reagents and solvents were used without further purification. Grignard reagents were purchased from *Aldrich* or synthesized with the described procedure. All microwave irradiation experiments were carried out in a CEM Explorer<sup>TM</sup> microwave apparatus, operating at a frequency of 2.45 GHz with continuous irradiation power from 0 to 200 W utilizing the standard absorbance level of 300 W maximum power. The reactions were carried out in 10 mL Pyrex vessels sealed with CEM plastic crimp tops equipped with magnetic stirrers. The temperature was measured with an infrared sensor on the outer surface of the process vial. After the irradiation period, the reaction vessel was cooled rapidly (1–2 min) to ambient temperature using a nitrogen jet.

Reactions were monitored by TLC with pre-coated silica gel 60 F<sub>254</sub> aluminium plates (Merck KGaA, Darmstadt) using UV light as the visualizing agent. The crude products were purified by standard flash chromatography using silica gel (35–70 µm) from *Acros Organics*. Analytical RP-HPLC was measured on a *JASCO* system with a *Phenomenex Luna* C18 column (5 µm, 250 × 4.6 mm). ESI- and HR-ESI-mass spectra were recorded on a Thermo Finnigan LTQ FT or on a Bruker maXis equipped with a *Waters Acquity UPLC* using a *Kinetex* C18 column (2.6 µm, 100 Å) at 40 °C. In all cases, mixtures of water (eluent A) and acetonitrile (eluent B) were used as solvents; if required, 0.05 % formic acid or 0.1 % TFA were added. <sup>1</sup>H, <sup>13</sup>C, and <sup>19</sup>F spectra were recorded on a Varian 300 MHz and 600 MHz spectrometer or on a Bruker Avance II 400 MHz spectrometer in DMSO-d<sub>6</sub> or CDCl<sub>3</sub>. The chemical shifts are reported in ppm relative to the signal of the deuterated solvent. Multiplicities are given as: s (singlet), br s (broad singlet), d (doublet), t (triplet), and m (multiplet). Melting points were measured on a Melting Point B-540 Büchi.

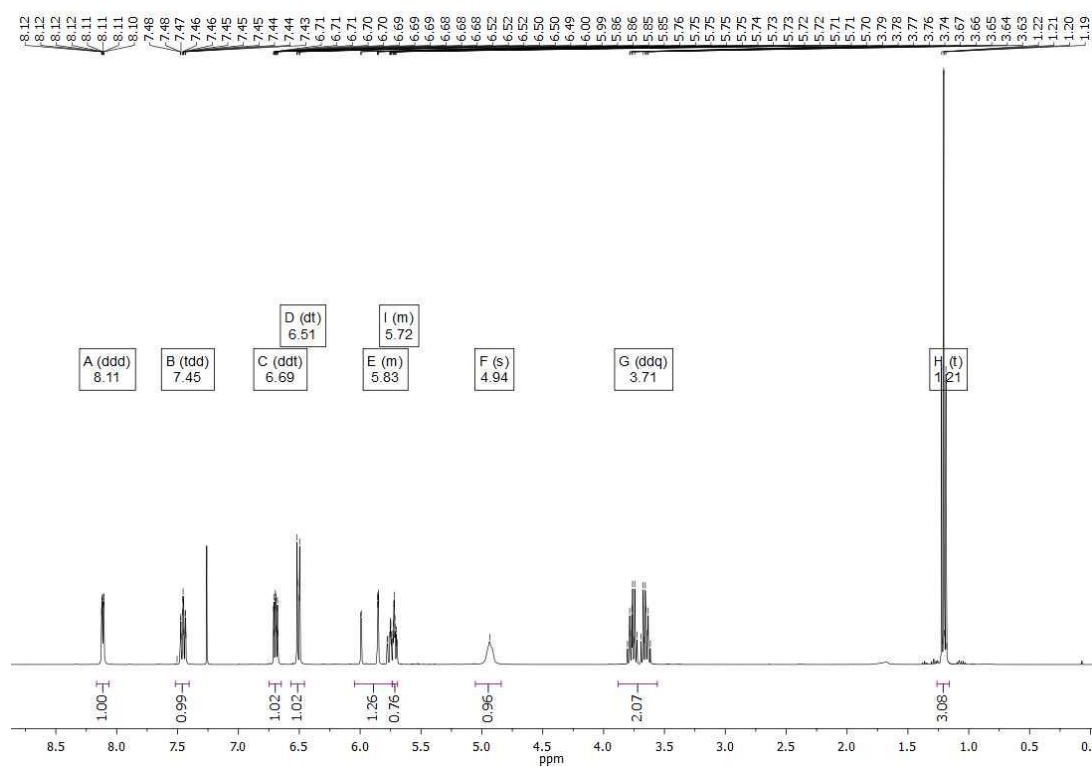
## 2. $^1\text{H}$ NMR, $^{19}\text{F}$ NMR and $^{13}\text{C}$ NMR spectra

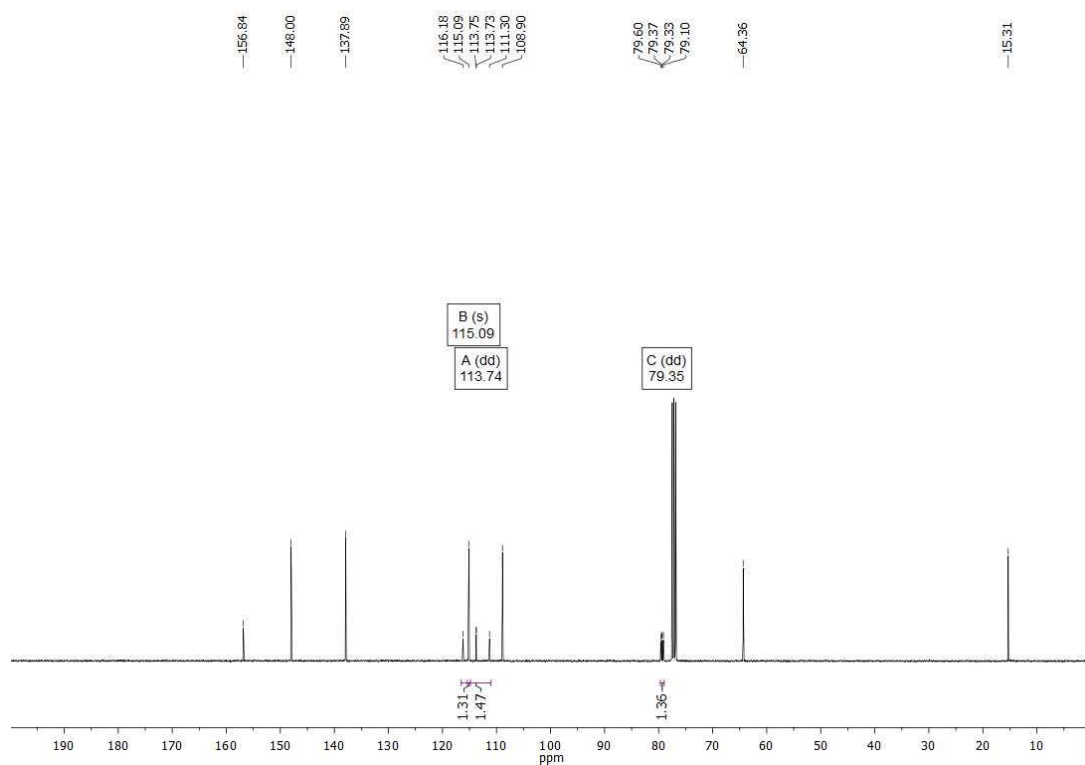
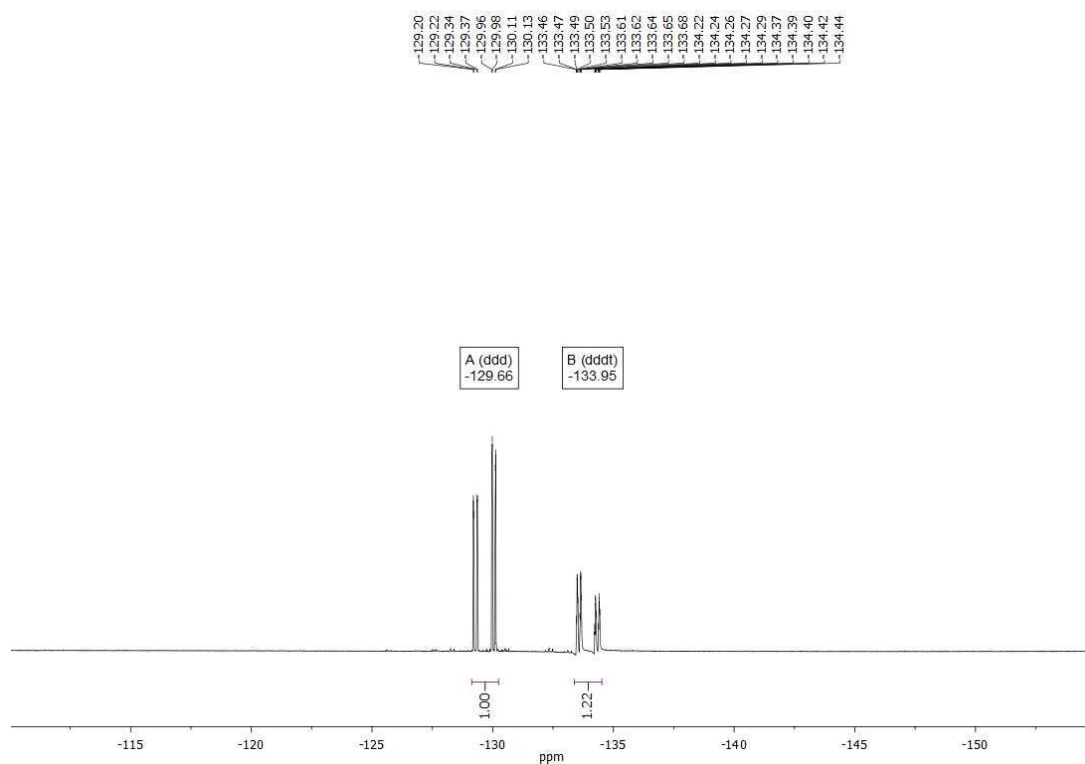
*N*-(1-Ethoxy-2,2,2-trifluoroethyl)pyridin-2-amine (1a):



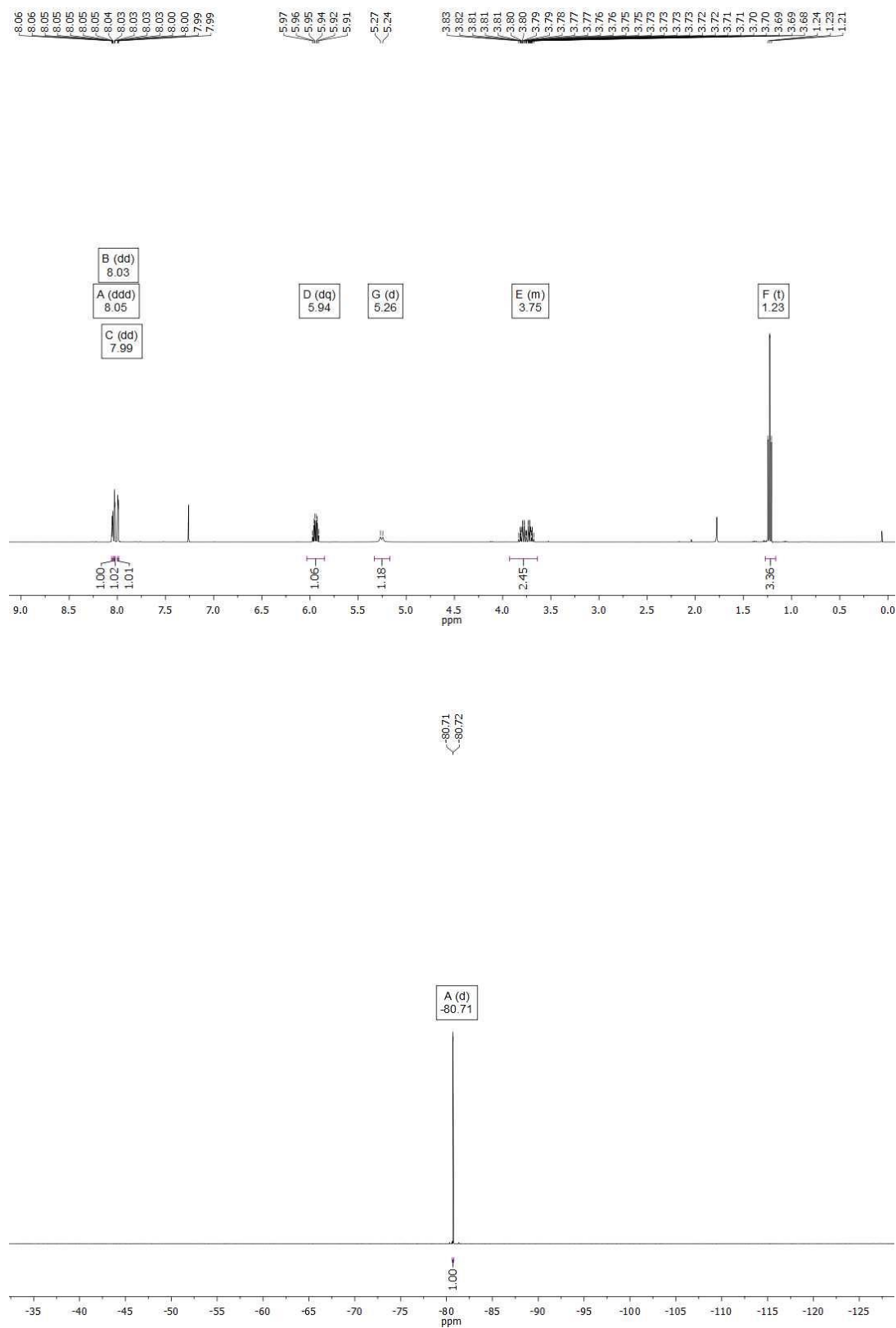


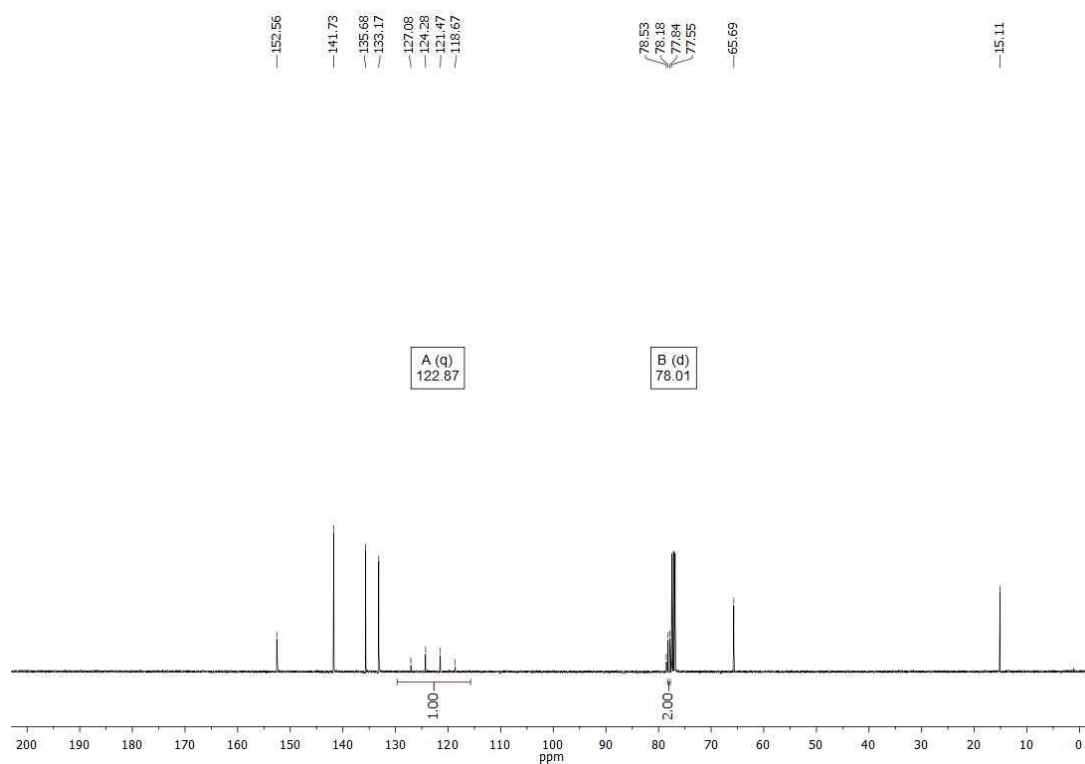
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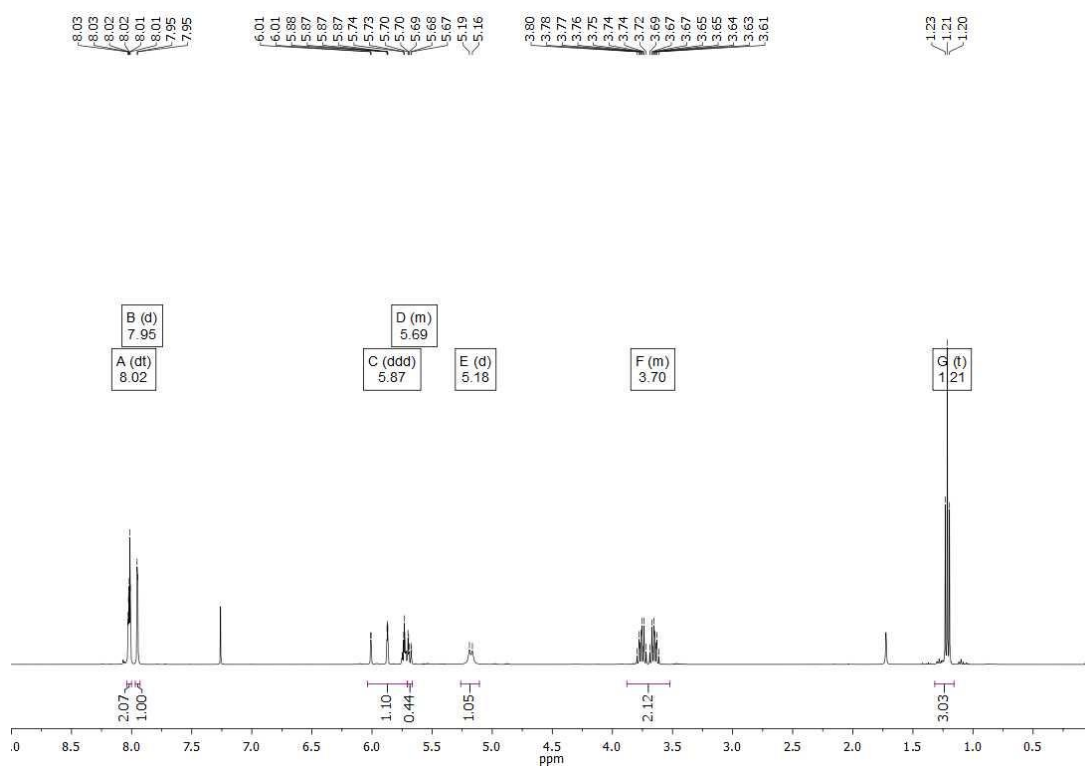


***N*-(1-Ethoxy-2,2,2-trifluoroethyl)pyrazin-2-amine (1c):**

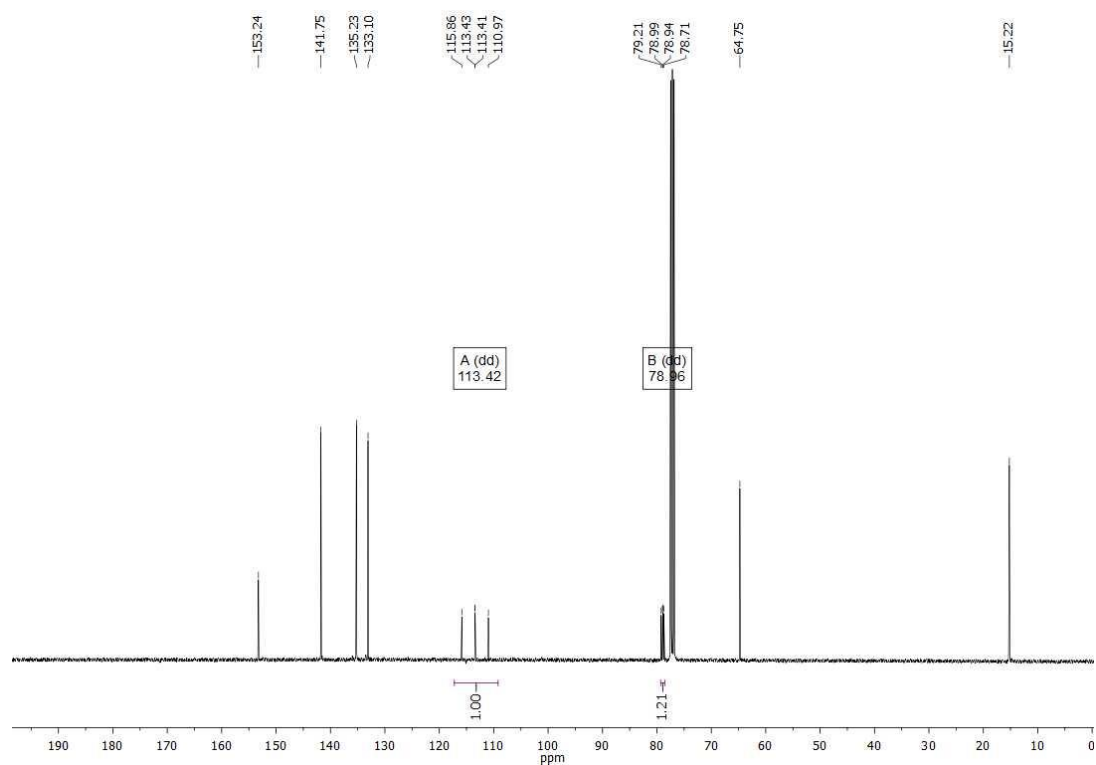
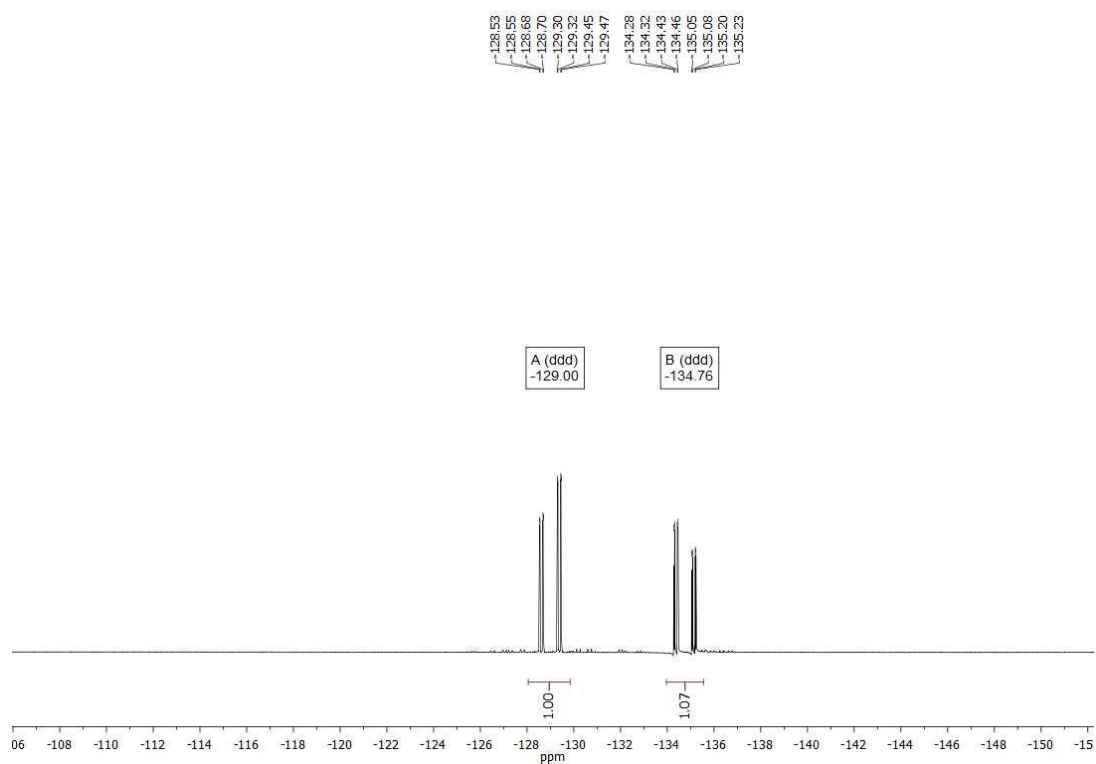




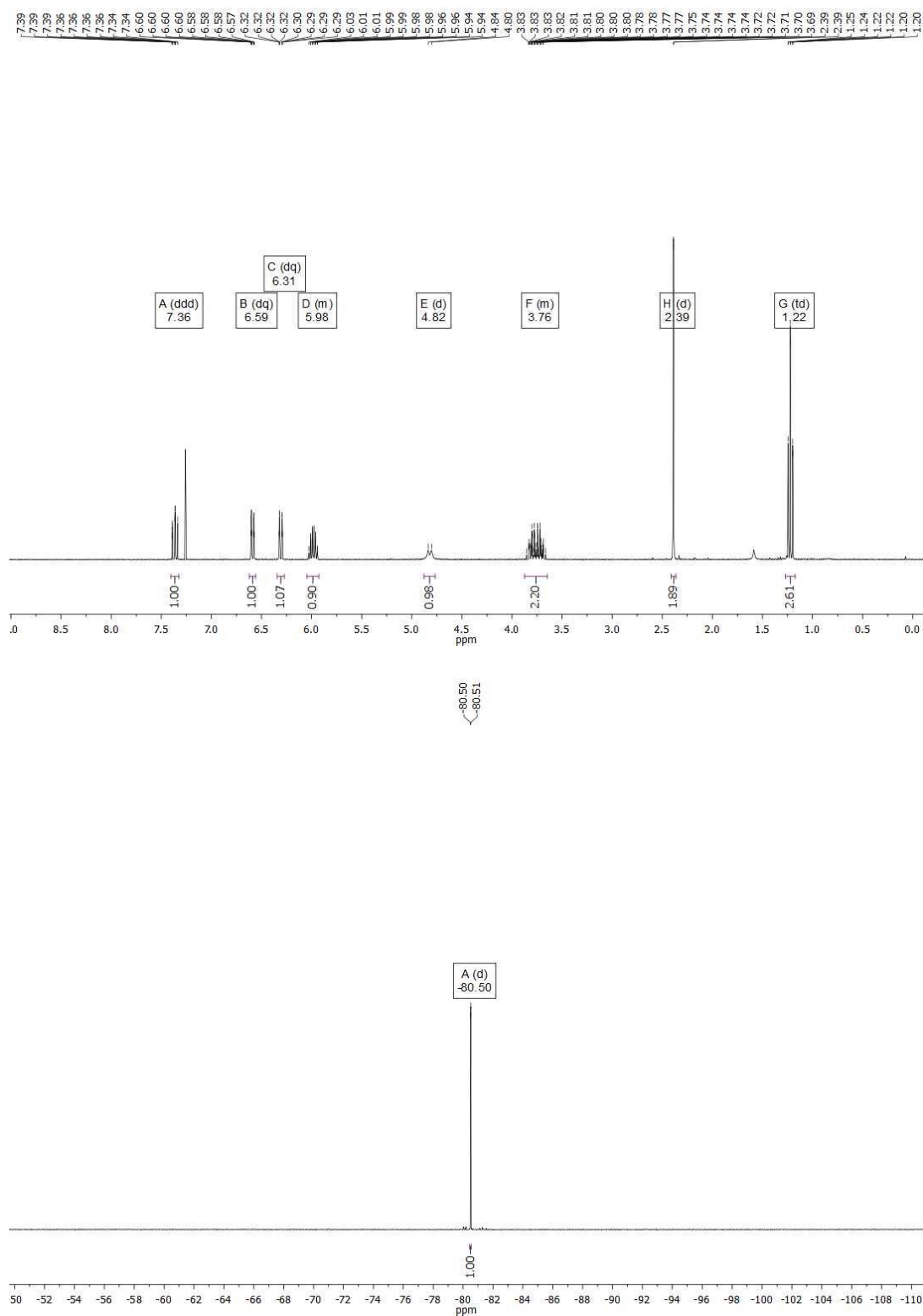
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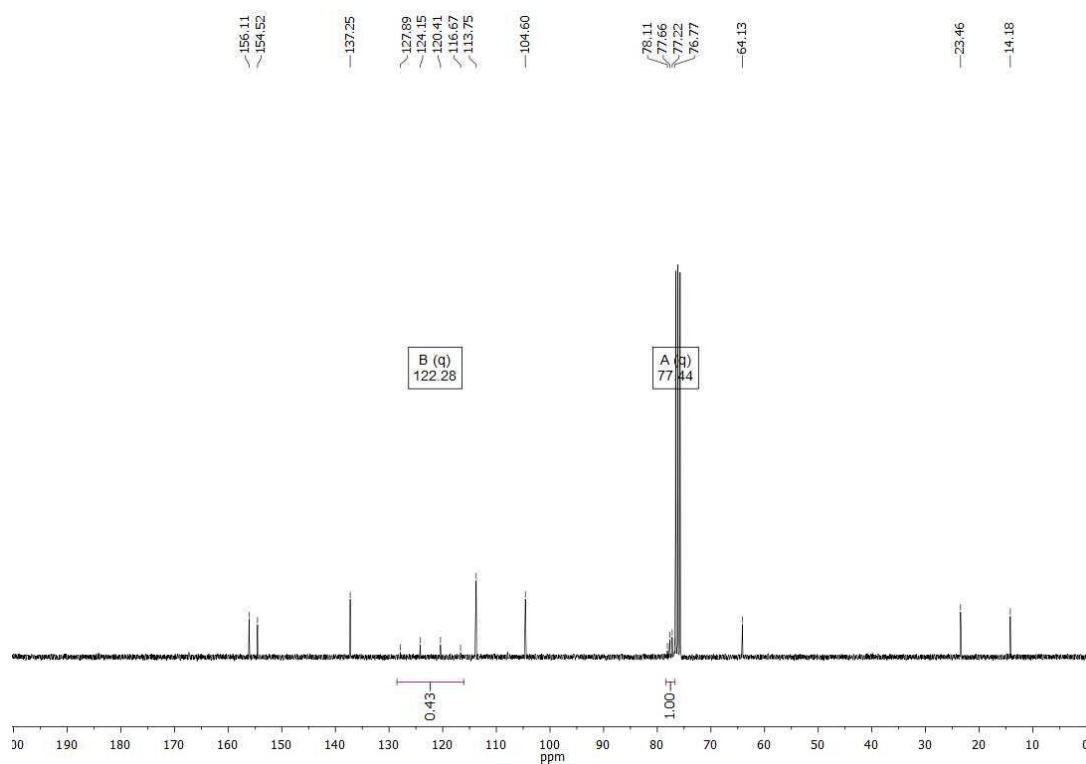




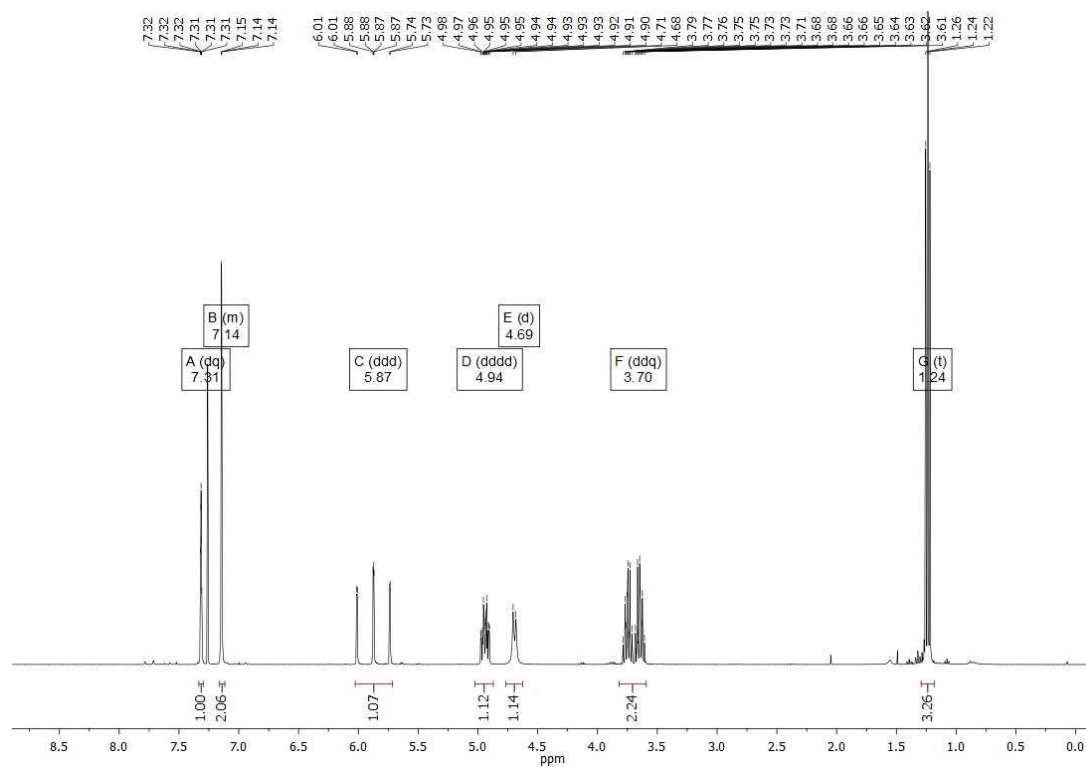


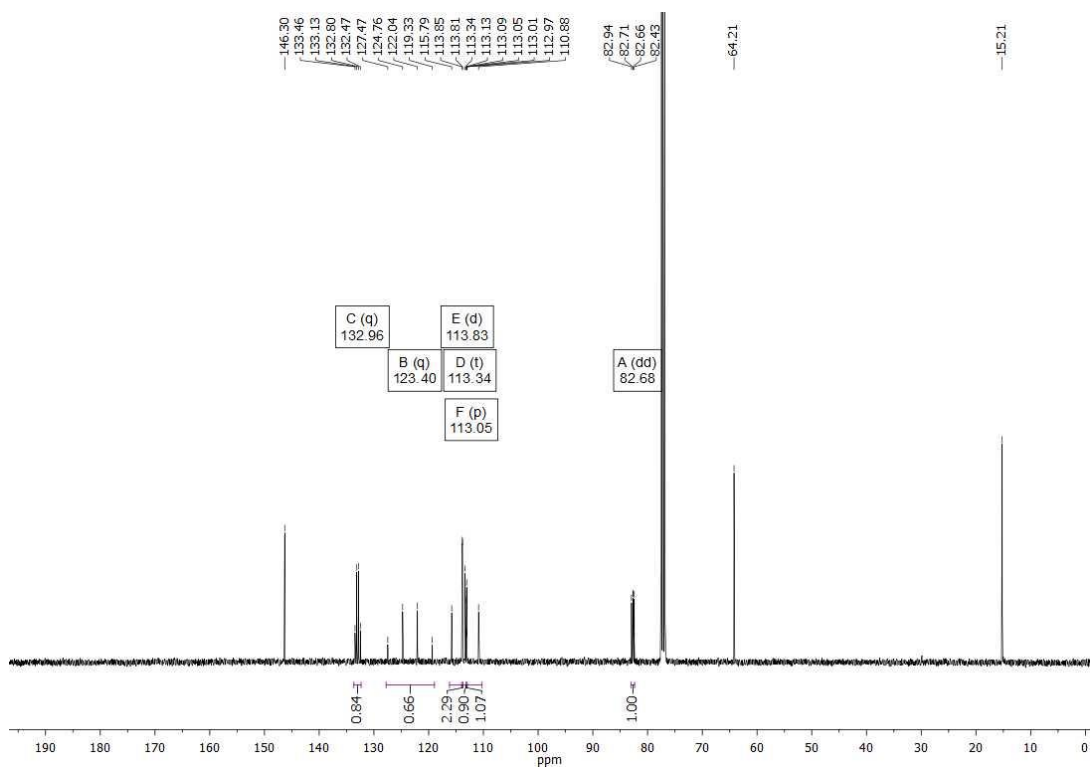
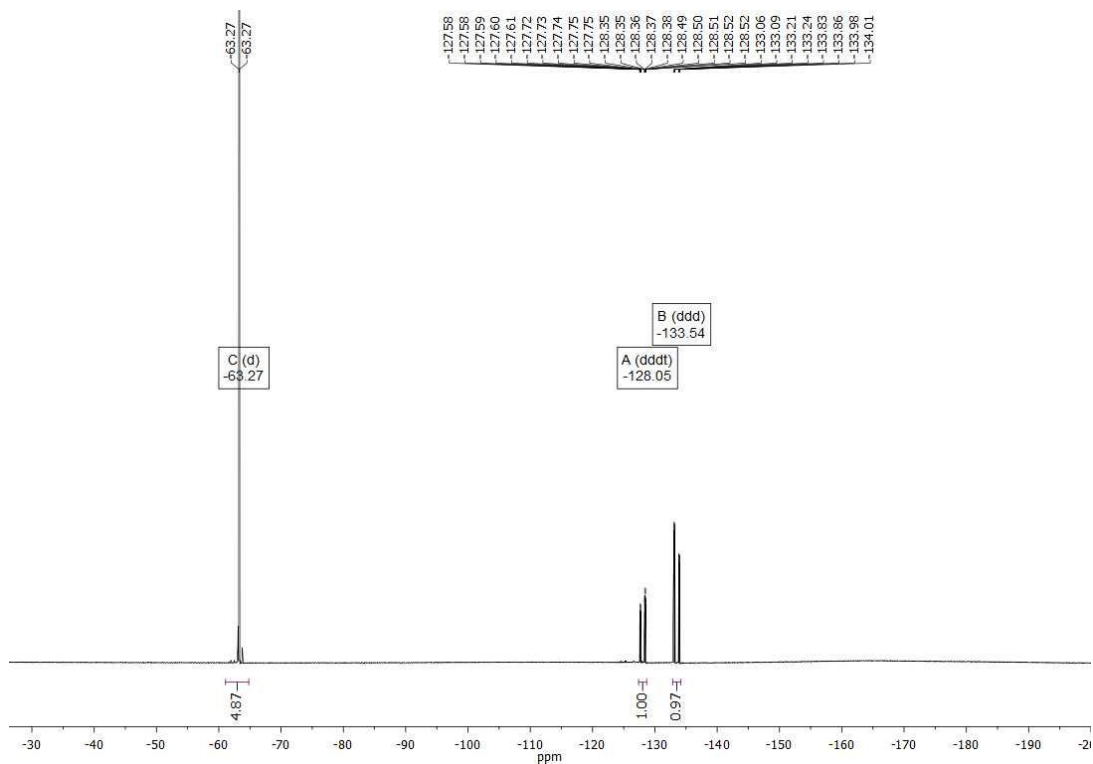
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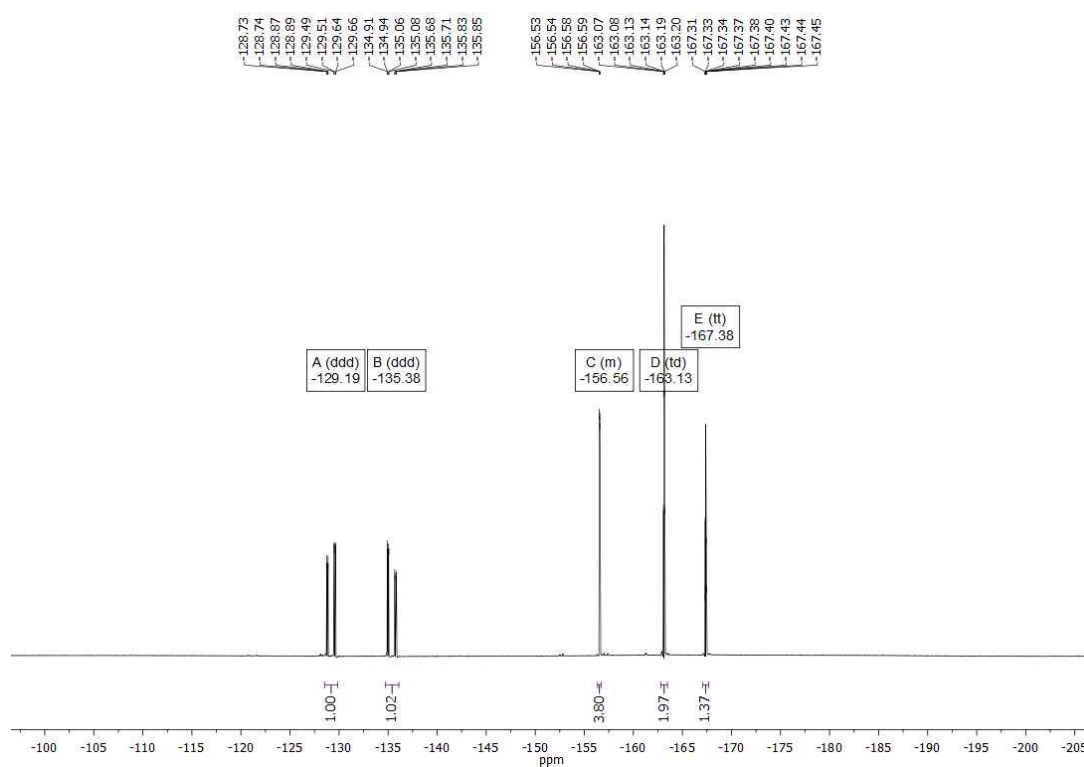
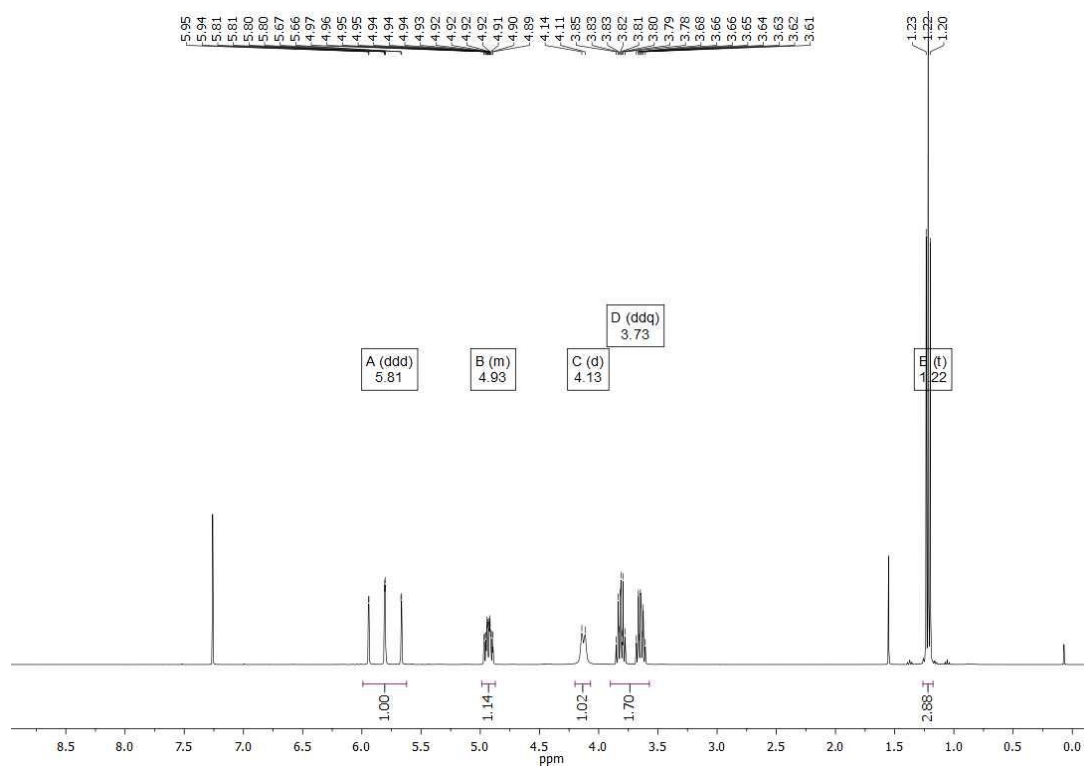


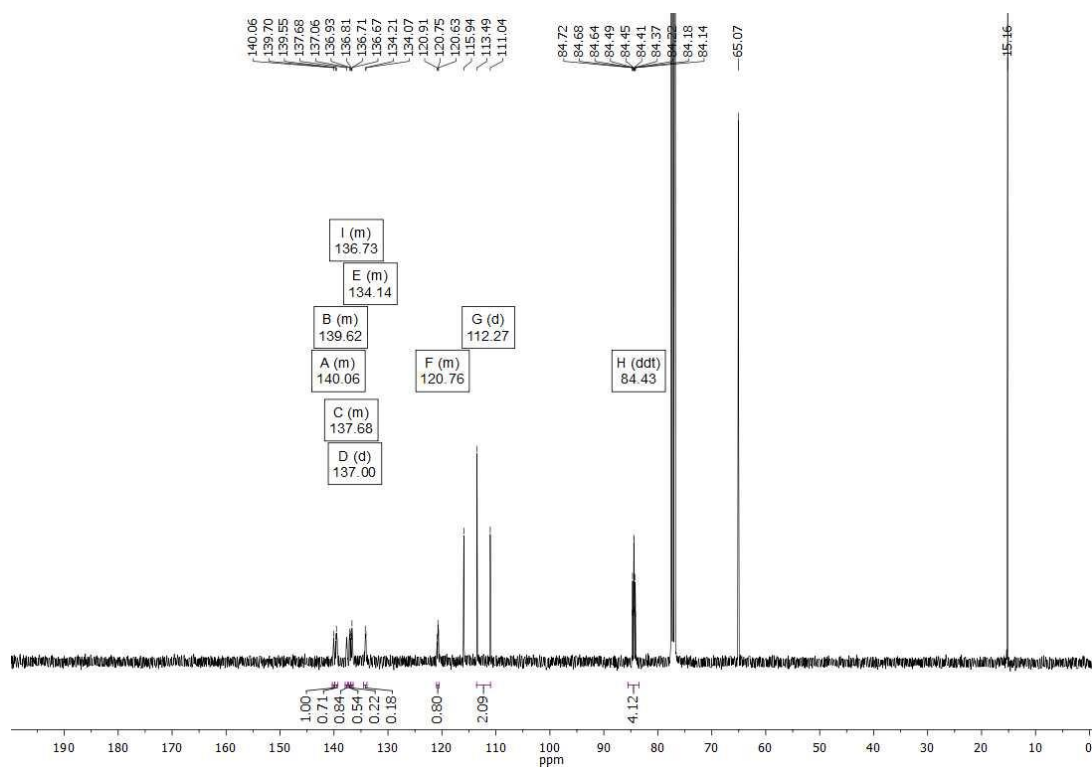
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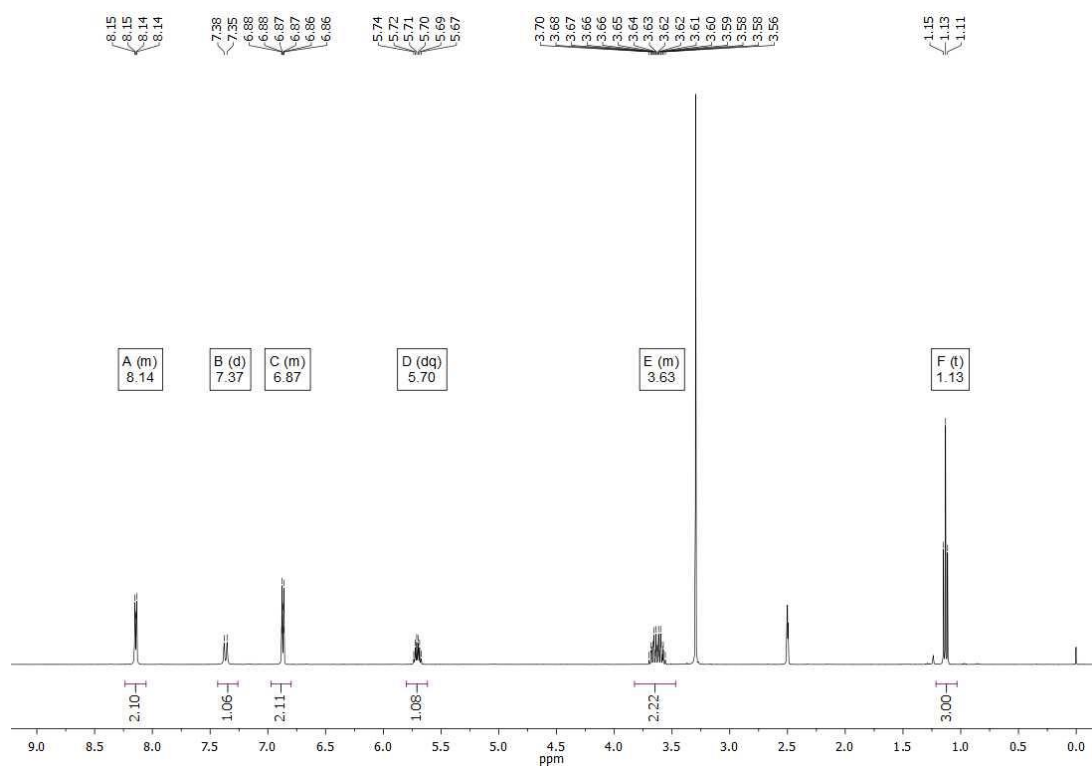


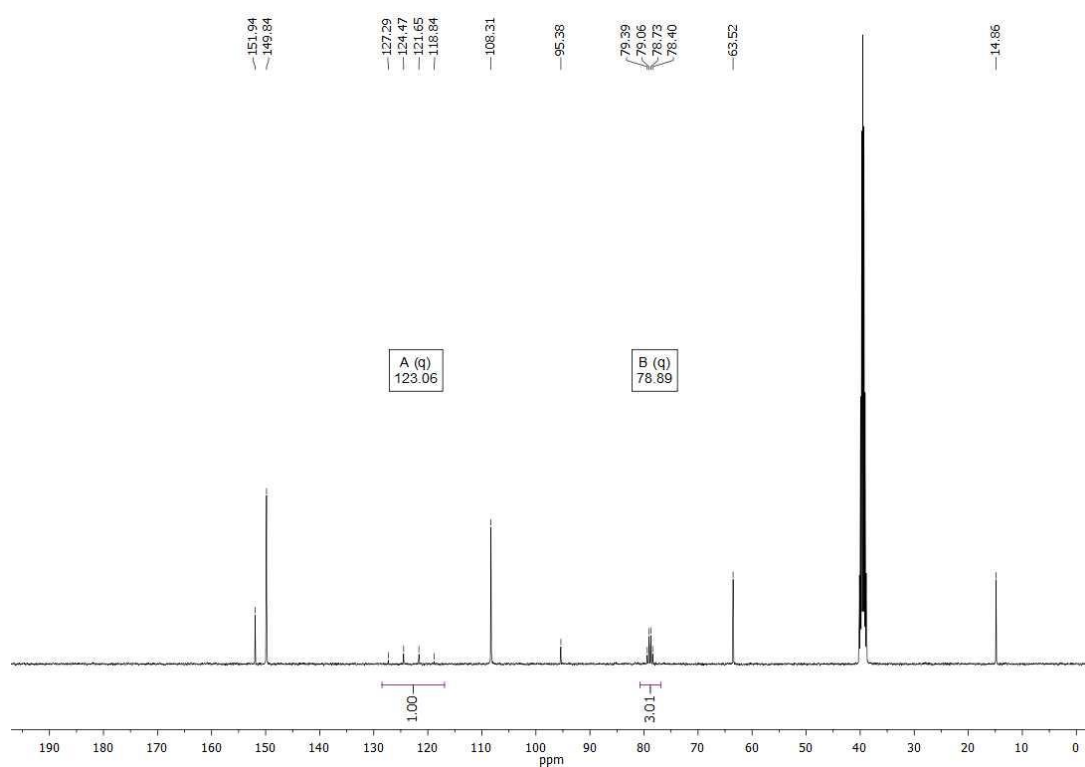
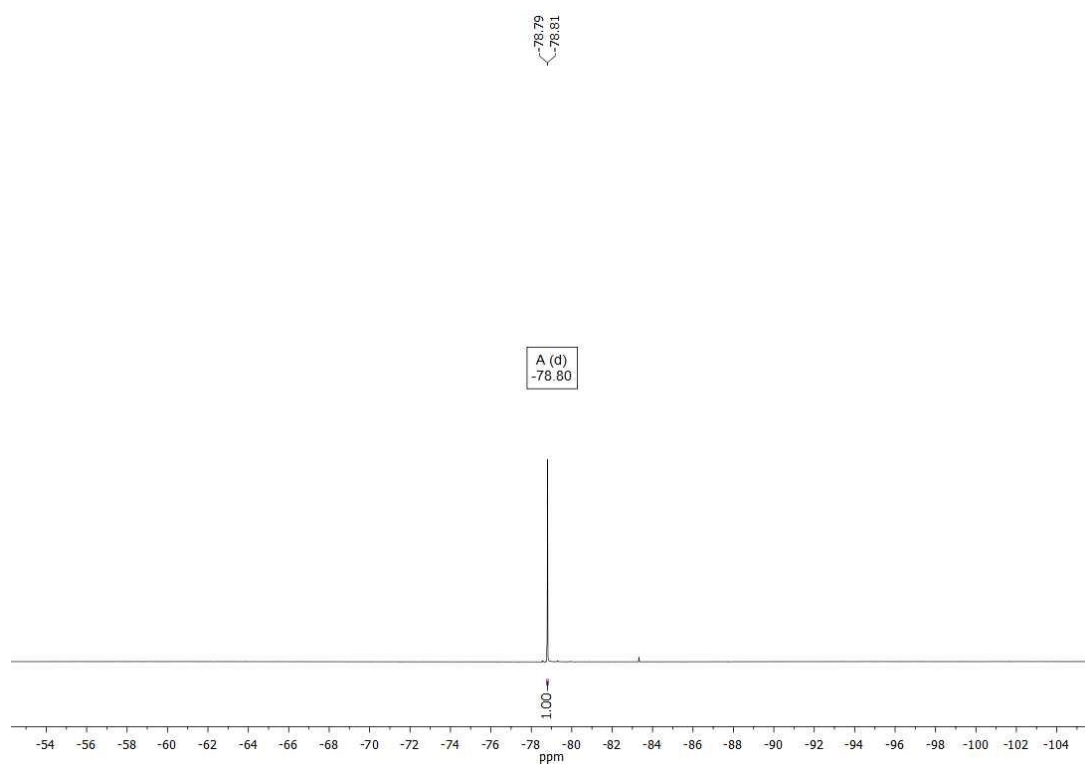
***N*-(1-Ethoxy-2,2-difluoroethyl)-2,3,4,5,6-pentafluoroaniline (1g):**



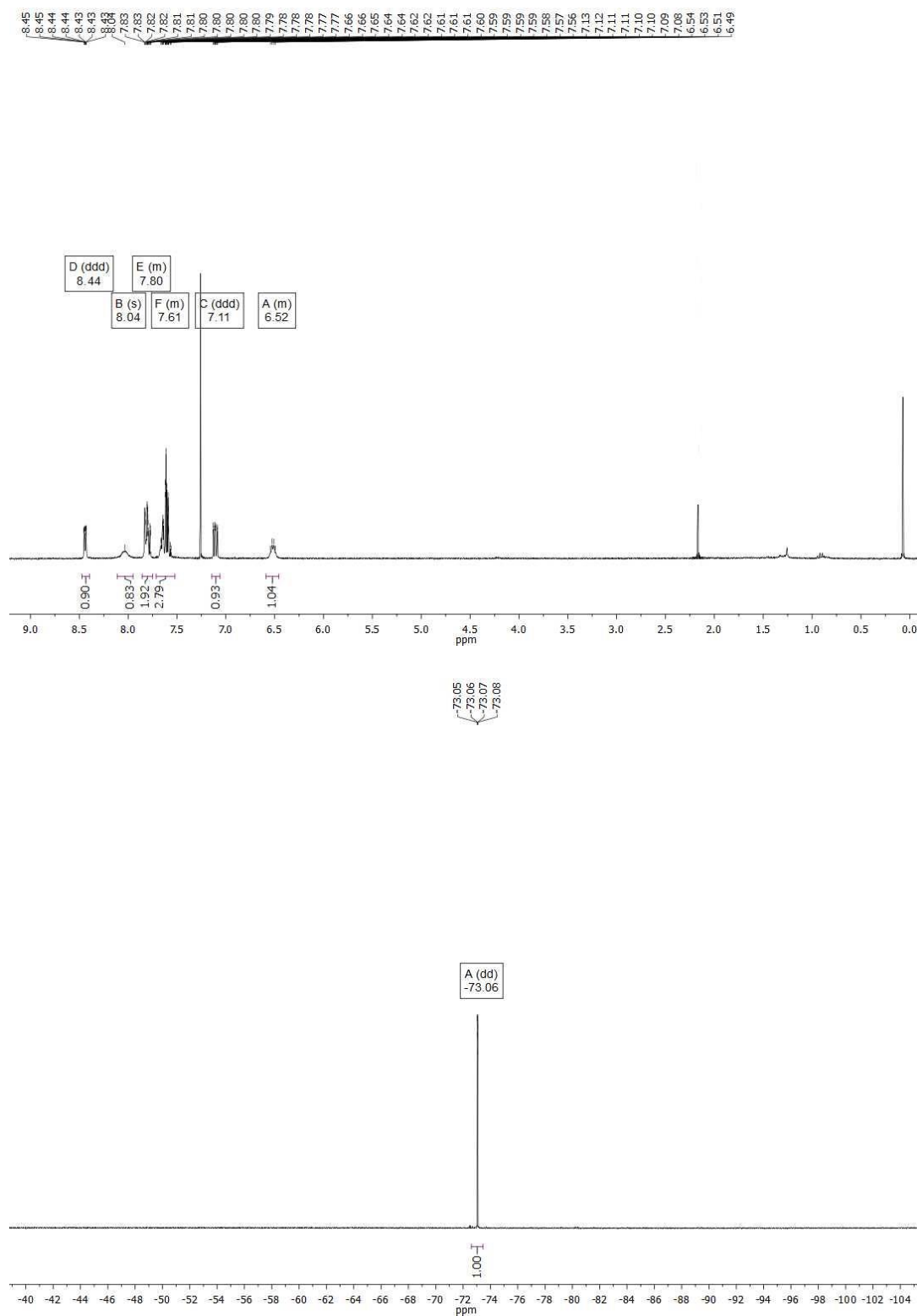


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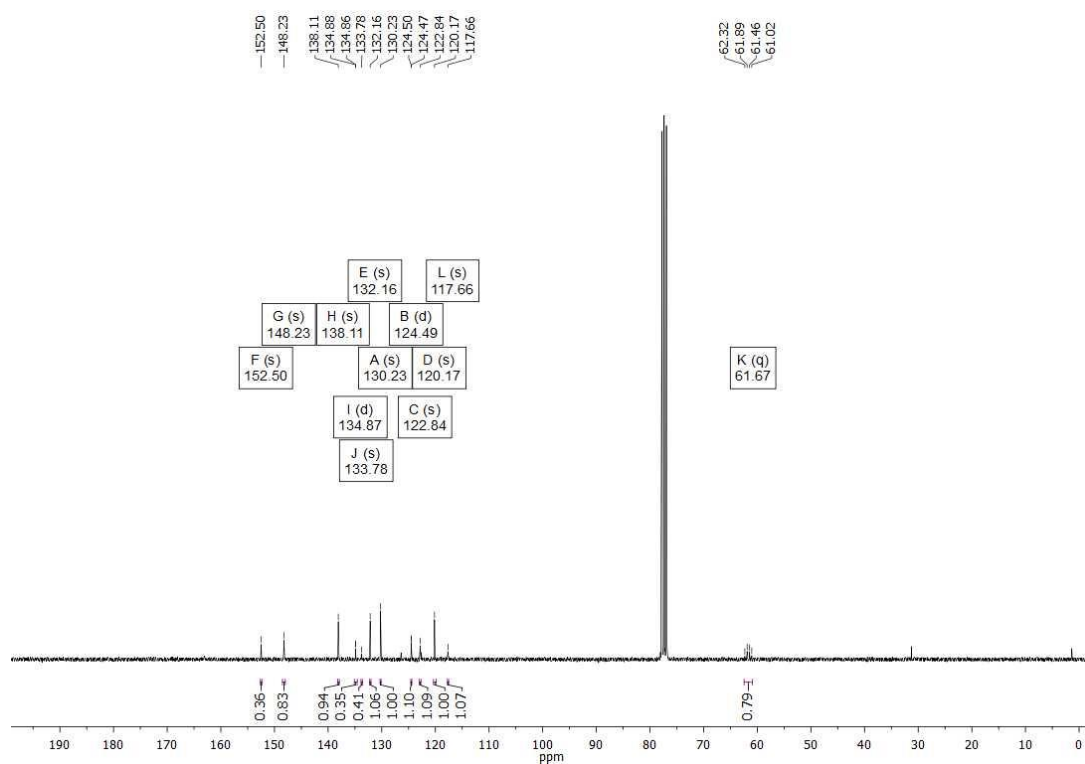




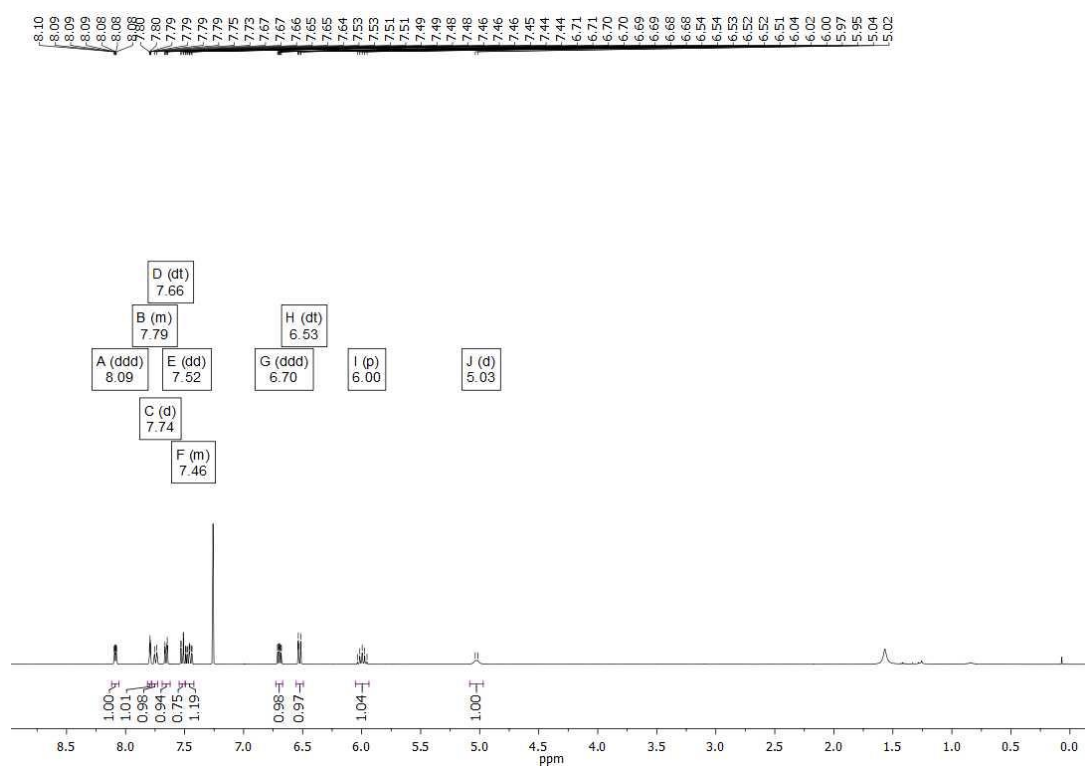
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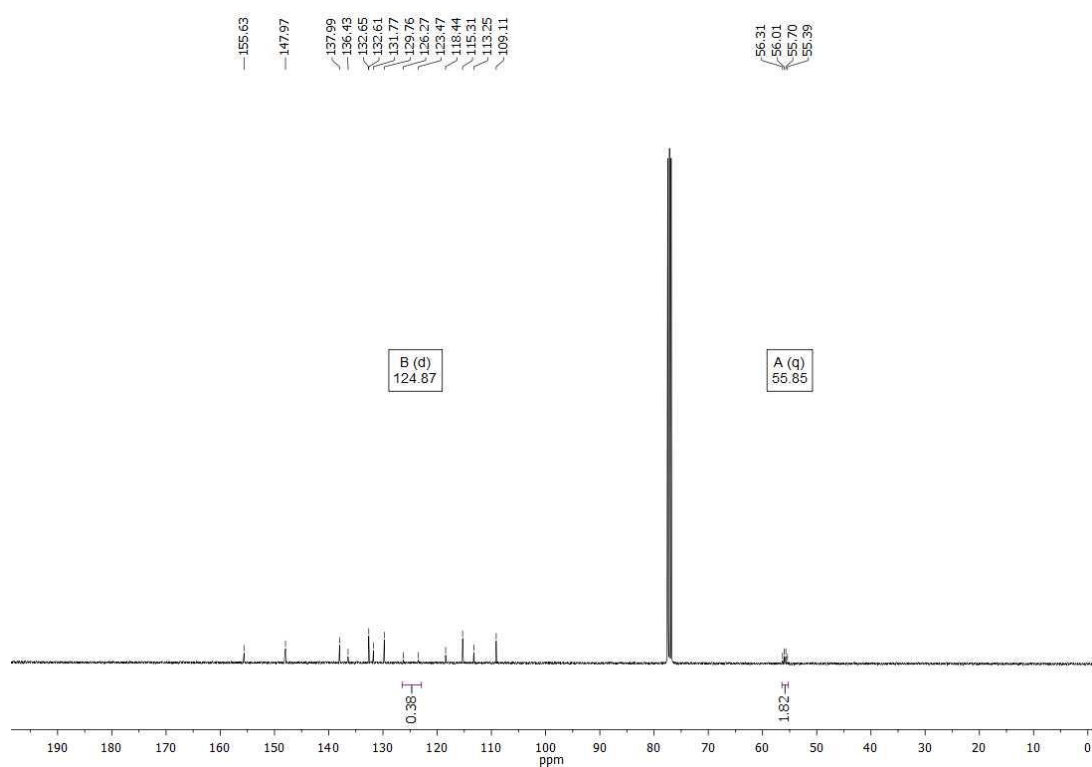
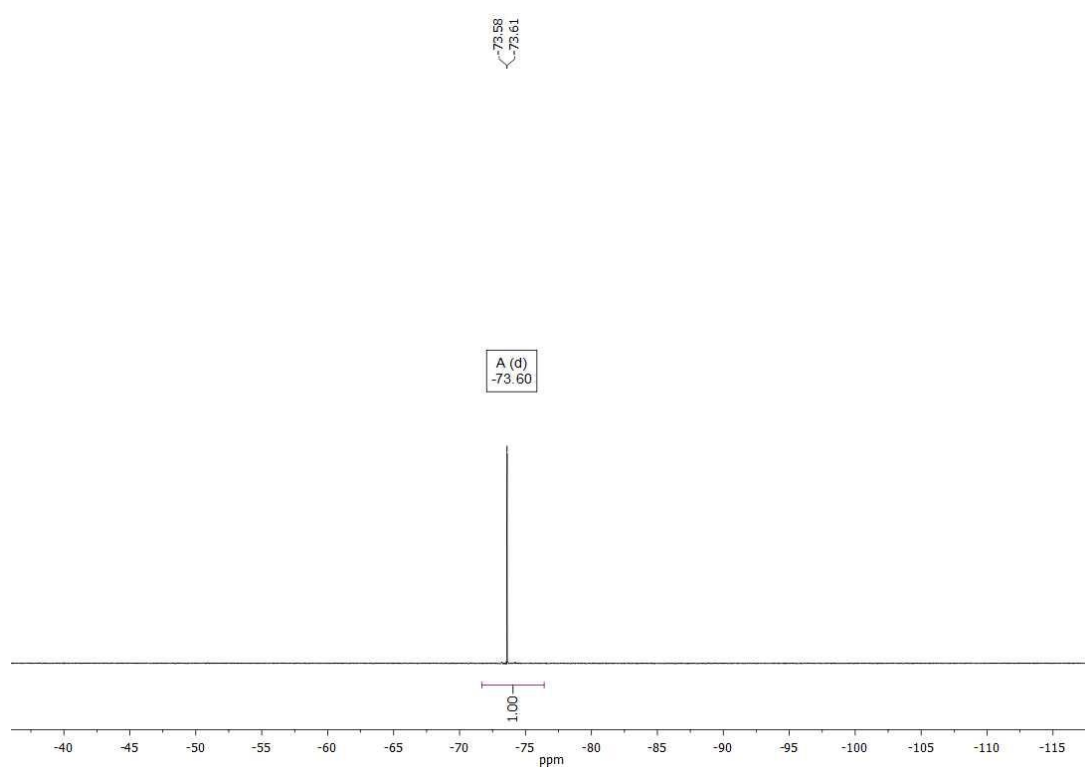




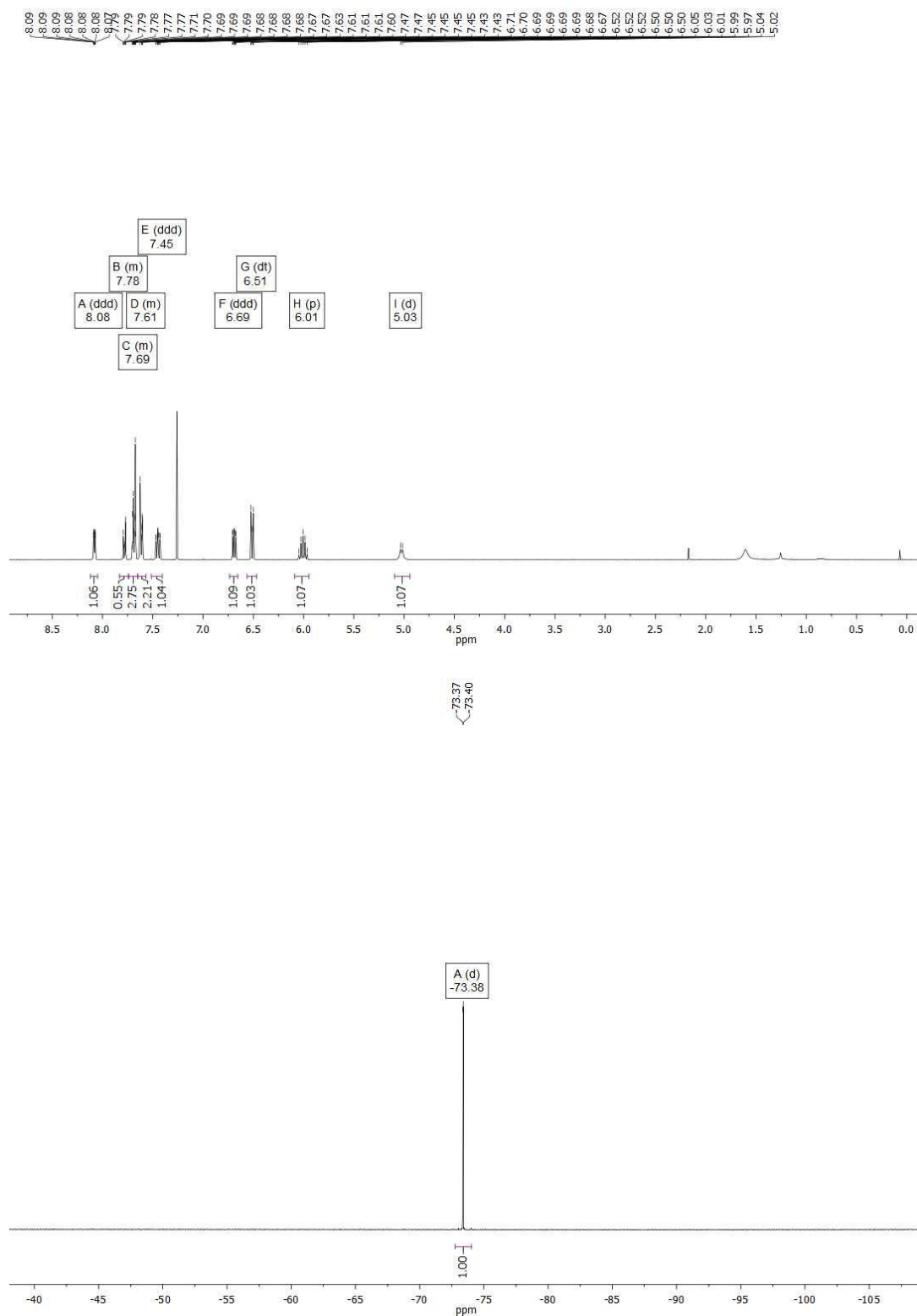


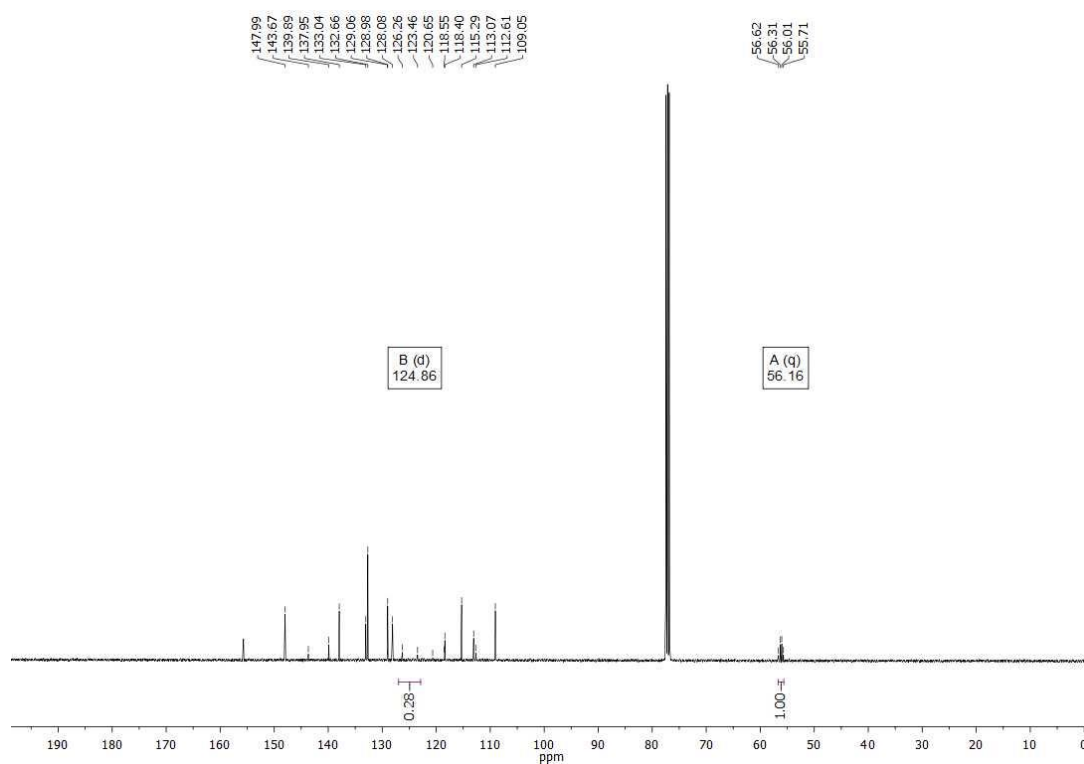
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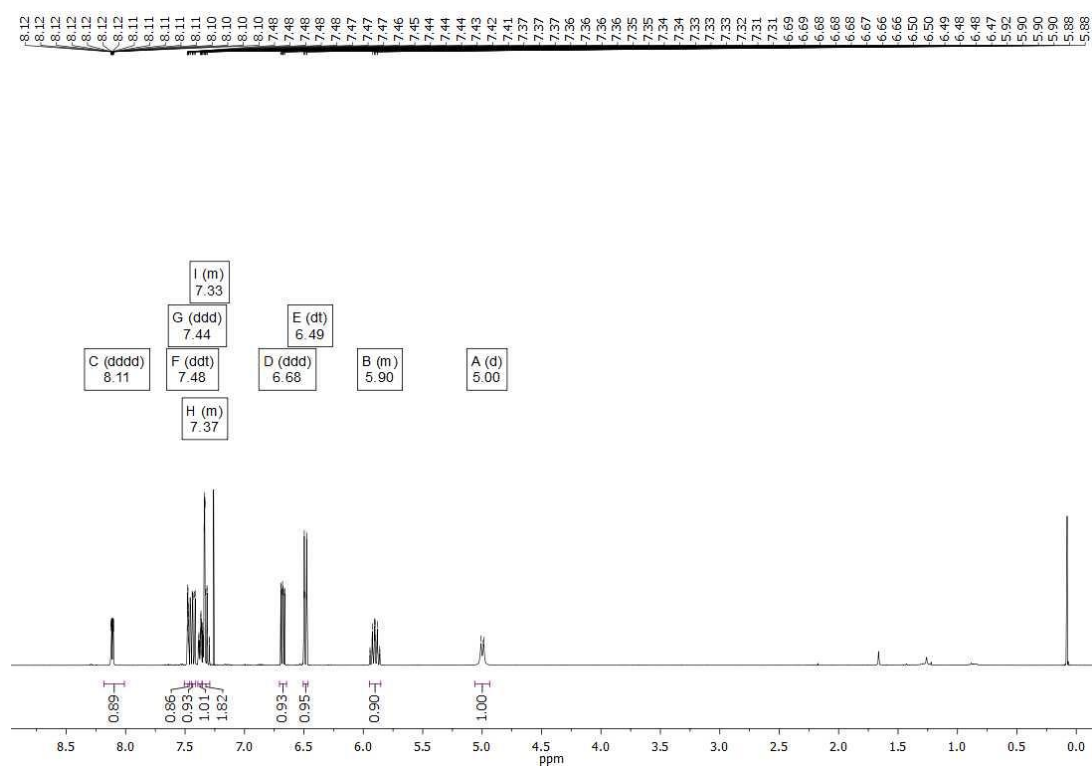


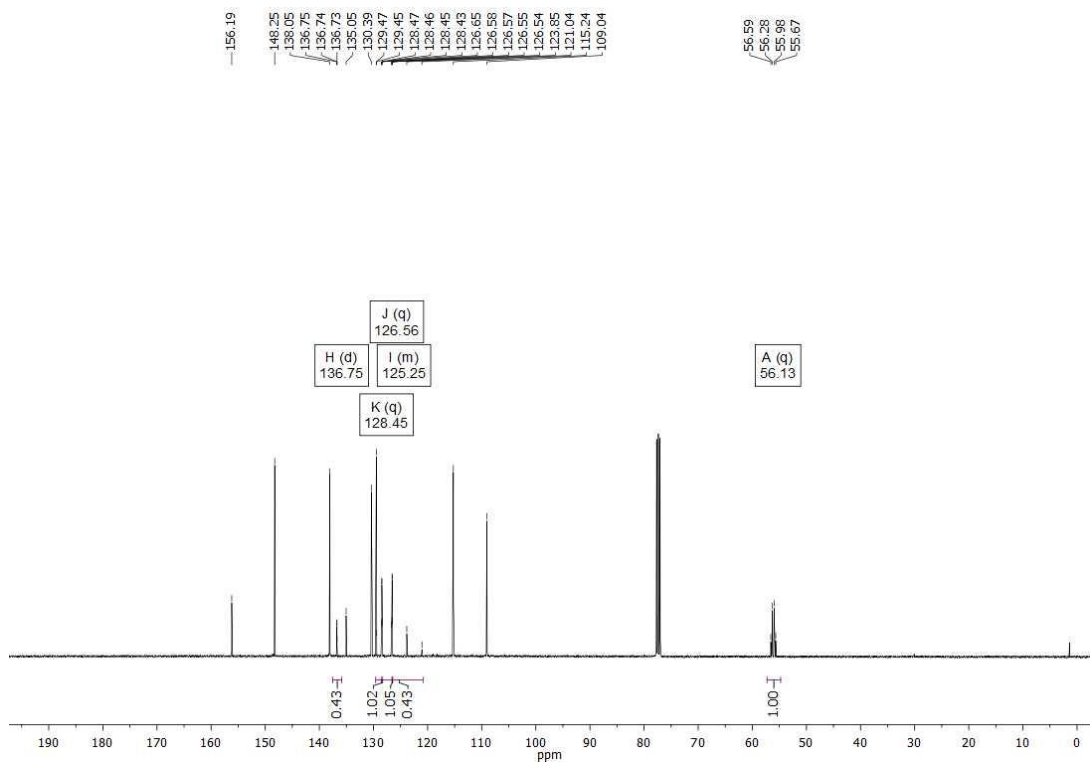
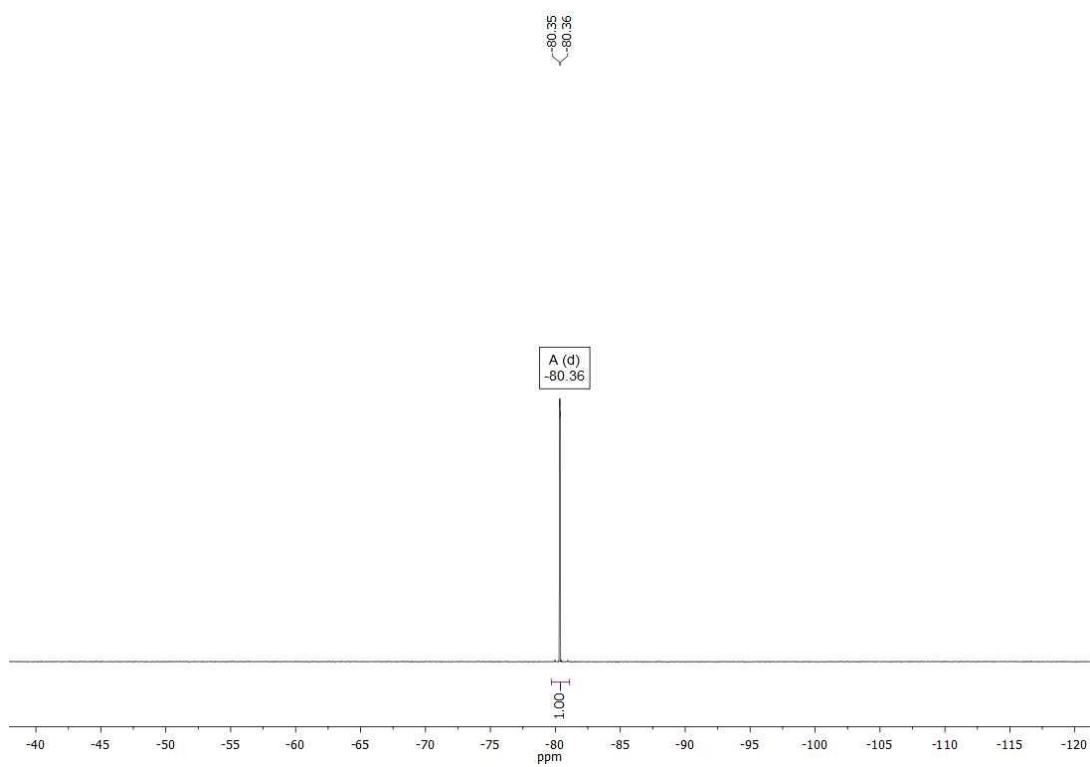
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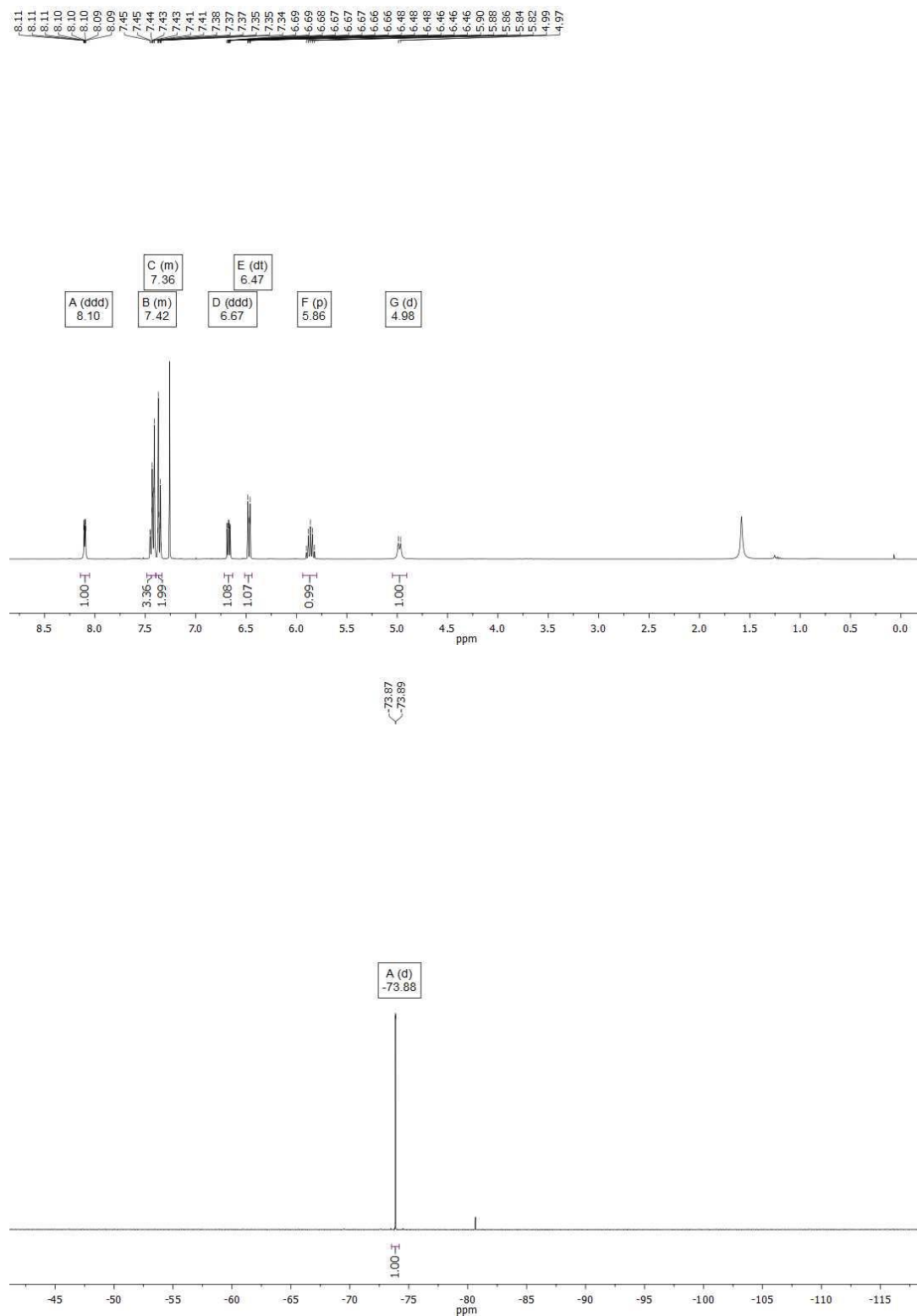


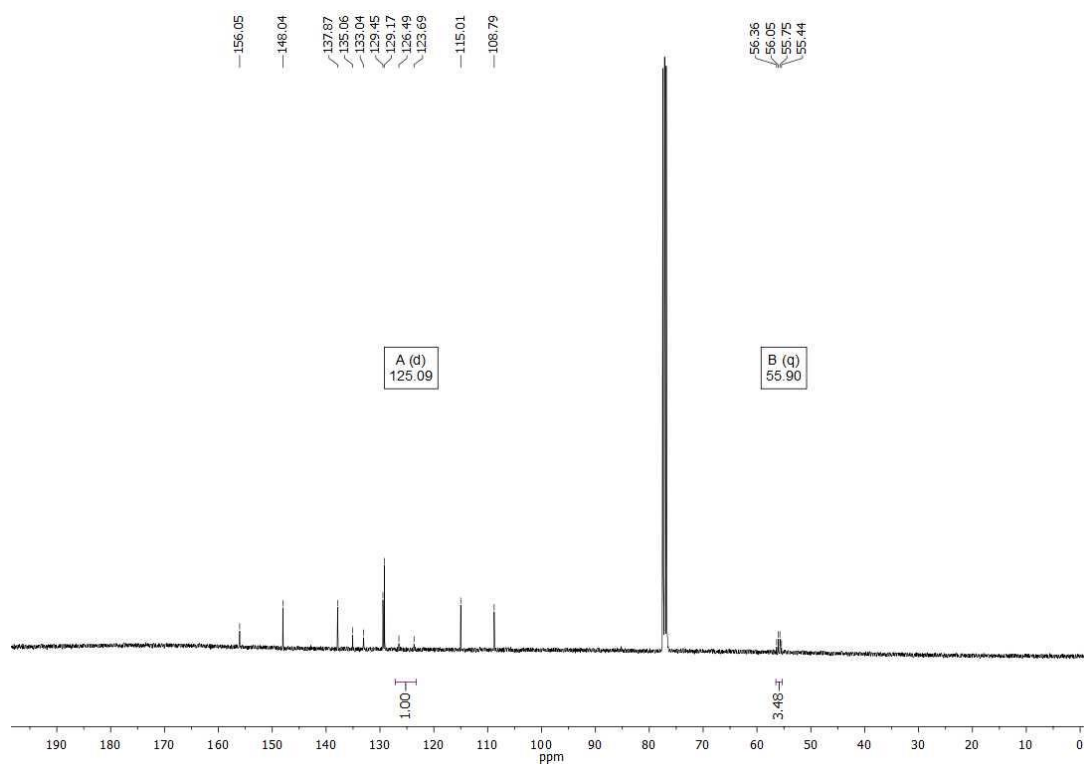
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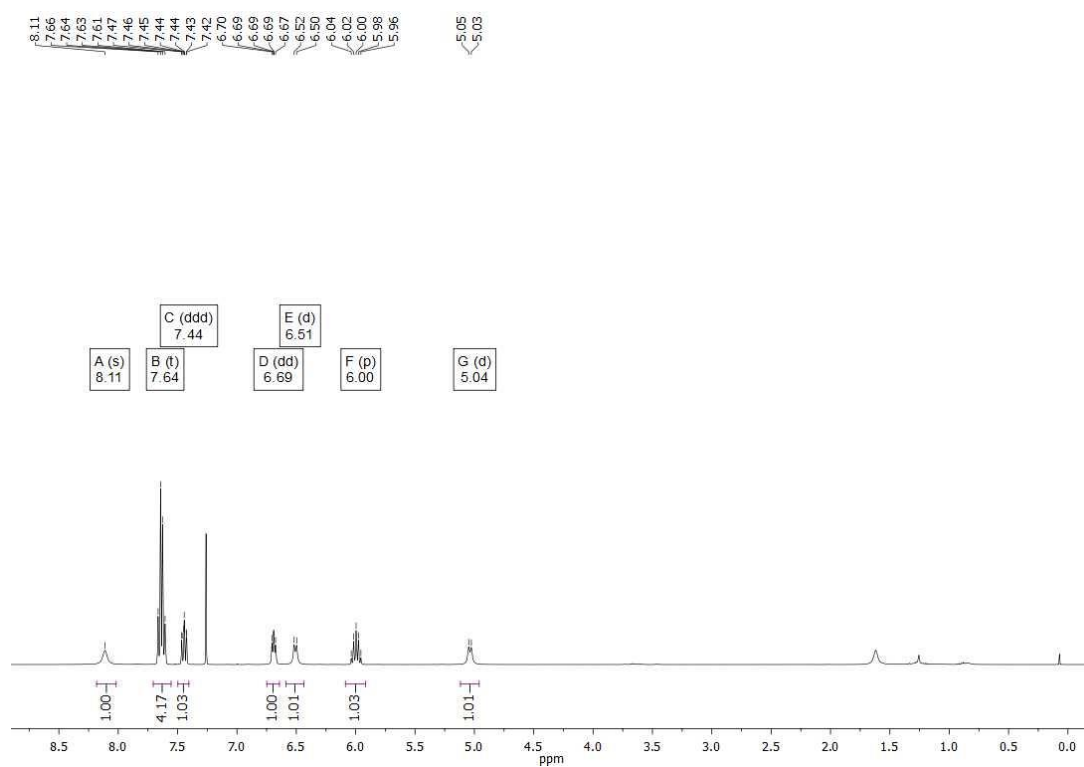


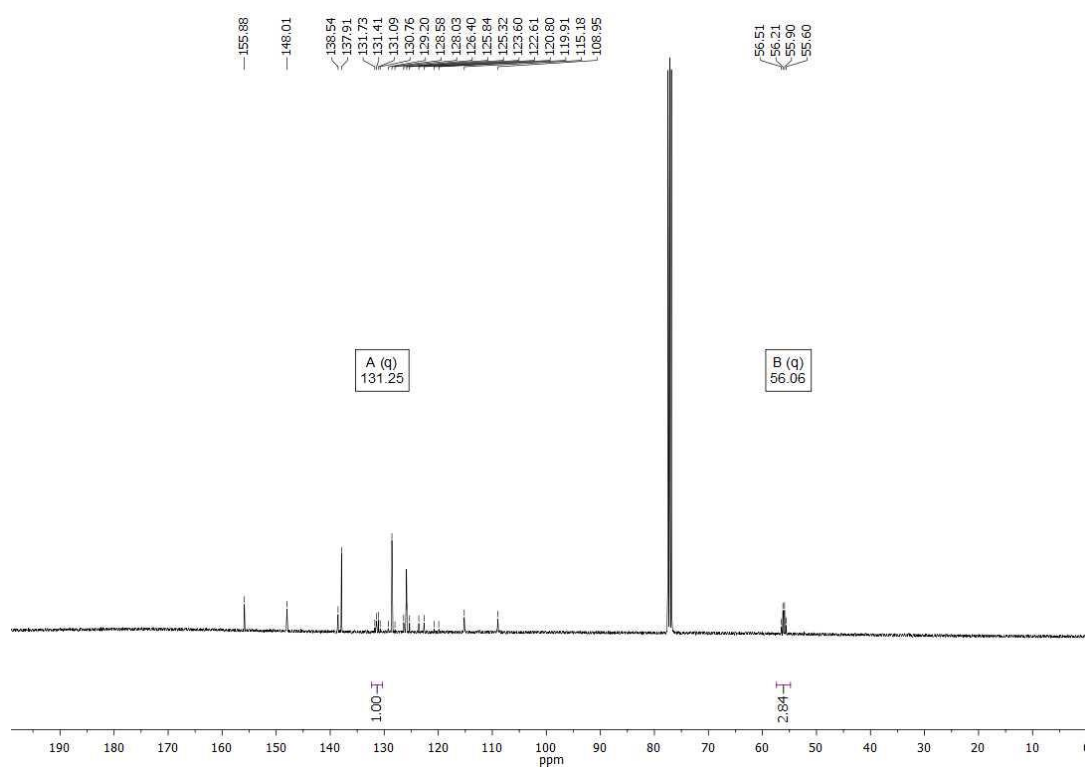
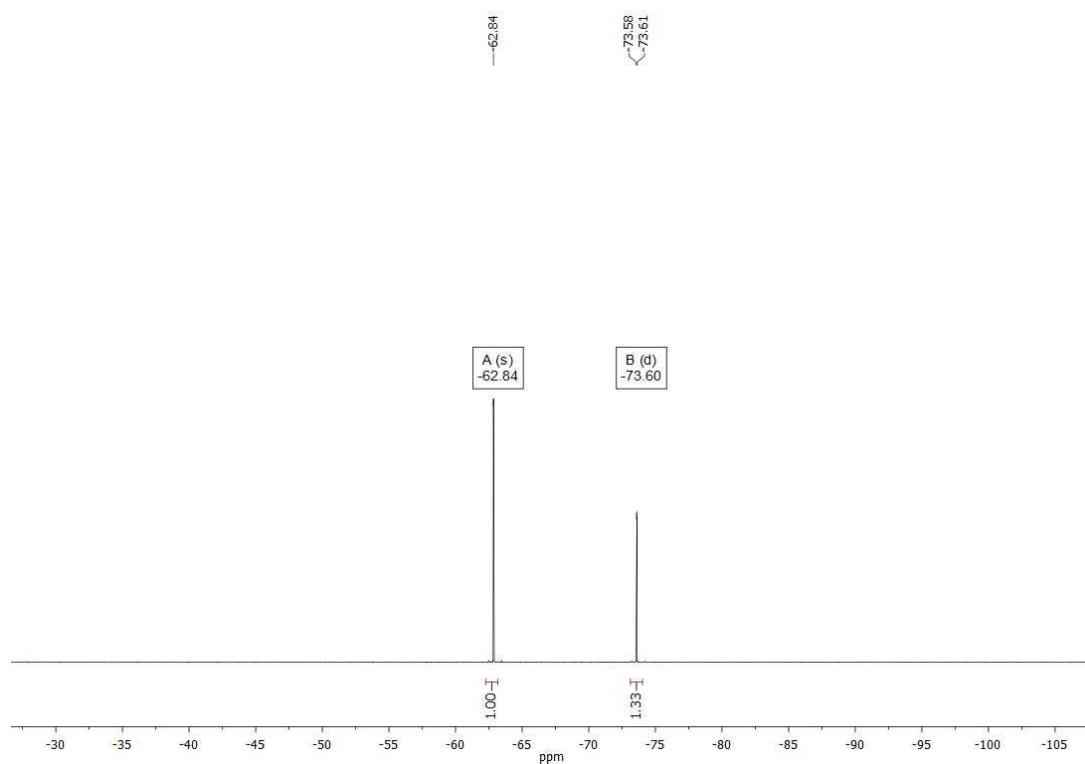
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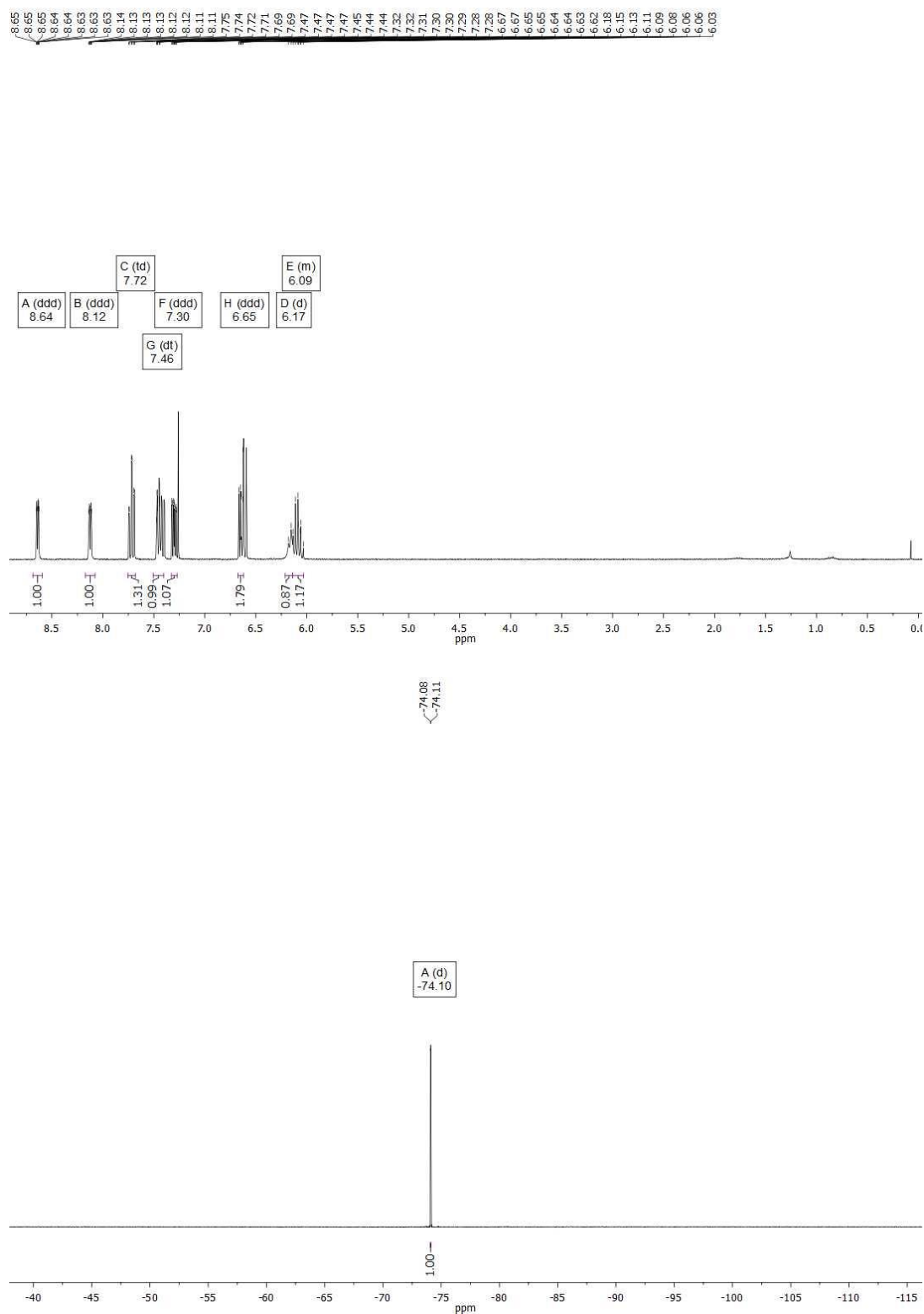
***N*-(2,2,2-Trifluoro-1-(4-(trifluoromethyl)phenyl)ethyl)pyridin-2-amine (2f):**

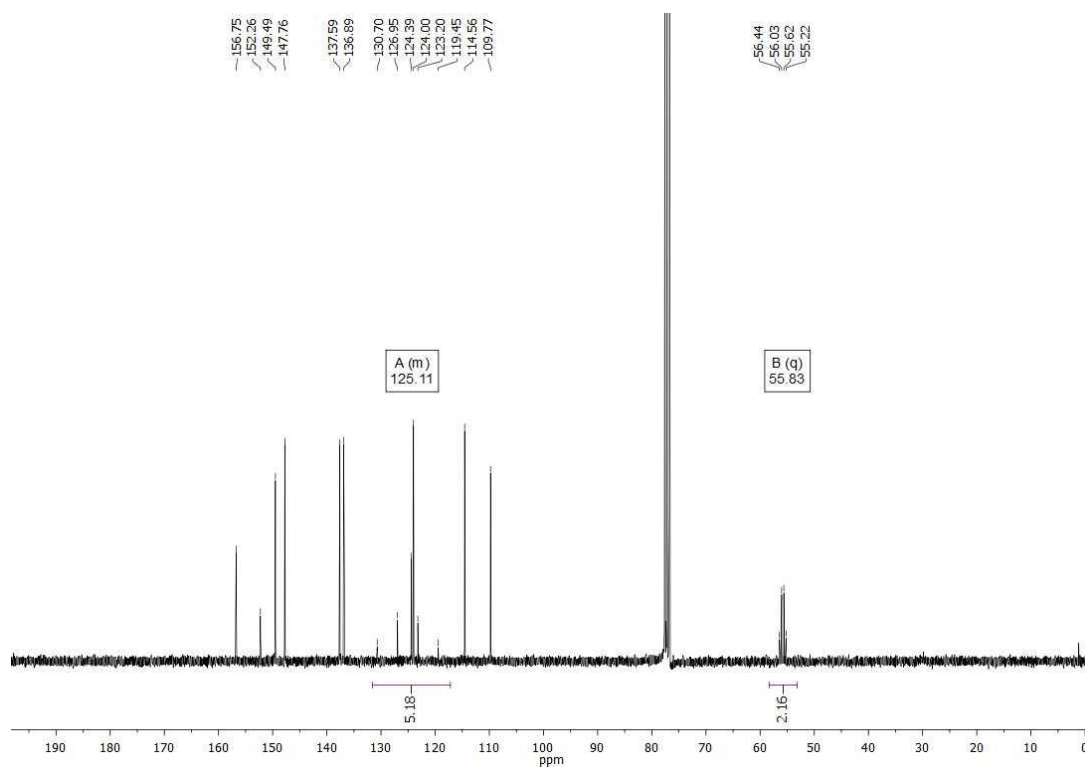




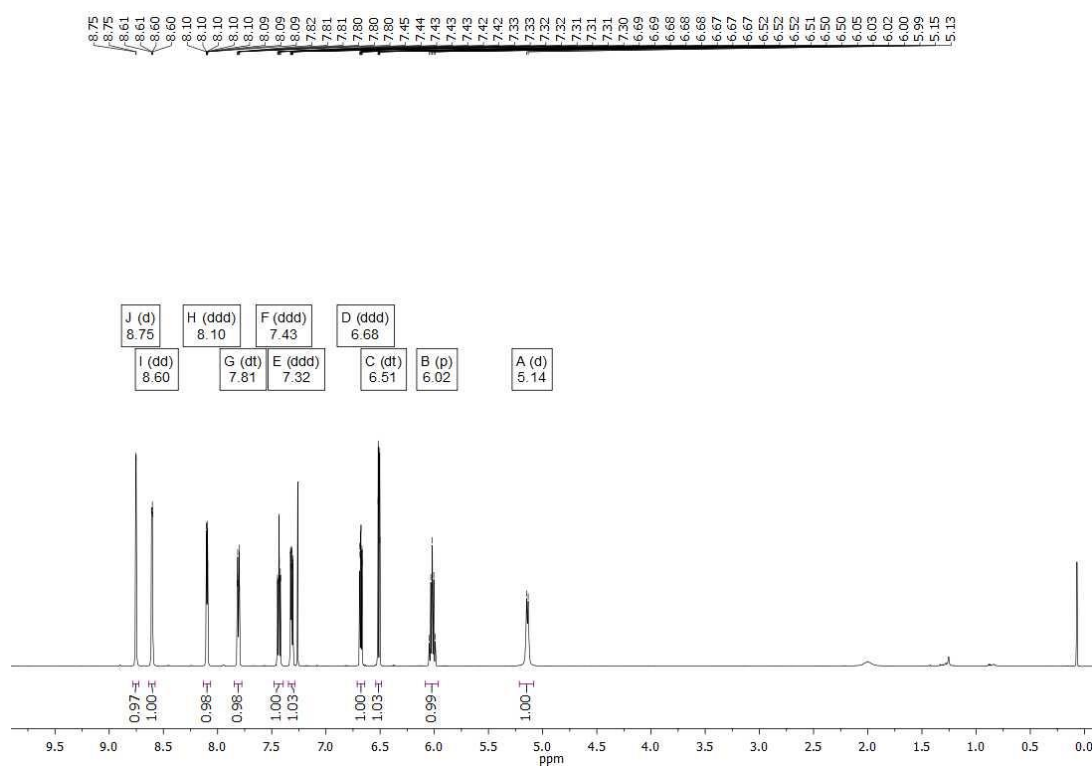


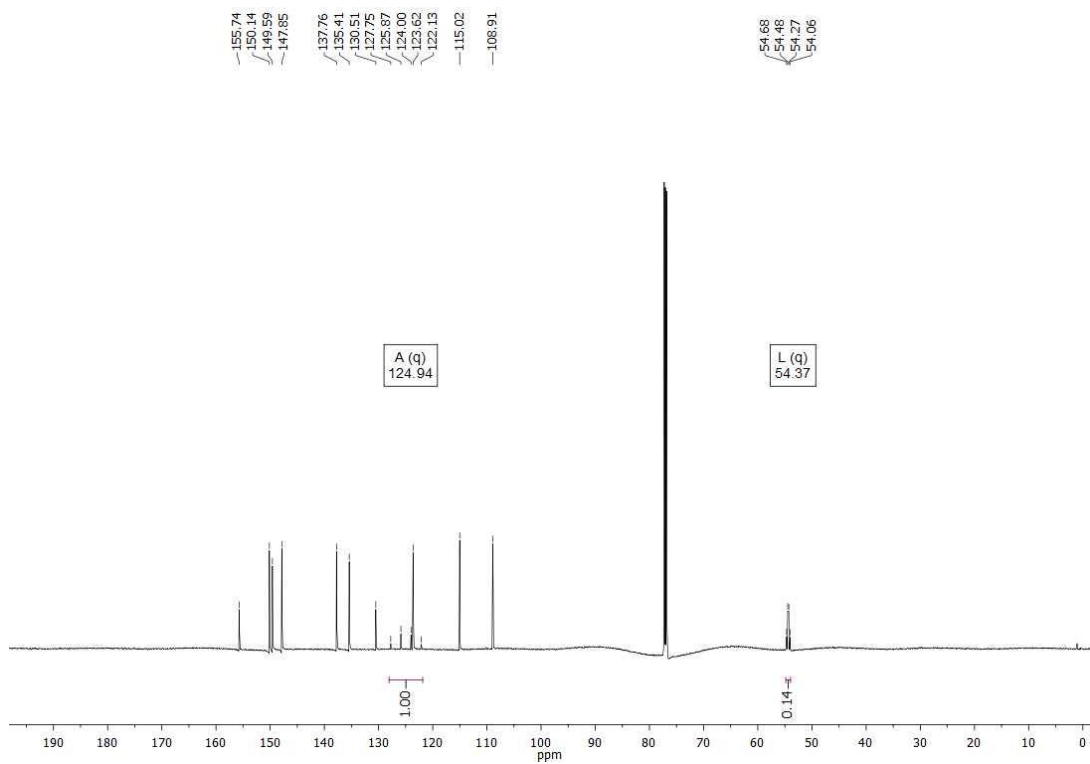
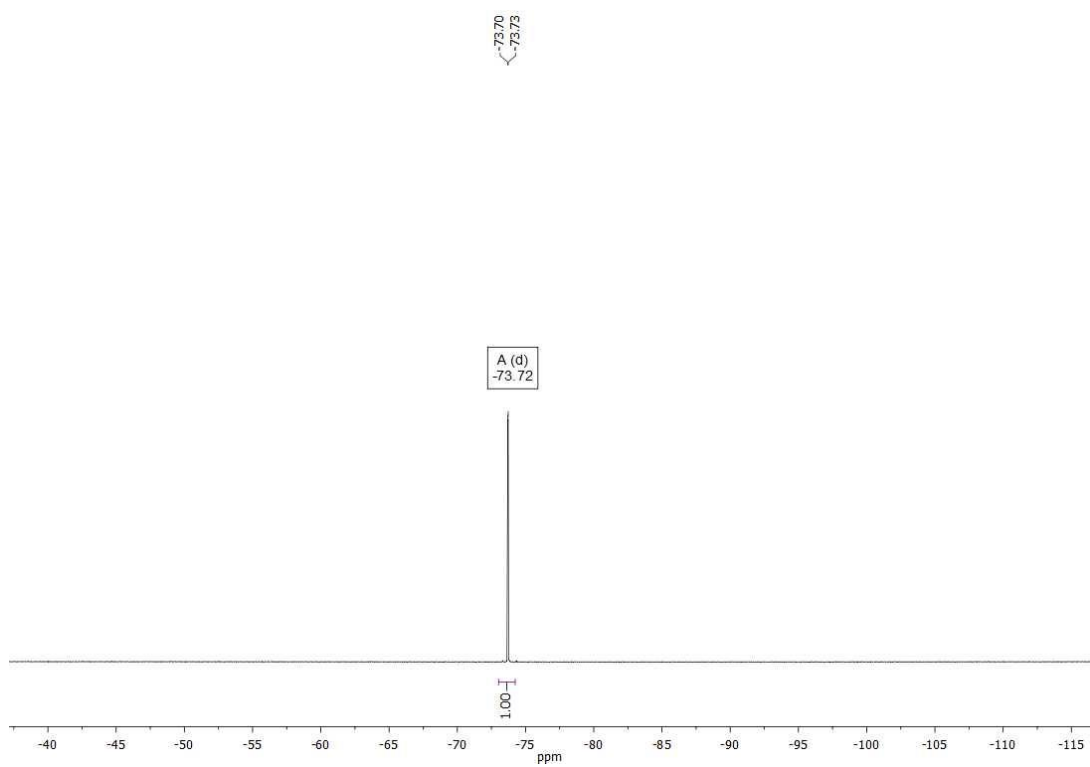
***N*-(2,2,2-Trifluoro-1-(pyridin-2-yl)ethyl)pyridin-2-amine (2g):**



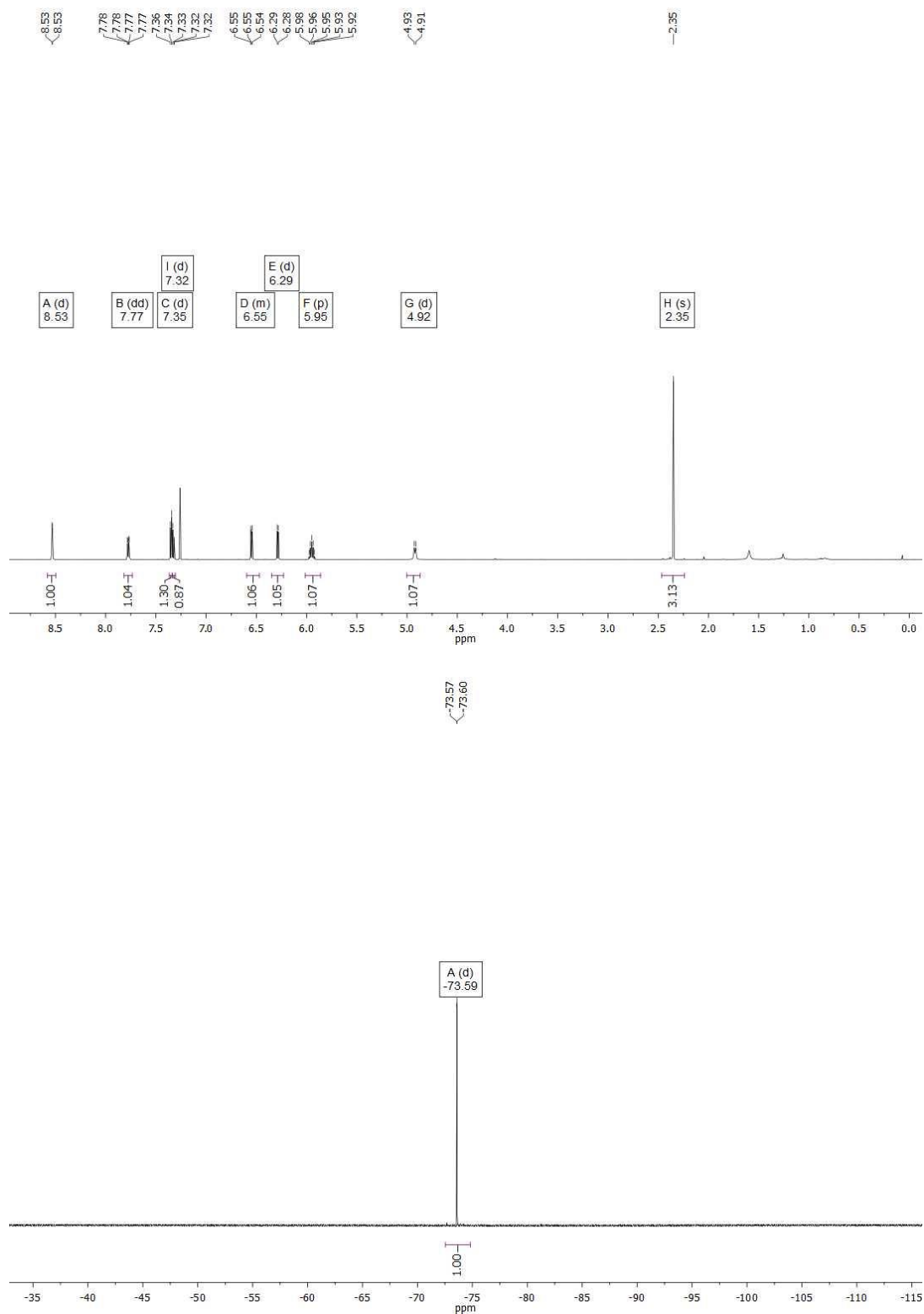


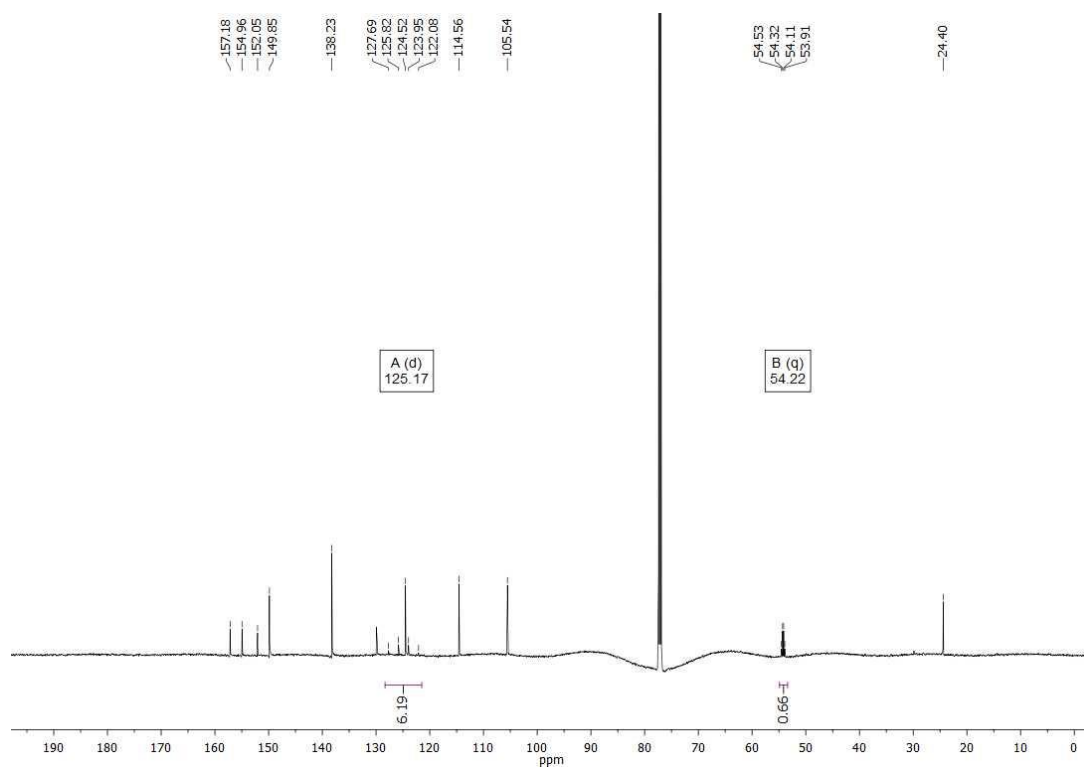
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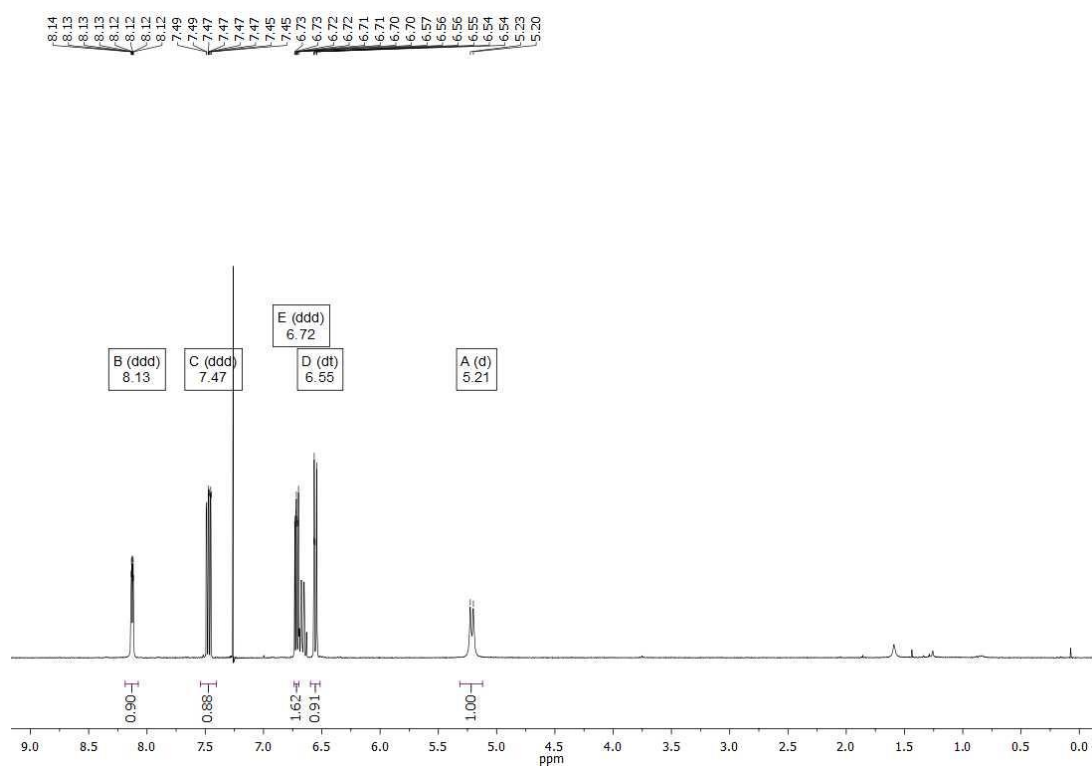


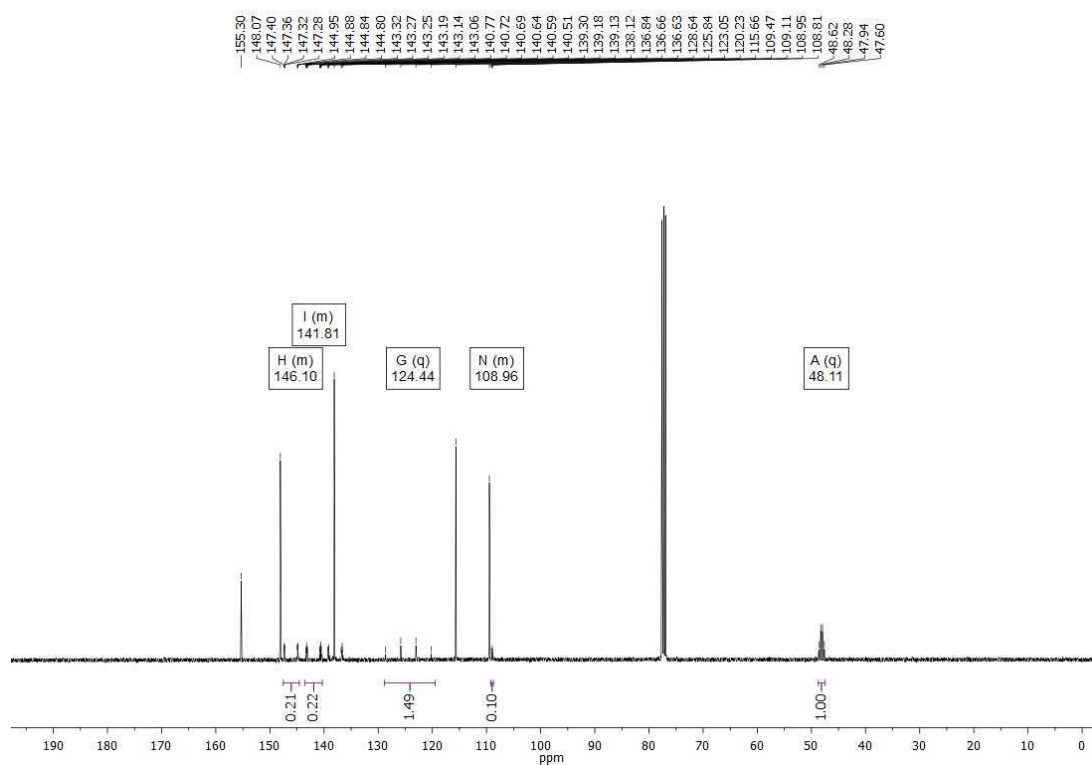
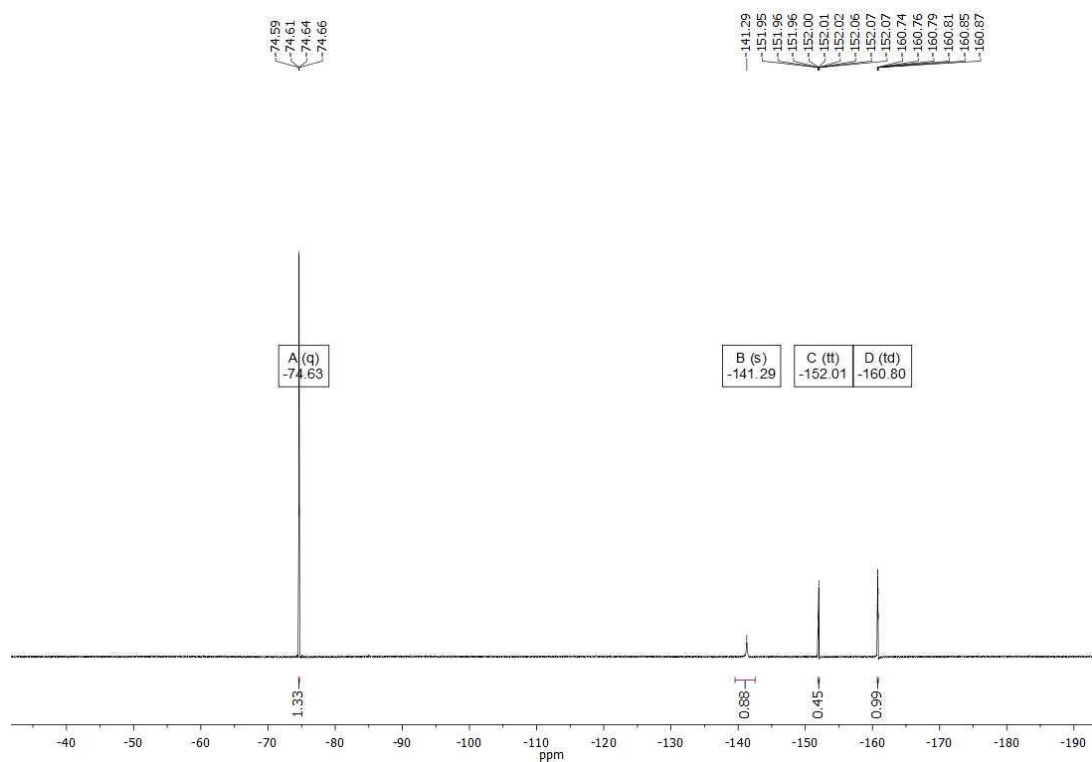
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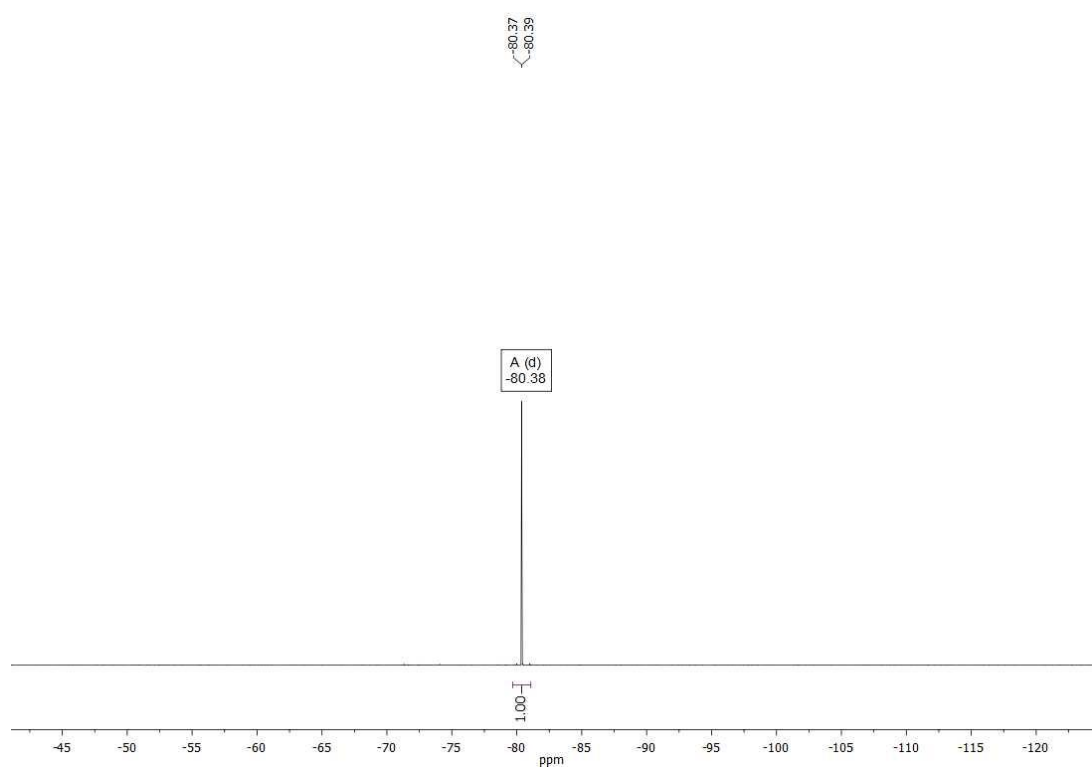
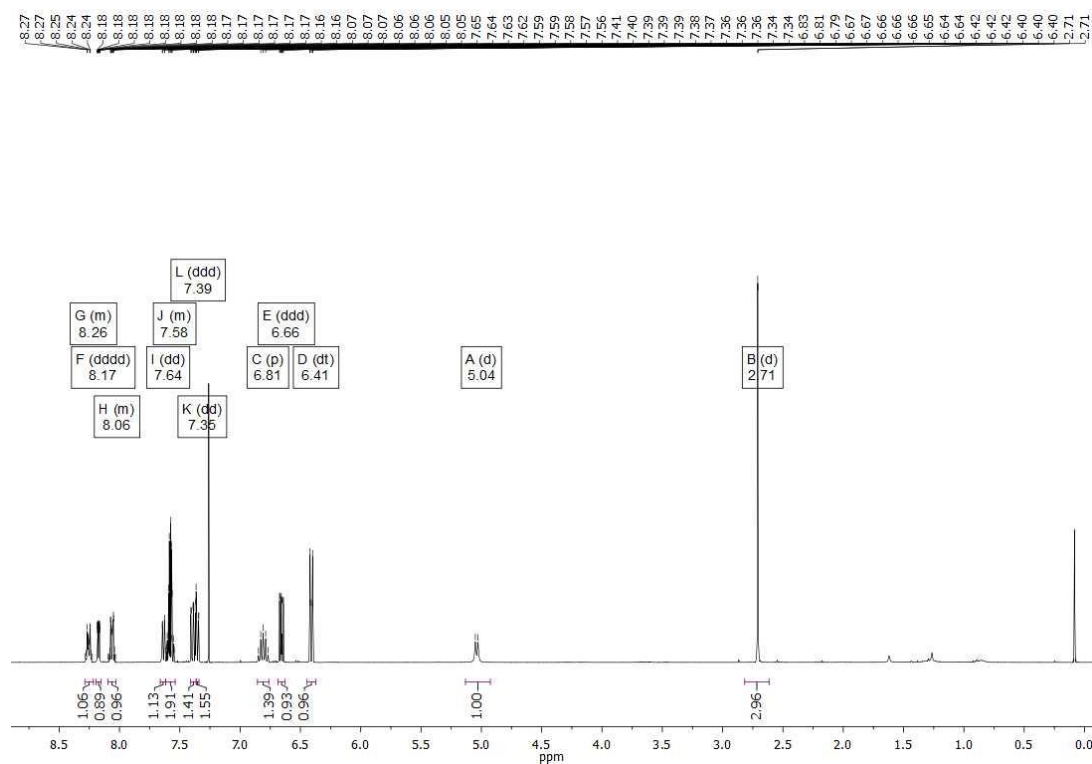


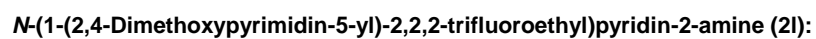
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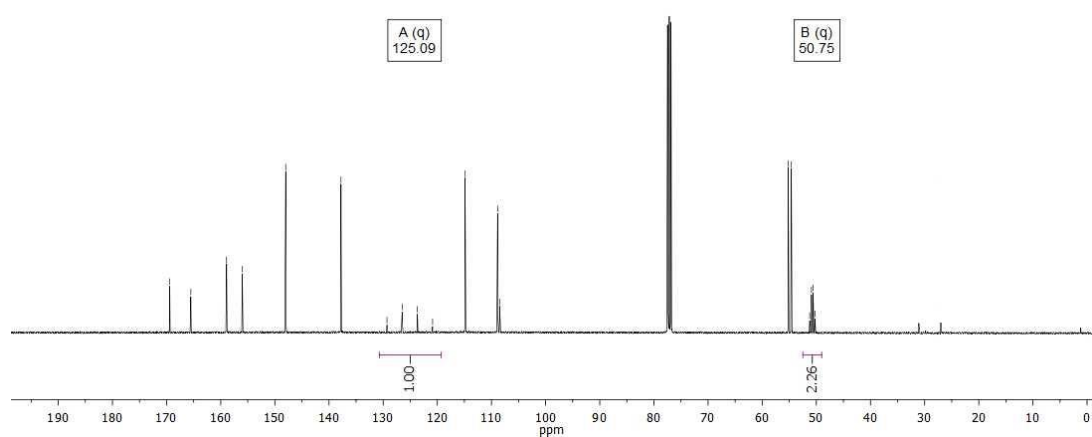
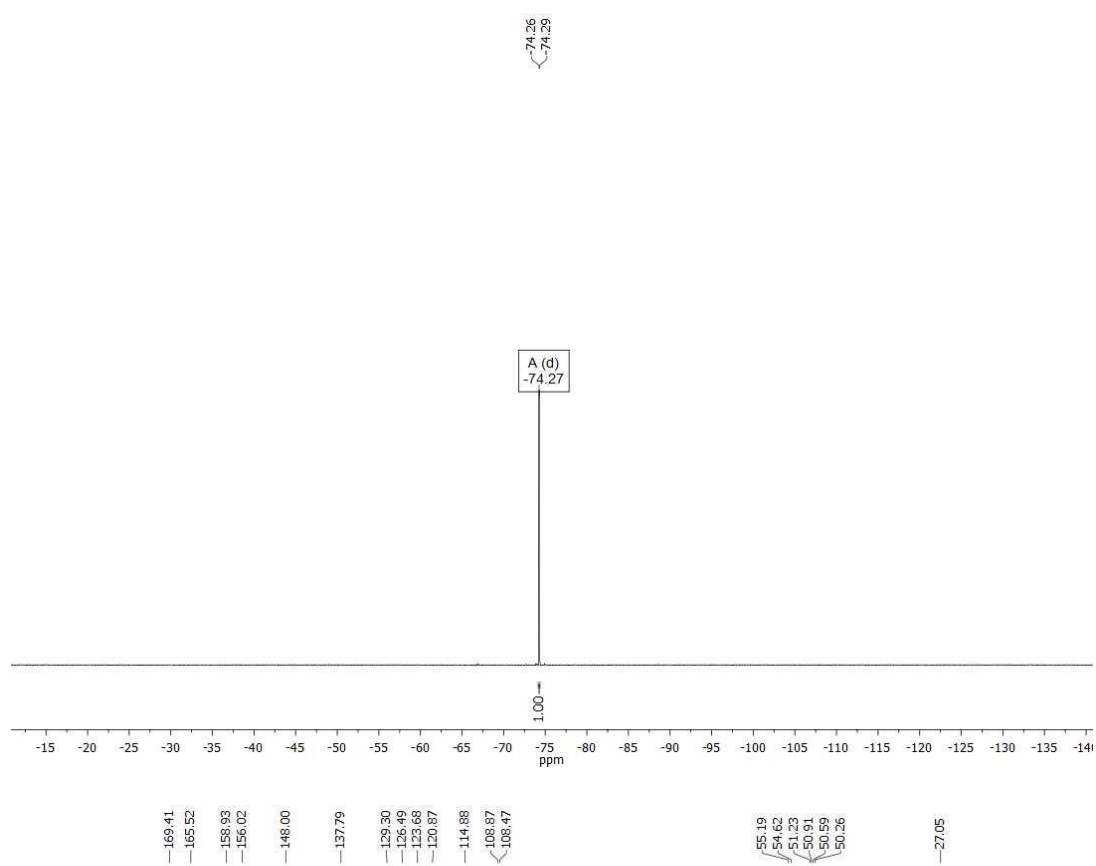


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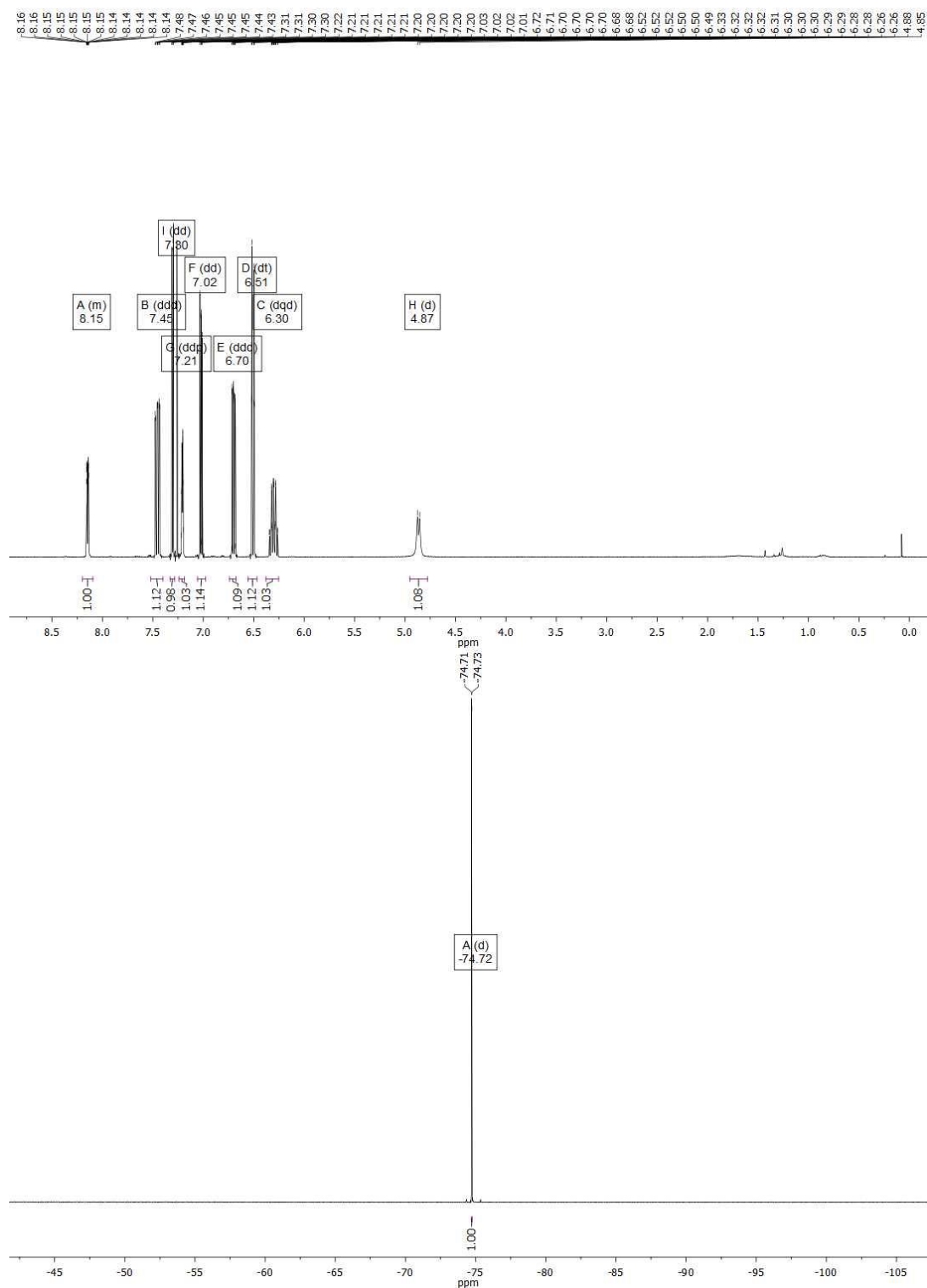


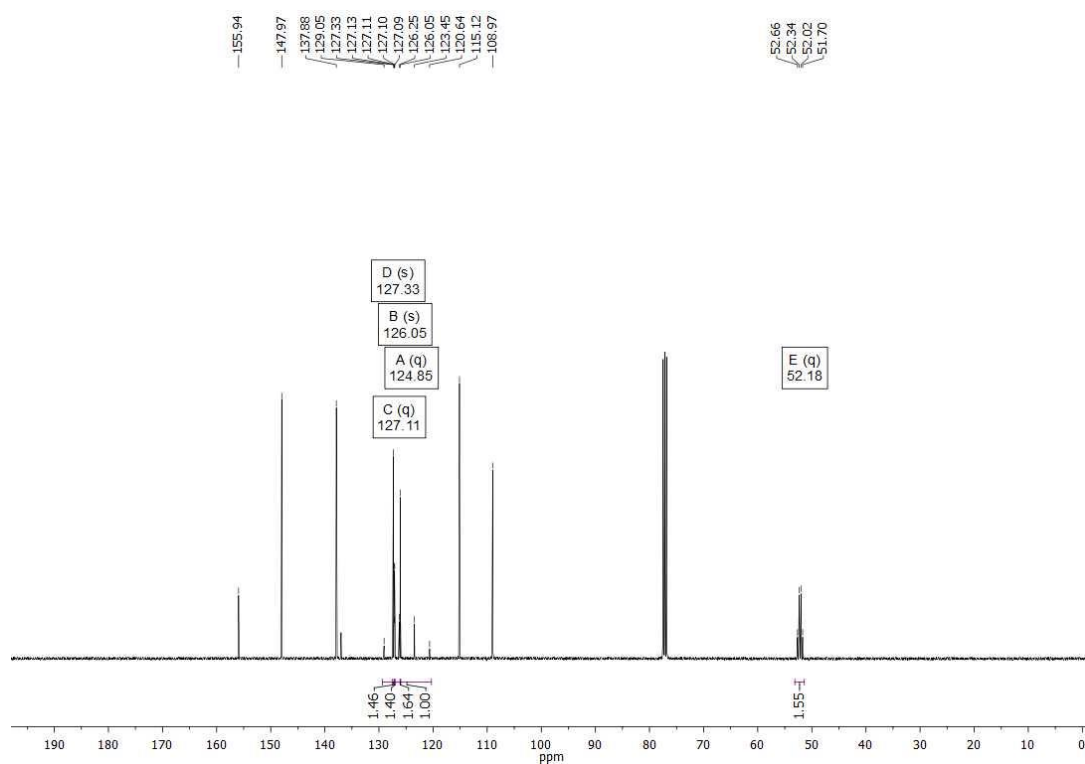




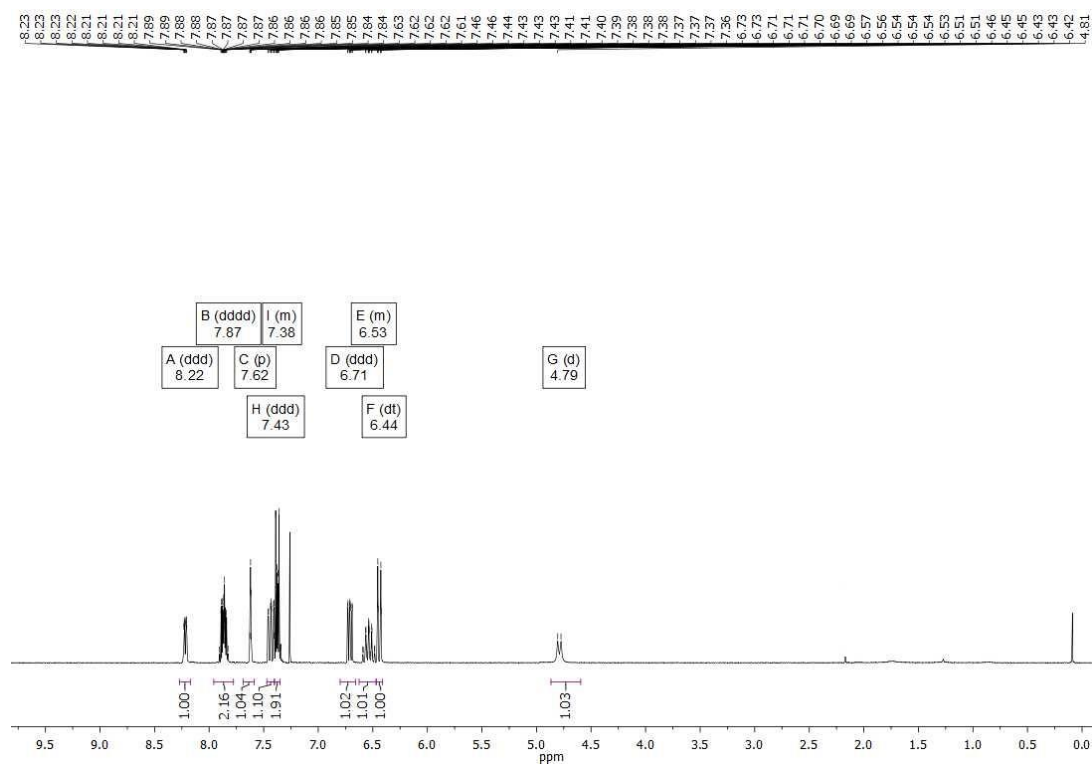


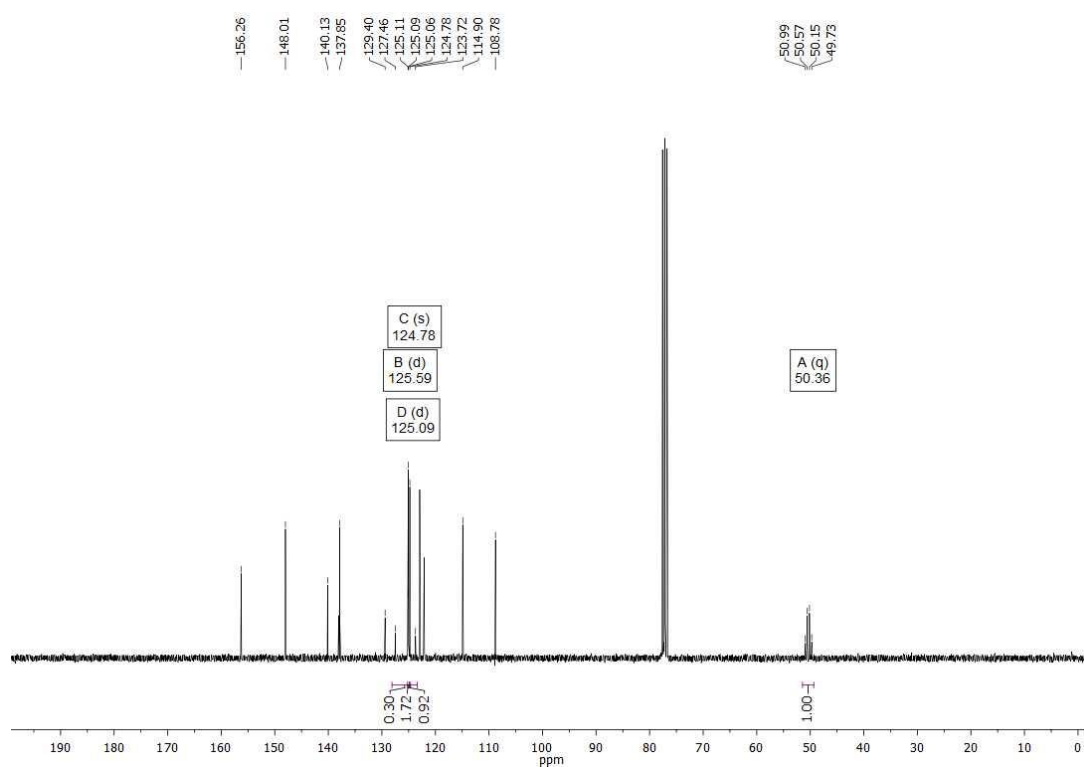
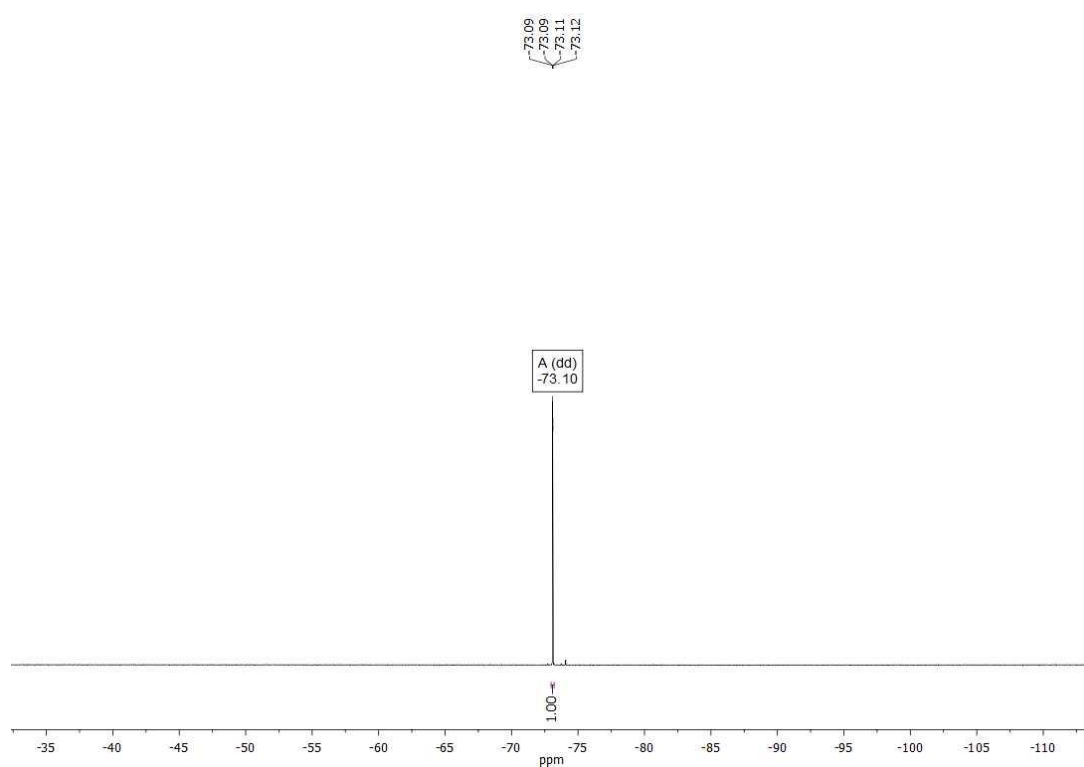
***N*-(2,2,2-Trifluoro-1-(thiophen-2-yl)ethyl)pyridin-2-amine (2m):**



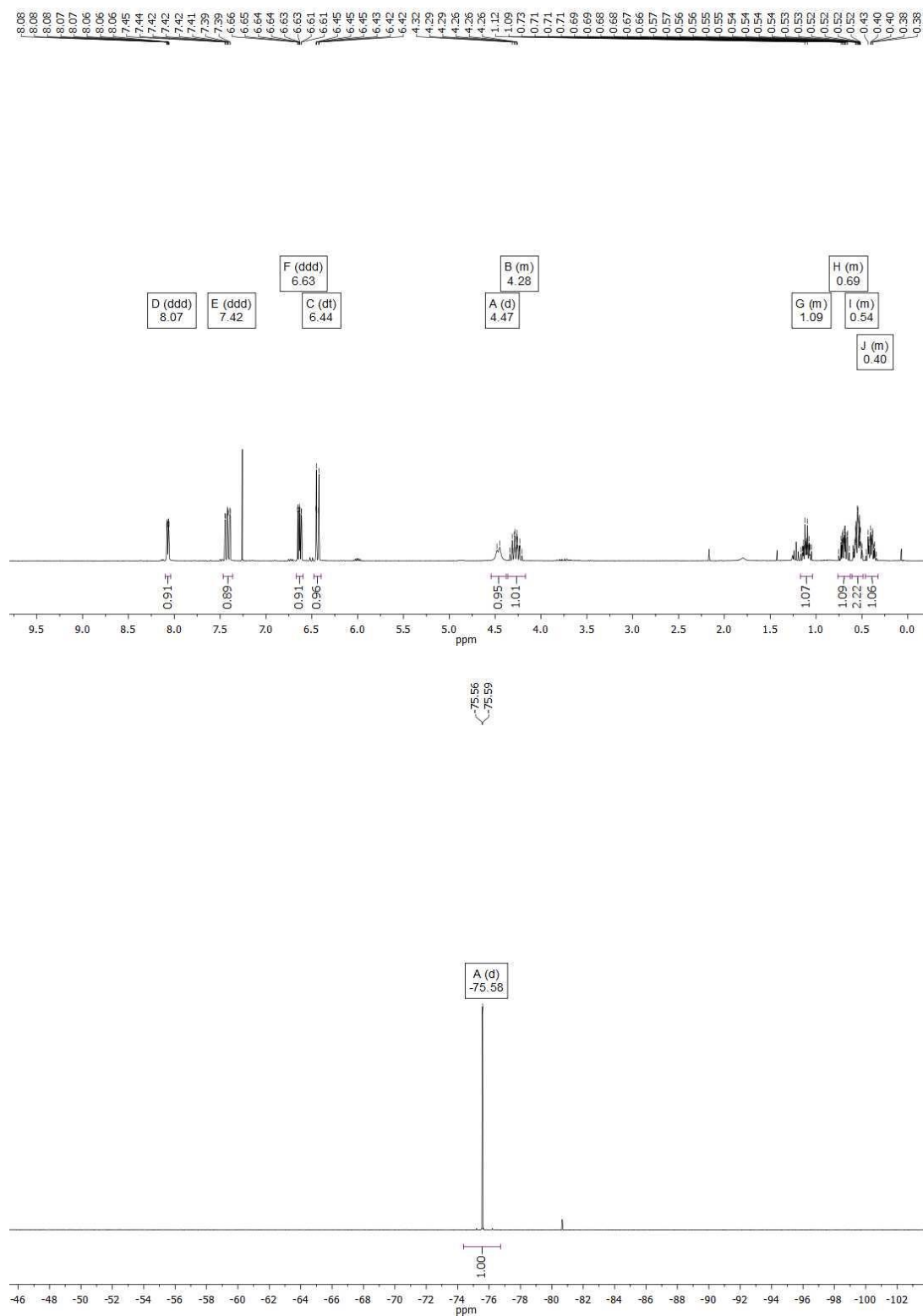


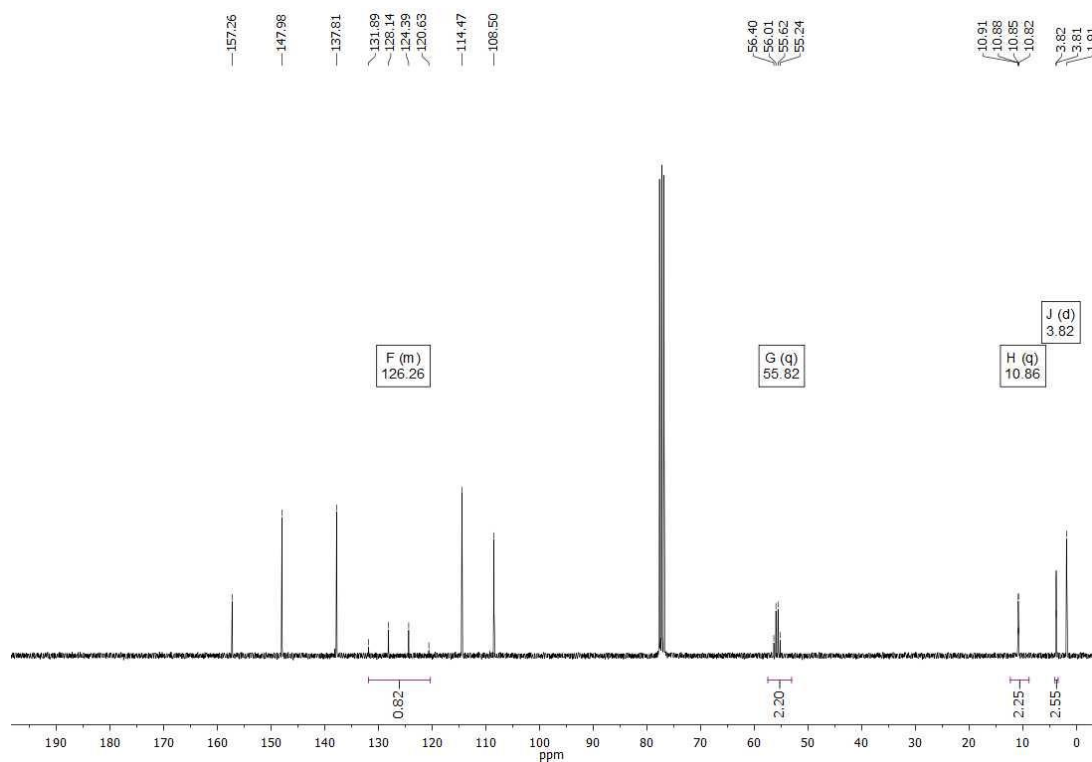
***N*-(1-(Benz[*b*]thiophen-3-yl)-2,2,2-trifluoroethyl)pyridin-2-amine (2n):**



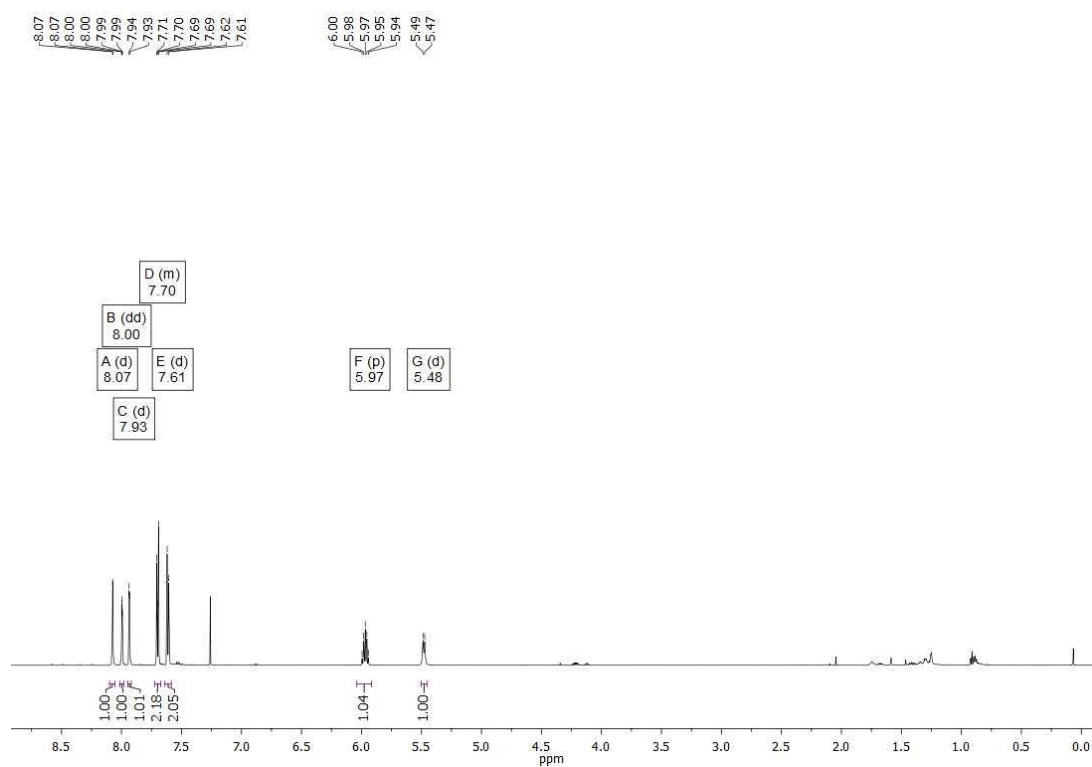


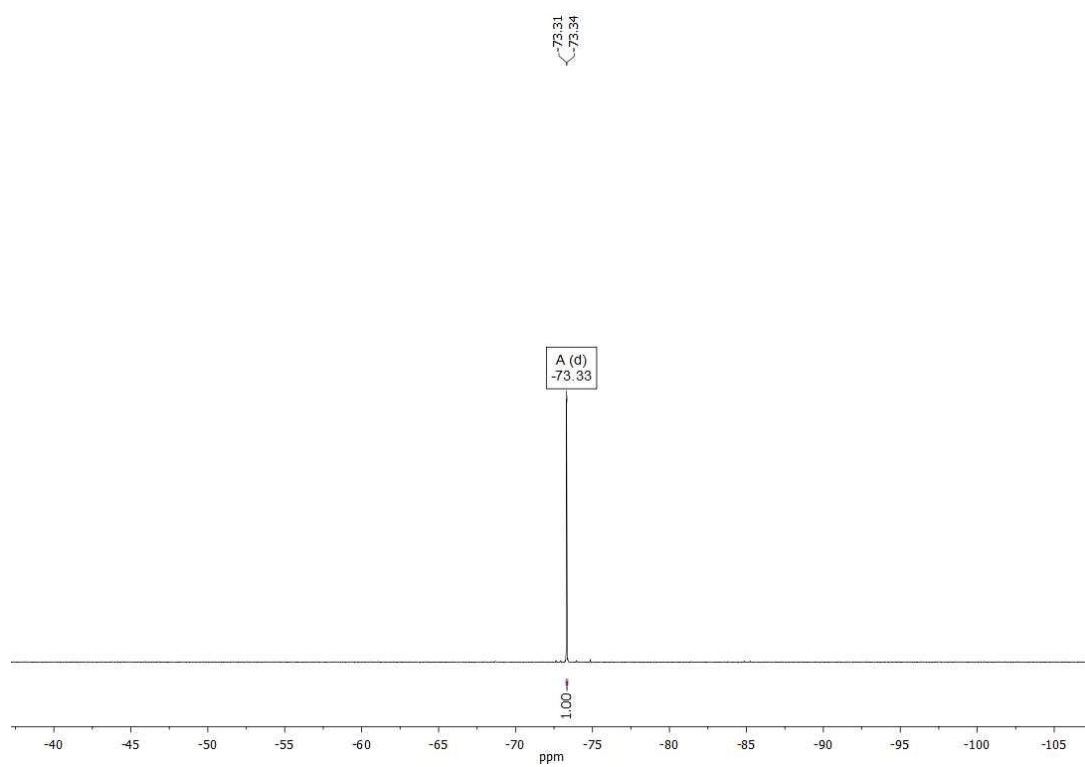
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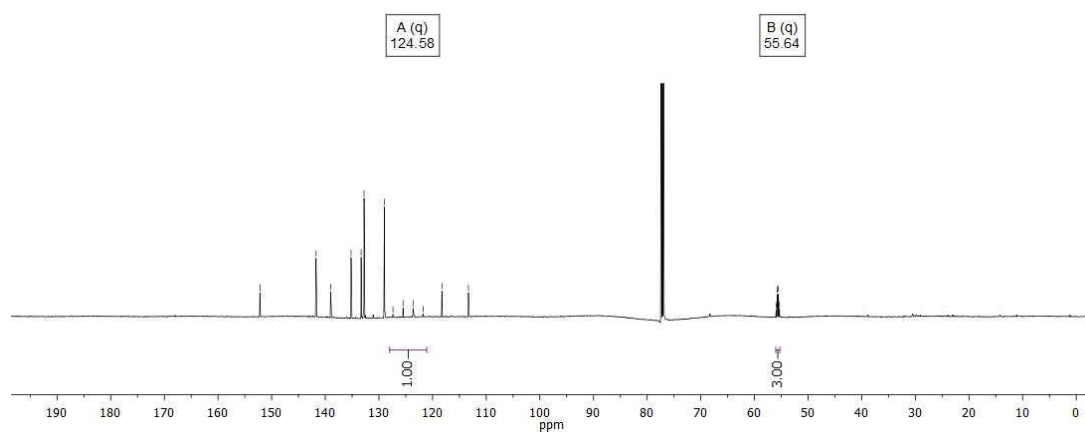


**4-(2,2,2-Trifluoro-1-(pyrazin-2-ylamino)ethyl)benzonitrile (2p):**

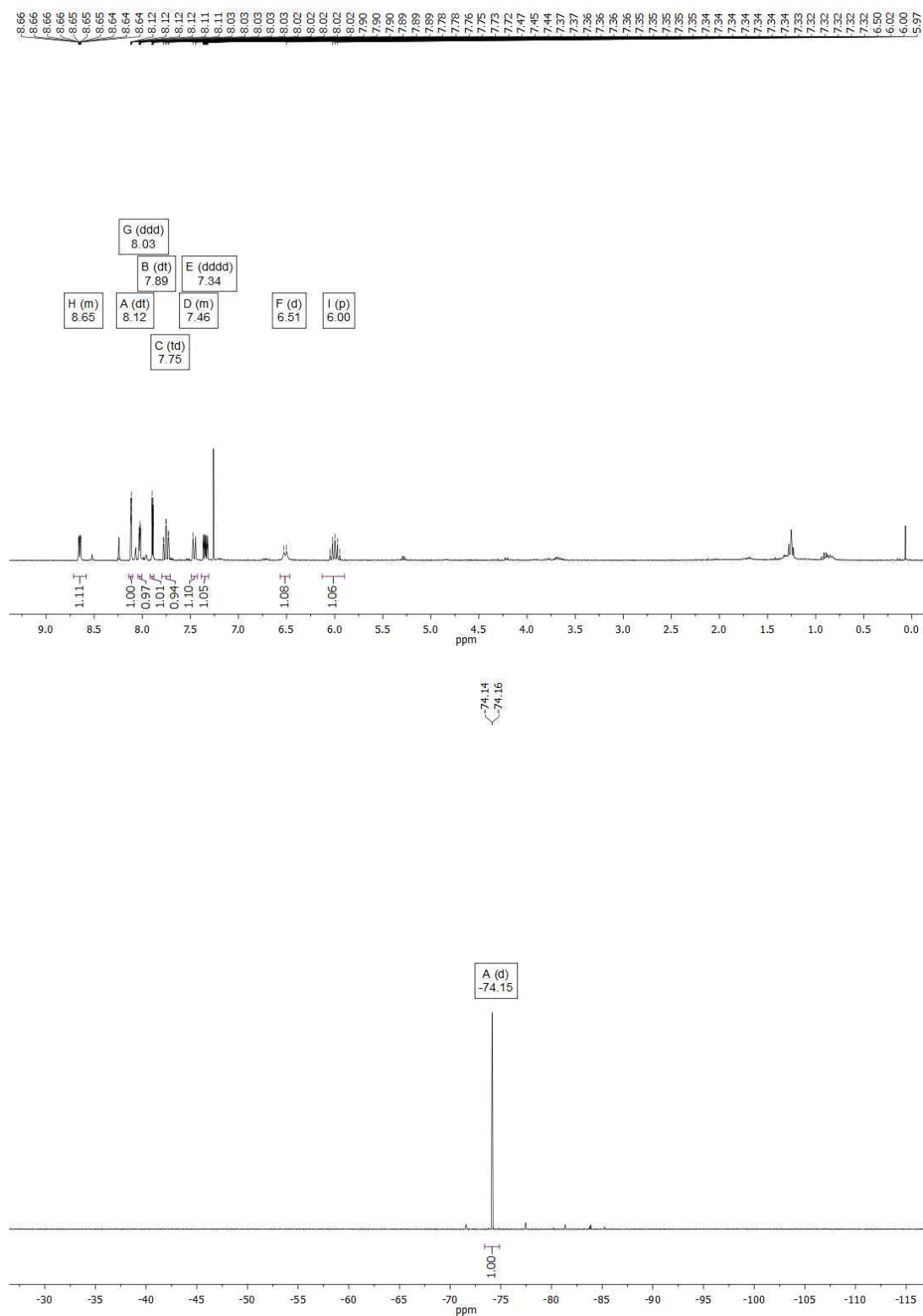




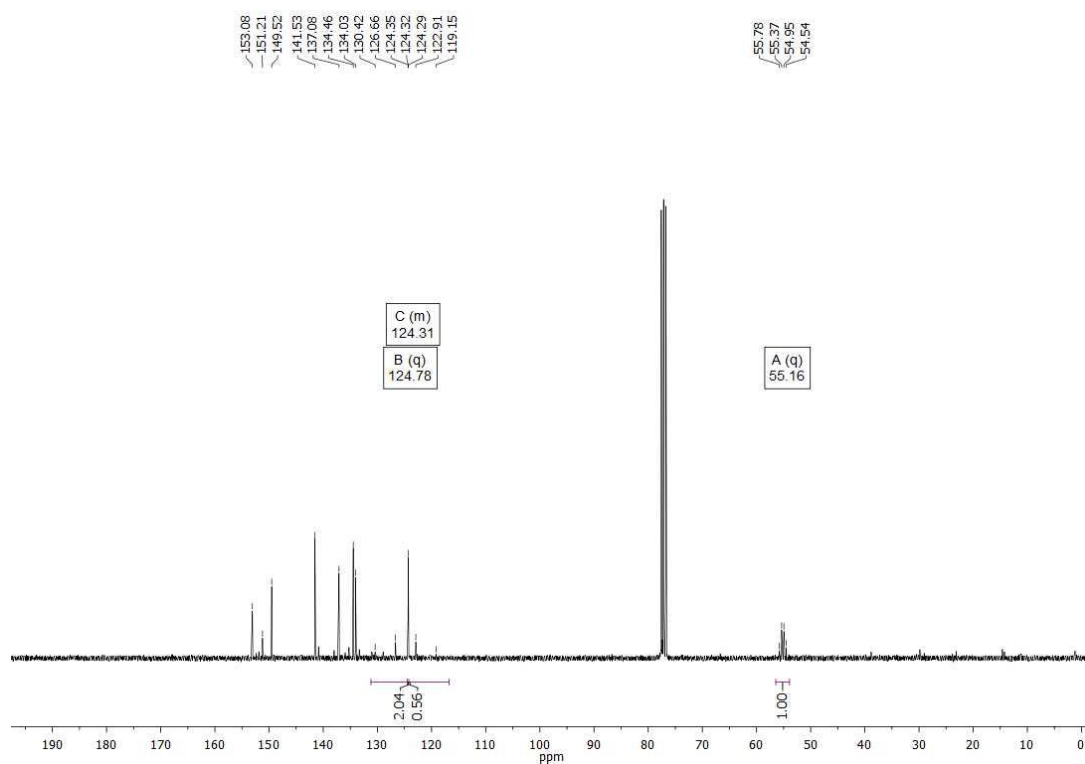
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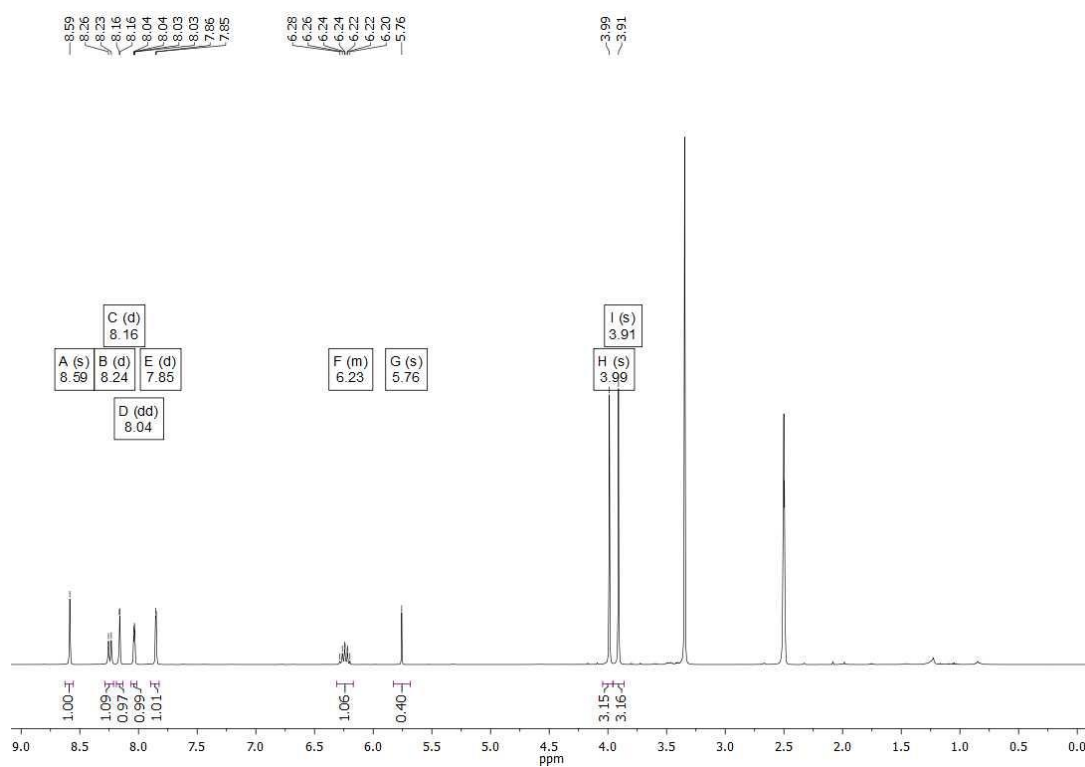
***N*-(2,2,2-Trifluoro-1-(pyridin-2-yl)ethyl)pyrazin-2-amine (2q):**

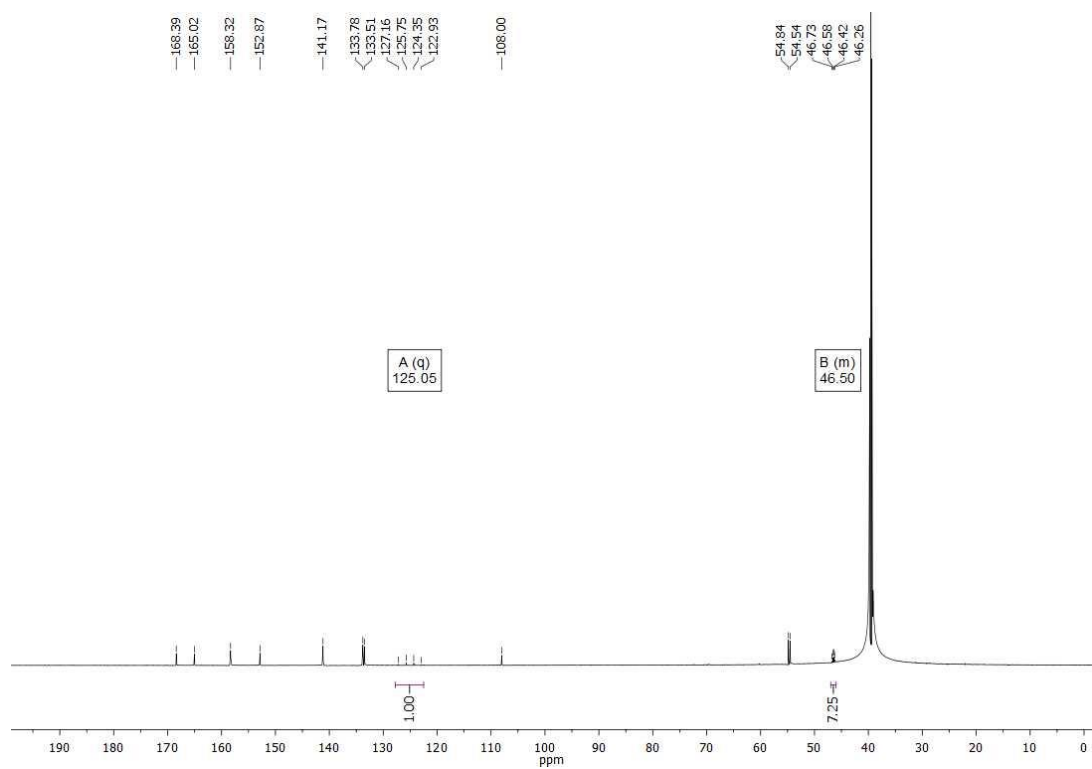
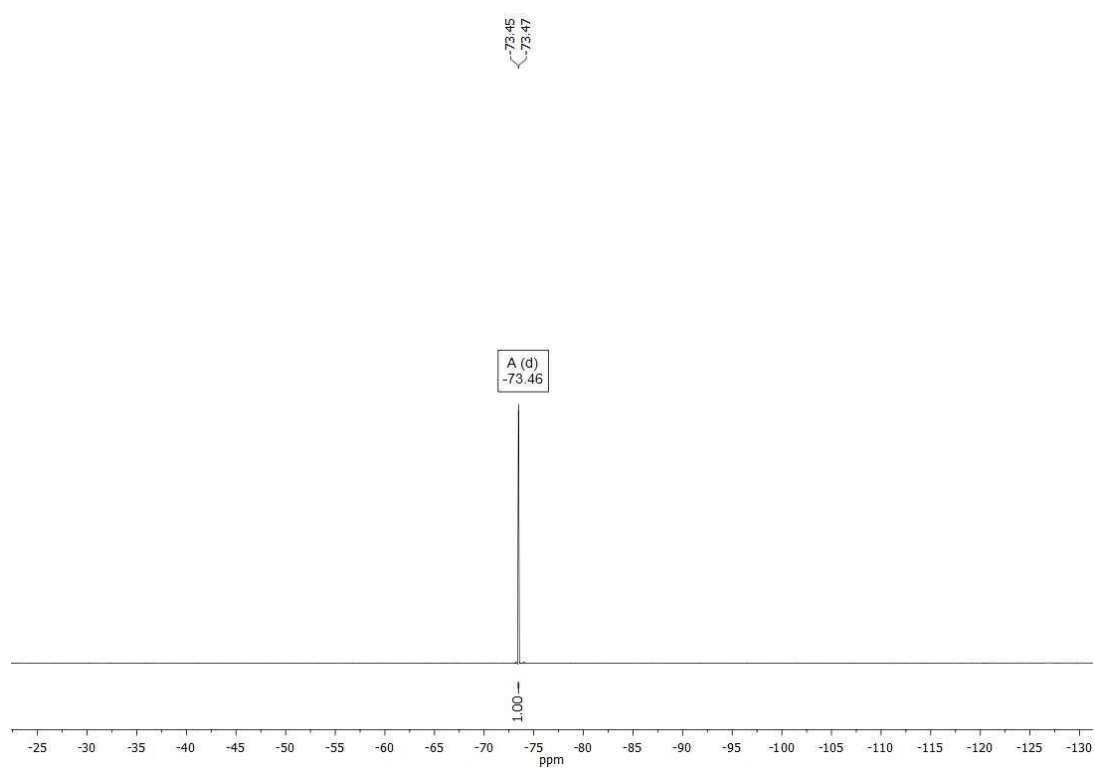




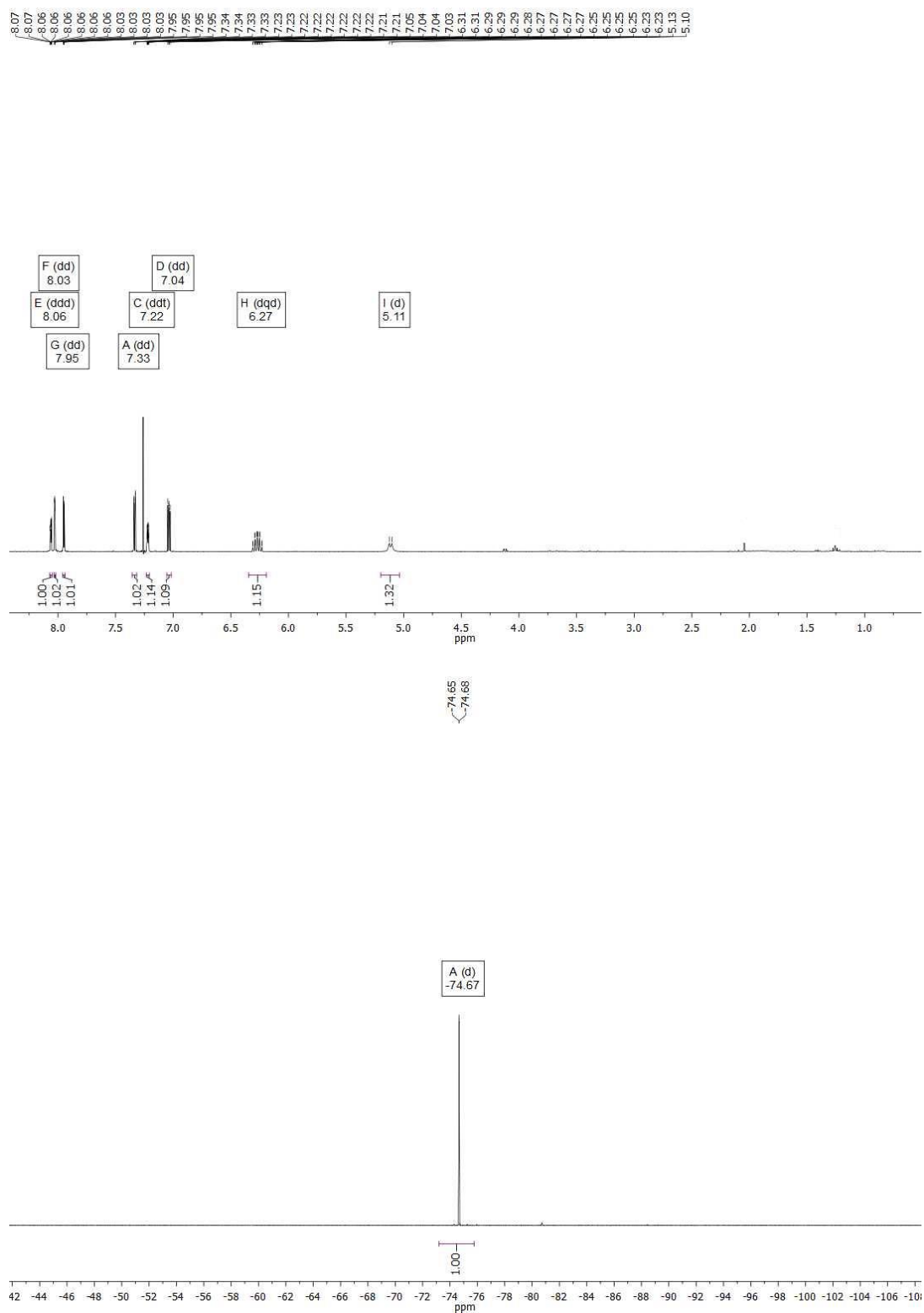


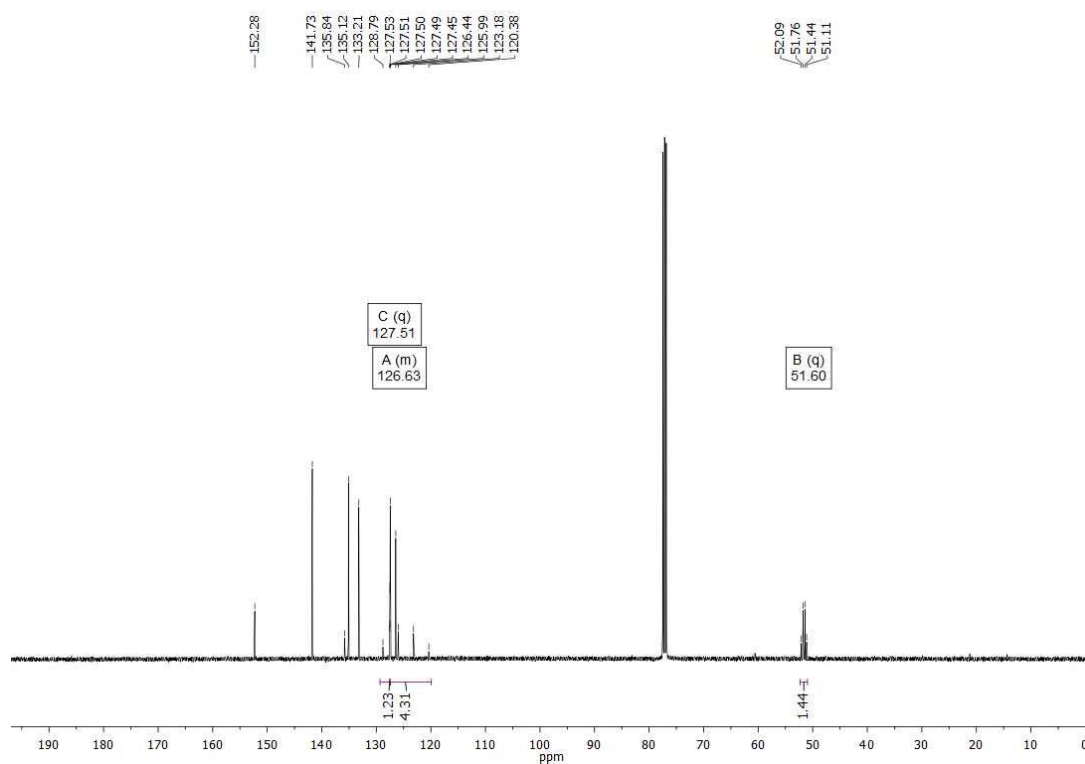
***N*-(1-(2,4-Dimethoxypyrimidin-5-yl)-2,2,2-trifluoroethyl)pyrazine-2-amine (2r):**



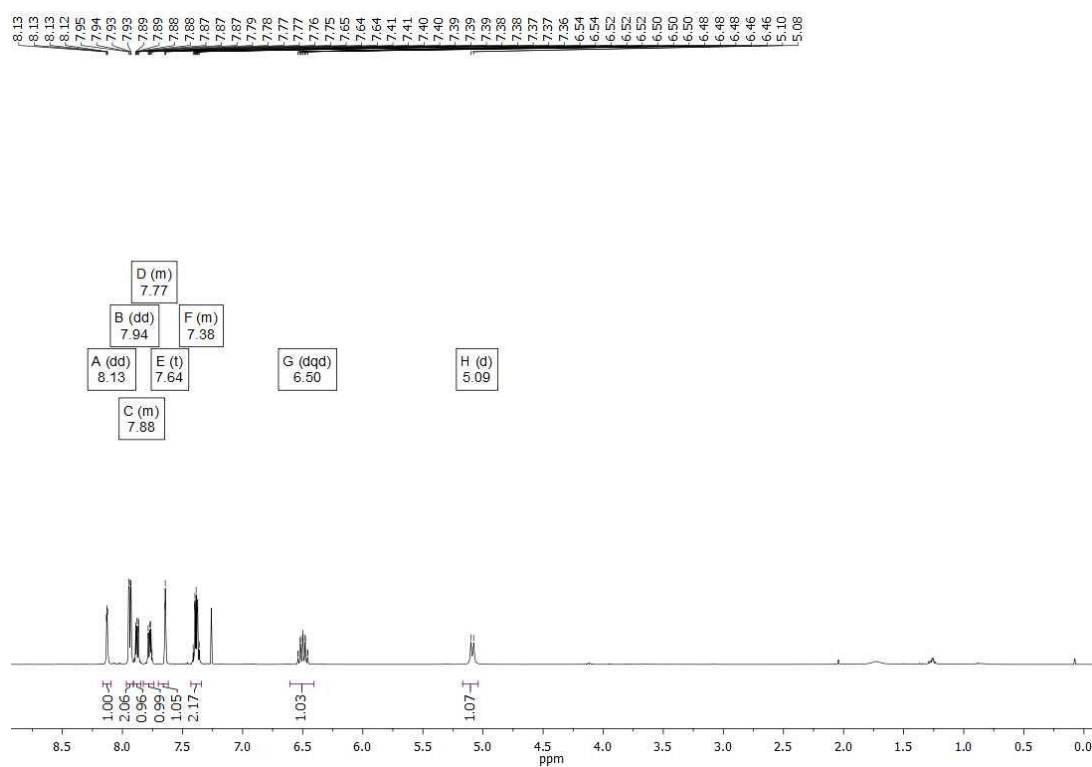


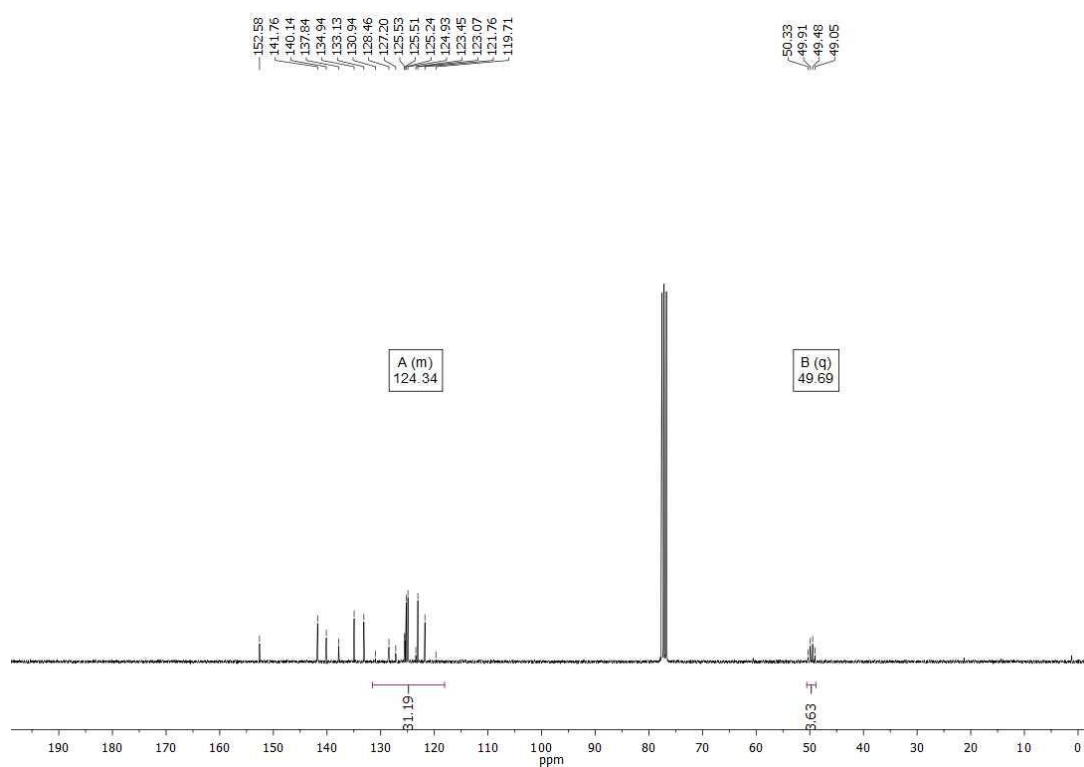
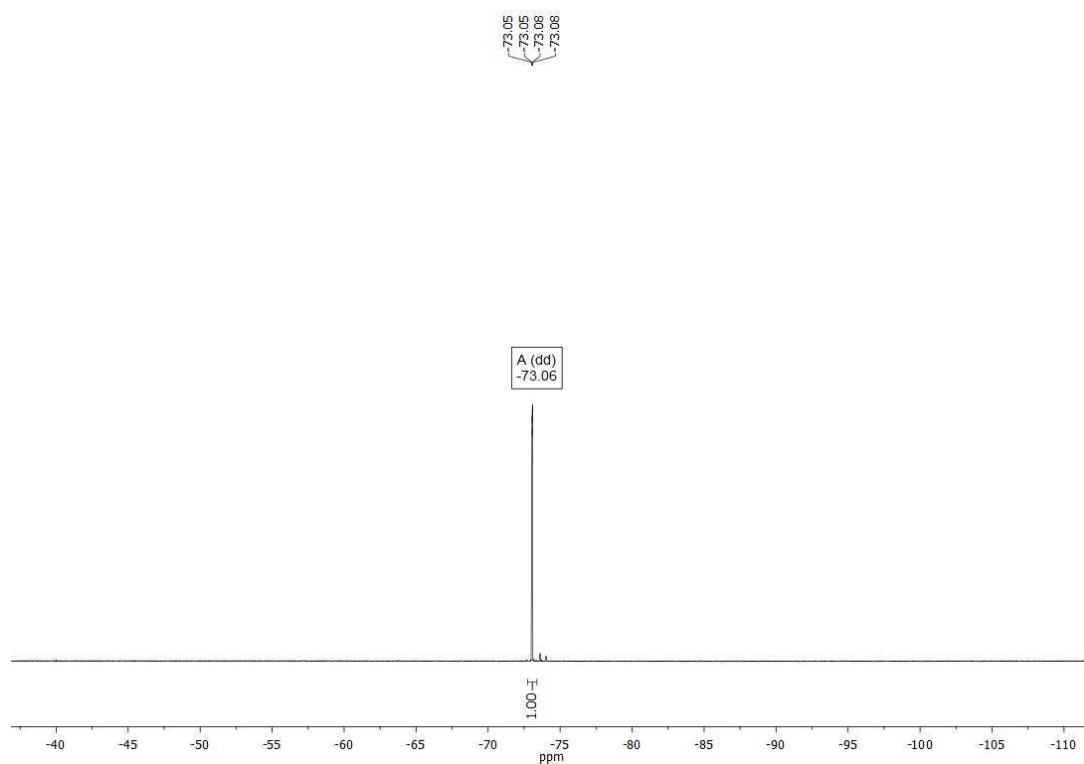
***N*-(2,2,2-Trifluoro-1-(thiophen-2-yl)ethyl)pyrazin-2-amine (2s):**



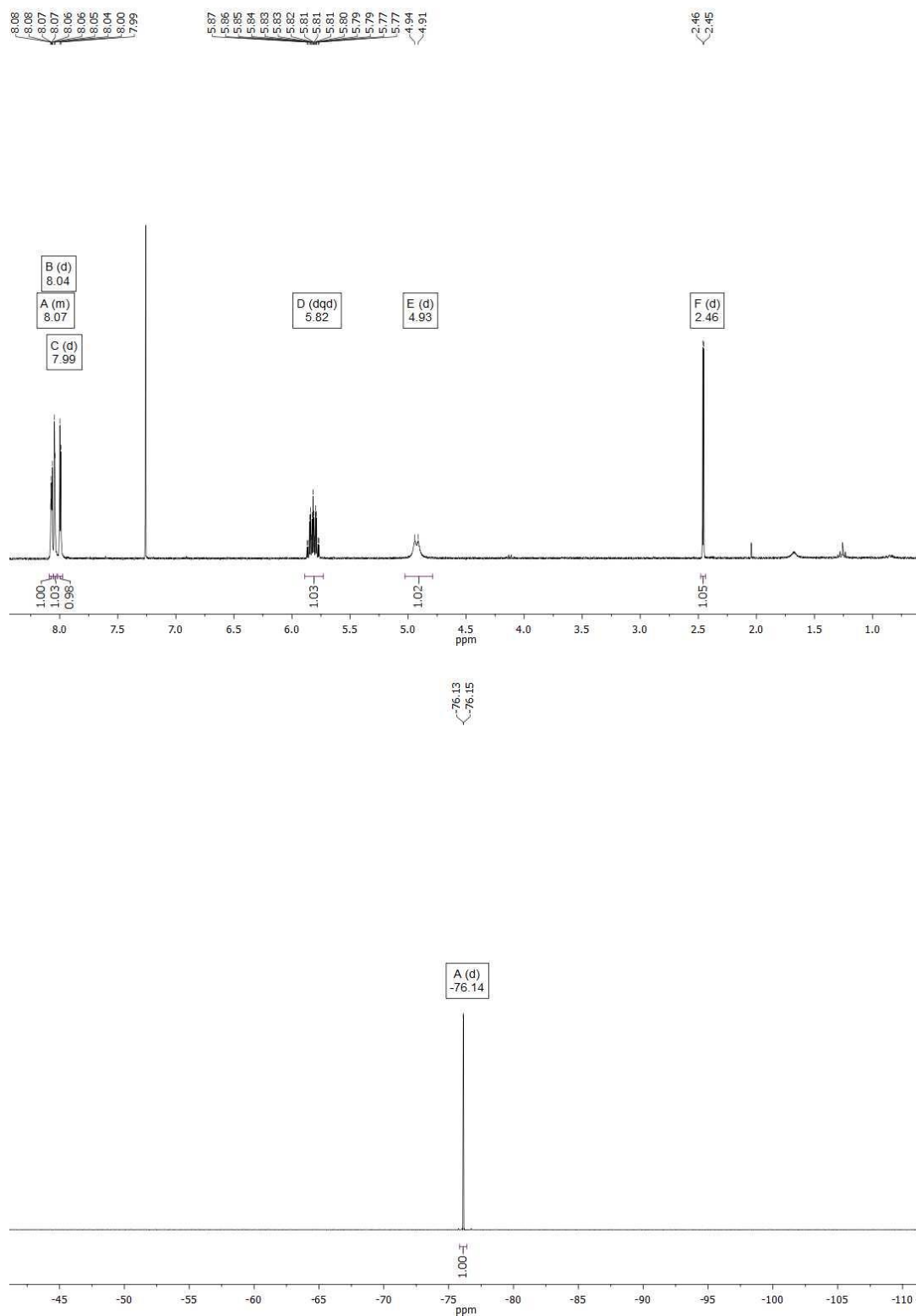


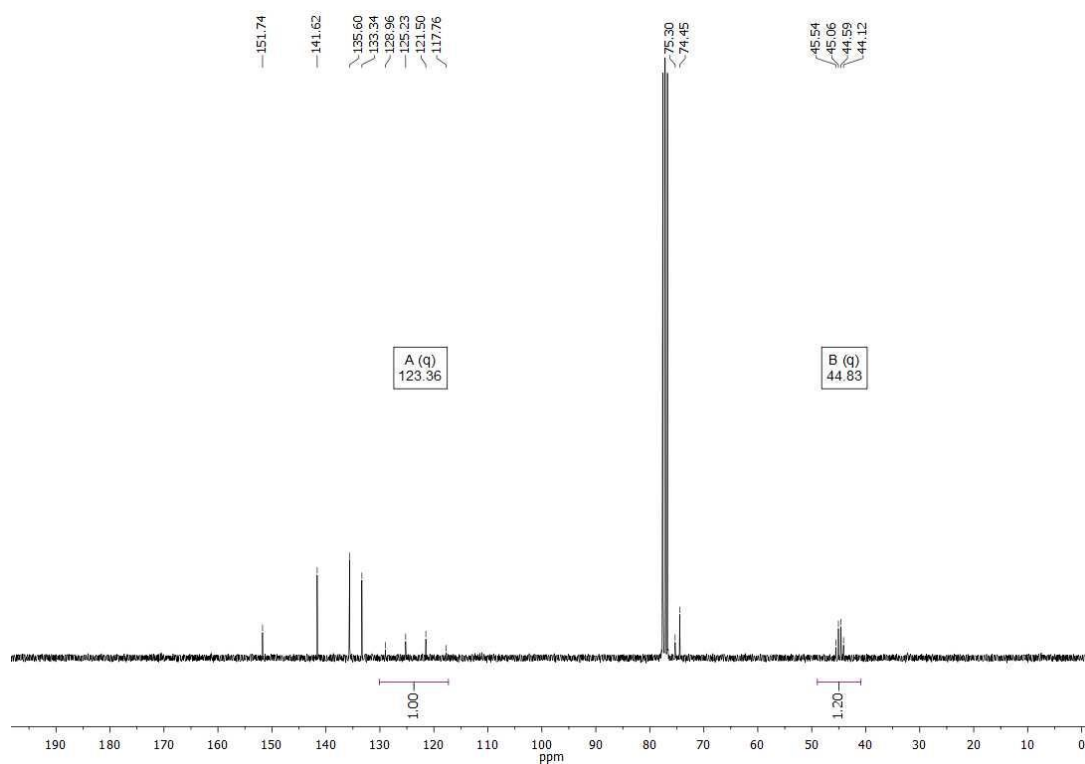
***N*-(1-(Benz[*b*]thiophen-3-yl)-2,2,2-trifluoroethyl)pyrazine-2-amine (2t):**



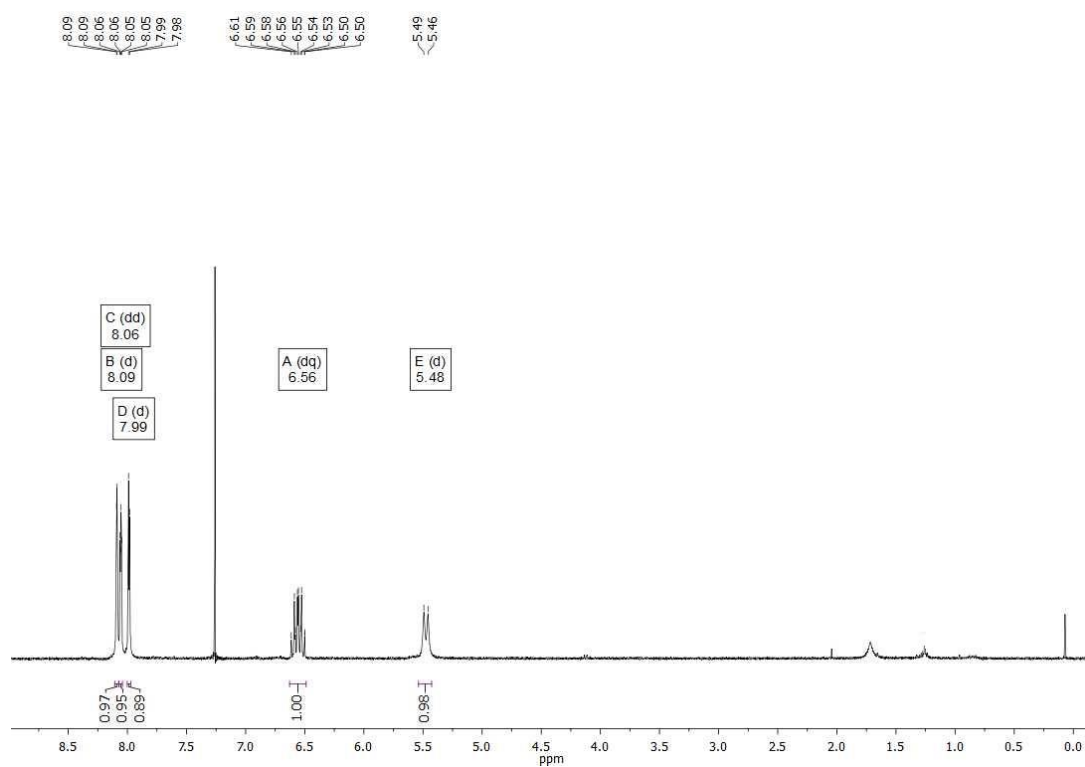


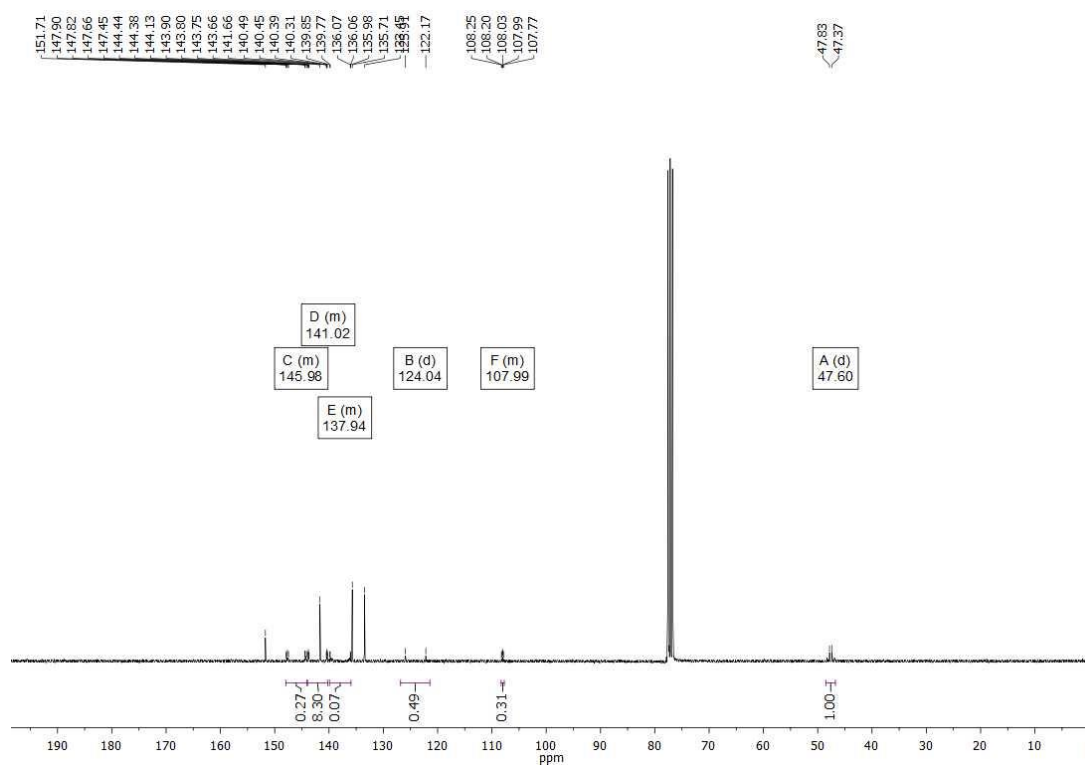
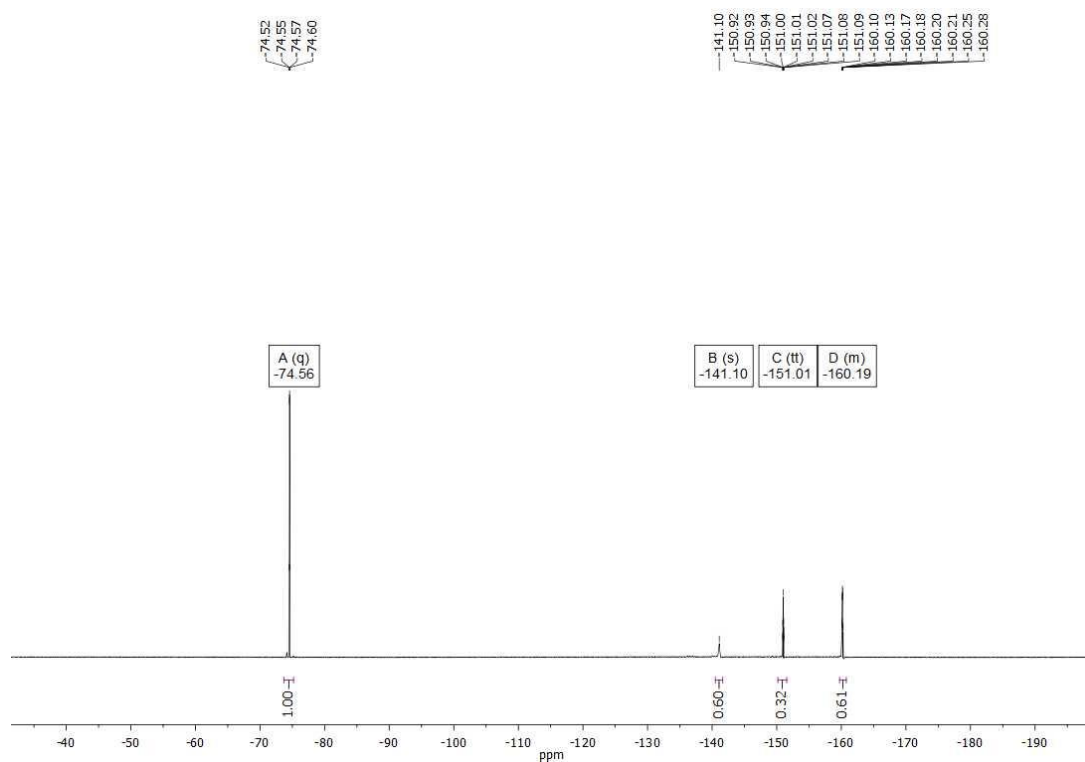
***N*-(1,1,1-Trifluoro-but-3-yn-2-yl)pyrazin-2-amine (2u):**





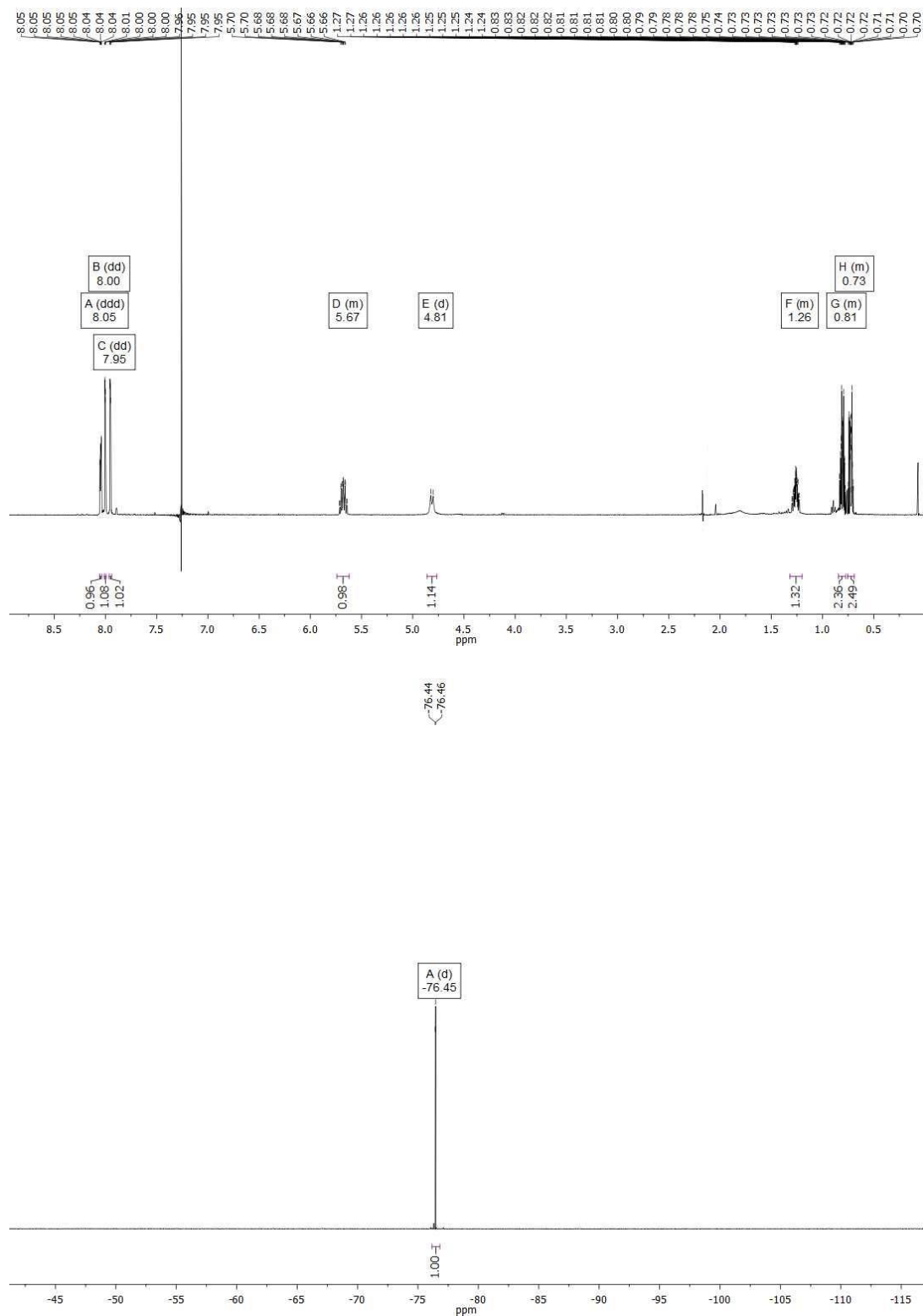
***N*-(2,2,2-Trifluoro-1-(perfluorophenyl)ethyl)pyrazin-2-amine (2v):**

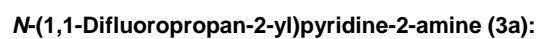


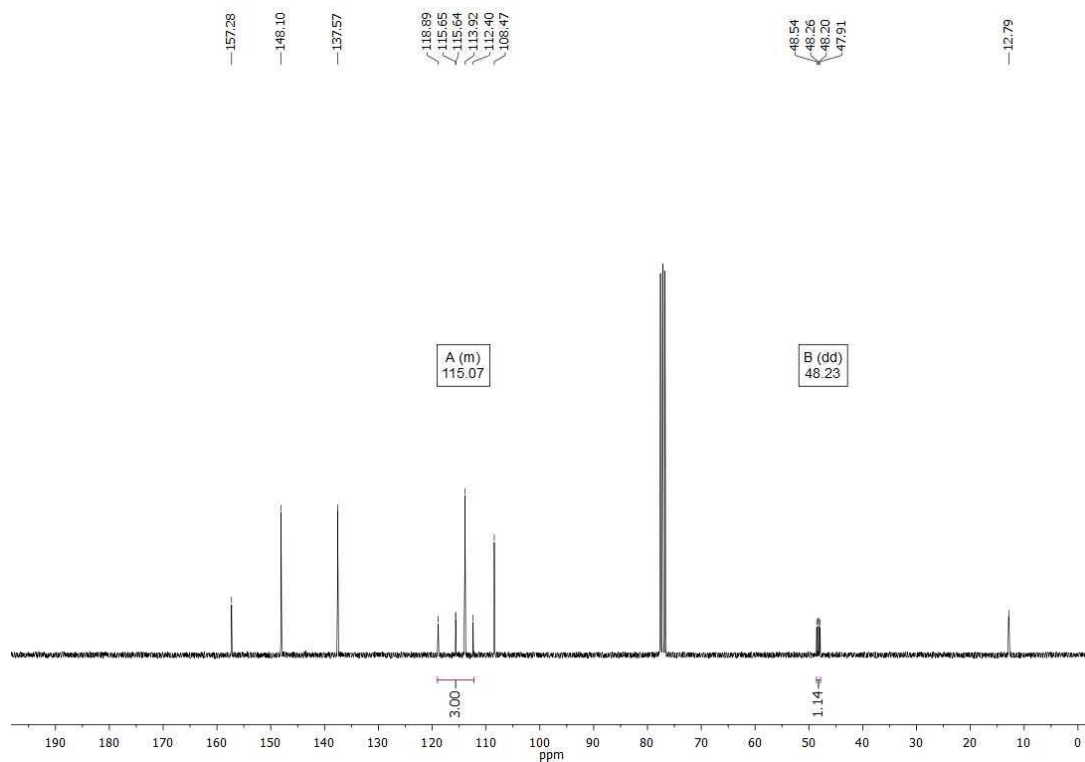
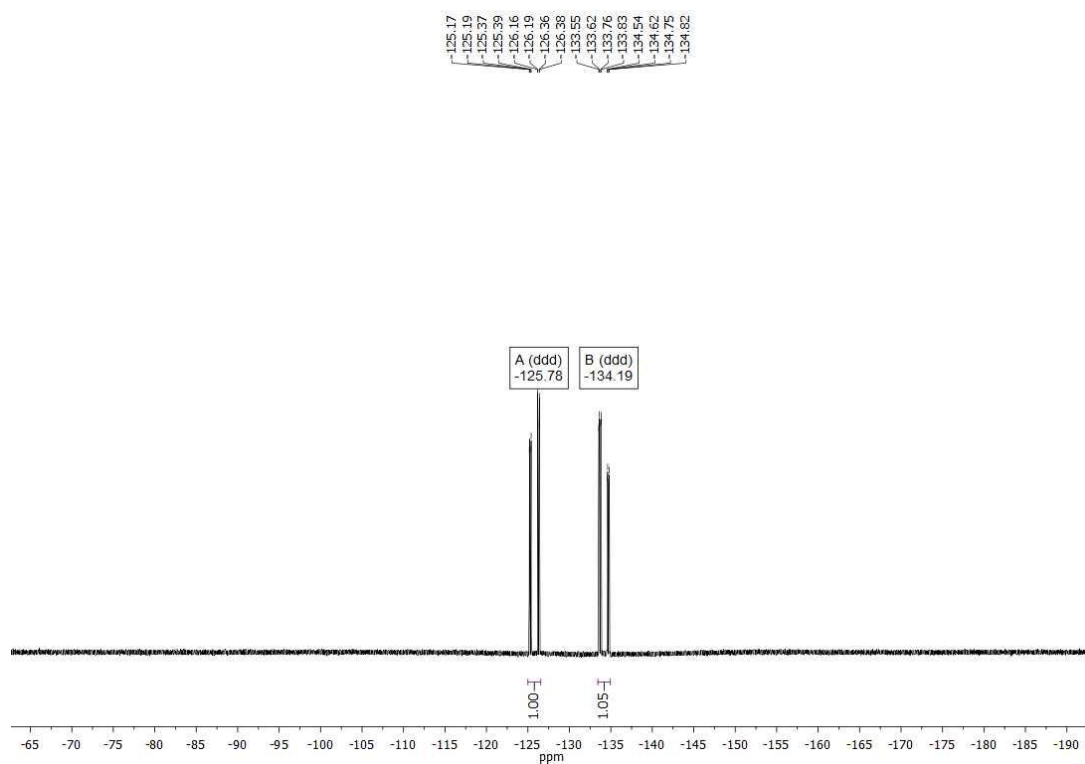




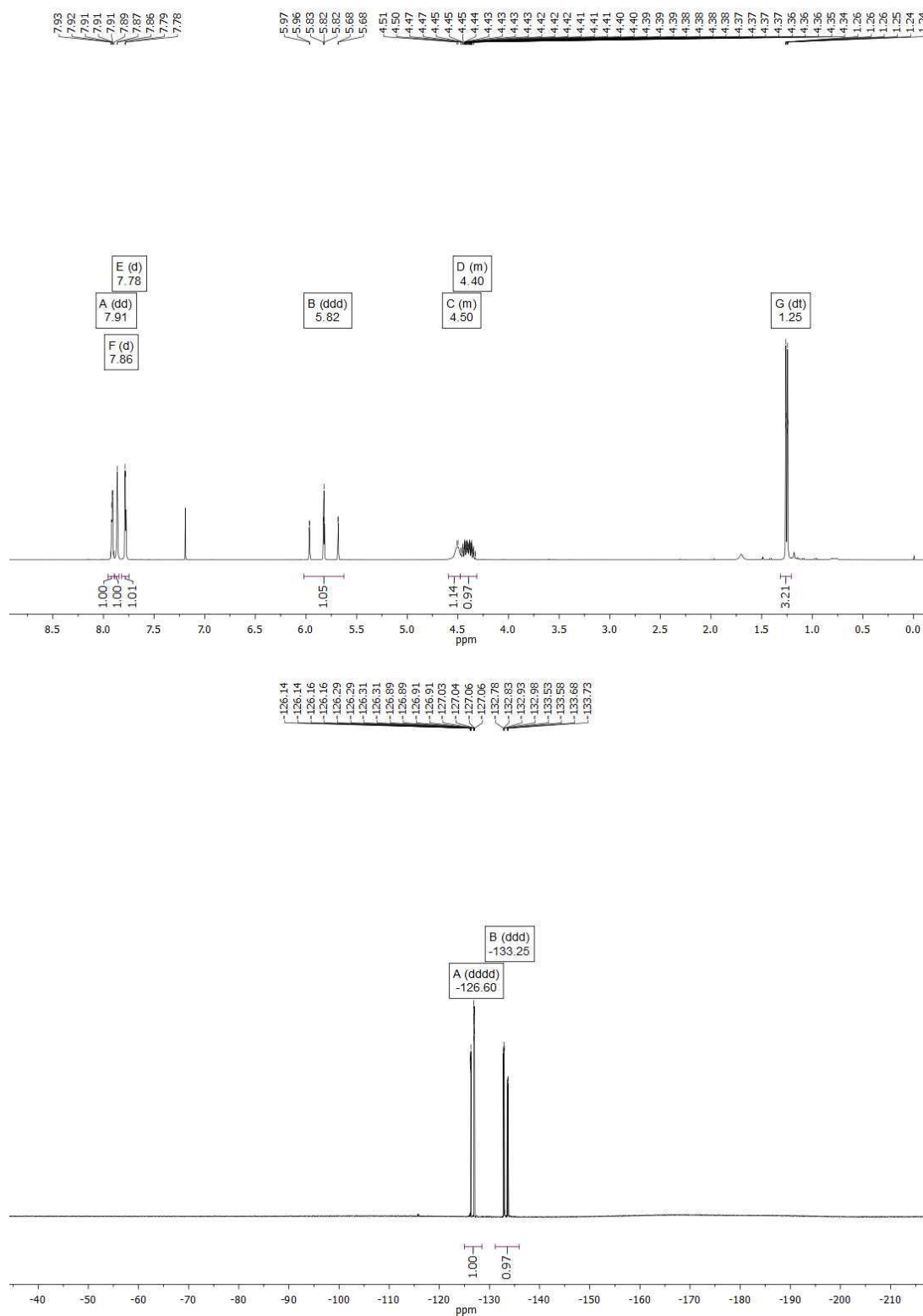
***N*-(4-Cyclopropyl-1,1,1-trifluorobut-3-yn-2-yl)pyrazin-2-amine (2w):**

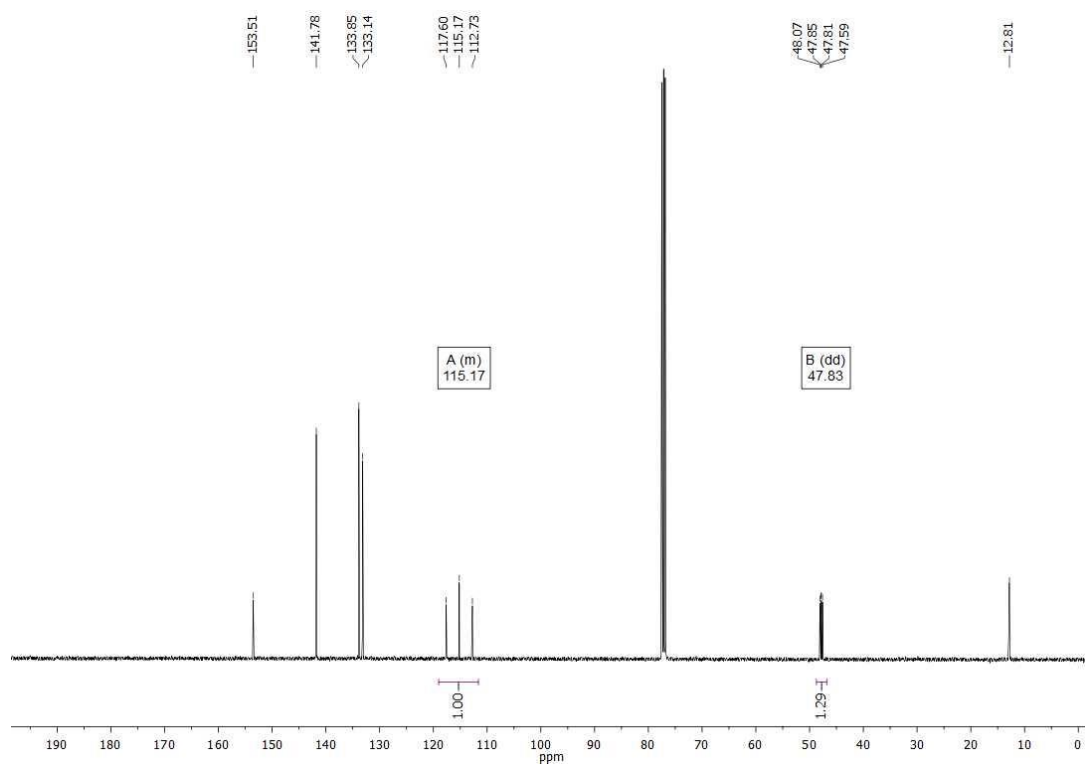




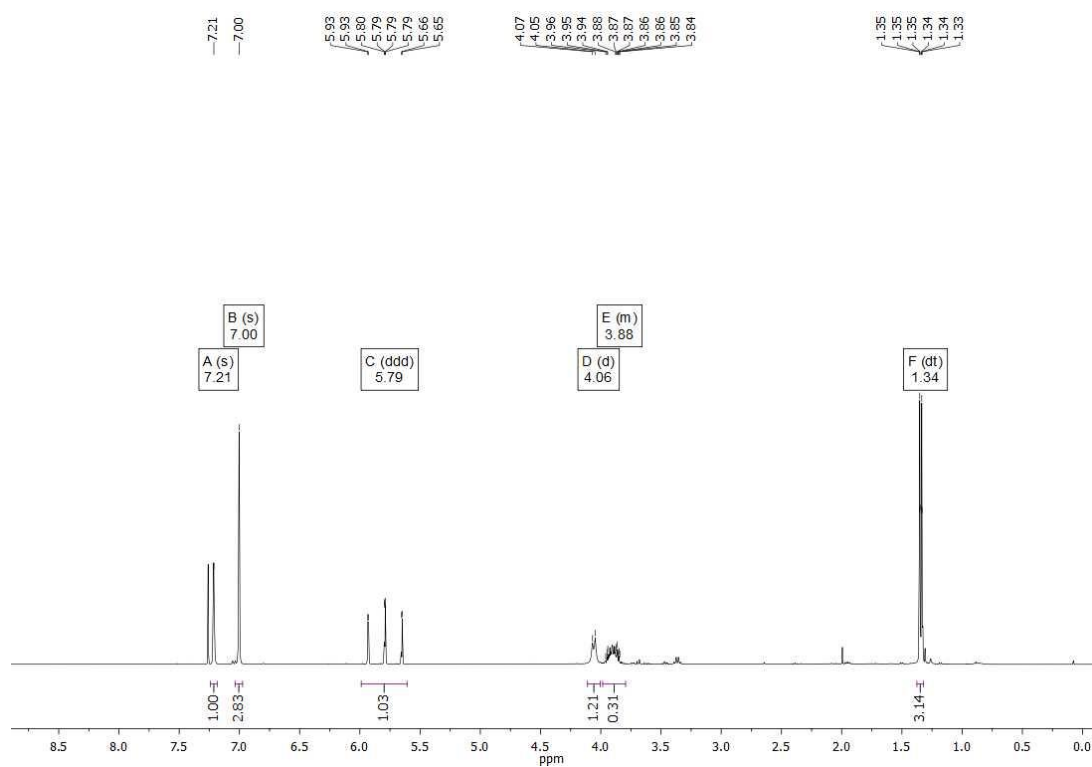


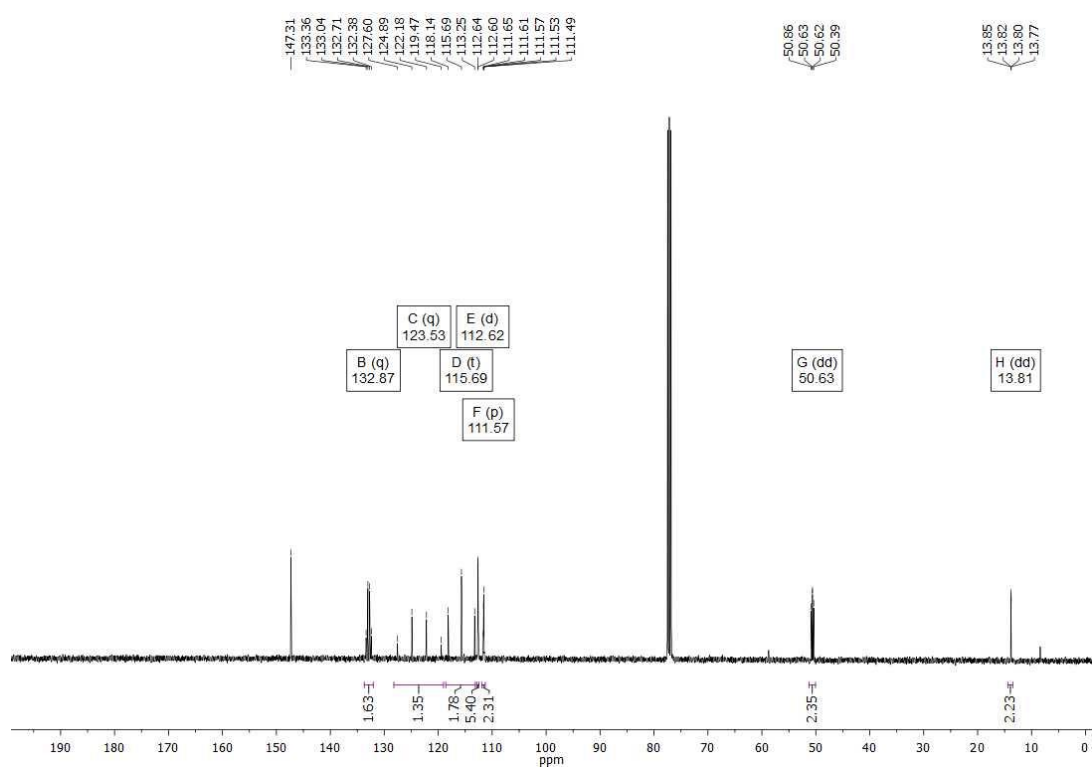
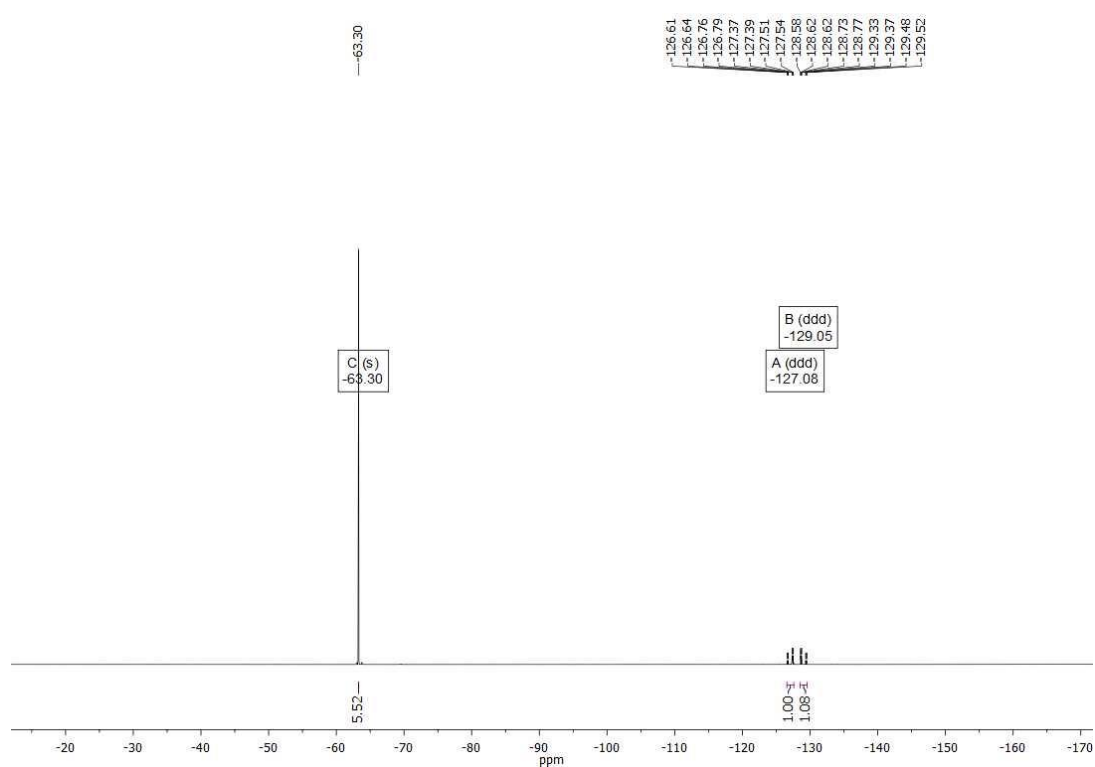
***N*-(1,1-Difluoropropan-2-yl)pyrazin-2-amine (3b):**



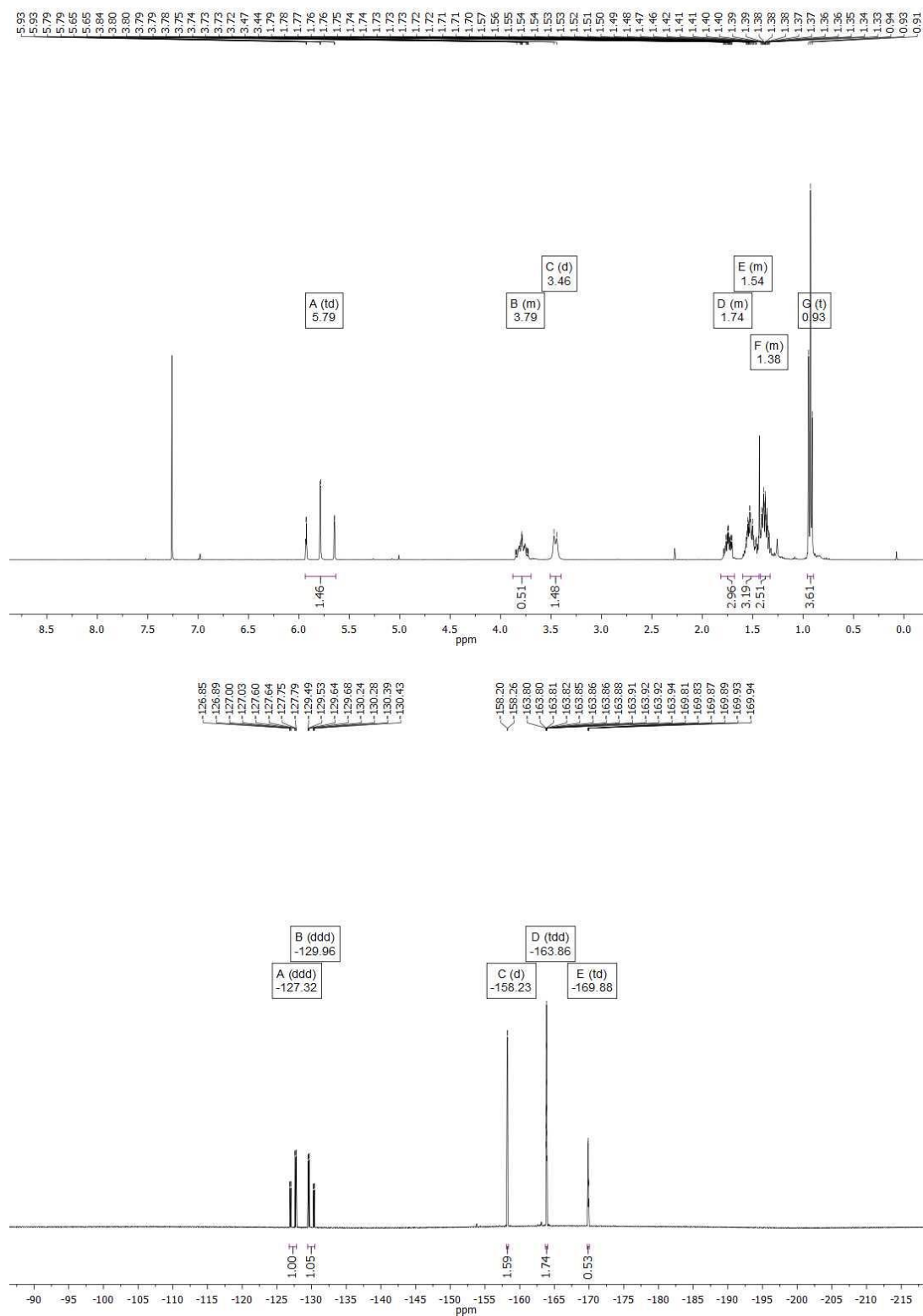


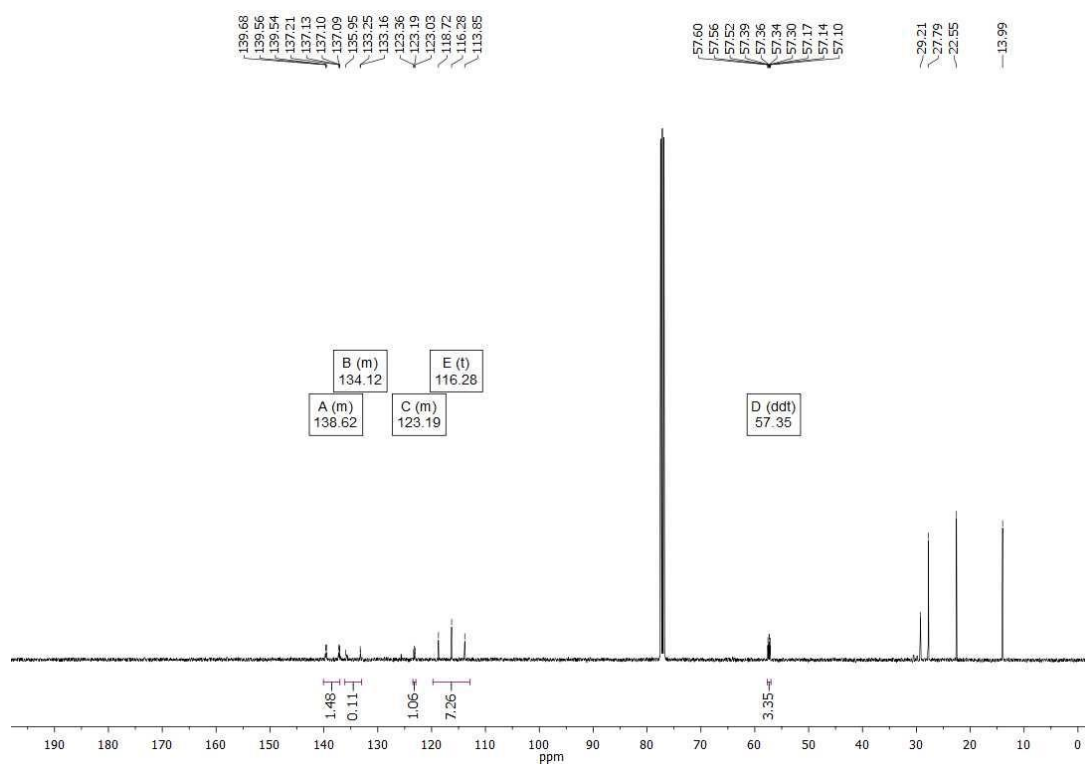
***N*-(1,1-Difluoropropan-2-yl)-3,5-bis(trifluoromethyl)aniline (3c):**



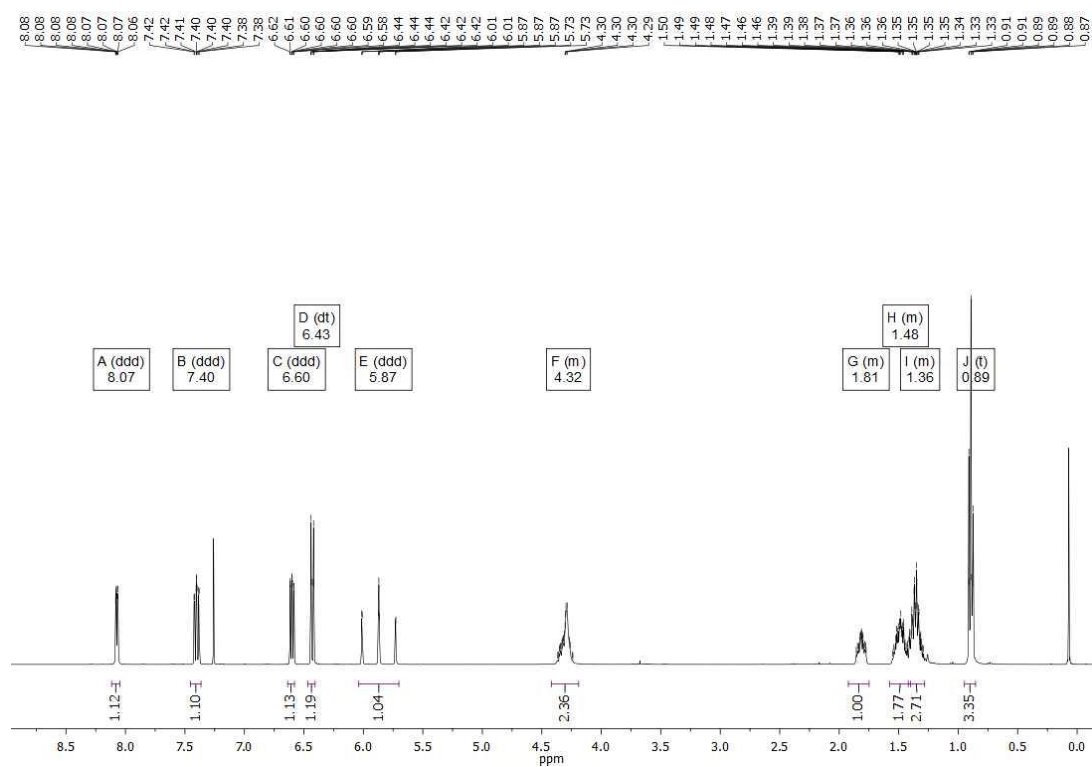


***N*-(1,1-Difluorohexan-2-yl)-2,3,4,5,6-pentafluoroaniline (3d):**

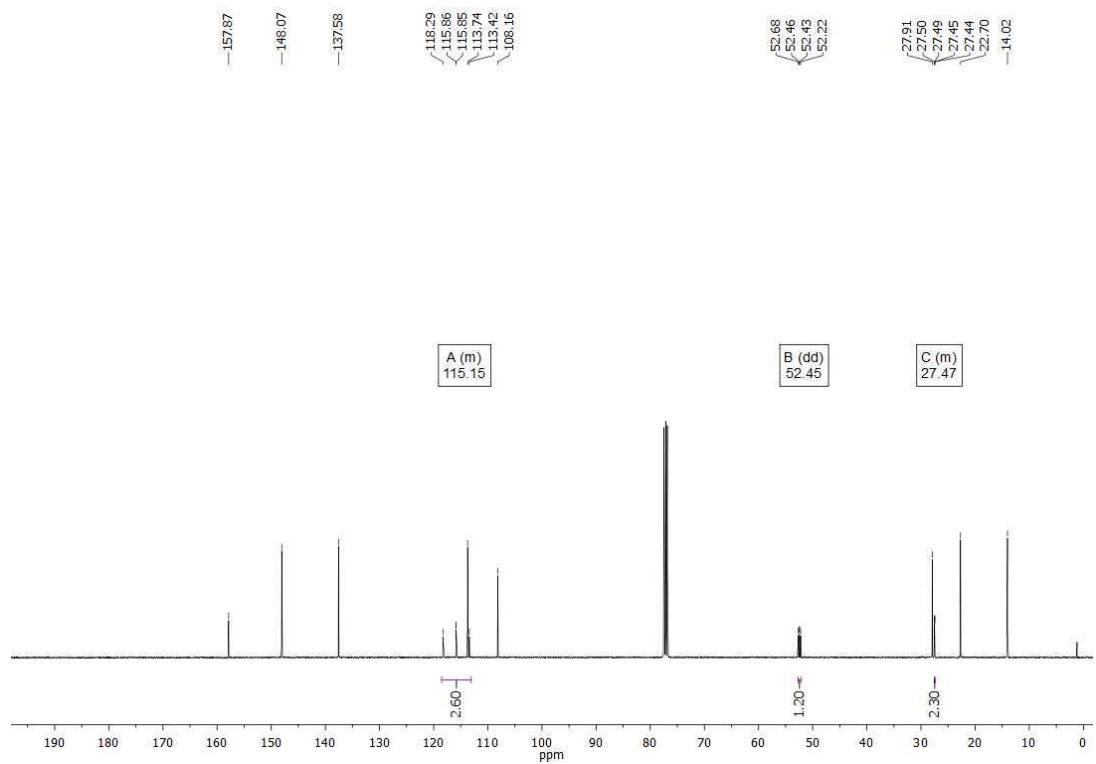
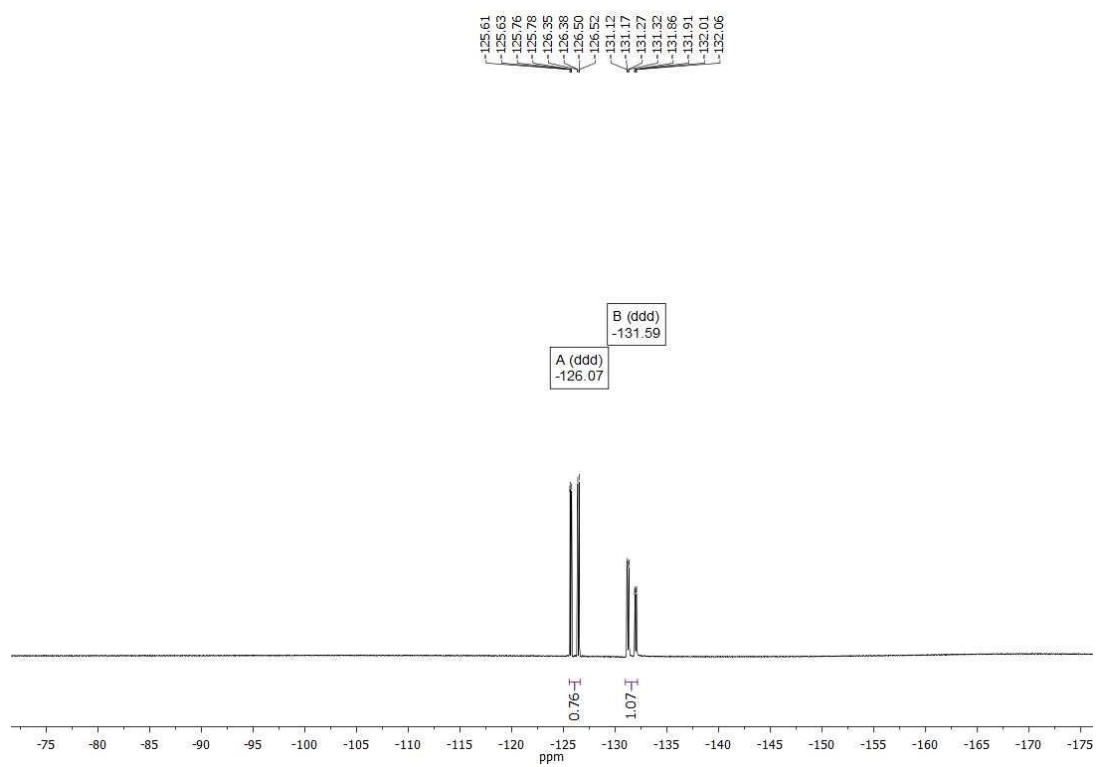




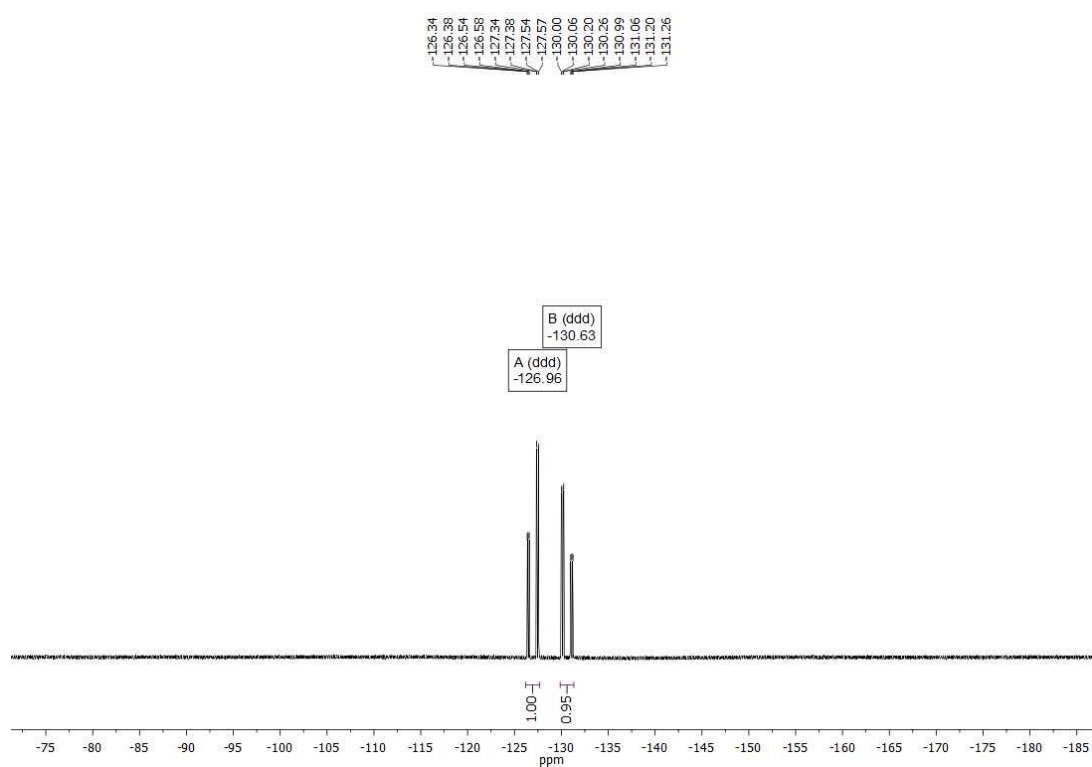
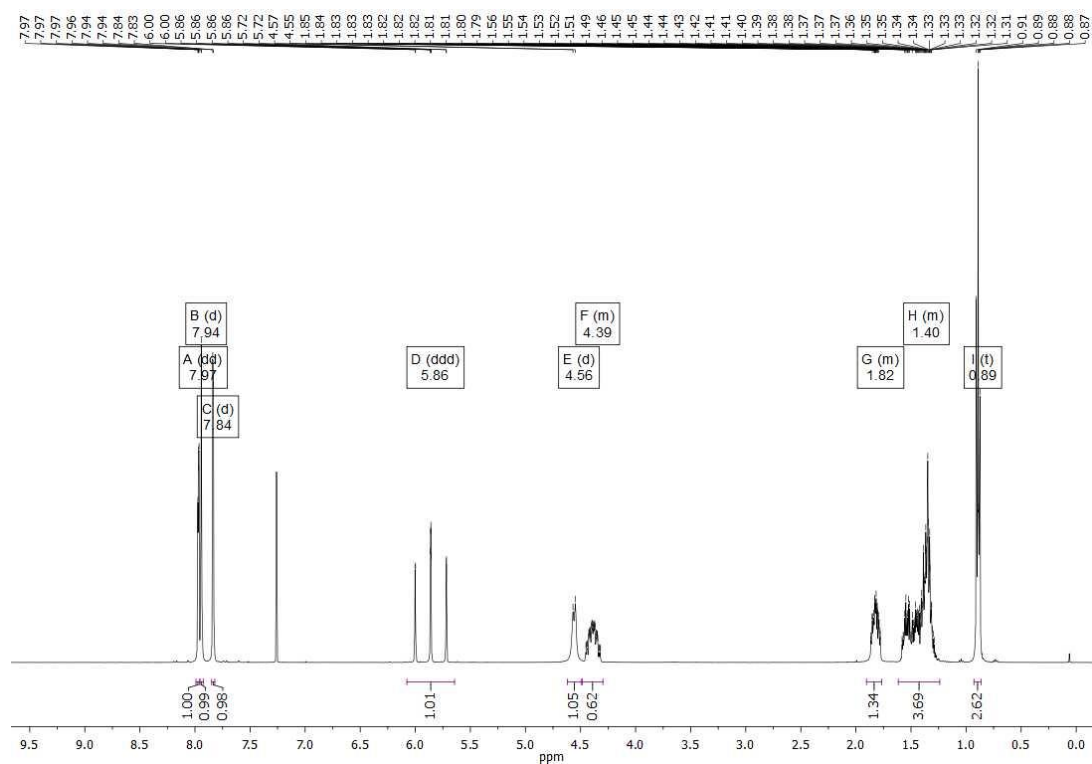
***N*-(1,1-Difluorohexan-2-yl)pyridine-2-amine (3e):**

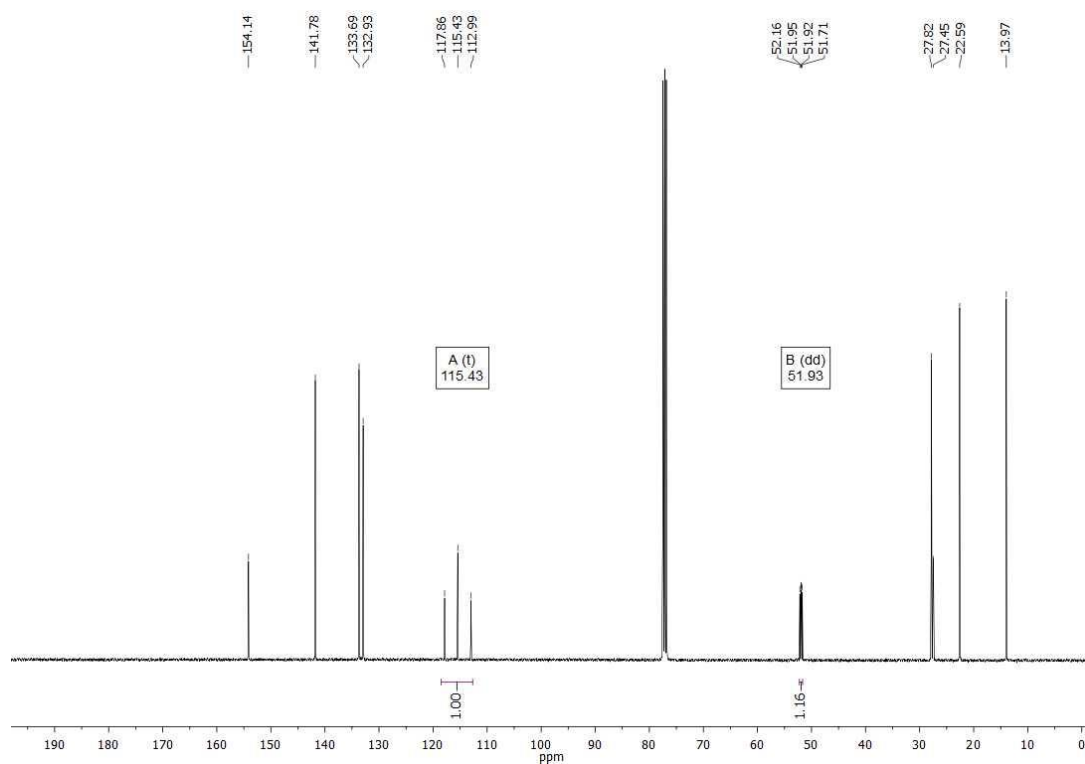




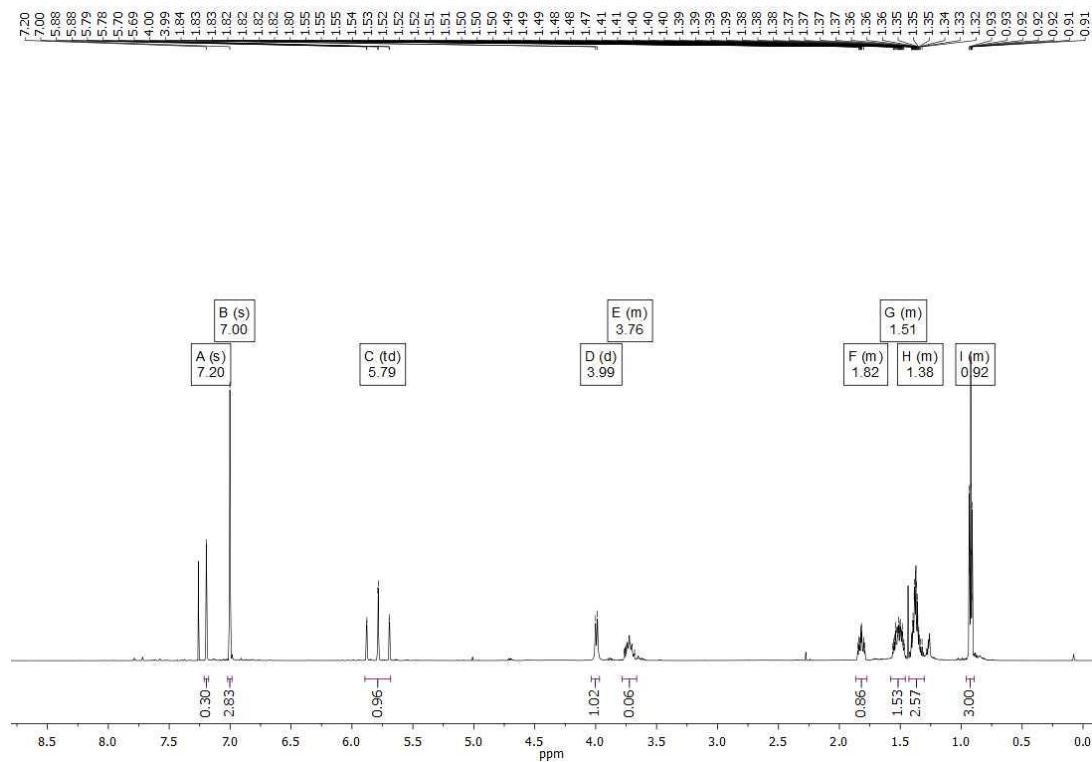


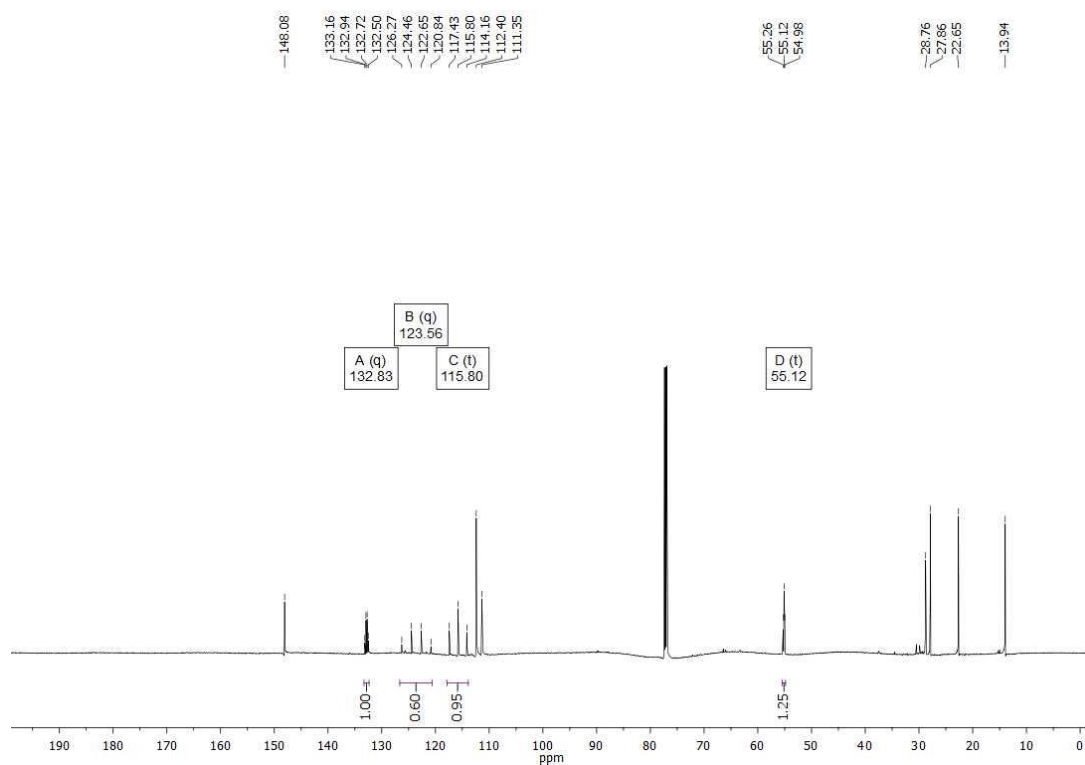
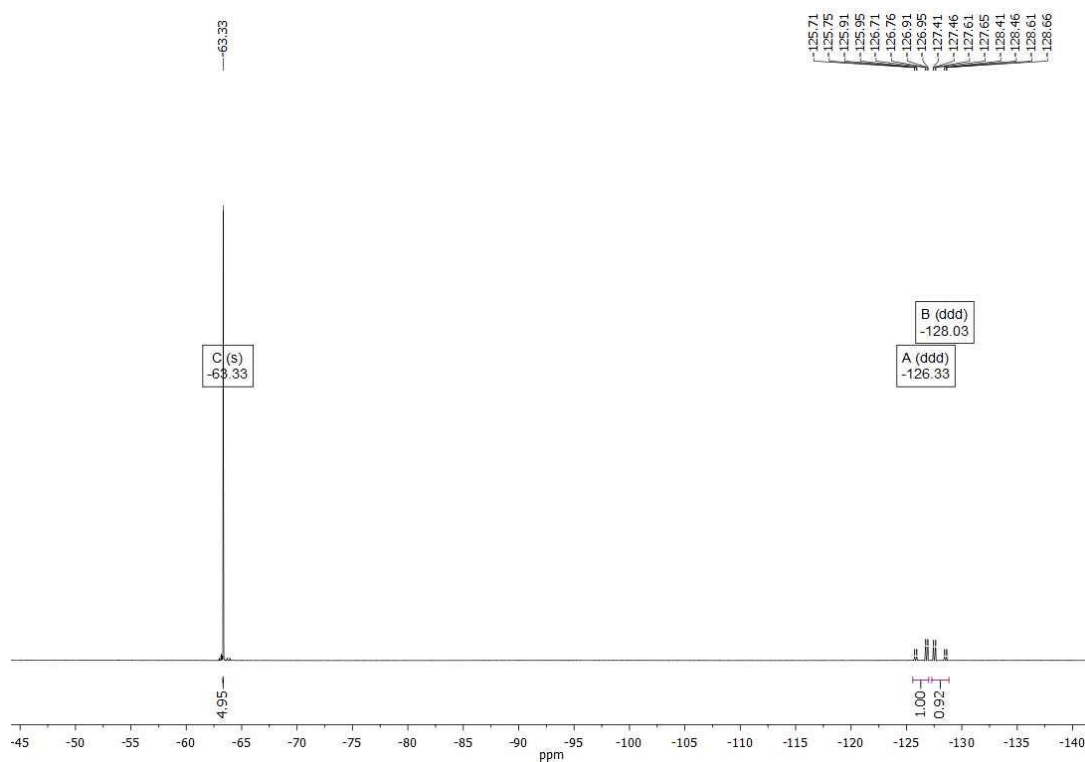
***N*-(1,1-Difluorohexan-2-yl)pyrazin-2-amine (3f):**



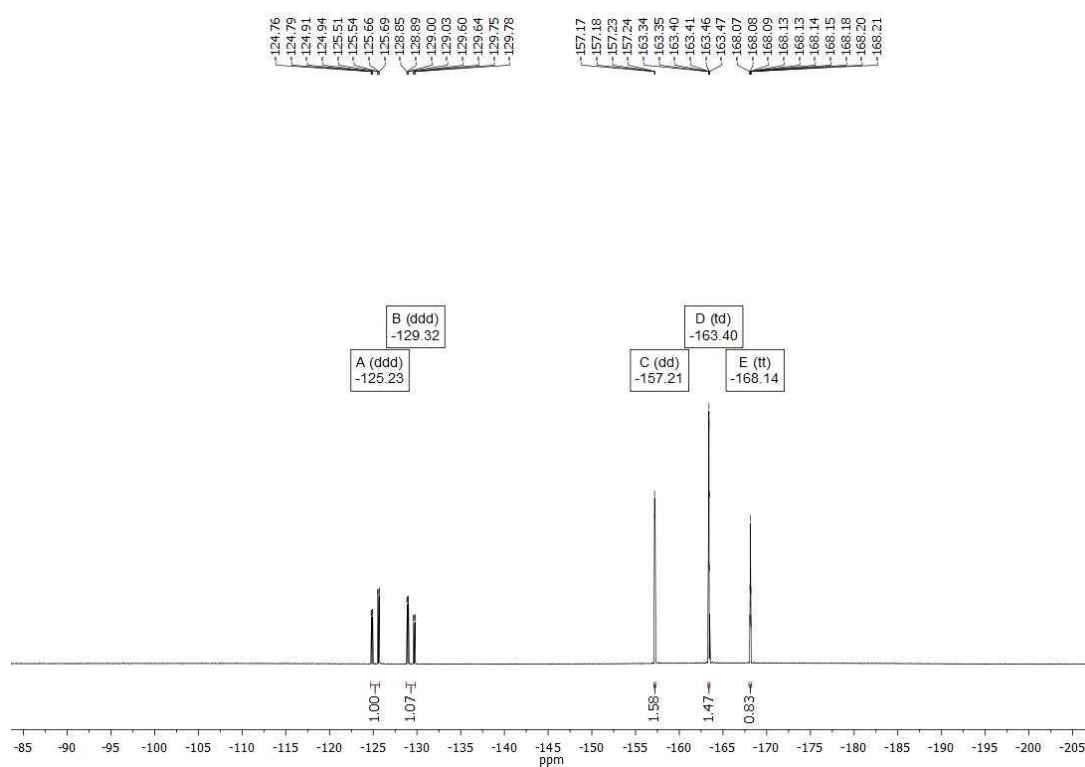
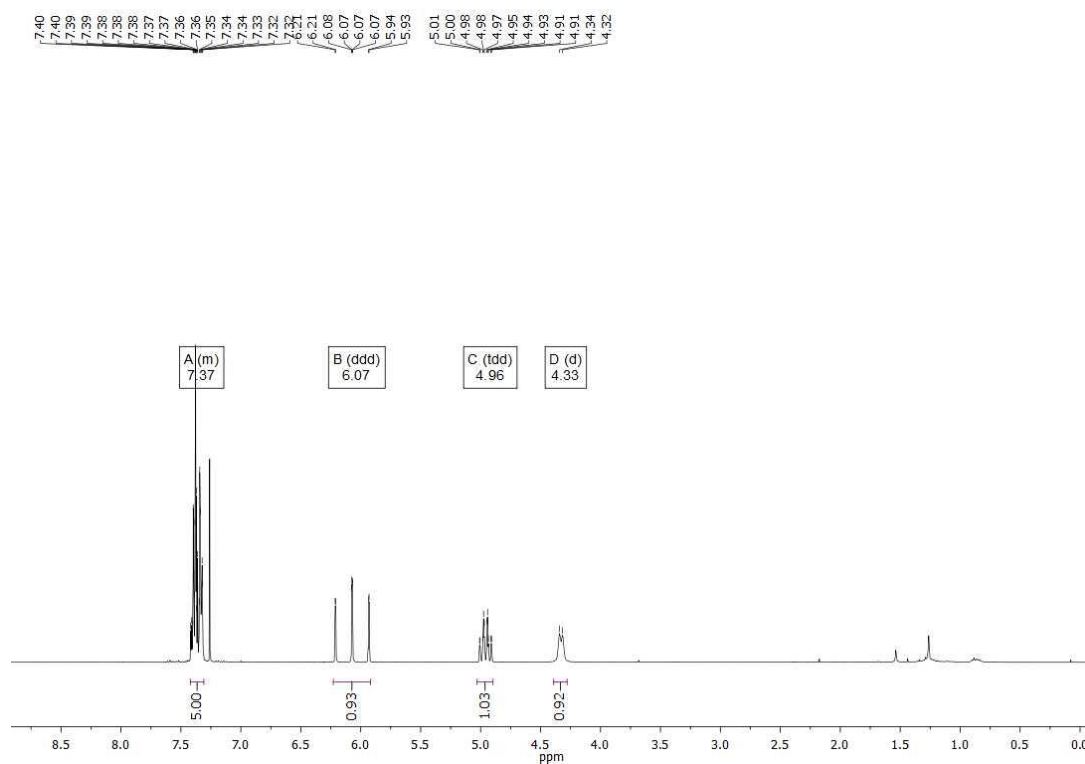


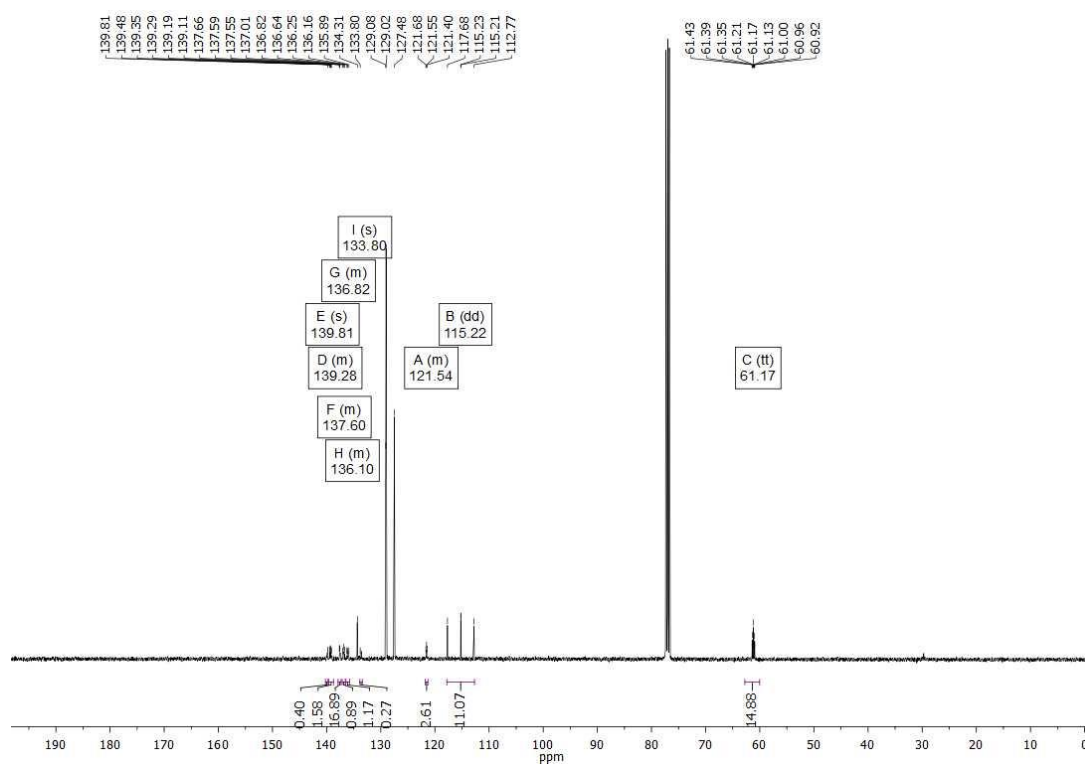
***N*-(1,1-Difluorohexan-2-yl)-3,5-bis(trifluoromethyl)aniline (3g):**



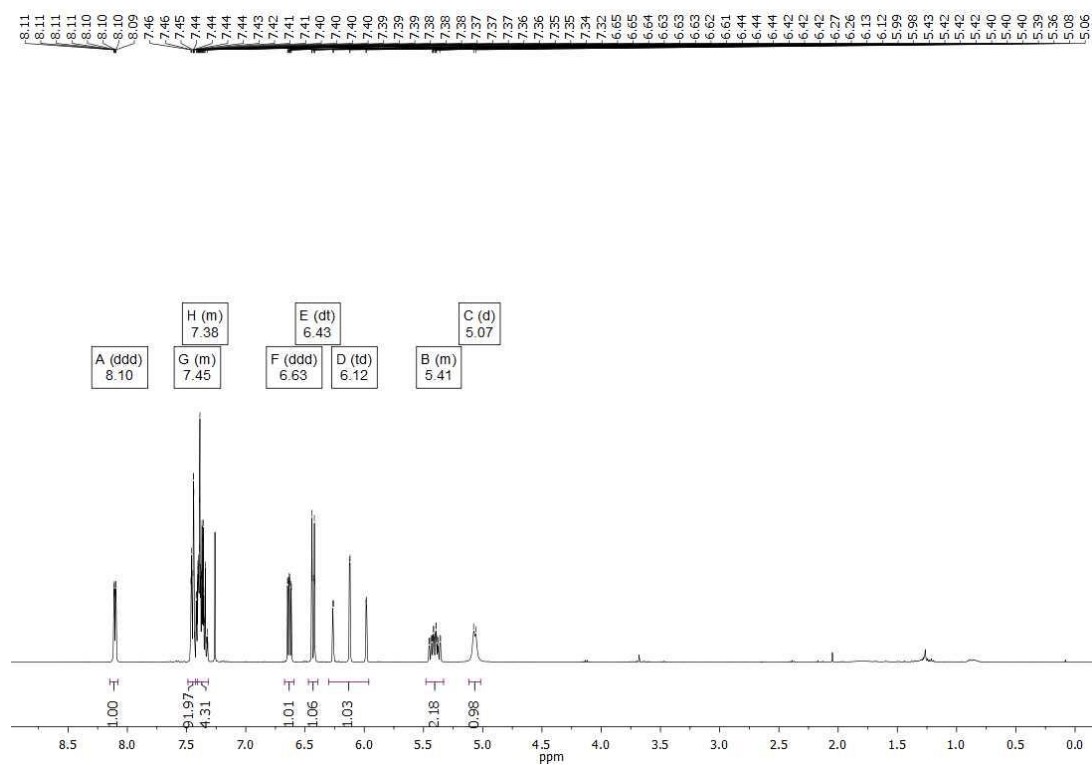


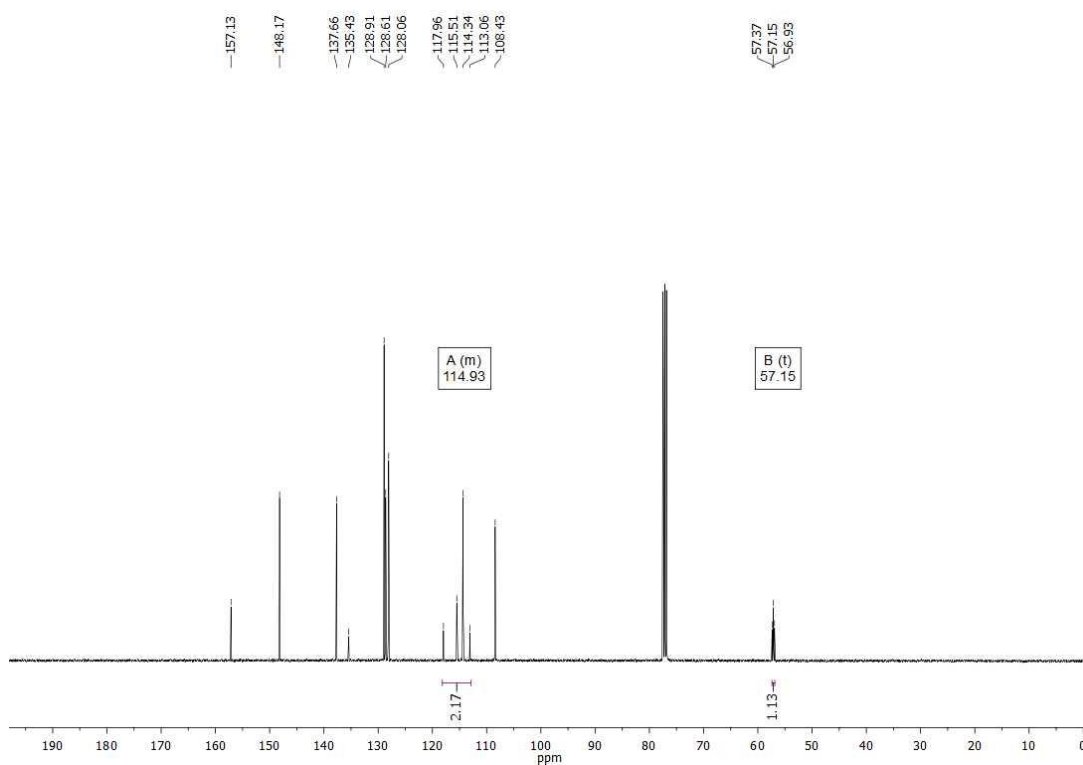
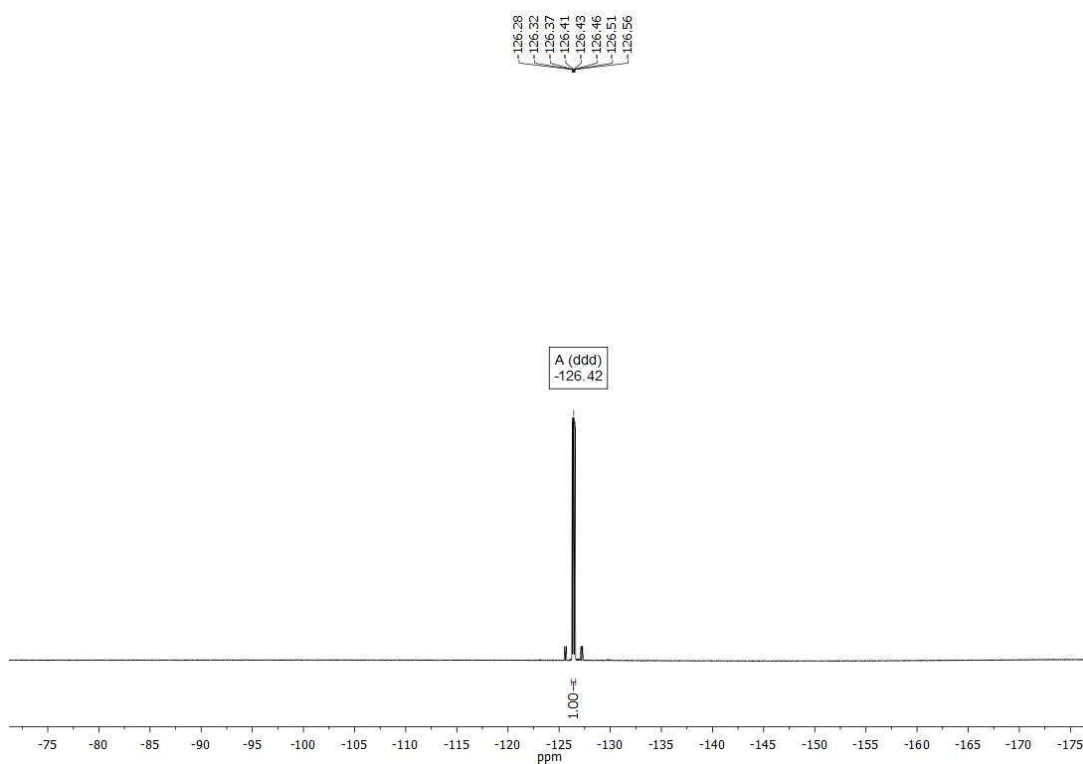
***N*-(1,1-Difluoro-1-phenylethyl)-2,3,4,5,6-pentafluoroaniline (3h):**



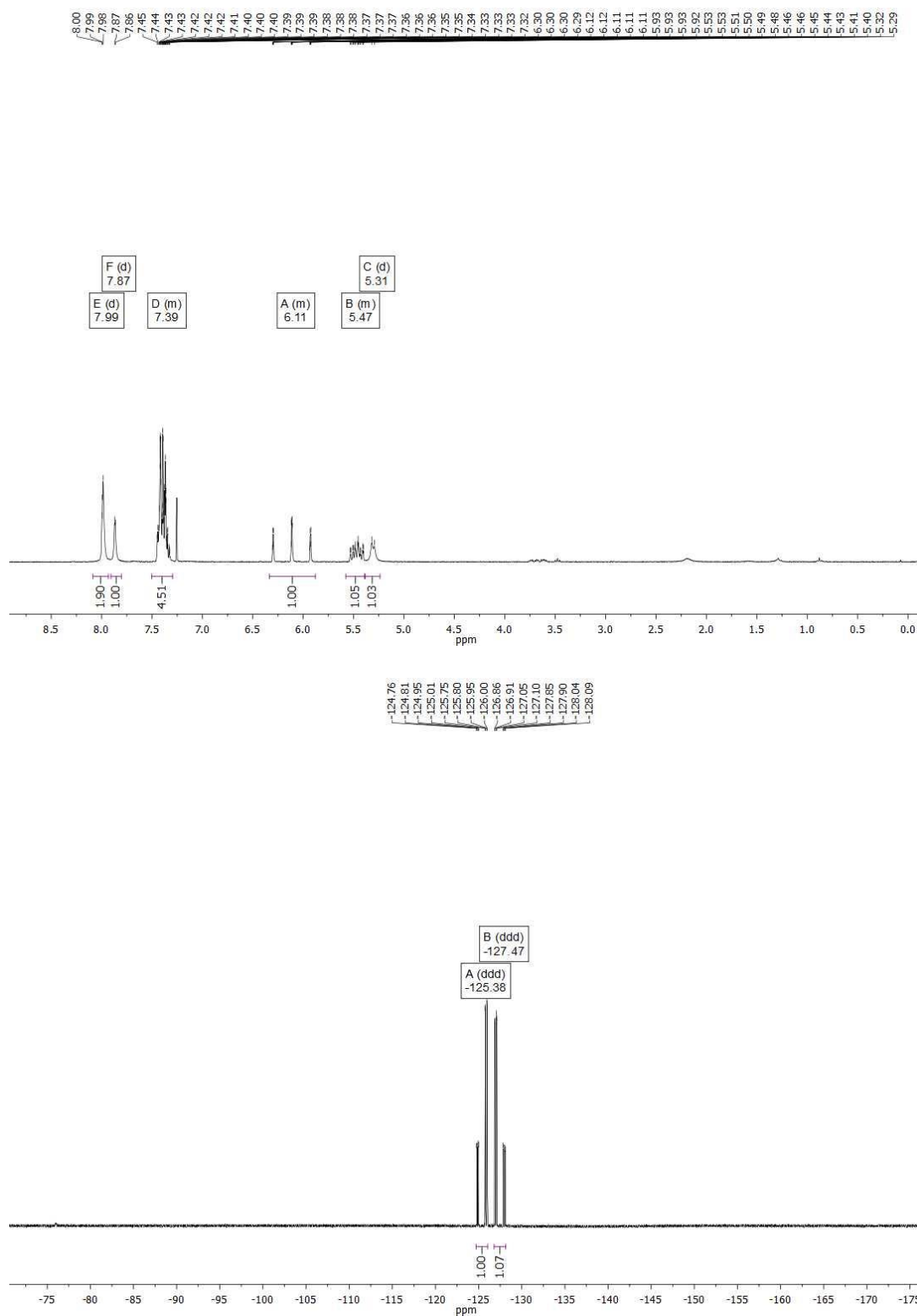


***N*-(1,1-Difluoro-1-phenylethyl)pyridine-2-amine (3i):**

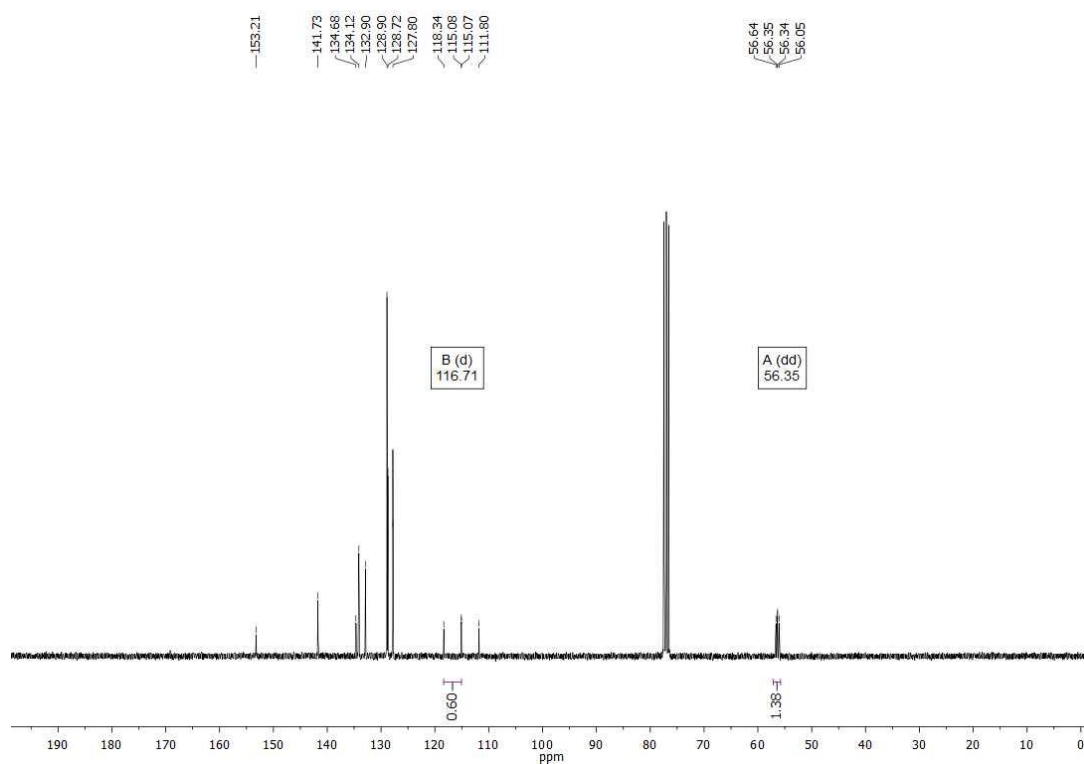




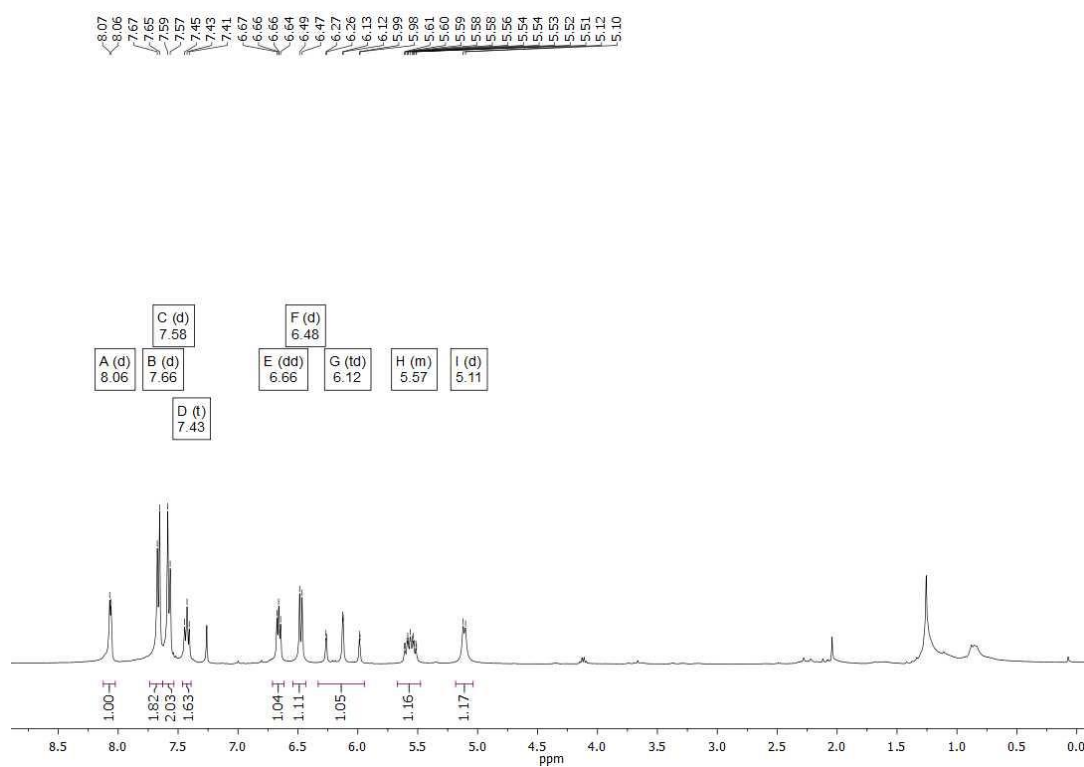
***N*-(1,1-difluoro-1-phenylethyl)pyrazin-2-amine (3j):**

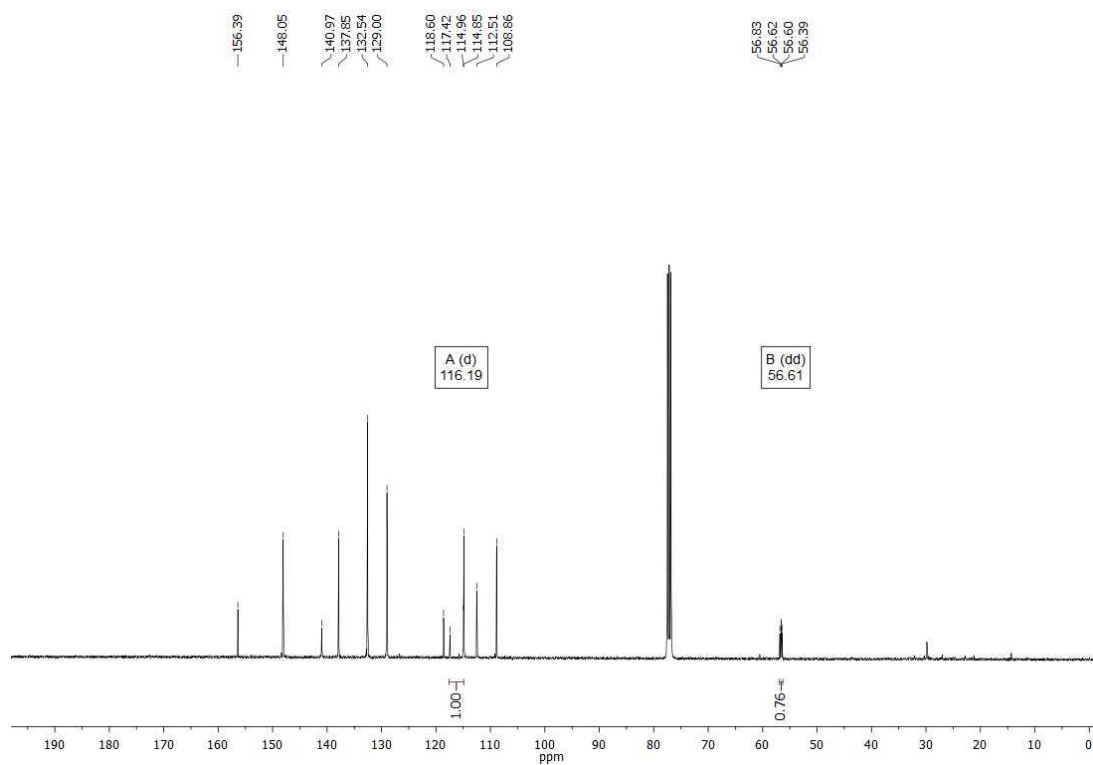
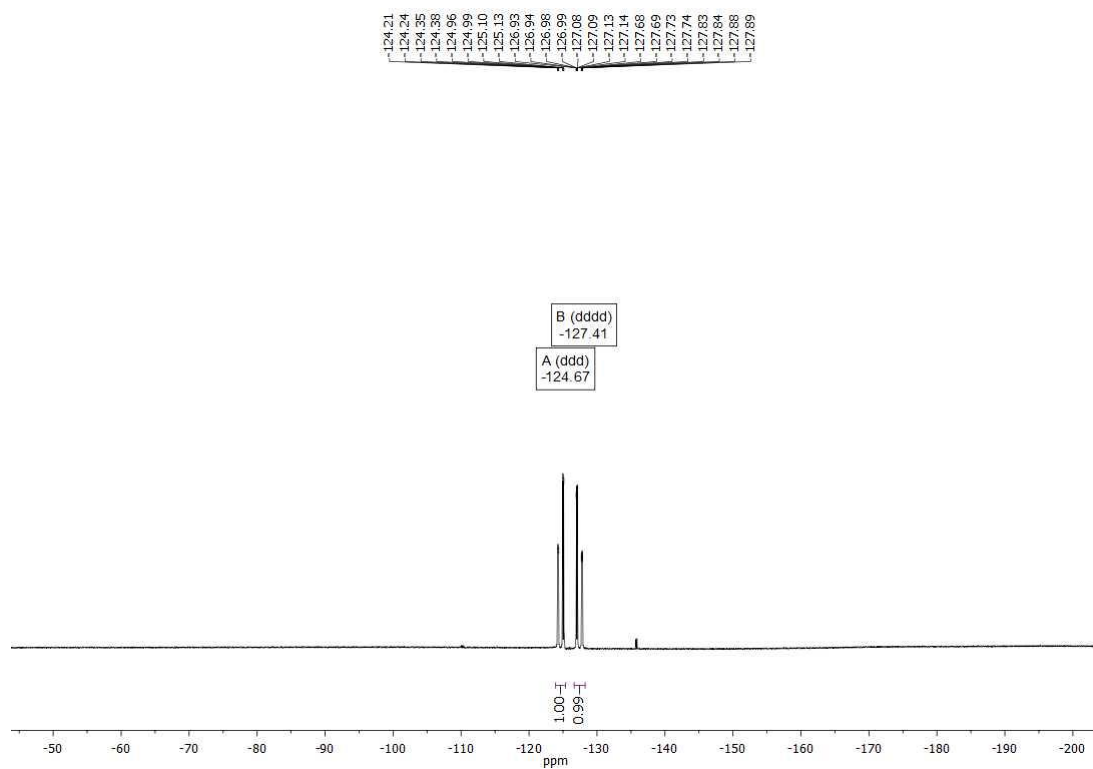




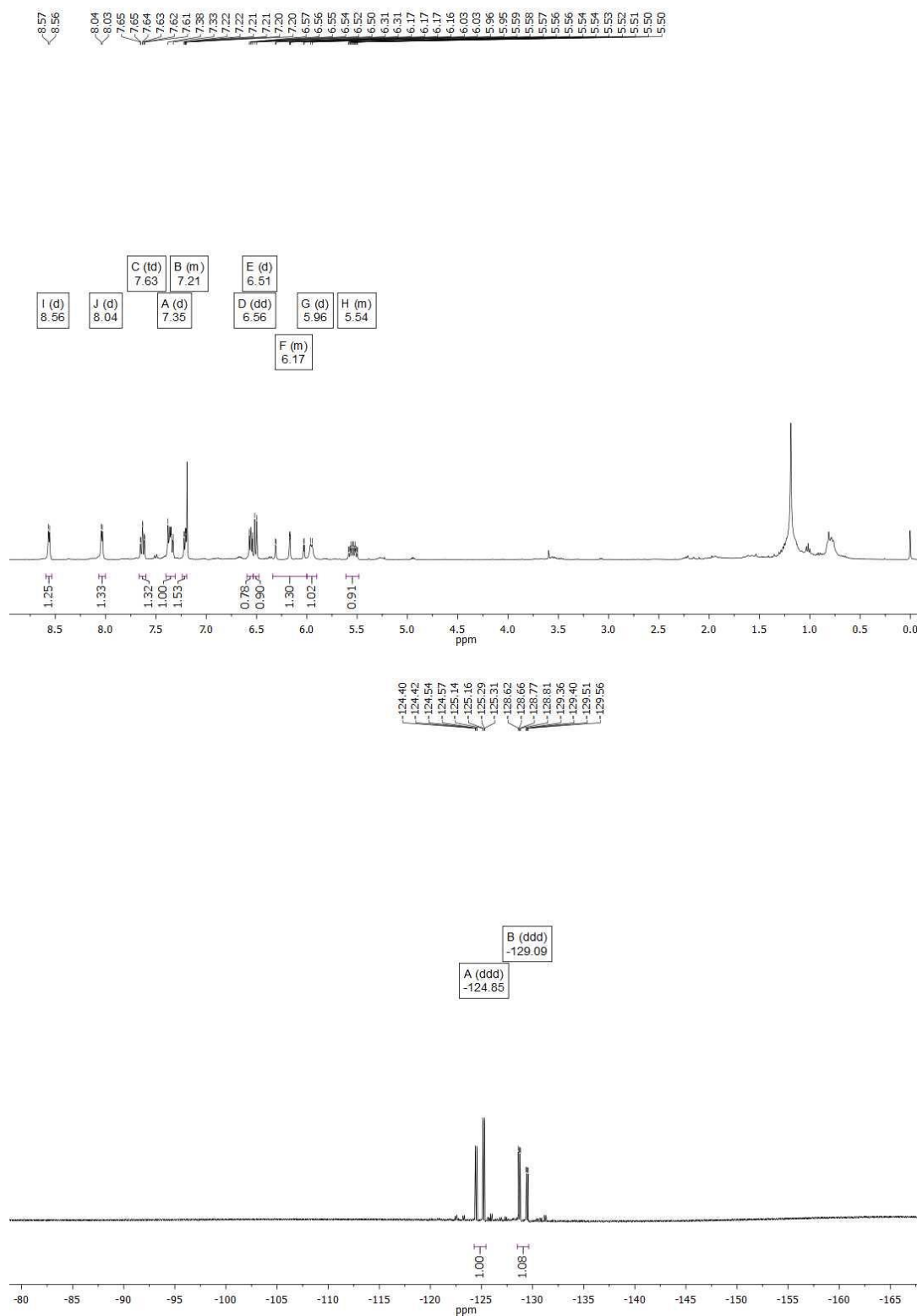


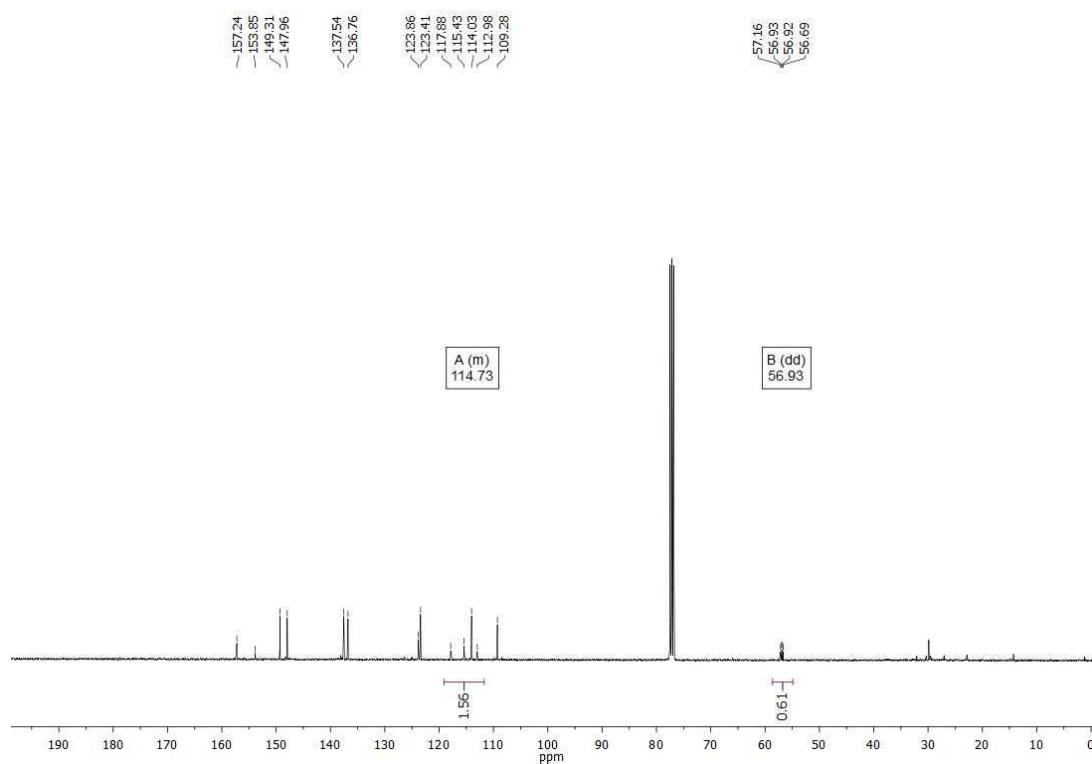
**4-(2,2-Difluoro-1-(pyridin-2-ylamino)ethyl)benzonitrile (3k):**



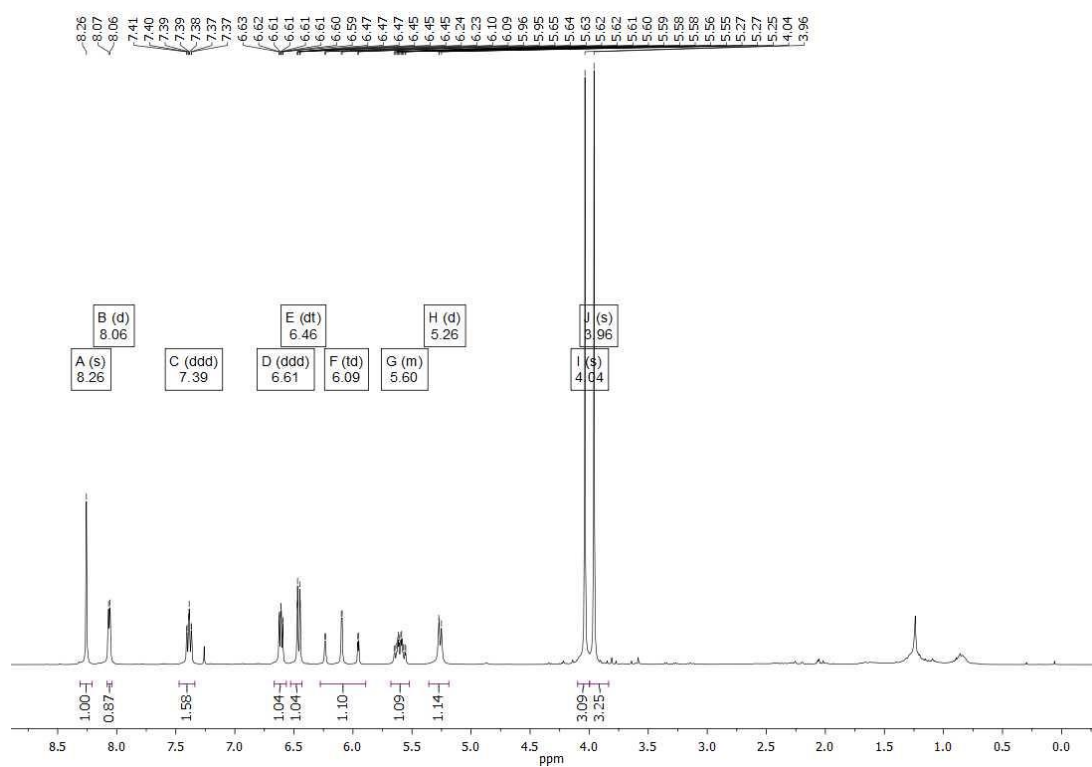


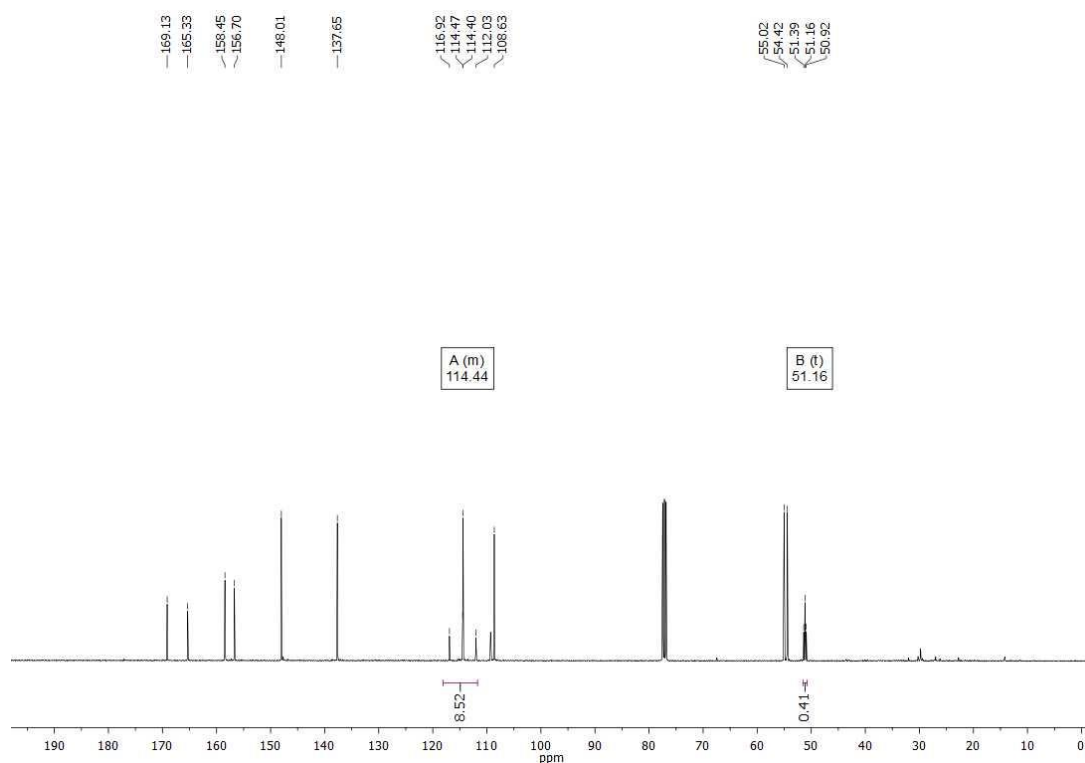
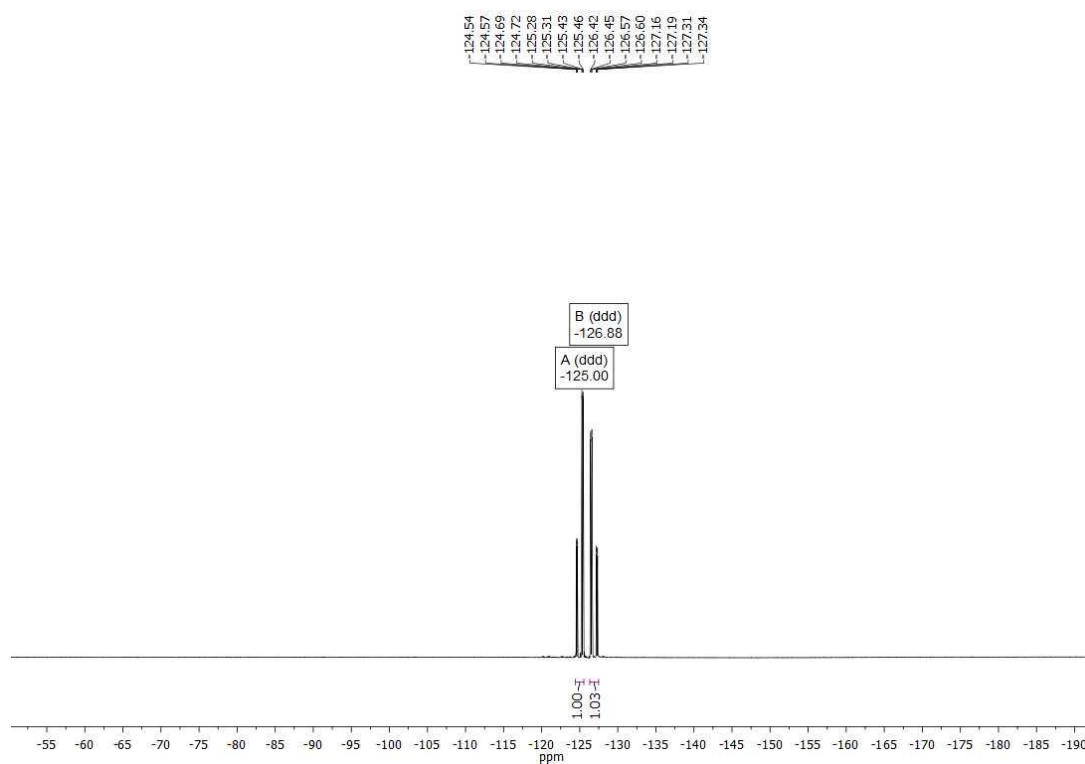
***N*-(2,2-Difluoro-1-(pyridin-2-yl)ethyl)pyridin-2-amine (3l):**



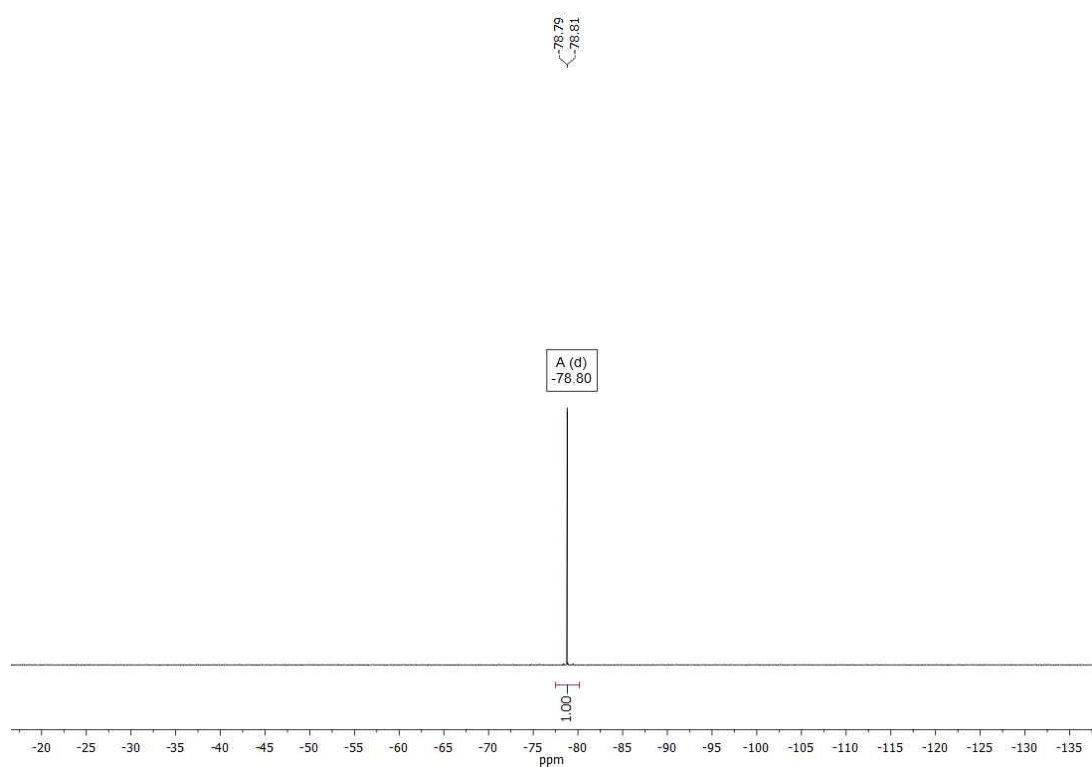
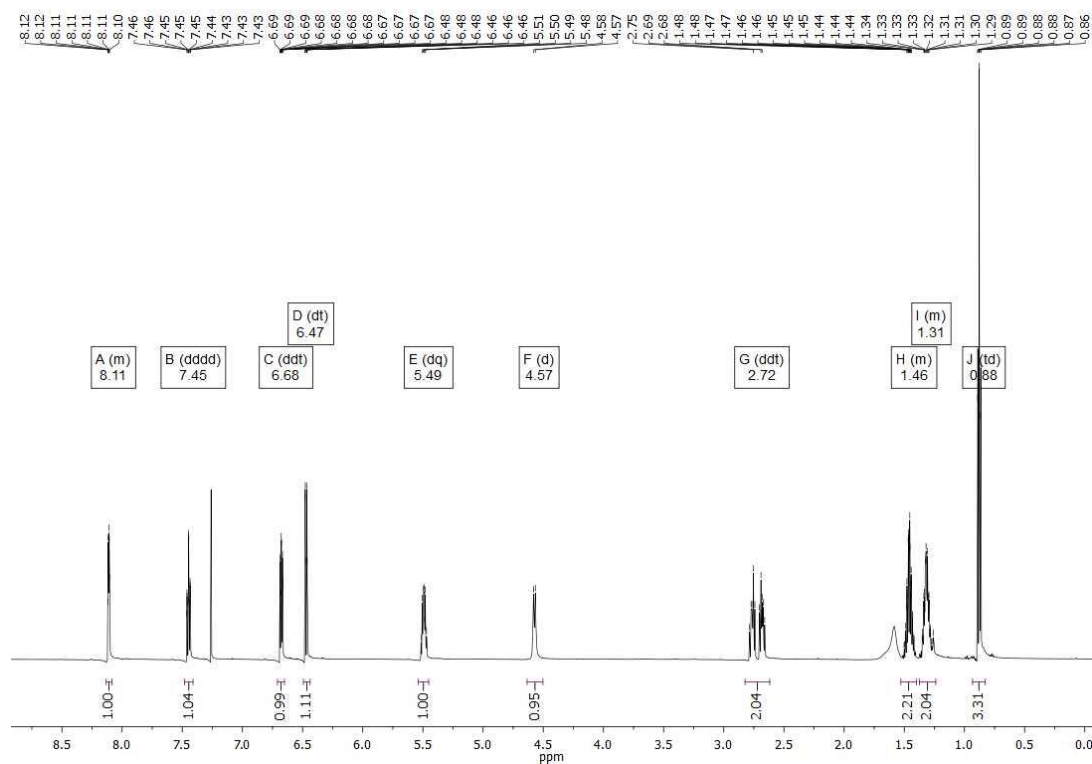


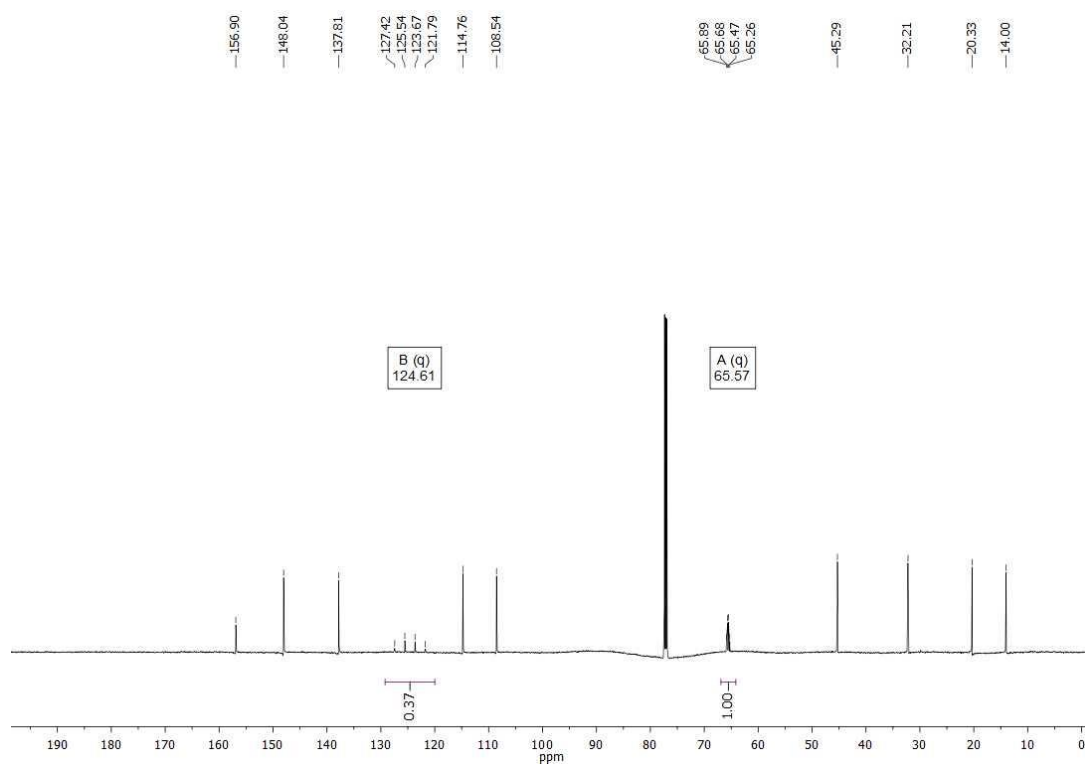
***N*-(1-(2,4-Dimethoxypyrimidin-5-yl)-2,2-difluoroethyl)pyridin-2-amine (3m):**



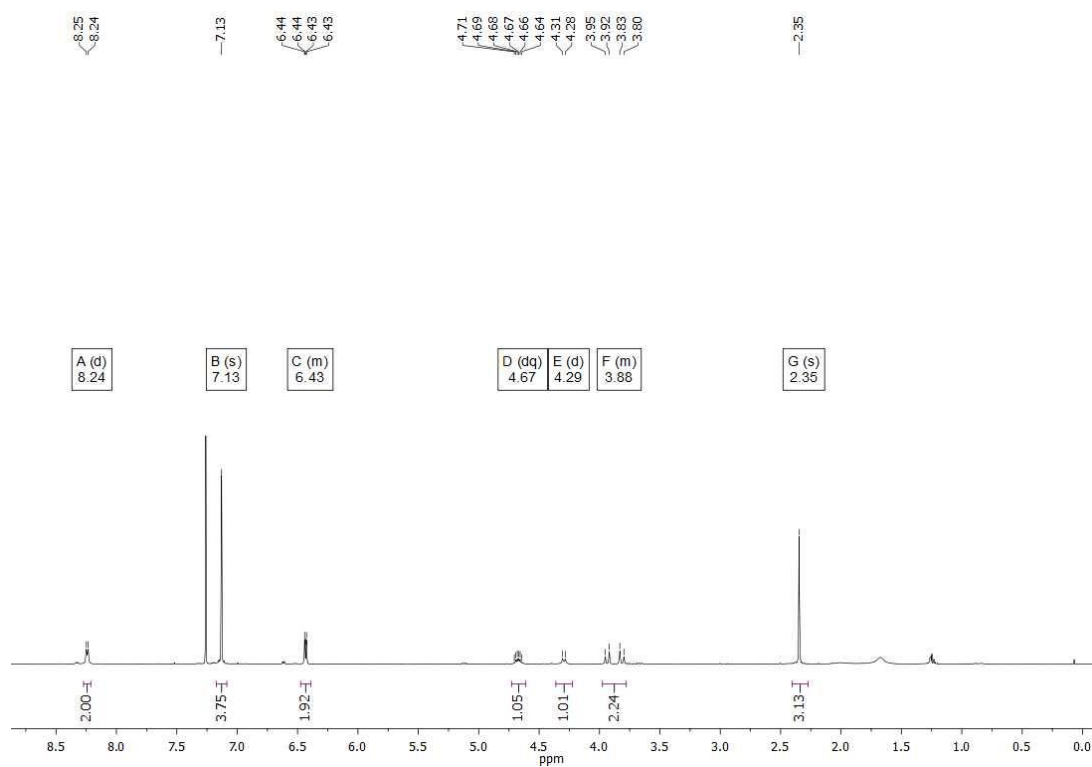


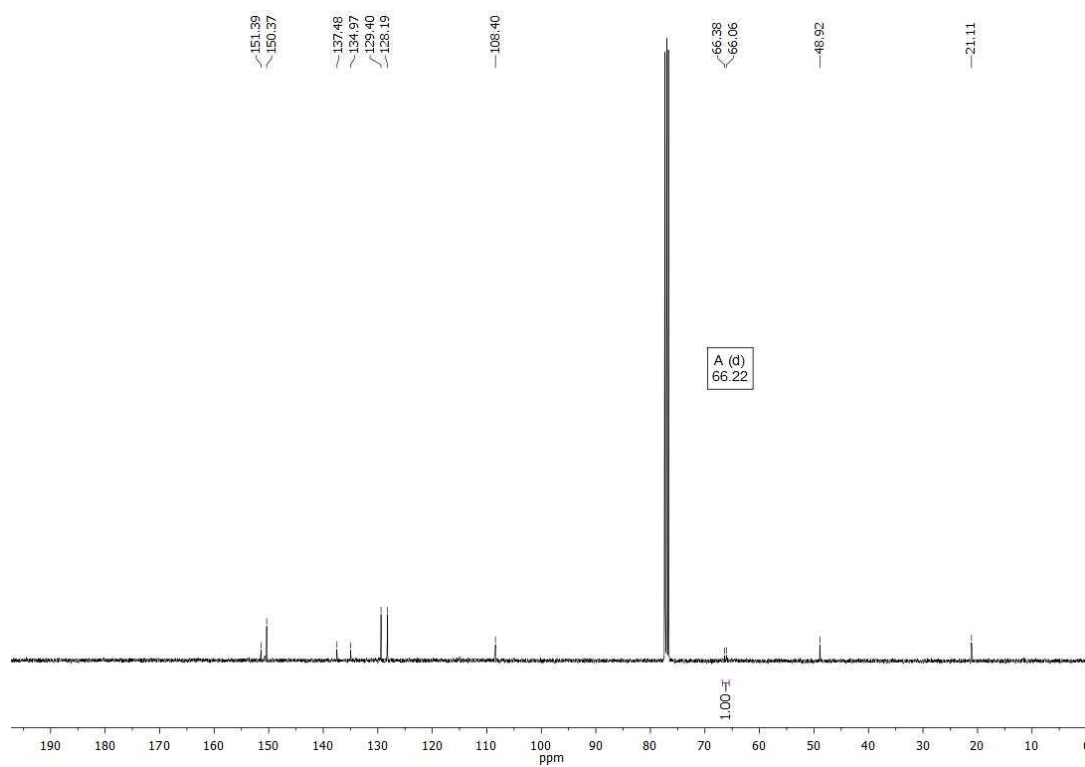
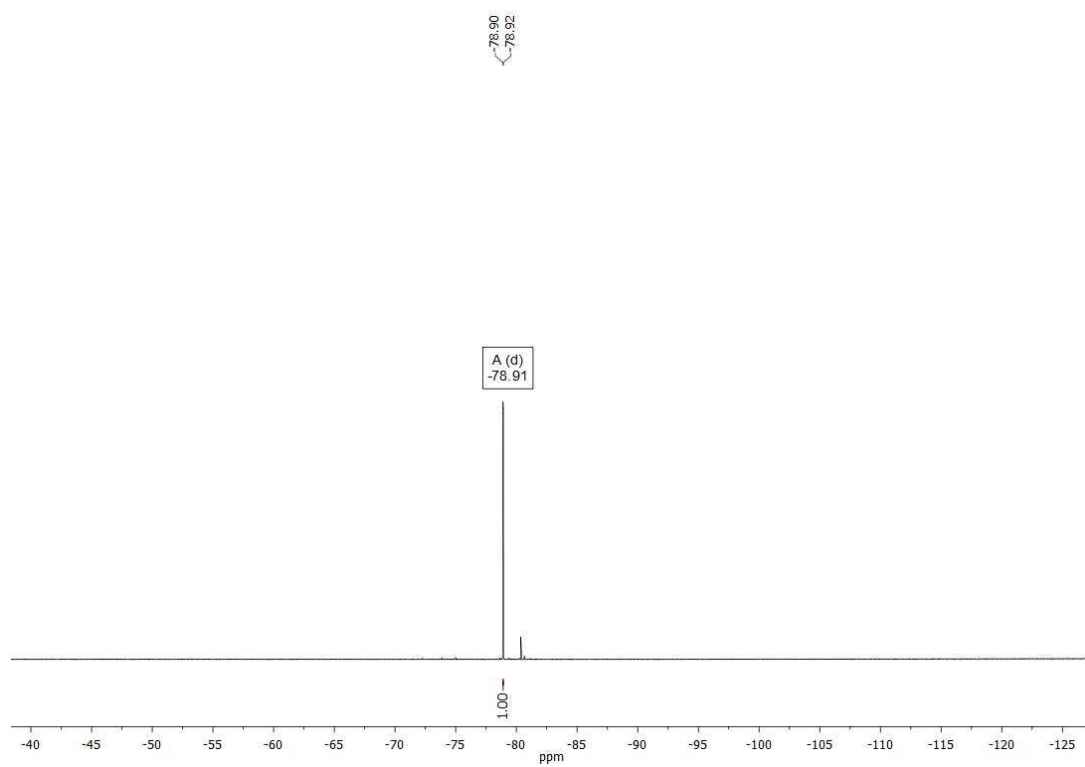
***N*-Butyl-2,2,2-trifluoro-*N*'-phenylethan-1,1-diamine (4a):**





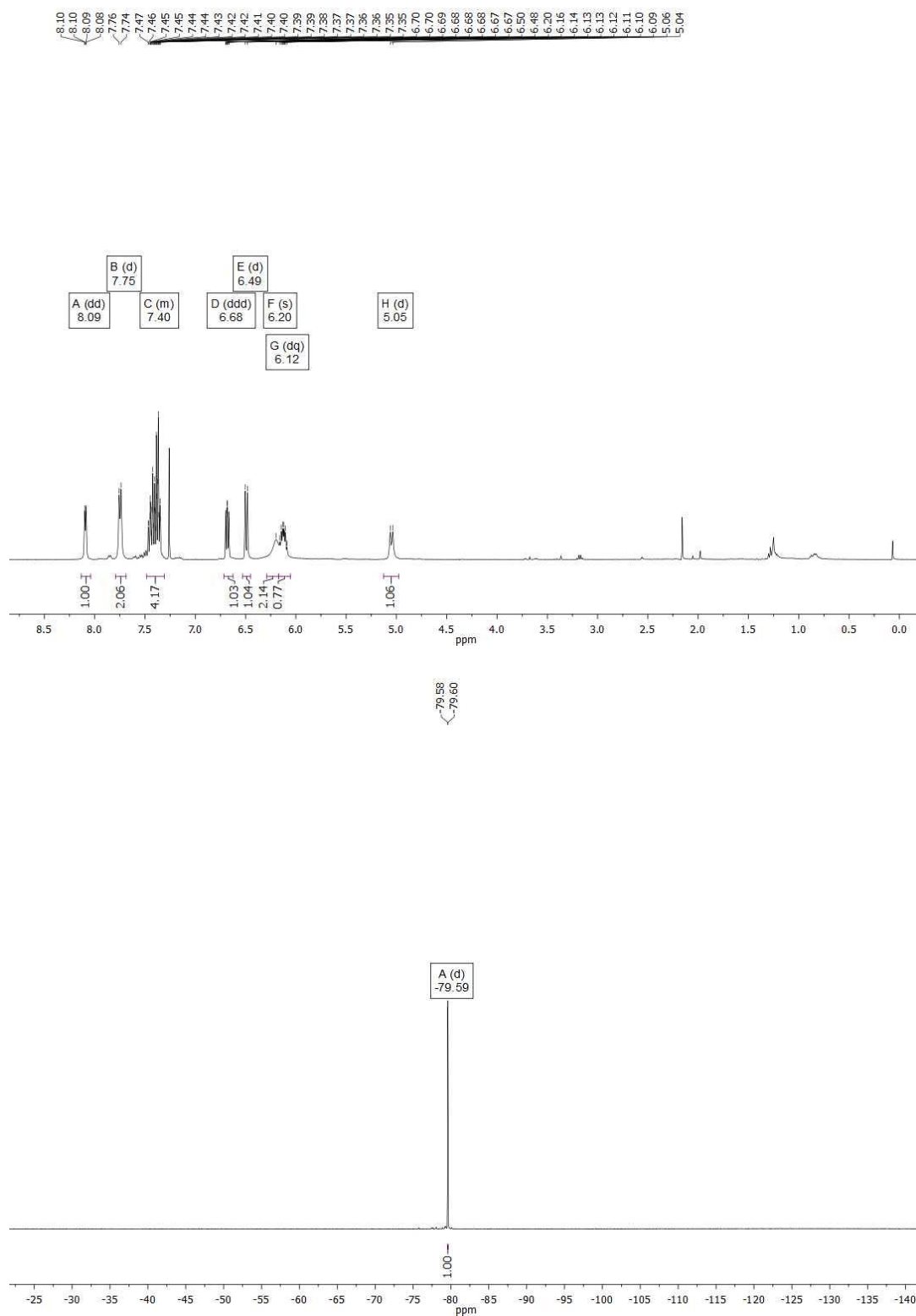
**2,2,2-Trifluoro-*N*-(4-methylbenzyl)-*N'*-(pyridin-4-yl)ethane-1,1-diamine (4b):**

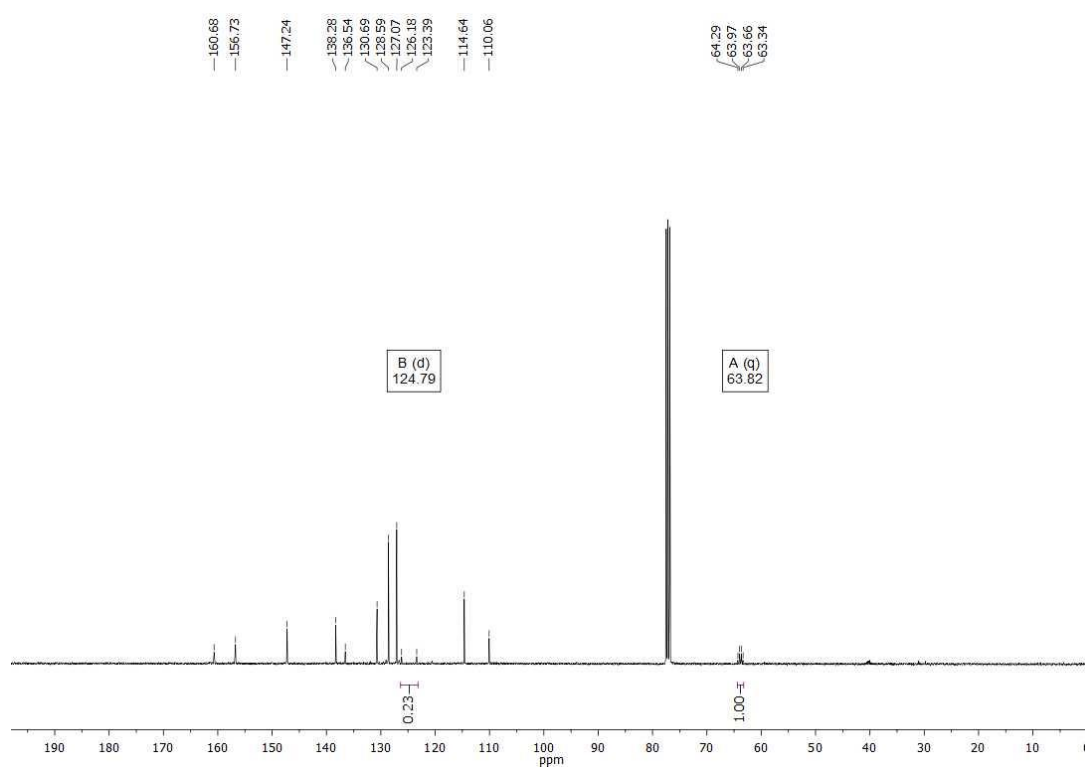




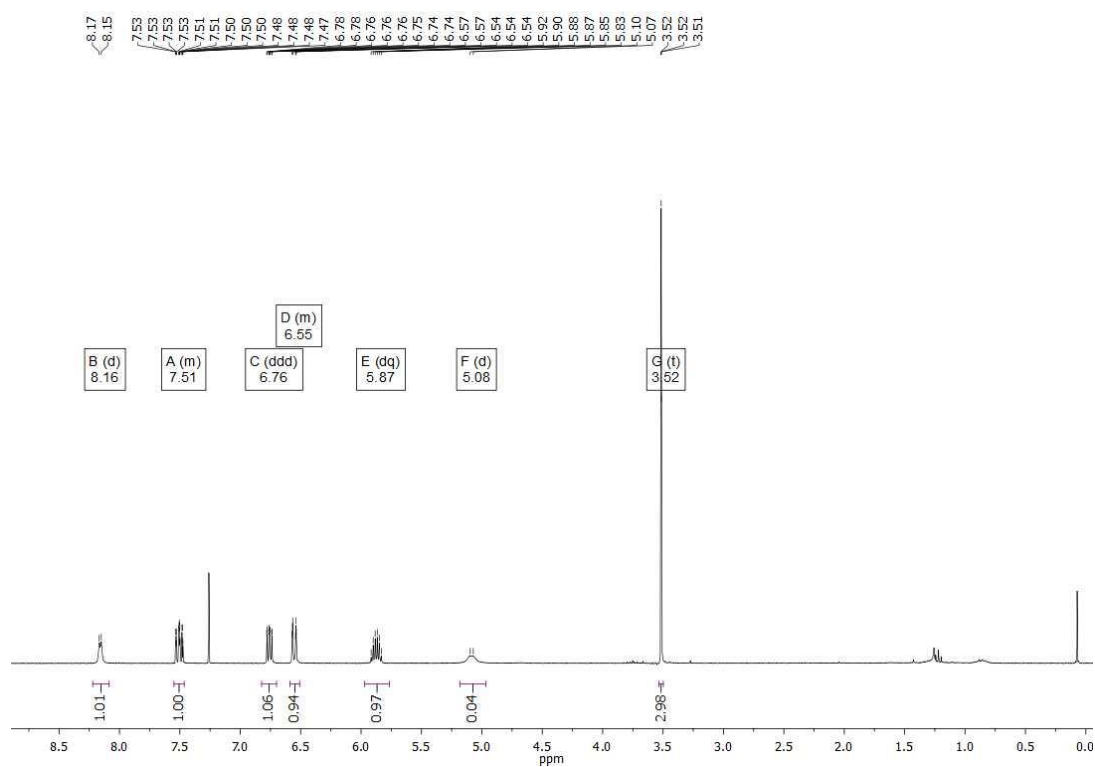


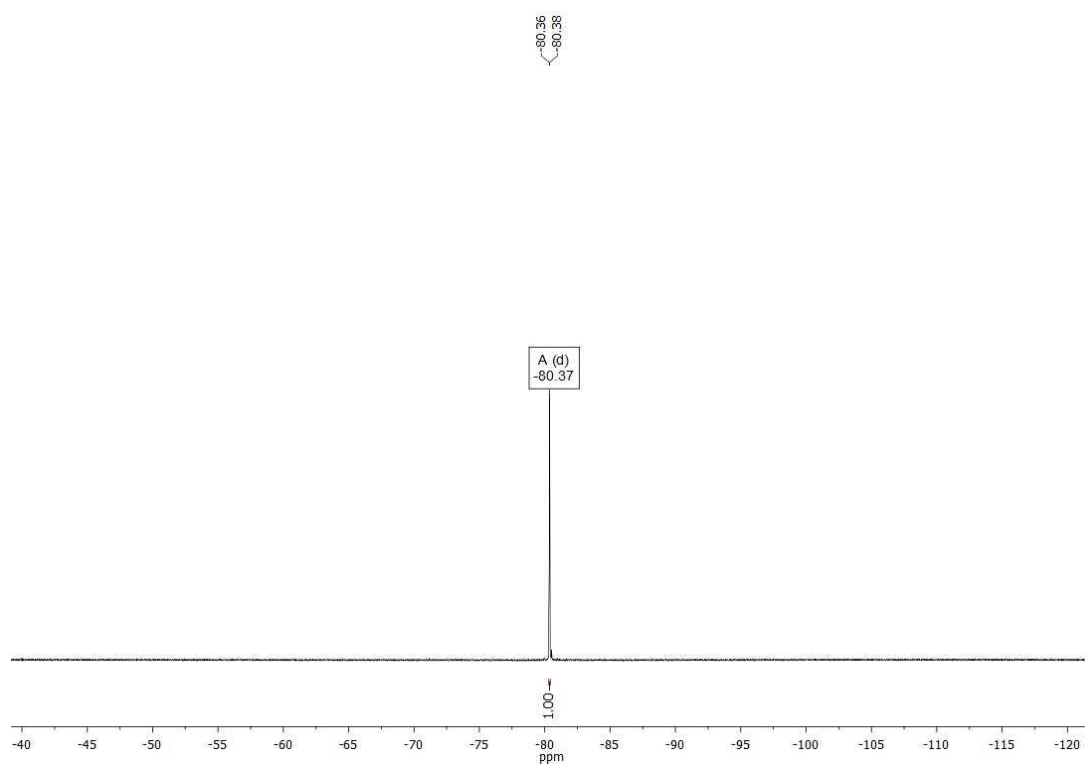
***N*-(2,2,2-Trifluoro-1-(pyridin-2-ylamino)ethyl)benzimidamide (4c):**



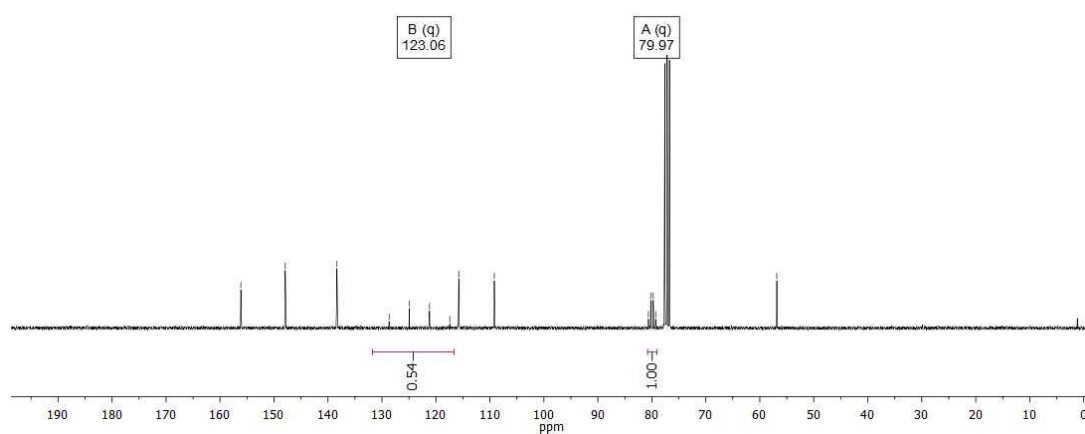


***N*-(2,2,2-Trifluoro-1-methoxyethyl)pyridin-2-amine (4d):**

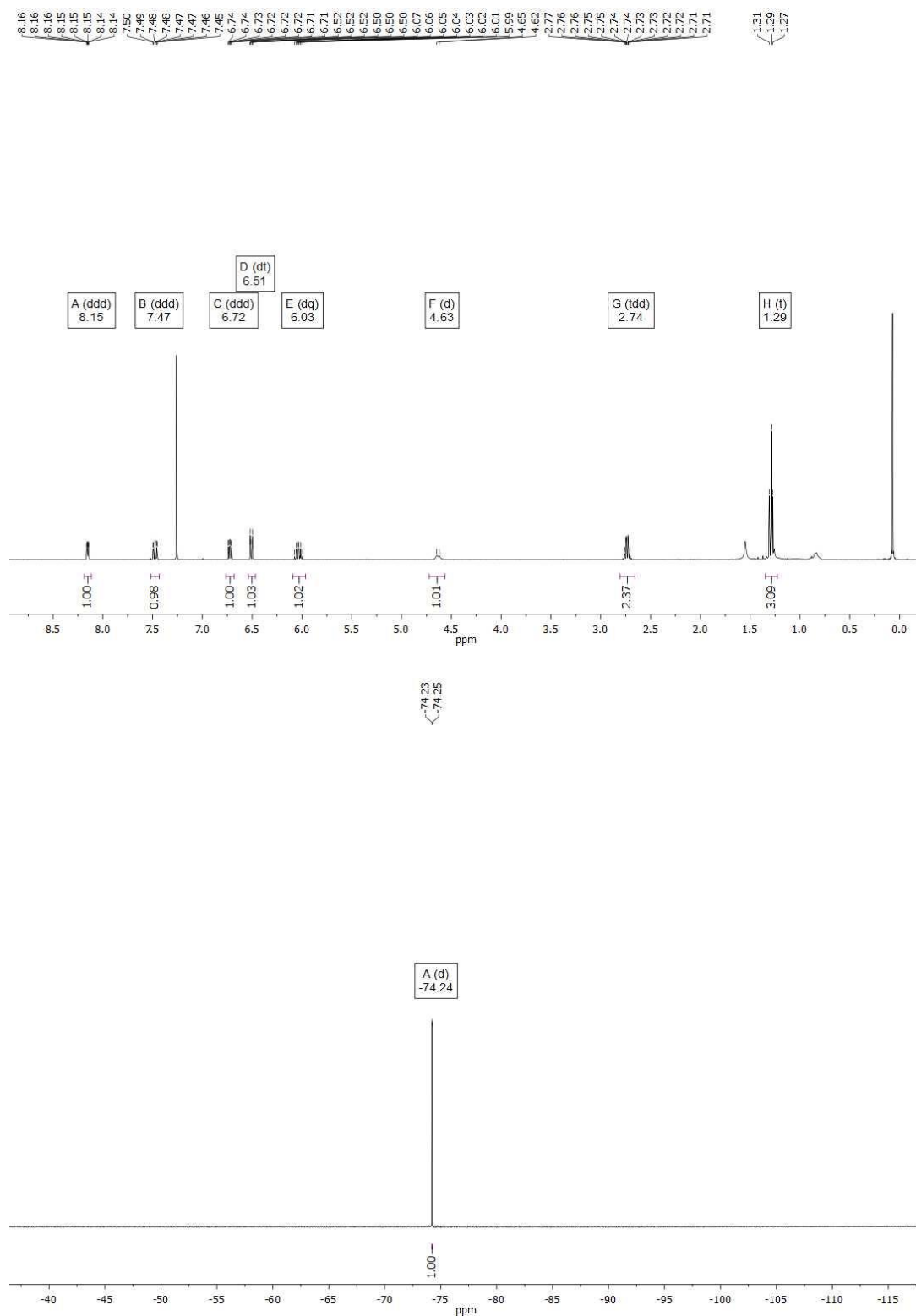


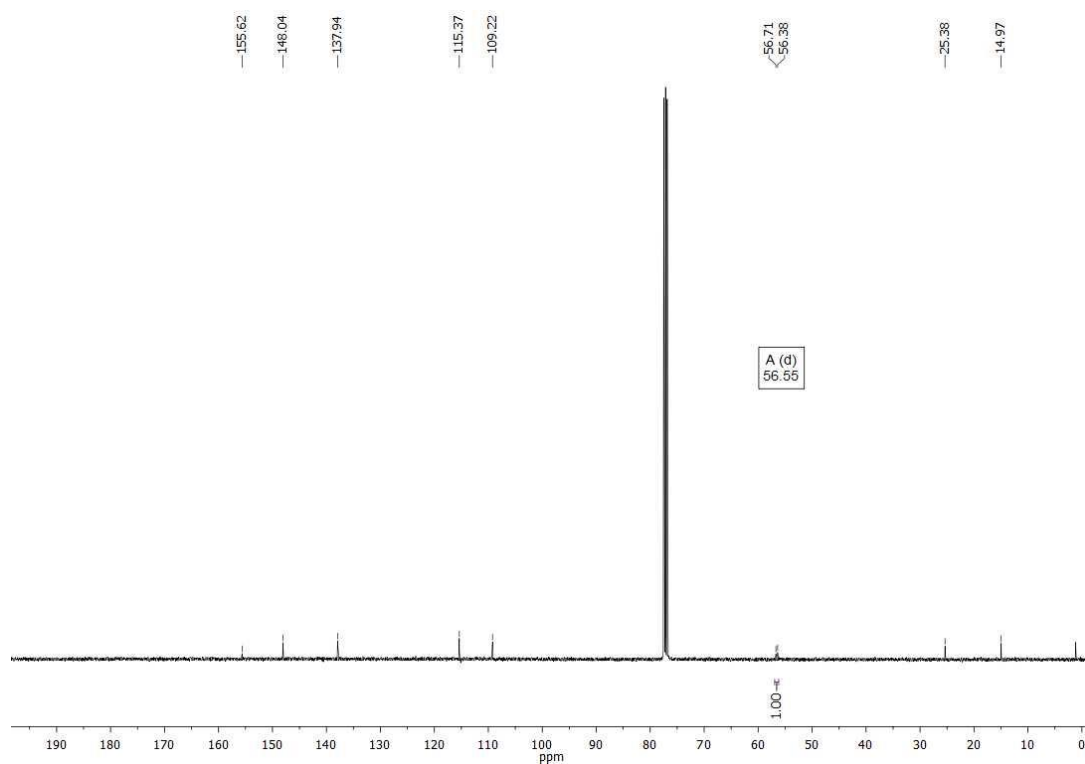


-156.14  
 -147.91  
 -138.34  
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 80.19  
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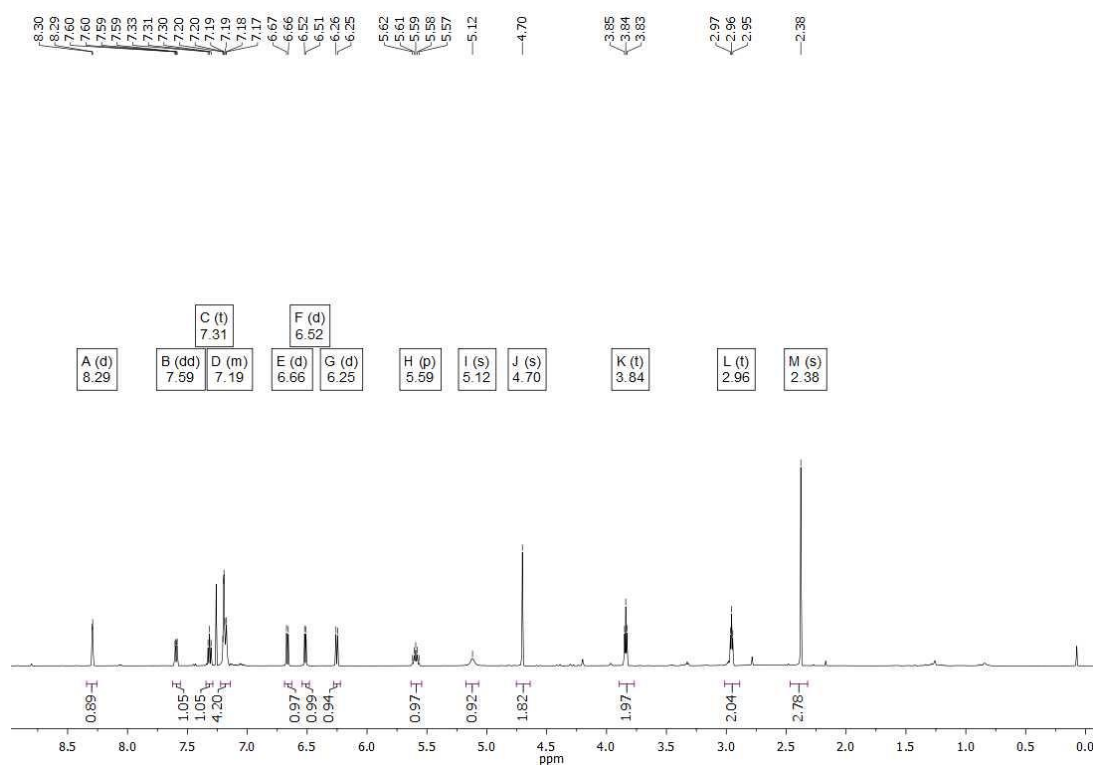


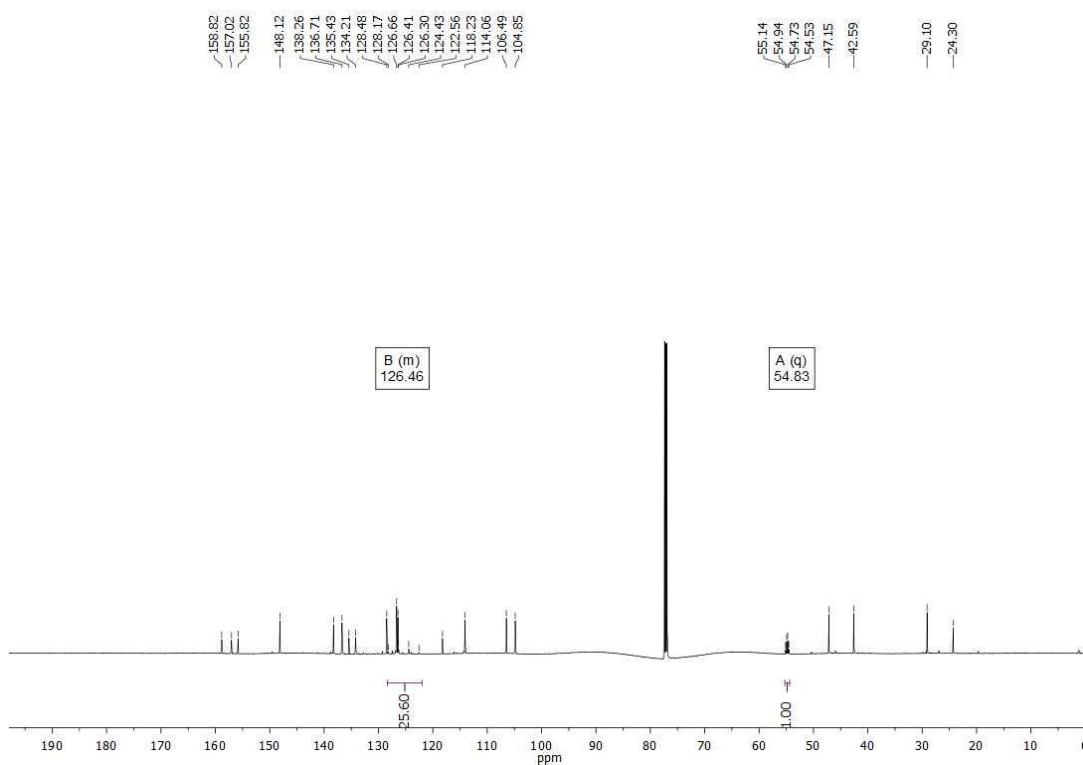
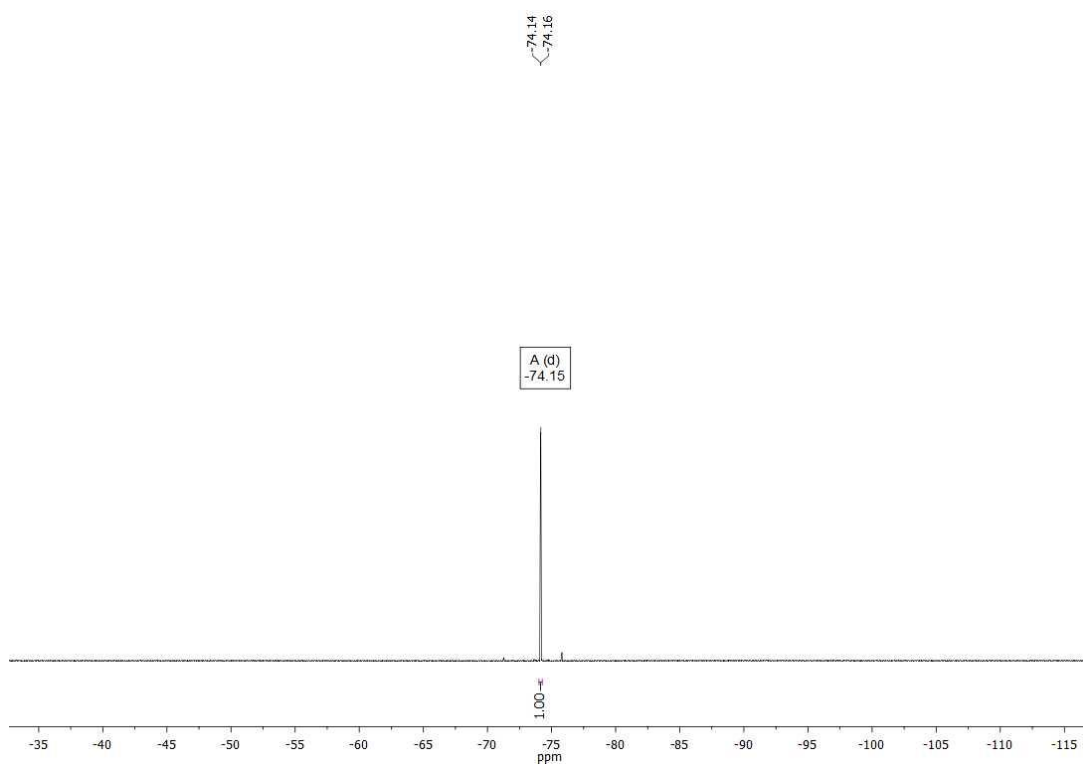
***N*-(1-(Ethylthio)-2,2,2-trifluoroethyl)pyridin-2-amine (4e):**



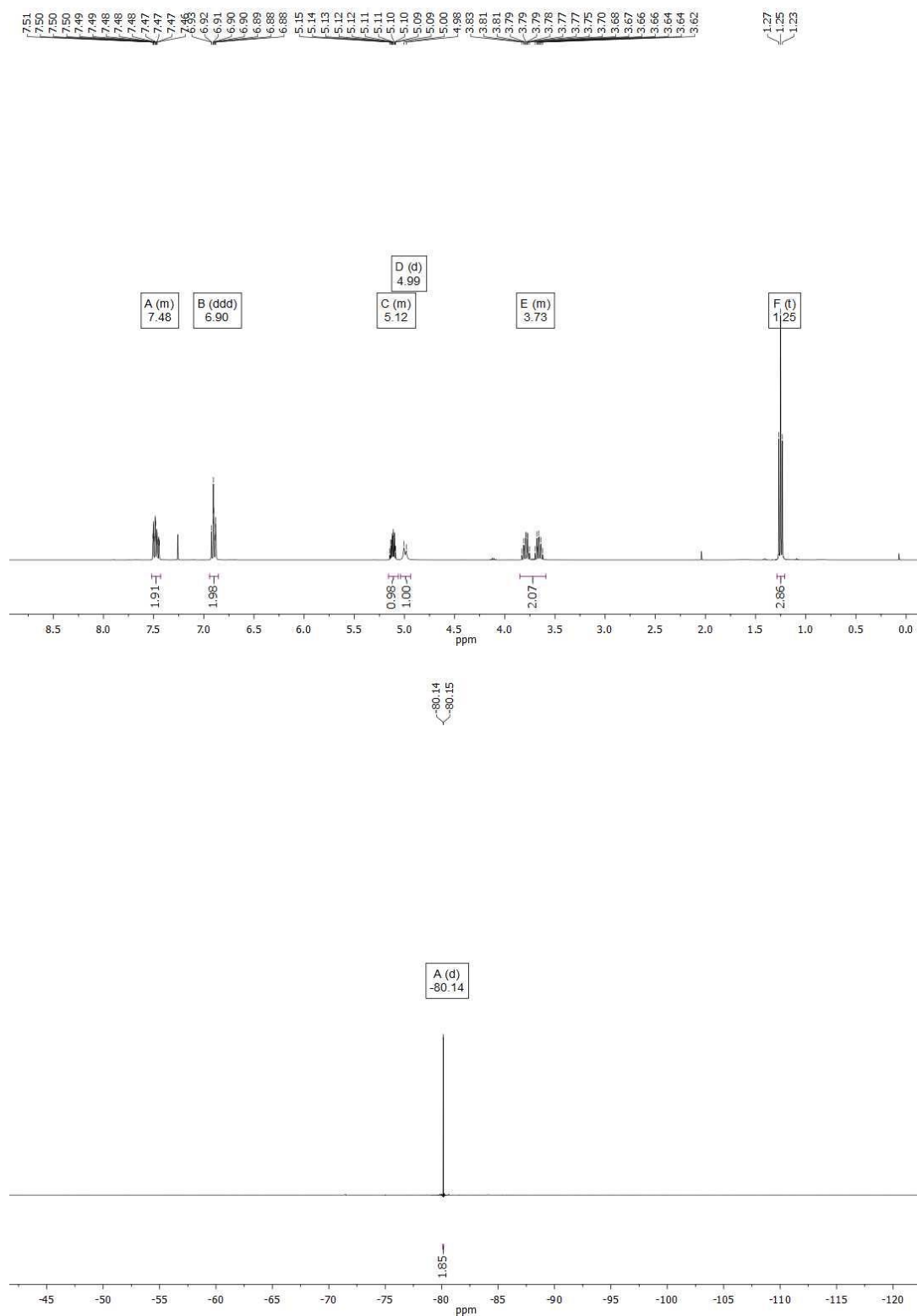


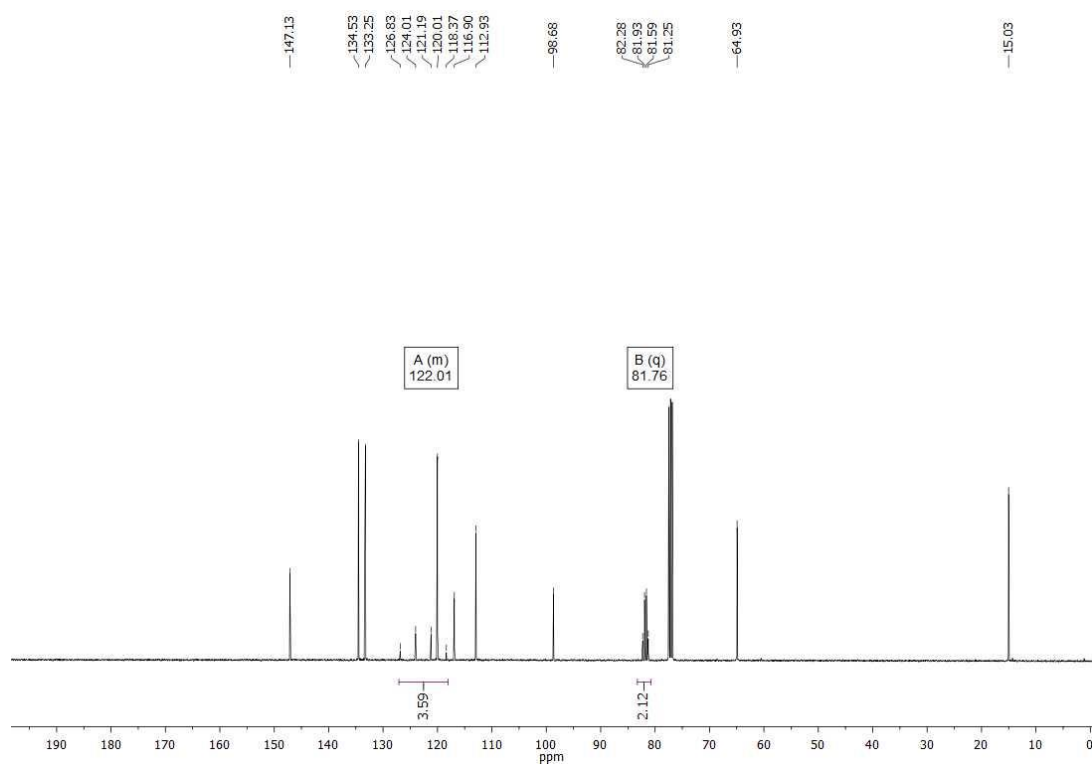
***N*-(1-(6-(3,4-Dihydroisoquinolin-2(1*H*)-yl)pyridin-3-yl)-2,2,2-trifluoroethyl)-6-methylpyridin-2-amine (5):**



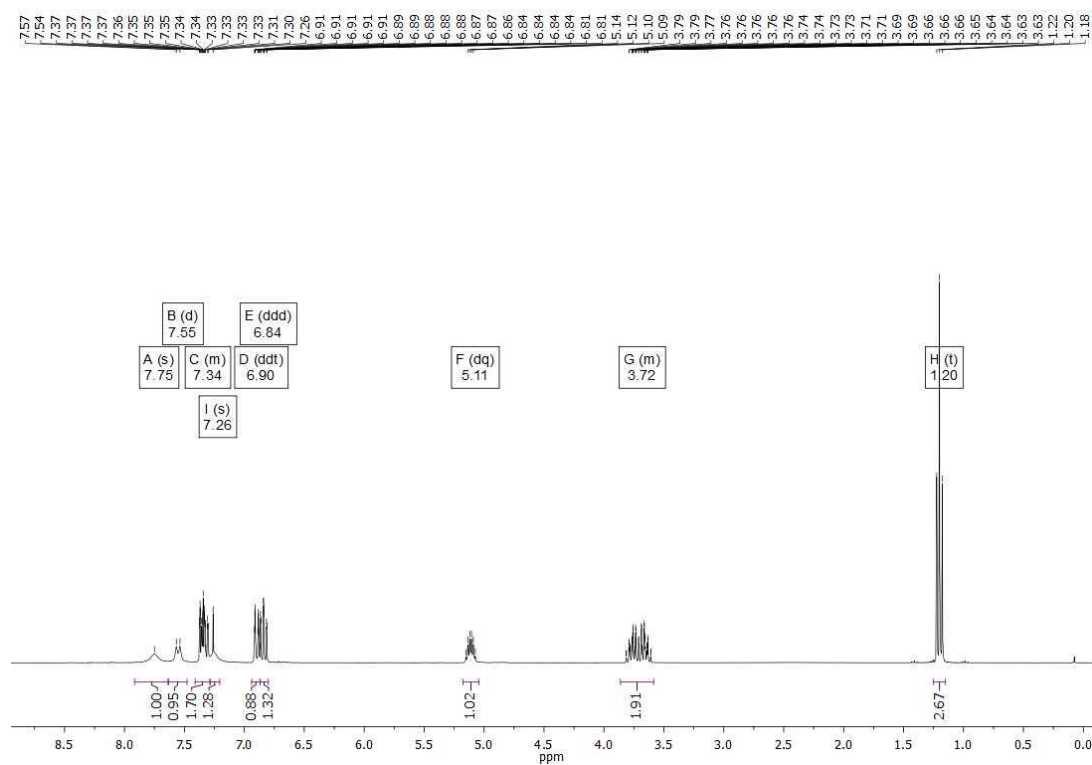


**2-((1-Ethoxy-2,2,2-trifluoroethyl)amino)benzonitrile (1i):**

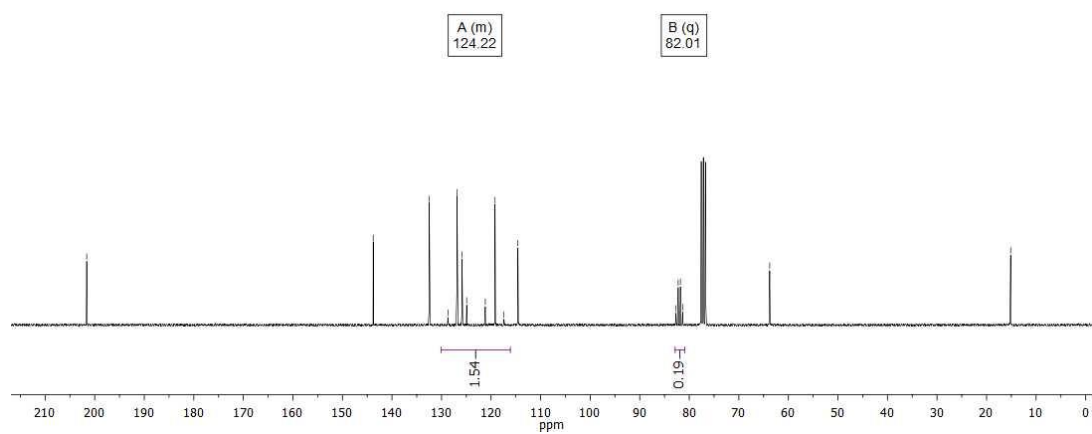
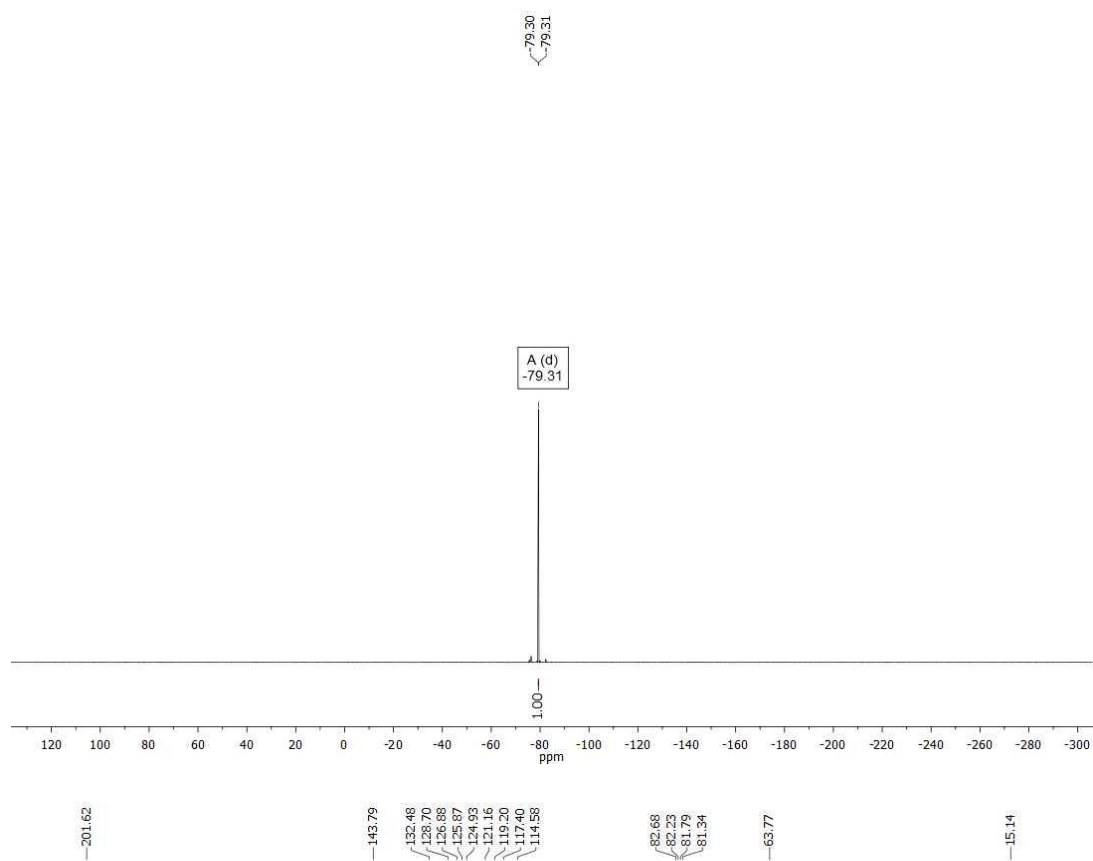




**2-((1-Ethoxy-2,2,2-trifluoroethyl)amino)benzothioamide (8):**







**2-(Trifluoromethyl)-2,3-dihydroquinazoline-4(1*H*)-thione (7):**

