

# Regioselective copper-catalyzed N(1)-(hetero)arylation of protected histidines

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## Supporting Information

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### General Considerations

Reagents were available from commercial suppliers and used without any additional purification unless otherwise noted. Histidine, aryl halides, base, solvent, copper catalyst and ligands were purchased from commercial sources such as Chem-Impex, Sigma-Aldrich, Alfa-aesar, Merck, and Avra chemicals. Nuclear magnetic resonance spectra (NMR) were recorded on a BrukerAvance-III 400 spectrometer as <sup>1</sup>H NMR (400 MHz), and <sup>13</sup>C-NMR (100 MHz). Chemical shifts for <sup>1</sup>H NMR were reported as  $\delta$  values and coupling constants were indicated in hertz (Hz). The following abbreviations were used for reported spin multiplicity: s = singlet, br.s. = broad singlet, d = doublet, t = triplet, dd = doublet of doublets, m =

multiplet and q = quadruplet. When splitting patterns could not be interpreted easily, was reported as multiplet (m). If required mixture of two deuterated solvents was used while recording the spectra to enhance the solubility and prevent precipitation of N-arylated histidines. Thin layer chromatography was performed on Merck precoated silica gel plates (0.25 mm, 60 Å pore size) impregnated with a fluorescent indicator (254 nm). Visualization on TLC was observed under UV light (254 nm) and staining with iodine vapours, or Dragendorff's solution. All the synthesized N-arylated compounds were isolated by automated flash chromatography on silica gel (200–400 mesh). High resolution mass spectra (HRMS) were recorded on Bruker Maxis and chiral HPLC experiments were performed on Shimadzu Prominence using an CHIRALPAK®-WH column (250mm L x 4.6mm i.d.) and the mobile phase used in this study was 0.50 mM copper(II) sulphate ( $\text{Cu}_2\text{SO}_4 \cdot 5\text{H}_2\text{O}$ ) in water and 2-propanol (95:5), gradient run for 70 min at flow rate of 1 mL/min at constant oven temperature of 50 °C.

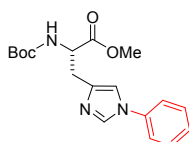
## **1. General procedure for the N-(hetero)arylation of protected histidine**

All the solid reagents were weighed in air, transferred to a 10 mL pre-dried MW vial with a septum and equipped with a magnetic stirring bar. In the MW vial, the solid materials such as Boc-His-OMe (0.25 mmol, 1.0 equiv.), copper iodide (10 mol%), and  $\text{K}_2\text{CO}_3$  (2.0 equiv.) was added and dried by applying vacuum and then back filling with argon or nitrogen. This procedure was repeated 3 times after which all the liquids reagents like aryl iodide (1.2 equiv., if it is liquid), ligand (20 mol%) and DMF (1 mL) were added under positive pressure of argon or nitrogen. After completion of this procedure, the MW vial was sealed and allowed to stir at constant temperature of 130 °C for 40 min. After the completion of reaction, the solvent was removed under reduced pressure and to crude mixture was added water (4 mL). The product was extracted with ethyl acetate (3 x 10 mL) and the combined organic phase was concentrated under reduced pressure. The reaction mixture was purified on a automated flash chromatography system (Biotage) to afford the N-arylated histidines using mobile combination of dichloromethane (97-90%) and methanol (3-10%).

## 2. Experimental section

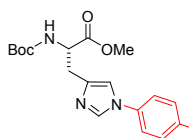
### 2.1. Characterization data of synthesized compounds

***N*- $\alpha$ -Boc-1-(phenyl)-L-histidine methyl ester (2a):** Yield = 89% (**2aa**), 23% (**2ab**);  $^1\text{H}$  NMR (400 MHz, CD<sub>3</sub>OD):  $\delta$  8.05 (s, 1H), 7.52 (d,  $J$  = 4.3, 4H), 7.42-7.37 (m, 2H), 4.50-4.46 (m, 1H), 3.74 (s, 3H), 3.12 (dd,  $J$  = 14.8, 5.2 Hz, 1H), 2.98 (dd,  $J$  = 14.6, 8.6 Hz, 1H), 1.40 (s, 9H);  $^{13}\text{C}$



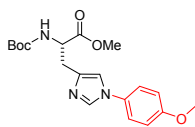
NMR (100 MHz, CD<sub>3</sub>OD): 172.8, 156.4, 138.1, 137.0, 135.1, 129.6, 127.2, 120.6, 116.0, 79.3, 53.7, 51.4, 29.8, 27.2; HRMS (ESI-TOF):  $m/z$  [(M+H)<sup>+</sup>] calculated for 346.1767, found 346.1761.

***N*- $\alpha$ -Boc-1-(4-methylphenyl)-L-histidine methyl ester (2b):** Yield = 91% (**2ba**), 27% (**2bb**);  $^1\text{H}$  NMR (400 MHz, CD<sub>3</sub>OD):  $\delta$  7.99 (s, 1H), 7.39-7.30 (m, 5H), 4.47 (t,  $J$  = 6.4 Hz, 1H), 3.73 (s, 3H), 3.10 (dd,  $J$  = 14.6, 4.8 Hz, 1H), 2.97 (dd,  $J$  = 14.5, 8.6 Hz, 1H), 2.39 (s, 3H), 1.40 (s, 9H);



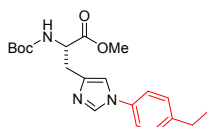
$^{13}\text{C}$  NMR (100 MHz, CD<sub>3</sub>OD): 172.7, 156.4, 137.9, 137.4, 135.0, 134.6, 130.0, 120.5, 116.1, 79.2, 53.7, 51.3, 29.8, 27.2, 19.5; HRMS (ESI-TOF):  $m/z$  [(M+H)<sup>+</sup>] calculated for 360.1923, found 360.1917.

***N*- $\alpha$ -Boc-1-(4-methoxyphenyl)-L-histidine methyl ester (2c):** Yield = 84%;  $^1\text{H}$  NMR [400 MHz, CD<sub>3</sub>OD]  $\delta$  7.92 (s, 1H), 7.41 (d,  $J$  = 8.9 Hz, 2H), 7.26 (s, 1H), 7.04 (d,  $J$  = 8.9 Hz, 2H), 4.48-4.45 (m, 1H), 3.84 (s, 3H), 3.73 (s, 3H), 3.10 (dd,  $J$  = 14.7, 5.1 Hz, 1H), 2.97 (dd,  $J$  = 14.5, 8.5 Hz,



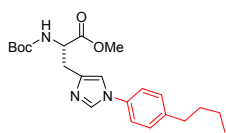
1H), 1.40 (s, 9H);  $^{13}\text{C}$  NMR [100 MHz, CD<sub>3</sub>OD]: 172.8, 159.1, 156.4, 137.7, 135.2, 130.2, 122.3, 116.5, 114.6, 79.3, 54.7, 53.8, 51.3, 29.7, 27.3; HRMS (ESI-TOF):  $m/z$  [(M+H)<sup>+</sup>] calculated for 376.1872, found 376.1866.

***N*- $\alpha$ -Boc-1-(4-ethylphenyl)-L-histidine methyl ester (2d):** Yield = 85%;  $^1\text{H}$  NMR (400 MHz, CD<sub>3</sub>OD):  $\delta$  8.24 (s, 1H), 7.46-7.37 (m, 5H), 4.49 (t,  $J$  = 6.8 Hz, 1H), 3.75 (s, 3H), 3.15 (dd,  $J$  = 15.1, 5.0 Hz, 1H), 3.01 (dd,  $J$  = 8.57, 14.6 Hz, 1H), 2.72 (q,  $J$  = 7.6 Hz, 2H), 1.40 (s, 9H), 1.27 (t,



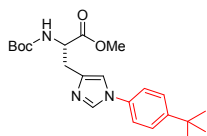
$J$  = 7.6 Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz, CD<sub>3</sub>OD): 174.0, 157.8, 145.8, 138.1, 136.2, 135.8, 130.4, 122.2, 118.1, 80.8, 54.9, 52.8, 30.7, 29.3, 28.6, 16.0; HRMS (ESI-TOF):  $m/z$  [(M+H)<sup>+</sup>] calculated for 374.2080, found 374.2067.

***N*- $\alpha$ -Boc-1-(4-butylphenyl)-L-histidine methyl ester (2e):** Yield = 81%;  $^1\text{H}$  NMR [400 MHz,  $\text{CD}_3\text{OD}$ ]  $\delta$  7.88 (s, 1H), 7.29 (d,  $J$  = 8.4 Hz, 2H), 7.21 (d,  $J$  = 8.4 Hz, 3H), 4.37-4.34 (m, 1H), 3.62 (s, 3H), 2.99 (dd,  $J$  = 15.0, 5.4 Hz, 1H), 2.85 (dd,  $J$  = 14.4, 8.4 Hz, 1H), 2.55 (t,  $J$  = 7.6 Hz, 2H), 1.55-1.47 (m, 2H), 1.31-1.21 (m, 11H), 0.84 (t,  $J$  = 7.3 Hz, 3H);  $^{13}\text{C}$  NMR [100 MHz,  $\text{CD}_3\text{OD}$ ]:



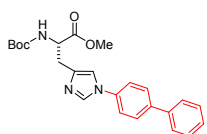
174.3, 157.8, 143.8, 139.3, 136.5, 136.2, 130.9, 122.0, 117.5, 80.8, 55.2, 52.8, 36.0, 34.7, 31.2, 28.7, 23.2, 14.3; HRMS (ESI-TOF):  $m/z$  [(M+H) $^+$ ] calculated for 402.2393, found 402.2383.

***N*- $\alpha$ -Boc-1-(4-*tert*-butylphenyl)-L-histidine methyl ester (2f):** Yield = 82%;  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  8.01 (s, 1H), 7.55 (d,  $J$  = 8.7 Hz, 2H), 7.43 (d,  $J$  = 8.6 Hz, 2H), 7.34 (s, 1H), 4.49-4.46 (m, 1H), 3.73 (s, 3H), 3.11 (dd,  $J$  = 14.6, 4.8 Hz, 1H), 2.98 (dd,  $J$  = 14.9, 8.6 Hz, 1H), 1.41 (s, 9H), 1.36 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ ): 172.8, 156.4, 150.6, 137.9, 135.0,



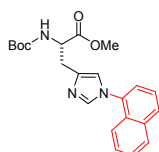
134.5, 126.5, 120.2, 116.1, 79.3, 53.8, 51.3, 34.0, 30.3, 29.8, 27.2; HRMS (ESI-TOF):  $m/z$  [(M+H) $^+$ ] calculated for 402.2393, found 402.2385.

***N*- $\alpha$ -Boc-1-(4-biphenyl)-L-histidine methyl ester (2g):** Yield = 83% (2ga), 25% (2gb);  $^1\text{H}$  NMR [400 MHz,  $\text{CD}_3\text{OD}$ ]  $\delta$  8.08 (s, 1H), 7.74 (d,  $J$  = 8.6 Hz, 2H), 7.64 (d,  $J$  = 7.1 Hz, 2H), 7.57 (d,  $J$  = 8.5 Hz, 2H), 7.46 (t,  $J$  = 7.5 Hz, 2H), 7.40-7.35 (m, 2H), 4.51-4.48 (m, 1H), 3.74 (s, 3H), 3.12 (dd,  $J$  = 14.5, 4.8 Hz, 1H), 3.49 (dd,  $J$  = 14.9, 8.9 Hz, 1H), 1.41 (s, 9H);  $^{13}\text{C}$  NMR [100 MHz,  $\text{CD}_3\text{OD}$ ]: 172.9, 156.4, 140.3, 139.5, 138.2, 136.0, 135.1, 128.6, 128.0, 127.4, 126.5, 120.8,



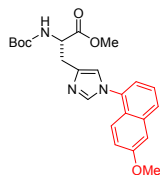
115.9, 79.4, 53.8, 51.4, 29.8, 27.3; HRMS (ESI-TOF):  $m/z$  [(M+H) $^+$ ] calculated for 422.2080, found 422.2771.

***N*- $\alpha$ -Boc-1-(1-naphthyl)-L-histidine methyl ester (2h):** Yield = 83%;  $^1\text{H}$  NMR [400 MHz,  $\text{CD}_3\text{OD}$ ]  $\delta$  8.01 (t,  $J$  = 8.5 ssHz, 2H), 7.82 (s, 1H), 7.61-7.50 (m, 5H), 7.22 (s, 1H), 4.54 (t,  $J$  = 6.0 Hz, 1H), 3.76 (s, 3H), 3.19 (dd,  $J$  = 14.6, 5.0 Hz, 1H), 3.07 (dd,  $J$  = 14.6, 8.4 Hz, 1H), 1.42 (s, 9H);  $^{13}\text{C}$  NMR [100 MHz,  $\text{CD}_3\text{OD}$ ]: 172.8, 156.4, 138.0, 134.3, 133.5, 129.3, 129.2, 128.1, 127.4,



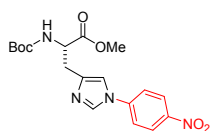
126.7, 125.0, 123.5, 121.6, 119.9, 113.3, 79.4, 53.9, 51.5, 29.8, 27.4; HRMS (ESI-TOF):  $m/z$  [(M+H) $^+$ ] calculated for 396.1923, found 396.1911.

**N- $\alpha$ -Boc-1-(6-methoxy-1-naphthyl)-L-histidine methyl ester (2i):** Yield = 79%;  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  8.13 (s, 1H), 7.93-7.83 (m, 3H), 7.59 (d,  $J$  = 8.6 Hz, 1H), 7.45 (s, 1H), 7.31 (s, 1H), 7.22 (d,  $J$  = 8.9 Hz, 1H), 4.52-4.49 (m, 1H), 3.94 (s, 3H) 3.75 (s, 3H), 3.14 (dd,  $J$  = 14.6 Hz,



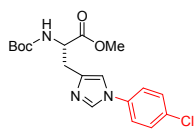
5.0 Hz, 1H), 3.01 (dd,  $J$  = 14.5, 8.7 Hz, 1H), 1.41 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  172.9, 158.2, 156.5, 138.0, 135.3, 133.7, 132.5, 129.0, 128.9, 128.5, 119.8, 118.2, 116.3, 105.4, 79.4, 54.5, 53.8, 51.5, 29.8, 27.2; HRMS (ESI-TOF):  $m/z$  [(M+H) $^+$ ] calculated for 426.2029, found 426.2018.

**N- $\alpha$ -Boc-1-(4-nitrophenyl)-L-histidine methyl ester (2j):** Yield = 92%;  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  8.37 (d,  $J$  = 8.9 Hz, 2H), 8.18 (s, 1H), 7.71 (d,  $J$  = 8.8 Hz, 2H), 7.47 (s, 1H), 4.54 (br.s., 1H), 3.74 (s, 3H), 3.17-2.98 (m, 2H), 1.40 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  172.7,



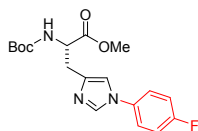
156.1, 146.2, 141.8, 135.6, 134.7, 125.6, 120.7, 116.5, 79.9, 53.3, 52.1, 30.3, 27.9; HRMS (ESI-TOF):  $m/z$  [(M+H) $^+$ ] calculated for 391.1617, found 391.1611.

**N- $\alpha$ -Boc-1-(4-chlorophenyl)-L-histidine methyl ester (2k):** Yield = 88%;  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  8.08 (s, 1H), 7.55-7.50 (m, 4H), 7.38 (s, 1H), 4.47 (br.s., 1H), 3.13-3.08 (m, 1H), 2.98 (dd,  $J$  = 13.7, 7.9 Hz, 1H), 1.40 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  172.7, 156.4,



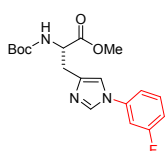
138.4, 135.7, 135.2, 132.6, 129.6, 122.0, 115.9, 79.3, 53.7, 51.3, 29.8, 27.2; HRMS (ESI-TOF):  $m/z$  [(M+H) $^+$ ] calculated for 380.1377, found 380.1369.

**N- $\alpha$ -Boc-1-(4-fluorophenyl)-L-histidine methyl ester (2l):** Yield = 83%;  $^1\text{H}$  NMR [400 MHz,  $\text{CD}_3\text{OD}$ ]  $\delta$  8.01 (s, 1H), 7.57-7.54 (m, 2H), 7.33 (s, 1H), 7.29-7.25 (m, 2H), 4.49-4.45 (m, 1H), 3.74 (s, 3H), 3.11 (dd,  $J$  = 14.7, 5.0 Hz, 1H), 2.98 (dd,  $J$  = 14.6, 8.7 Hz, 1H), 1.40 (s, 9H);  $^{13}\text{C}$



NMR [100 MHz,  $\text{CD}_3\text{OD}$ ]: 172.8, 161.7 (d,  $J$  = 244 Hz), 156.4, 138.1, 135.3, 133.4, 122.8, 116.4, 116.2, 79.4, 53.7, 51.4, 29.7, 27.2; HRMS (ESI-TOF):  $m/z$  [(M+H) $^+$ ] calculated for 364.1672, found 364.1666.

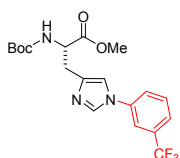
**N- $\alpha$ -Boc-1-(3-fluorophenyl)-L-histidine methyl ester (2m):** Yield = 88%;  $^1\text{H}$  NMR [400 MHz,  $\text{CD}_3\text{OD}$ ]  $\delta$  8.11 (s, 1H), 7.57-7.51 (m, 1H), 7.41-7.36 (m, 3H), 7.17-7.12 (m, 1H), 4.50-4.46 (m, 1H), 3.74 (s, 3H), 3.11 (dd,  $J$  = 14.9, 5.3 Hz, 1H), 2.98 (dd,  $J$  = 14.6, 8.7 Hz, 1H), 1.40 (s, 9H);



$^{13}\text{C}$  NMR [100 MHz,  $\text{CD}_3\text{OD}$ ]: 172.8, 163.3 (d,  $J$  = 245 Hz), 156.4, 138.3, 135.2,

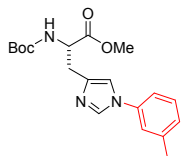
131.3, 116.1, 113.9, 113.6, 107.7, 79.4, 53.7, 51.4, 29.7, 27.1; HRMS (ESI-TOF):  $m/z$  [(M+H)<sup>+</sup>] calculated for 364.1672, found 364.1668.

***N*- $\alpha$ -Boc-1-(3-trifluoromethylphenyl)-L-histidine methyl ester (2n):** Yield = 83%; <sup>1</sup>H NMR [400 MHz, CD<sub>3</sub>OD]  $\delta$  8.17 (s, 1H), 7.84 (d,  $J$  = 12.0 Hz, 2H), 7.76-7.69 (m, 2H), 7.47 (s, 1H), 4.51-4.48 (m, 1H), 3.75 (s, 3H), 3.13 (dd,  $J$  = 14.6, 4.6 Hz, 1H), 2.99 (dd,  $J$  = 14.6, 8.8 Hz, 1H), 1.40 (s, 9H); <sup>13</sup>C NMR [100 MHz, CD<sub>3</sub>OD]  $\delta$  172.9, 156.5, 138.1, 137.5, 135.4, 131.9 (q,  $J$  = 33



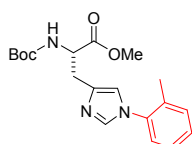
Hz), 130.8, 124.2, 123.7, 123.6 (q,  $J$  = 271 Hz), 117.2, 115.9, 79.5, 53.6, 51.5, 29.8, 27.2; HRMS (ESI-TOF):  $m/z$  [(M+H)<sup>+</sup>] calculated for 414.1640, found 414.1634.

***N*- $\alpha$ -Boc-1-(3-methylphenyl)-L-histidine methyl ester (2o):** Yield = 84%; <sup>1</sup>H NMR [400 MHz, CD<sub>3</sub>OD]  $\delta$  8.01 (s, 1H), 7.39-7.20 (m, 5H), 4.48 (br.s., 1H), 3.74 (s, 3H), 3.11 (d,  $J$  = 16.0 Hz, 1H), 3.01-2.95 (m, 1H), 2.39 (s, 3H), 1.39 (s, 9H); <sup>13</sup>C NMR [100 MHz, CD<sub>3</sub>OD]: 172.9, 156.4,



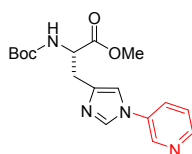
140.1, 137.9, 136.9, 135.0, 129.5, 127.9, 121.0, 117.6, 116.0, 79.4, 53.7, 51.5, 29.8, 27.3, 20.0; HRMS (ESI-TOF):  $m/z$  [(M+H)<sup>+</sup>] calculated for 360.1923, found 360.1916.

***N*- $\alpha$ -Boc-1-(2-methylphenyl)-L-histidine methyl ester (2p):** Yield = 77%; <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD):  $\delta$  7.96 (s, 1H), 7.42-7.29 (m, 4H), 7.16 (s, 1H), 4.49 (br.s., 1H), 3.75 (s, 3H), 3.17 (d,  $J$  = 13.8 Hz, 1H), 3.02 (dd,  $J$  = 14.3, 9.8 Hz, 1H), 2.20 (s, 3H), 1.42 (s, 9H); <sup>13</sup>C NMR (100 MHz,



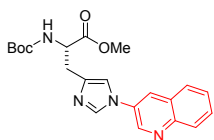
CD<sub>3</sub>OD): 172.6, 156.4, 136.9, 135.9, 133.6, 131.1, 129.2, 126.8, 126.0, 119.3, 79.5, 53.6, 51.5, 29.2, 27.3, 16.2; HRMS (ESI-TOF):  $m/z$  [(M+H)<sup>+</sup>] calculated for 360.1923, found 360.1917.

***N*- $\alpha$ -Boc-1-(3-pyridyl)-L-histidine methyl ester (2q):** Yield = 85%; <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD):  $\delta$  8.72 (s, 1H), 8.47 (s, 1H), 8.08 (s, 1H), 7.94 (d,  $J$  = 8.3 Hz, 1H), 7.50-7.47 (m, 1H), 7.37 (s, 1H), 4.37 (br.s., 1H), 3.62 (s, 3H), 3.01 (dd,  $J$  = 15.3, 4.4 Hz, 1H), 2.88 (dd,  $J$  = 14.6, 8.1 Hz, 1H), 1.29 (s, 9H); <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD):  $\delta$  174.0, 157.8, 149.1, 142.9, 140.0, 136.9,



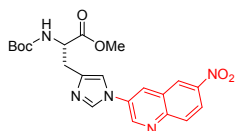
135.3, 130.4, 126.1, 117.2, 80.6, 54.8, 52.7, 31.2, 28.6; HRMS (ESI-TOF):  $m/z$  [(M+H)<sup>+</sup>] calculated for 347.1719, found 347.1714.

***N*- $\alpha$ -Boc-1-(3-quinolinyl)-L-histidine methyl ester (2r):** Yield = 83%;  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  9.06 (s, 1H), 8.44 (d,  $J$  = 2.2 Hz, 1H), 8.29 (s, 1H), 8.06 (d,  $J$  = 8.4 Hz, 1H), 7.98 (d,  $J$  = 8.0 Hz, 1H), 7.80-7.76 (m, 1H), 7.67 (t,  $J$  = 7.5 Hz, 1H), 7.59 (s, 1H), 4.53 (br.s., 1H), 3.76 (s, 3H), 3.16 (dd,  $J$  = 15.3, 5.6 Hz, 1H), 3.03 (dd,  $J$  = 15.7, 8.1 Hz, 1H), 1.40 (s, 9H);  $^{13}\text{C}$  NMR (100

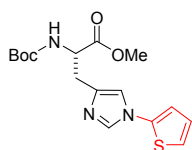


MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  172.7, 156.4, 146.2, 143.6, 138.9, 135.7, 130.6, 129.9, 128.0, 127.9, 127.9, 127.8, 126.5, 116.1, 79.3, 53.7, 51.4, 29.8, 27.2; HRMS (ESI-TOF):  $m/z$  [(M+H) $^+$ ] calculated for 397.1876, found 397.1867.

***N*- $\alpha$ -Boc-1-(6-nitro-3-quinolinyl)-L-histidine methyl ester (2s):** Yield = 86%;  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  9.33 (d,  $J$  = 2.5 Hz, 1H), 8.97 (d,  $J$  = 2.4 Hz, 1H), 8.72 (d,  $J$  = 2.3 Hz, 1H), 8.51-8.48 (m, 1H), 8.39 (s, 1H), 8.25 (d,  $J$  = 9.2 Hz, 1H), 7.66 (s, 1H), 4.53 (br.s., 1H), 3.76 (s, 3H), 3.17 (dd,  $J$  = 13.5, 4.5 Hz, 1H), 3.04 (dd,  $J$  = 15.3, 8.7 Hz, 1H), 1.41 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  172.6, 156.4, 148.0, 147.1, 146.5, 131.9, 130.3, 127.4, 127.0, 124.4, 122.8, 115.8, 79.3, 53.6, 51.4, 29.8, 27.2; HRMS (ESI-TOF):  $m/z$  [(M+Na) $^+$ ] calculated for 464.1546, found 464.1540.

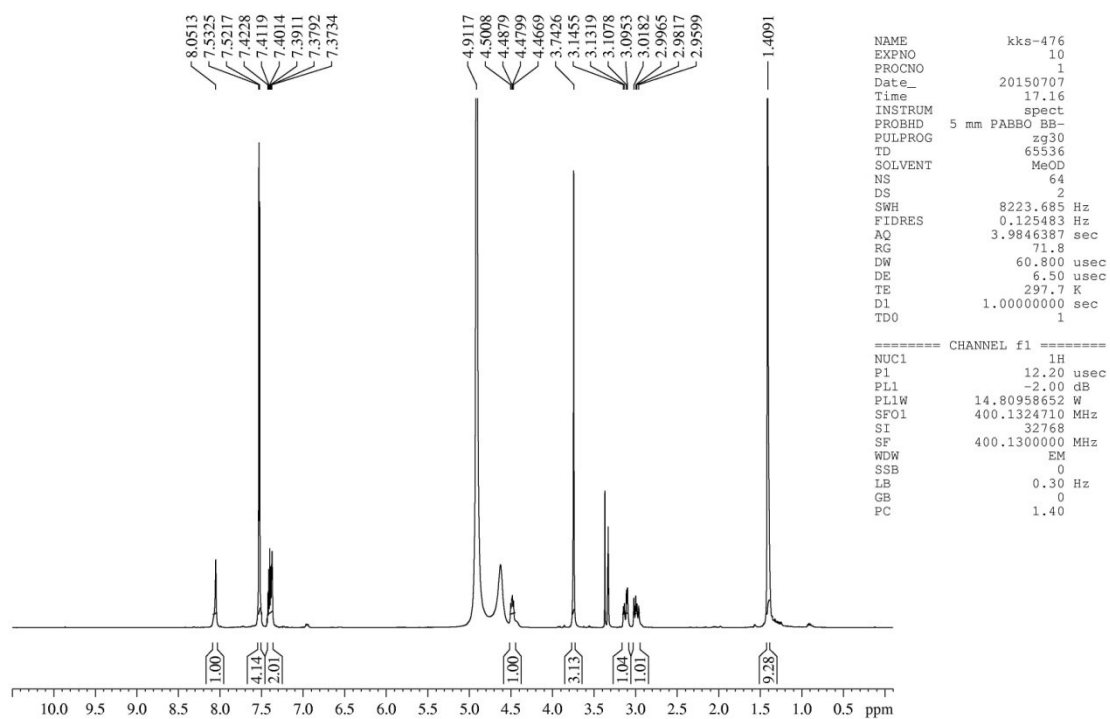


***N*- $\alpha$ -Boc-1-(2-thiophenyl)-L-histidine methyl ester (2t):** Yield = 75%;  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  7.94 (s, 1H), 7.33-7.31 (m, 1H), 7.25 (s, 1H), 7.18-7.17 (m, 1H), 7.06-7.03 (m, 1H), 4.48-4.44 (m, 1H), 3.74 (s, 3H), 3.12-3.07 (m, 1H), 2.98-2.92 (m, 1H), 1.42 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  172.6, 156.4, 138.8, 136.8, 126.1, 121.1, 118.7, 118.1, 79.2, 53.6, 51.3, 29.3, 27.2; HRMS (ESI-TOF):  $m/z$  [(M+H) $^+$ ] calculated for 352.1331, found 352.1319.

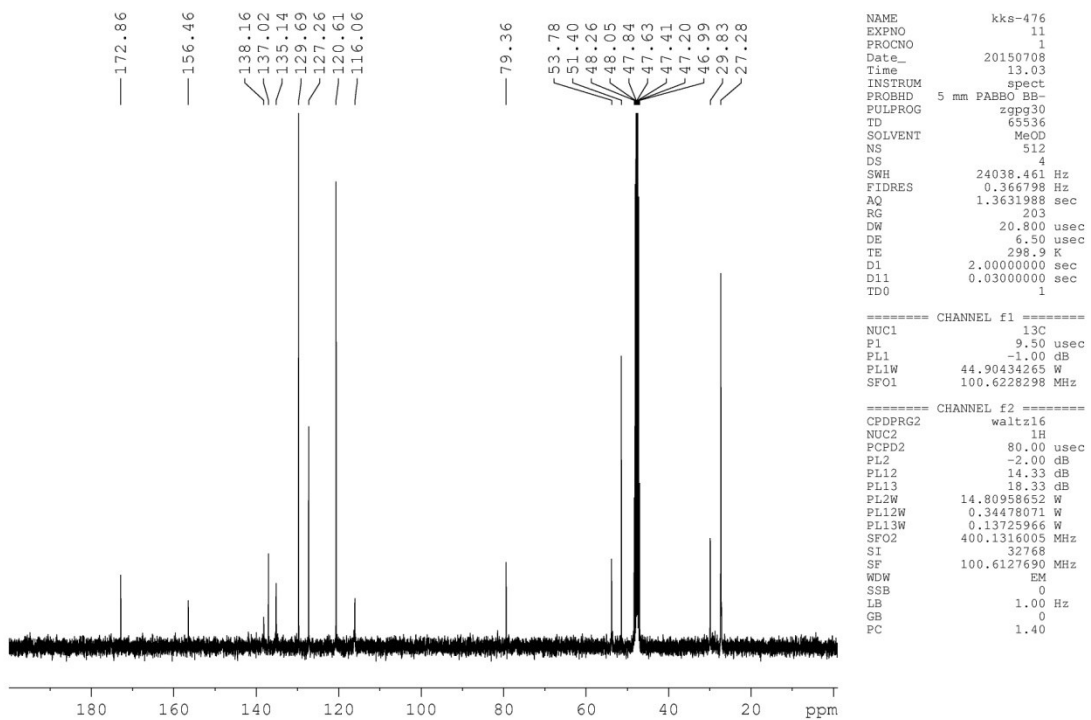


## 2.2. <sup>1</sup>H and <sup>13</sup>C NMR spectral data

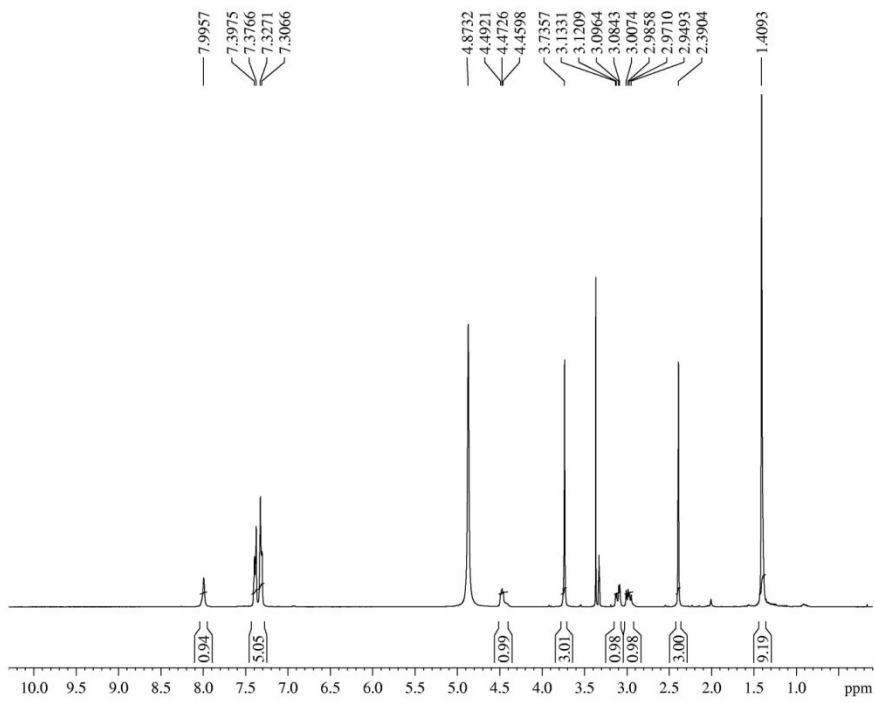
### *N*-α-Boc-1-(phenyl)-L-histidine methyl ester (2a)







***N*- $\alpha$ -Boc-1-(4-methylphenyl)-L-histidine methyl ester (2b)**

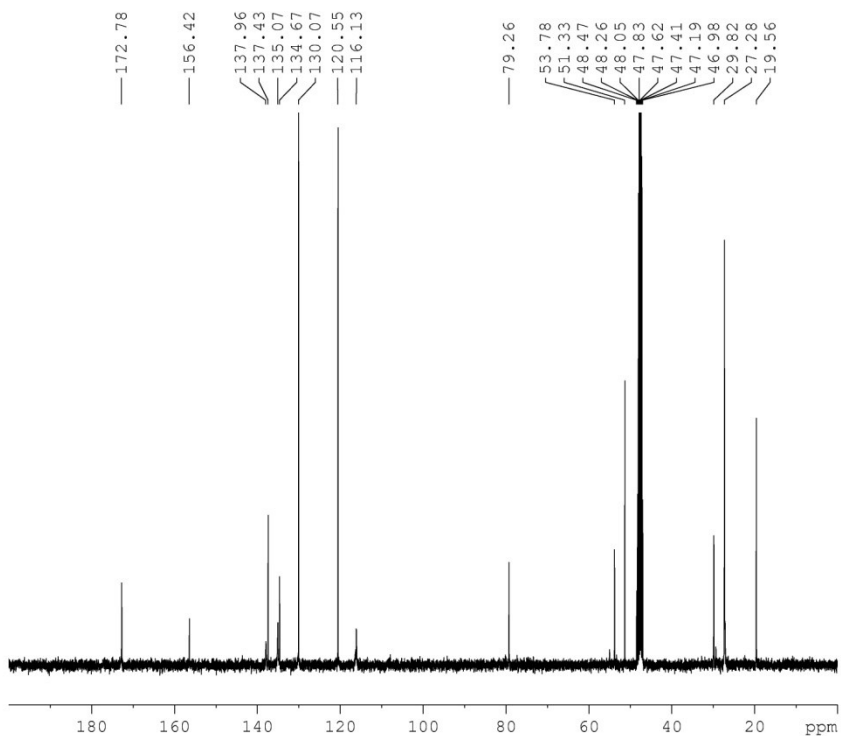


```

NAME          kks-482
EXPNO         10
PROCNO        1
Date_         20150713
Time          17.43
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            71.8
DW            60.800 usec
DE            6.50 usec
TE            298.5 K
D1            1.00000000 sec
TDO           1

===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1           -2.00 dB
PLLW          14.80958652 W
SFO1          400.1324710 MHz
SI            32768
SF            400.1300000 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.40

```



```

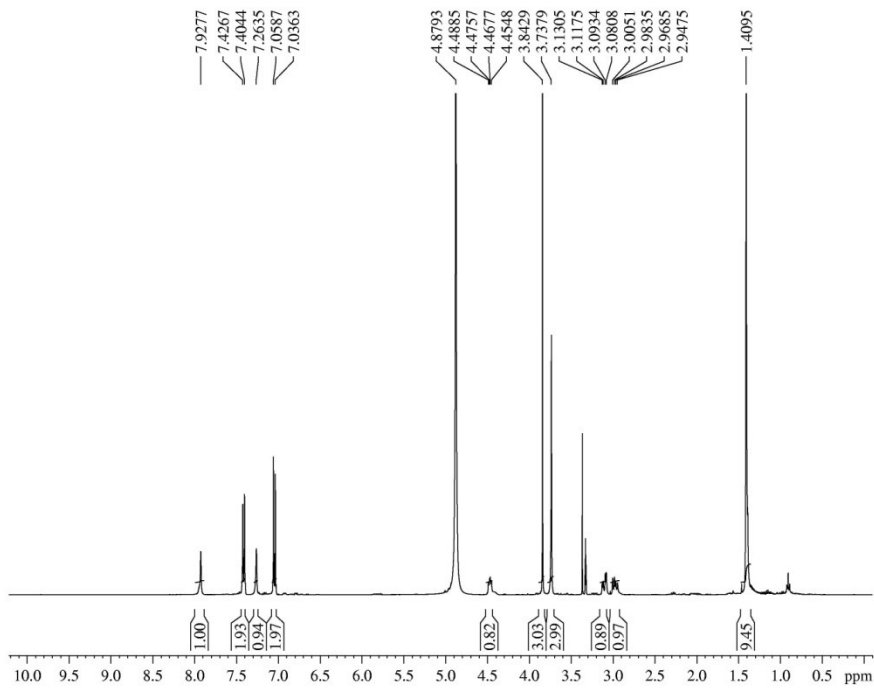
NAME          kks-482
EXPNO         11
PROCNO        1
Date_         20150713
Time          23.45
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zgpg30
TD            65536
SOLVENT       MeOD
NS            512
DS            4
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631988 sec
RG            203
DW            20.800 usec
DE            6.50 usec
TE            298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          13C
P1            9.50 usec
PL1           -1.00 dB
PL1W          44.90434265 W
SFO1          100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2       waltz16
NUC2          1H
PCPD2         80.00 usec
PL2           -2.00 dB
PL12          14.33 dB
PL13          18.33 dB
PL2W          14.80958652 W
PL12W         0.34478071 W
PL13W         0.13725966 W
SFO2          400.1316005 MHz
SI            32768
SF            100.6127690 MHz
WDW           EM
SSB           0
LB            1.00 Hz
GB            0
PC            1.40

```

***N*- $\alpha$ -Boc-1-(4-methoxyphenyl)-L-histidine methyl ester (2c)**

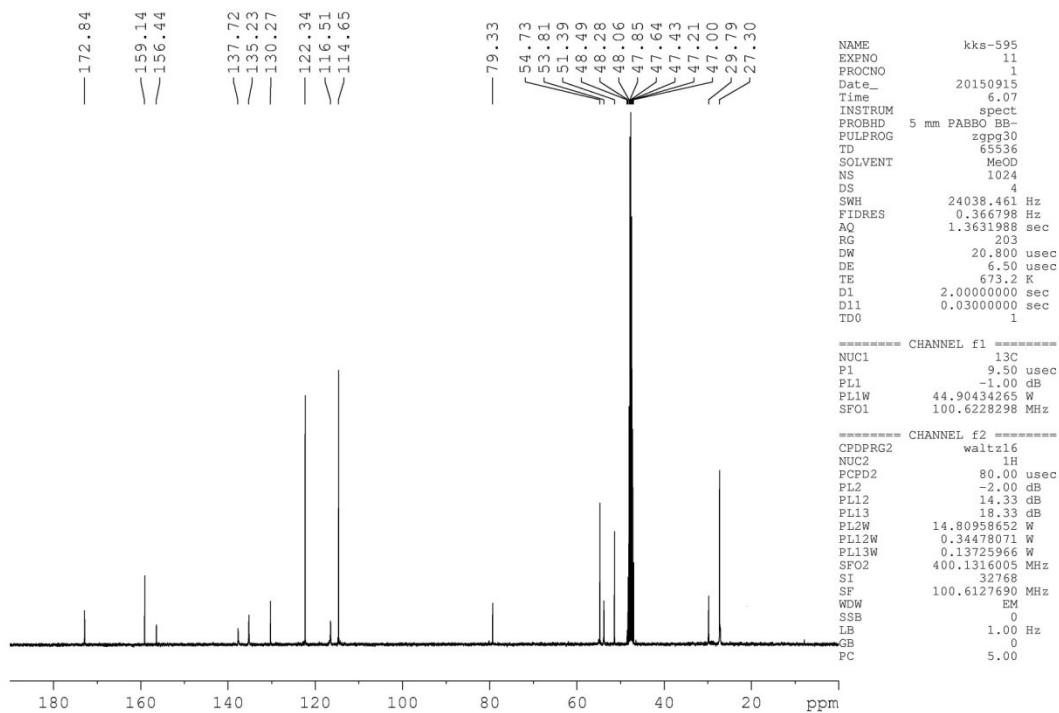


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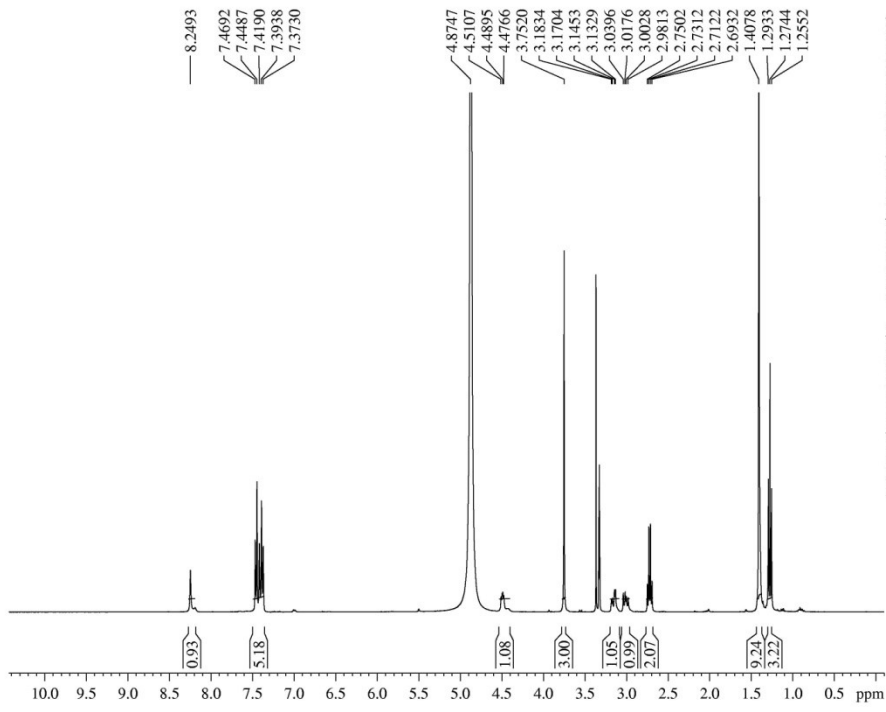
NAME          kks-595
EXPNO         10
PROCNO        1
Date_         20150914
Time          17.57
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            57
DW            60.800 usec
DE            6.50 usec
TE            673.2 K
D1            1.00000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1           -2.00 dB
PL1W         14.80958652 W
SFO1         400.1324710 MHz
SI            32768
SF            400.1300000 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.40

```



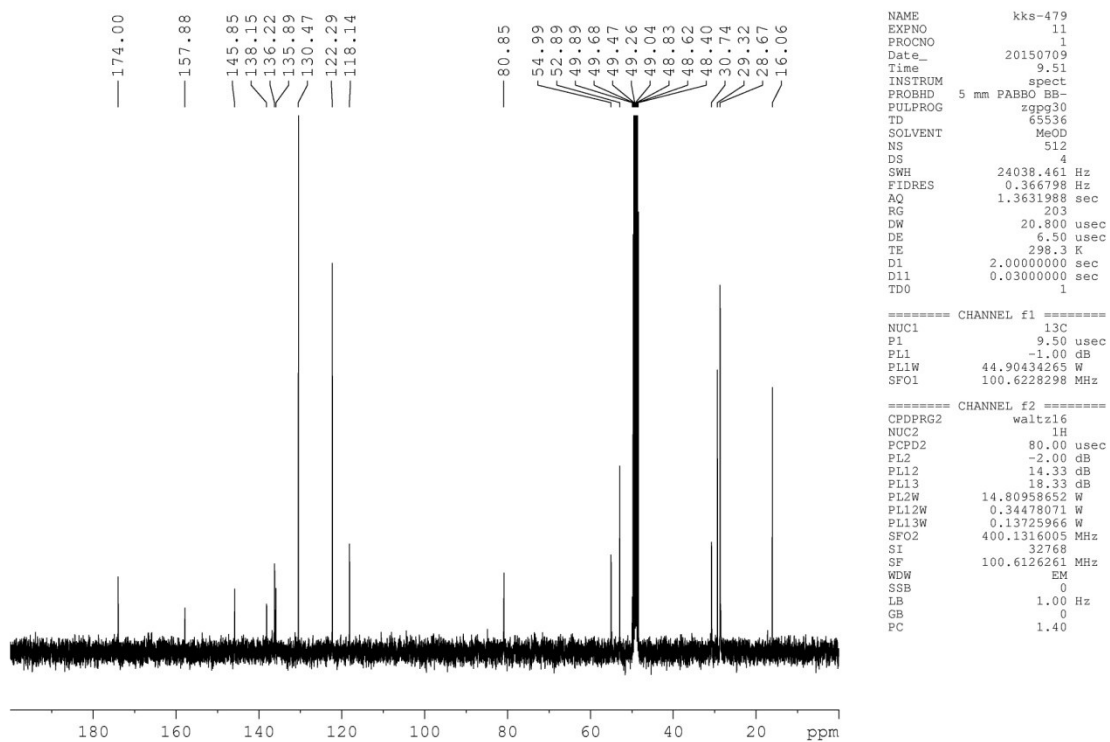
***N*- $\alpha$ -Boc-1-(4-ethylphenyl)-L-histidine methyl ester (2d)**



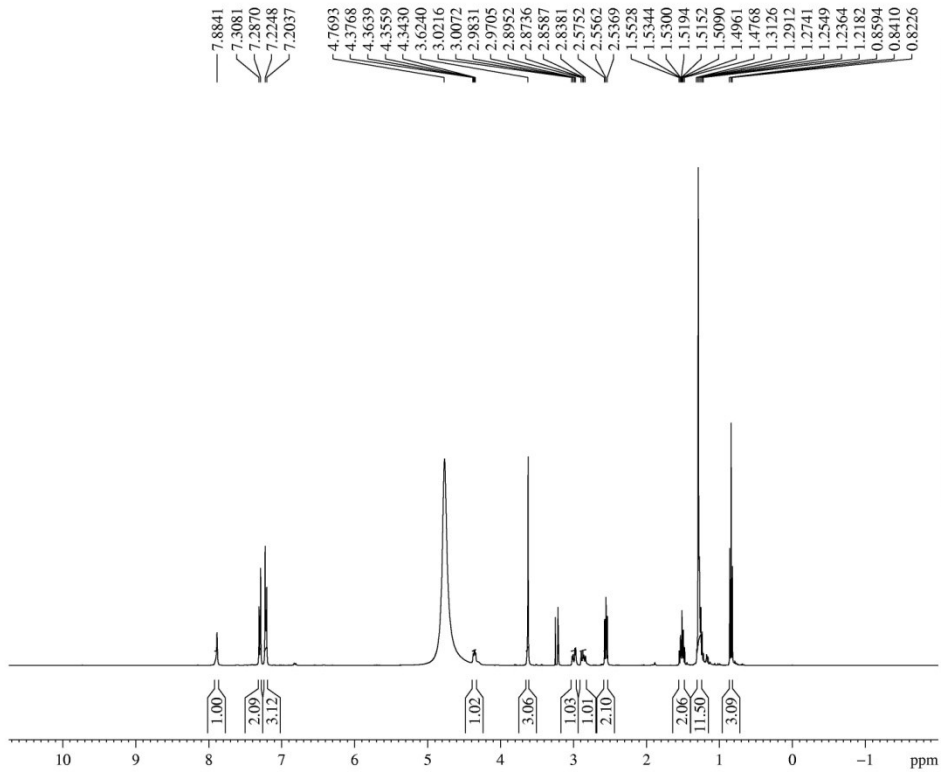
```

NAME          kks-479
EXPNO         10
PROCNO        1
Date_         20150709
Time          9.27
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            80.6
DW            60.800 usec
DE            6.50 usec
TE            297.5 K
D1            1.00000000 sec
TDO           1
===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1           -2.00 dB
PL1W          14.80958652 W
SFO1          400.1324710 MHz
SI            32768
SF            400.1300000 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            8.00

```



***N*- $\alpha$ -Boc-1-(4-butylphenyl)-L-histidine methyl ester (2e)**



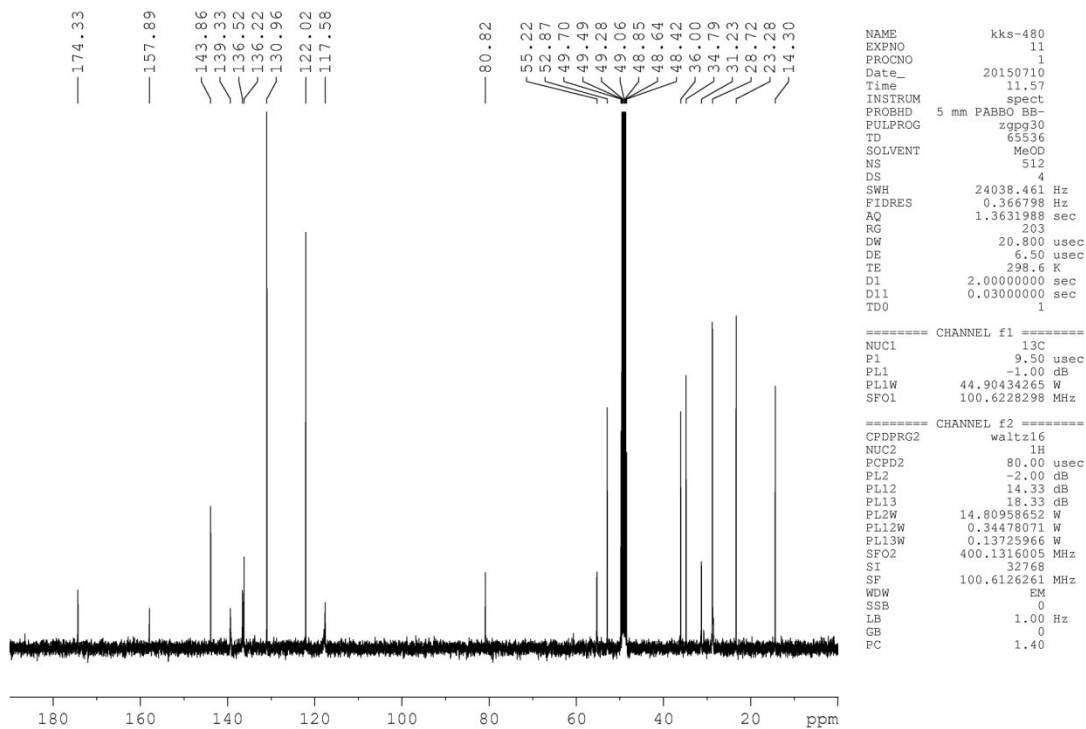
```

NAME          kks-481
EXPNO         11
PROCNO        :
Date_         20150710
Time          10.5:
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg31
TD            65536
SOLVENT       MeOH
NS            64
DS            :
SWH           8223.681
FIDRES        0.125481
AQ            3.984638
RG            5
DW            60.800
DE            6.50
TE            297.
D1            1.0000000
TD0           :

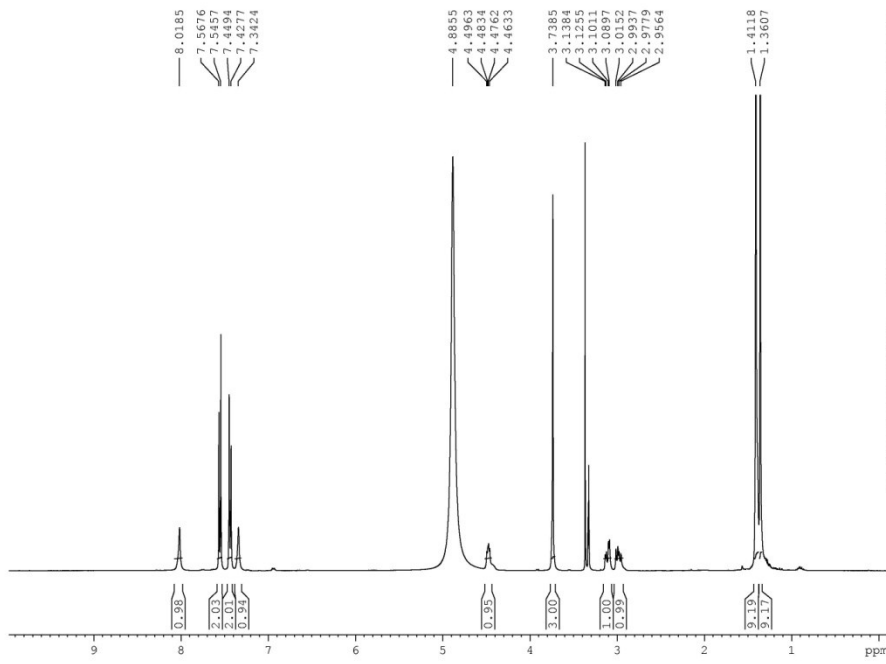
===== CHANNEL f1 =====
NUC1          1H
P1            12.20
PL1          -2.00
PL1W         14.8095865
SFO1         400.132471
SI           3276
SF           400.130046
WDW           EI
SSB           0
LB            0.30
GB            0
PC            5.00

```





***N*- $\alpha$ -Boc-1-(4-*tert*-butylphenyl)-L-histidine methyl ester (2f)**

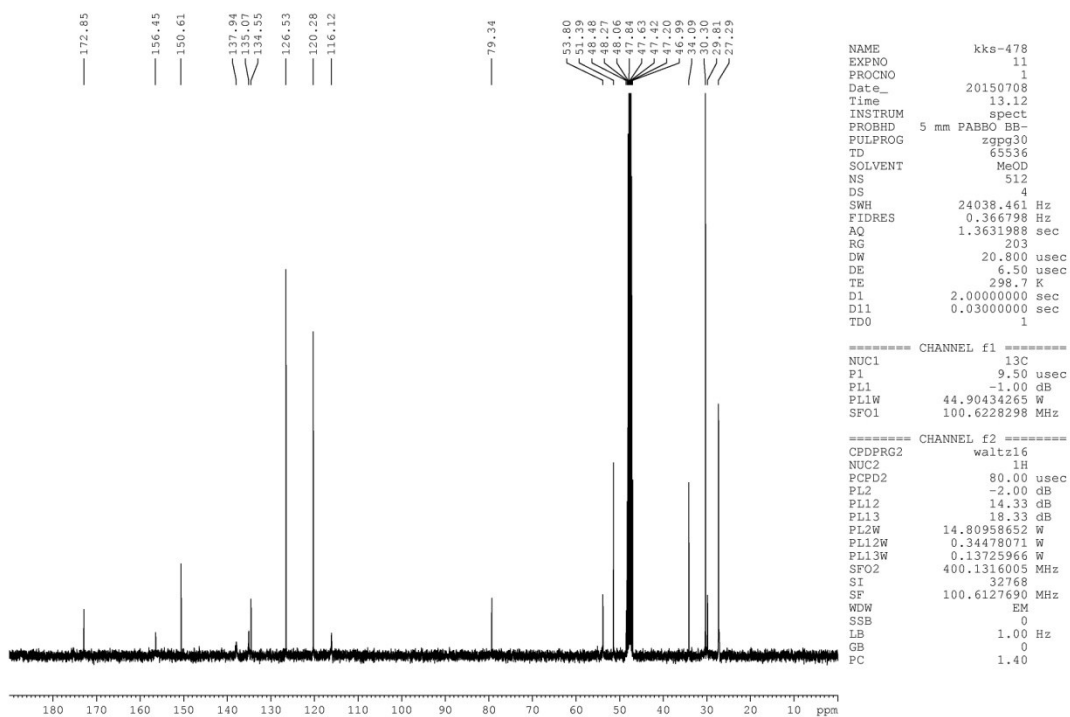


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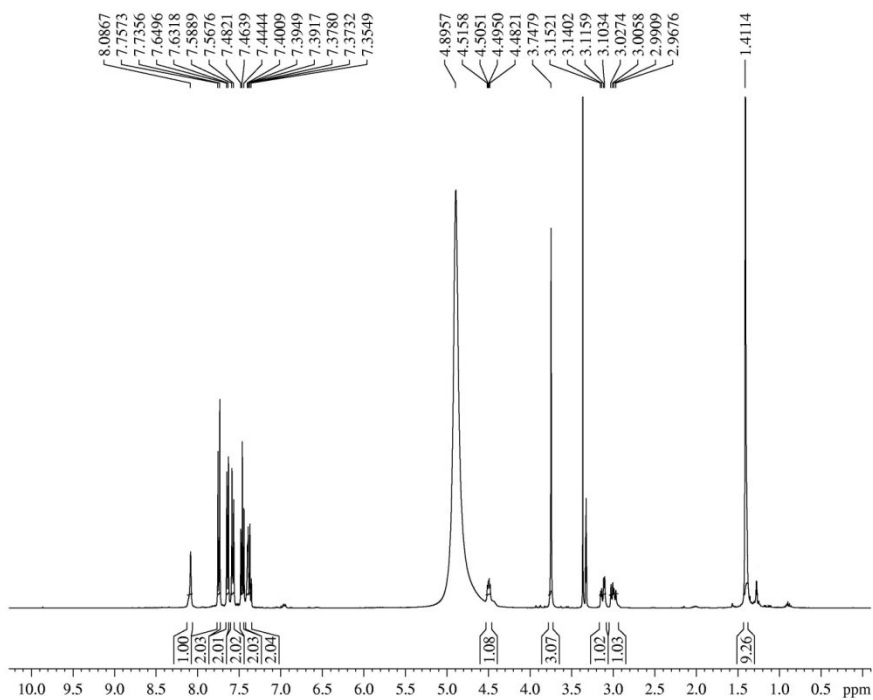
NAME          kks-478
EXPNO         10
PROCNO        1
Date_         20150707
Time          17.31
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            64
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            64
DW            60.800 usec
DE            6.50 usec
TE            297.5 K
D1            1.00000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1           -2.00 dB
PL1W          14.80958652 W
SFO1          400.1324710 MHz
SI            32768
SF            400.1300000 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            10.00

```



***N*- $\alpha$ -Boc-1-(4-biphenyl)-L-histidine methyl ester (2g)**

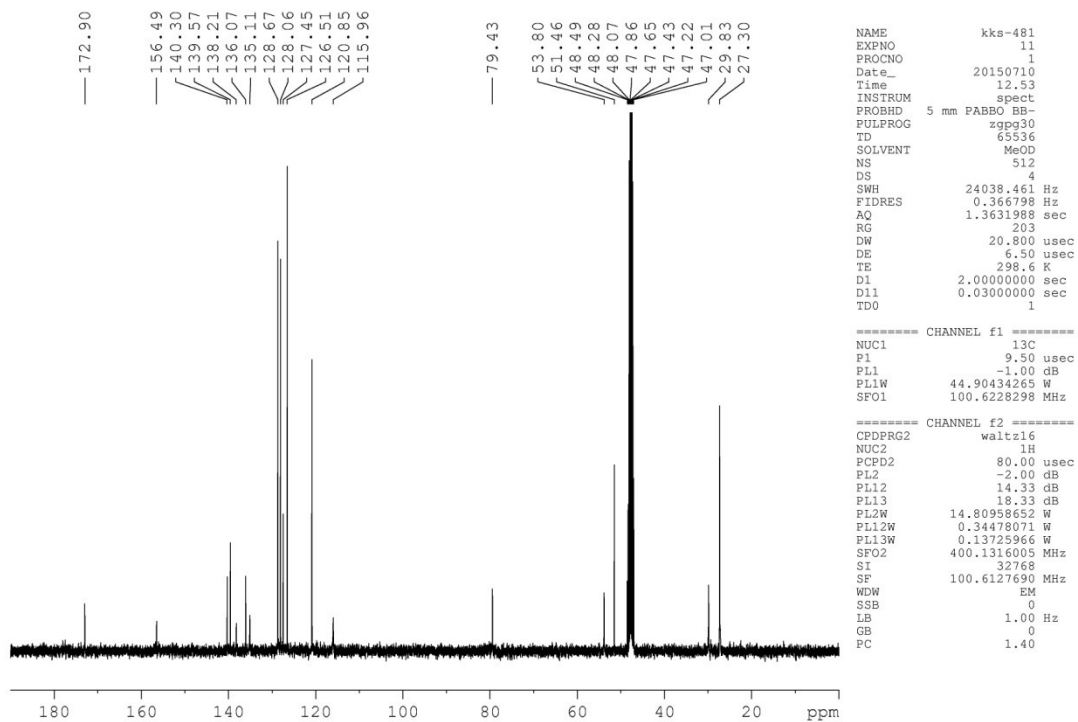


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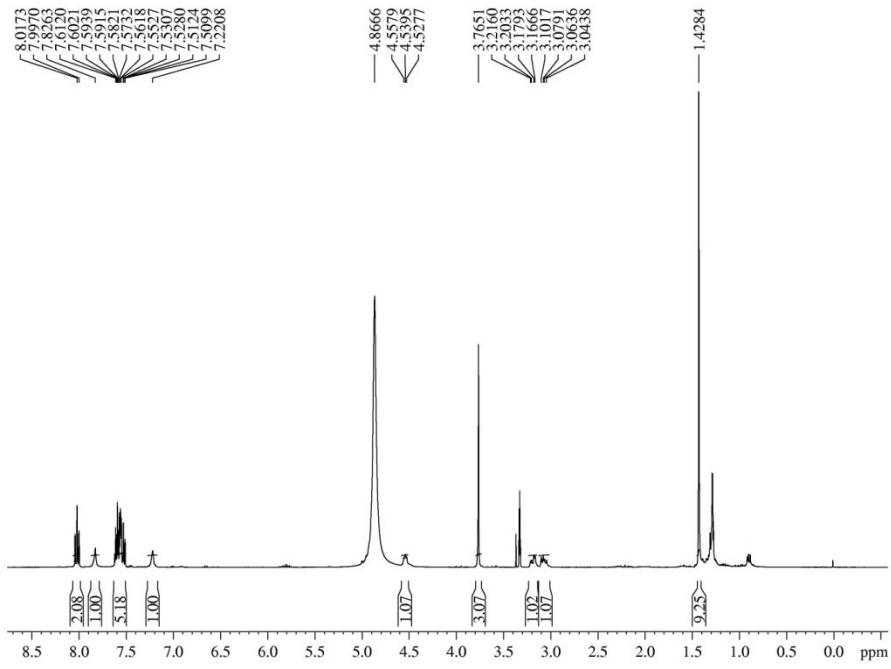
NAME          kks-481
EXPNO         10
PROCNO        1
Date_         20150710
Time          10.58
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            64
DW            60.800 usec
DE            6.50 usec
TE            297.8 K
D1            1.00000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1           -2.00 dB
PL1W          14.80958652 W
SFO1          400.1324710 MHz
SI            32768
SF            400.1300000 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            8.00

```



***N*- $\alpha$ -Boc-1-(1-naphthyl)-L-histidine methyl ester (2h)**

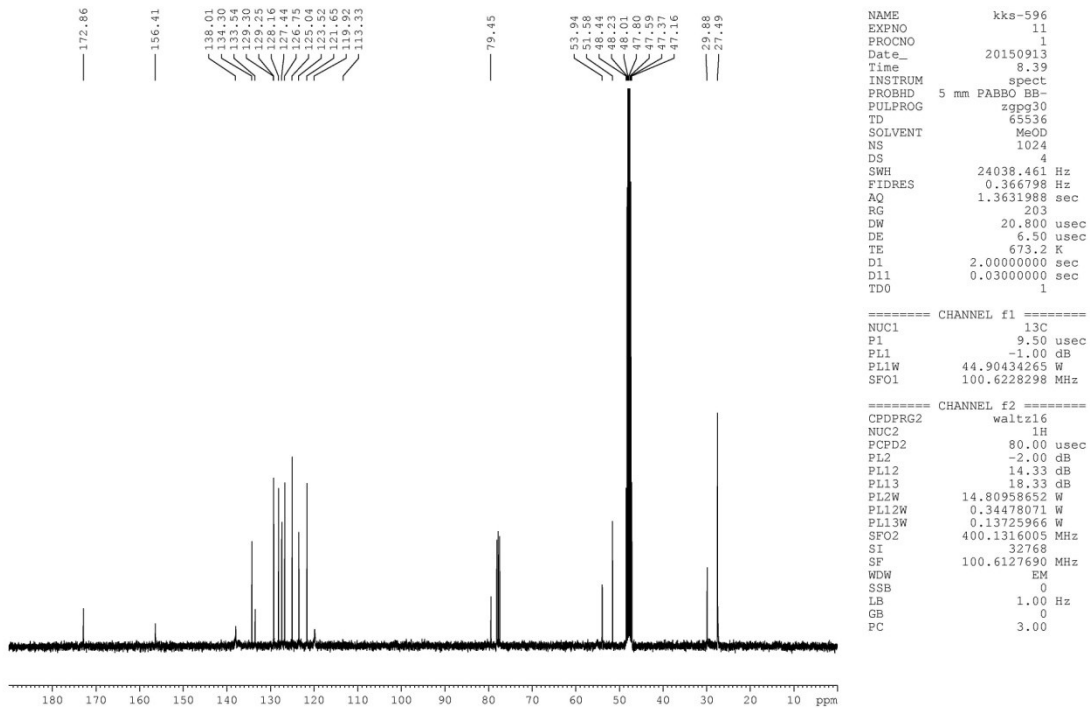


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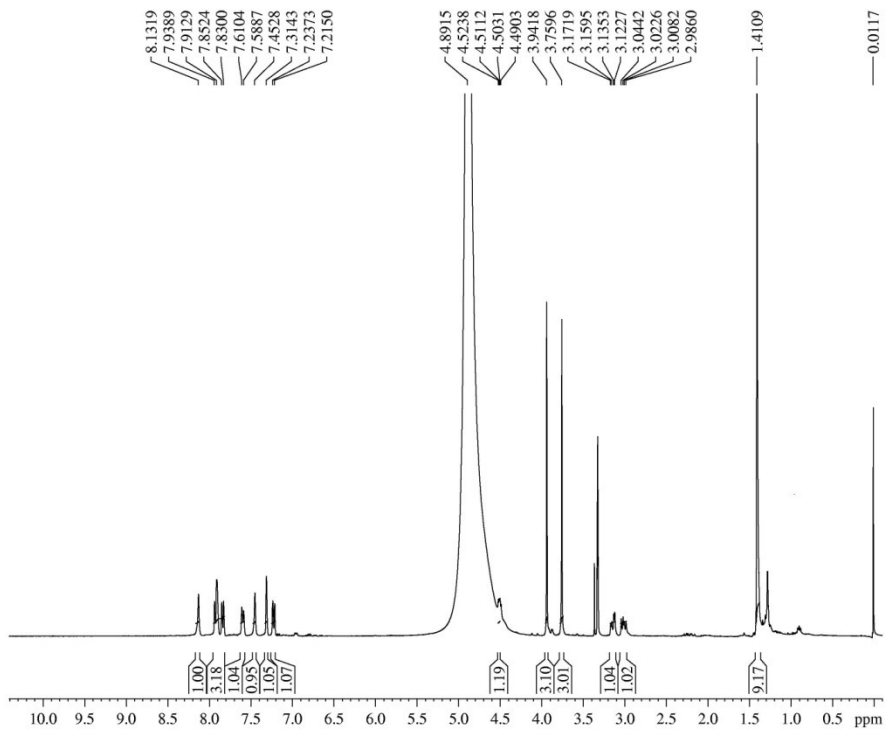
NAME          kks-596
EXPNO         10
PROCNO        1
Date_         20150913
Time          7.39
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 se
RG            90.5
DW            60.800 us
DE            6.50 us
TE            673.2 K
D1            1.00000000 se
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            12.20 us
PL1           -2.00 dB
PL1W          14.80958652 W
SFO1          400.1324710 MH
SI            32768
SF            400.1300000 MH
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.40

```



***N*- $\alpha$ -Boc-1-(6-methoxy-1-naphthyl)-L-histidine methyl ester (2i)**



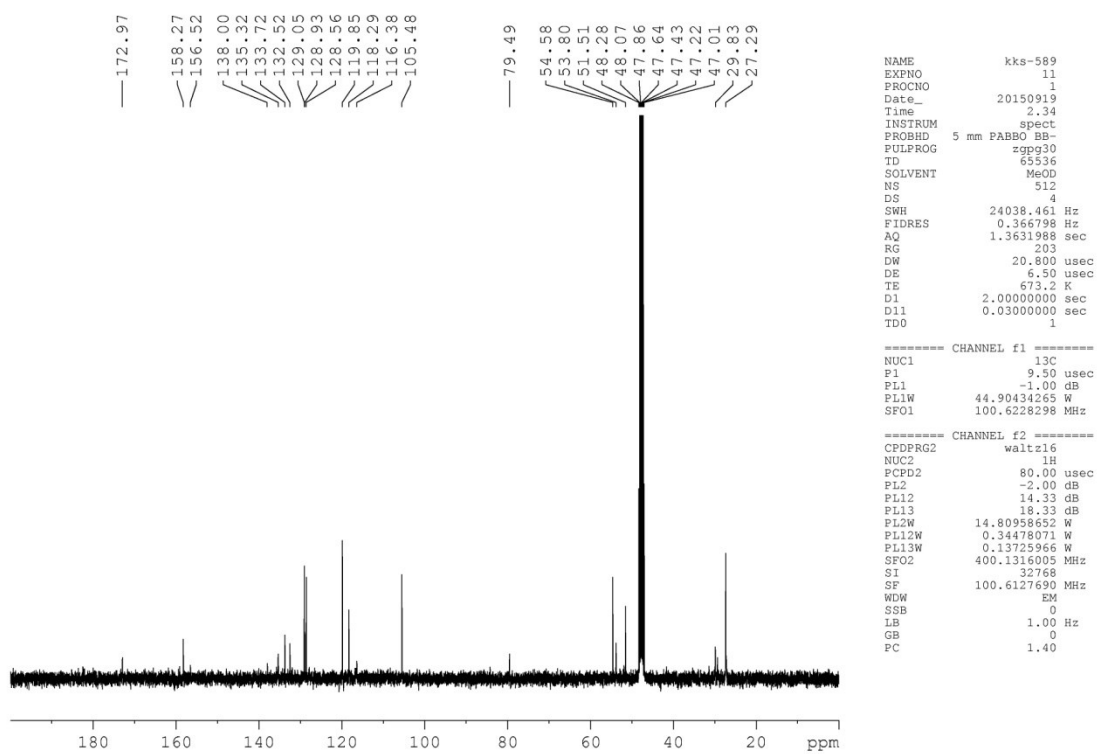
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NAME          kks-589
EXPNO         10
PROCNO        1
Date_         20150918
Time          16.42
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            71.8
DW            60.800 use
DE            6.50 use
TE            673.2 K
D1            1.00000000 sec
TDO           1

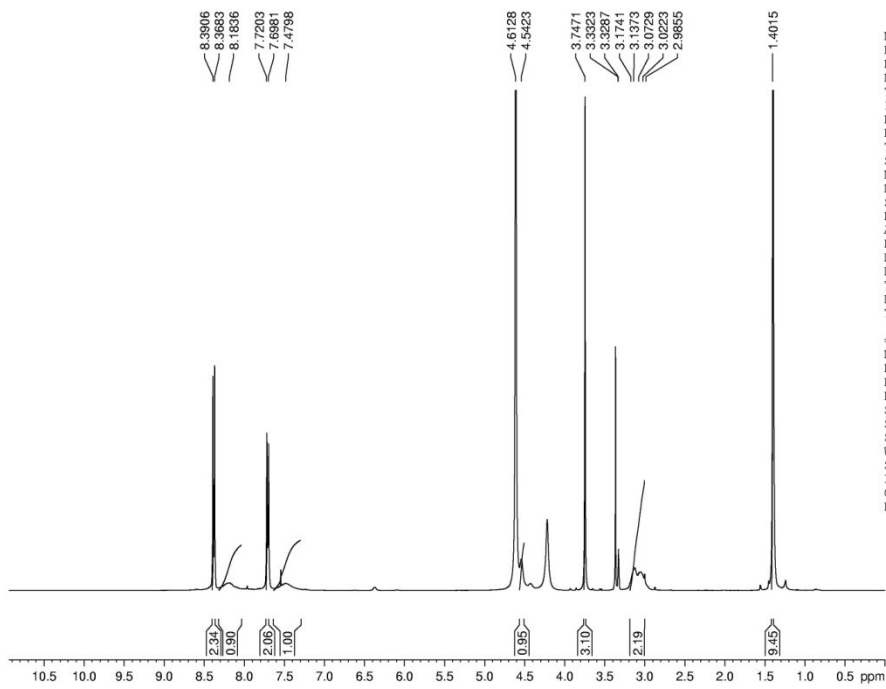
===== CHANNEL f1 =====
NUC1           1H
P1             12.20 use
PL1            -2.00 dB
PLLW          14.80958652 W
SFO1          400.1324710 MHz
SI            32768
SF            400.1300000 MHz
WDW            EM
SSB            0
LB             0.30 Hz
GB            0
PC            1.40

```





***N*- $\alpha$ -Boc-1-(4-nitrophenyl)-L-histidine methyl ester (2j)**

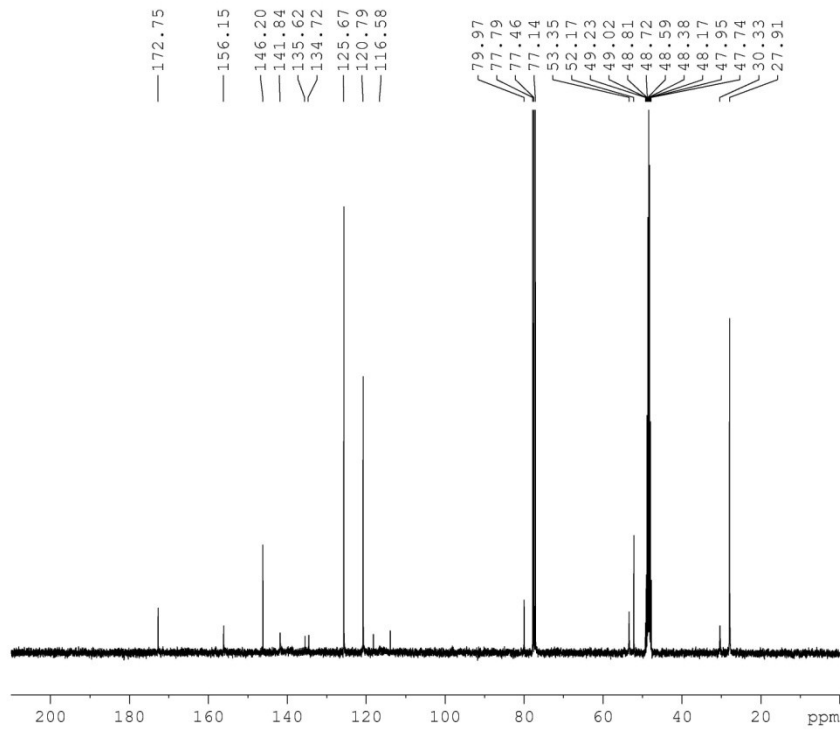


```

NAME          kks-641f
EXPNO         10
PROCNO        1
Date_         20160315
Time          13.25
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            64
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            80.6
DW            60.800 usec
DE            6.50 usec
TE            295.4 K
D1            1.00000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1           -2.00 dB
PL1W          14.80958652 W
SFO1          400.1324710 MHz
SI            32768
SF            400.1300000 MHz
WDF           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.40

```



```

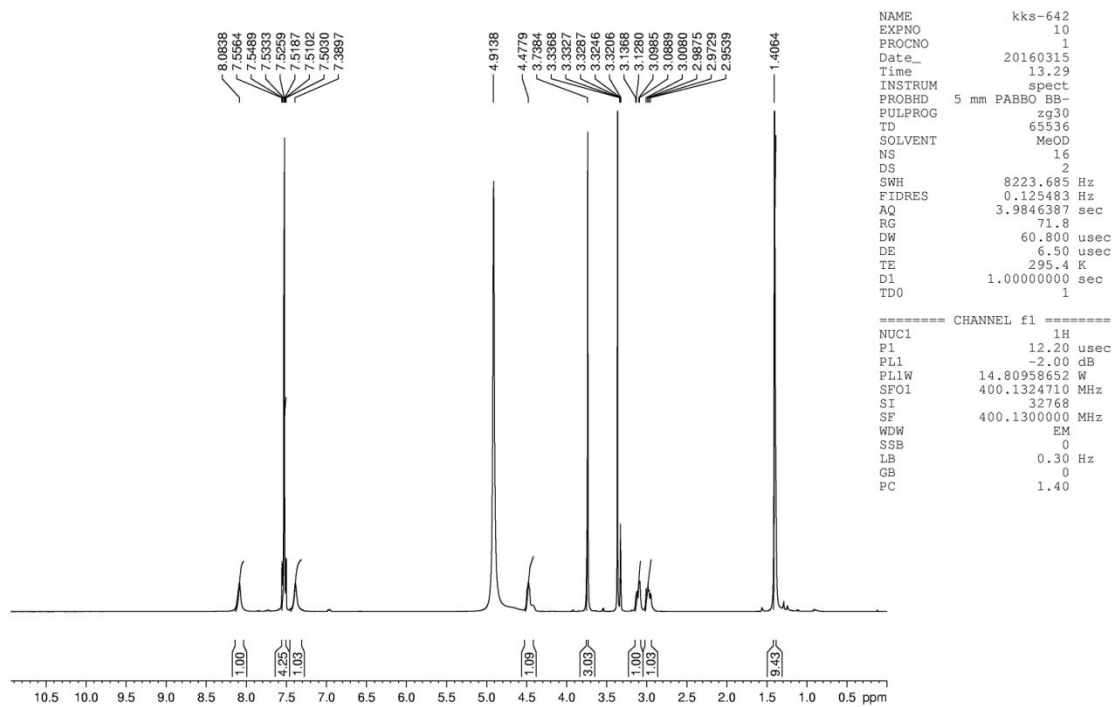
NAME          kks-641f
EXPNO         11
PROCNO        1
Date_         20160315
Time          23.30
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zgpg30
TD             65536
SOLVENT       MeOD
NS             1024
DS             4
SWH            24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631988 sec
RG             203
DW             20.800 usec
DE             6.50 usec
TE             297.1 K
D1             2.0000000 sec
D11            0.03000000 sec
TD0            1

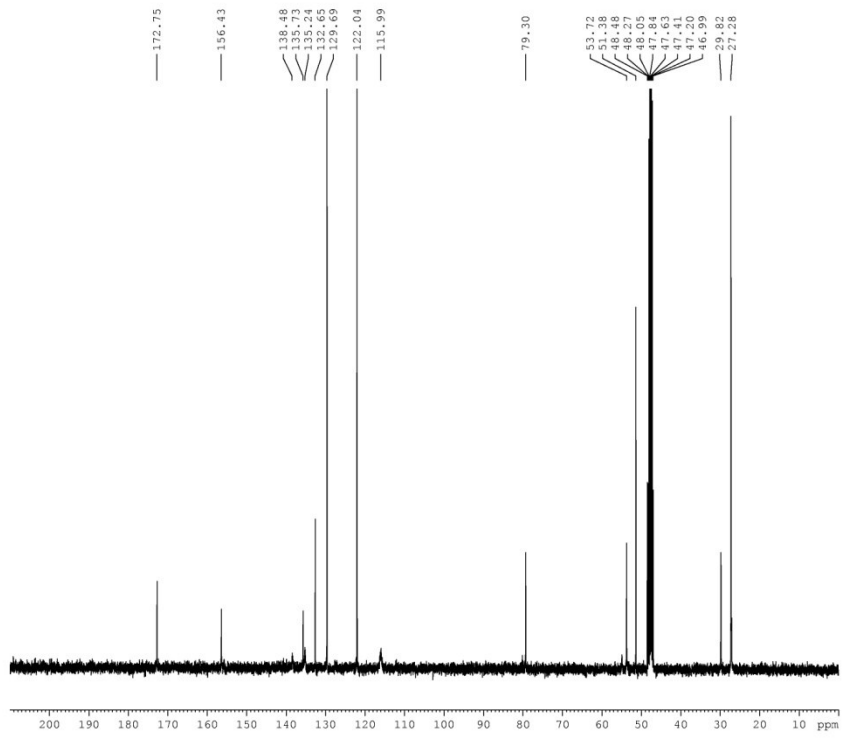
===== CHANNEL f1 =====
NUC1           13C
P1              9.50 usec
PL1             -1.00 dB
PL1W           44.90434265 W
SF01           100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2        waltz16
NUC2            1H
PCPD2           80.00 usec
PL2             -2.00 dB
PL12            14.33 dB
PL13            18.33 dB
PL2W           14.80958652 W
PL12W           0.34478071 W
PL13W           0.13725966 W
SF02           400.1316005 MHz
SI              32768
SF             100.6127690 MHz
WDW             EM
SSB             0
LB              1.00 Hz
GB              0
PC              1.40

```

**N- $\alpha$ -Boc-1-(4-chlorophenyl)-L-histidine methyl ester (2k)**





```

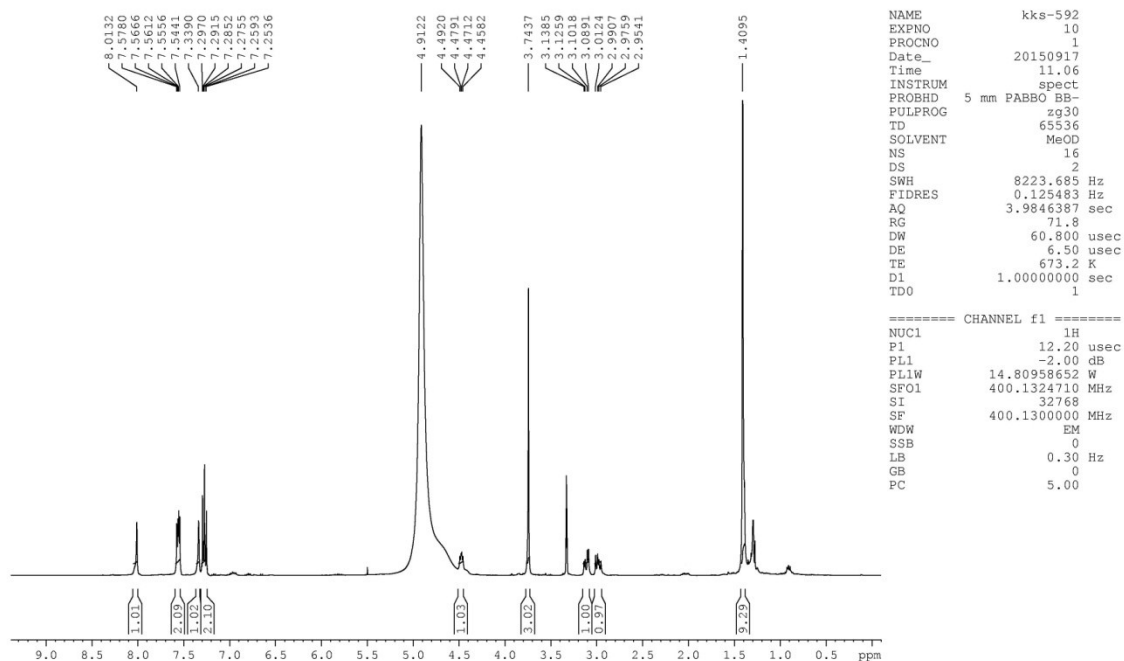
NAME          kks-642
EXPNO         11
PROCNO        1
Date_         20160315
Time          15.41
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zgpg30
TD            65536
SOLVENT       MeOD
NS            512
DS            4
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631988 sec
RG            203
DW            20.800 usec
DE            6.50 usec
TE            296.6 K
D1            2.0000000 sec
D11           0.0300000 sec
TDO           1

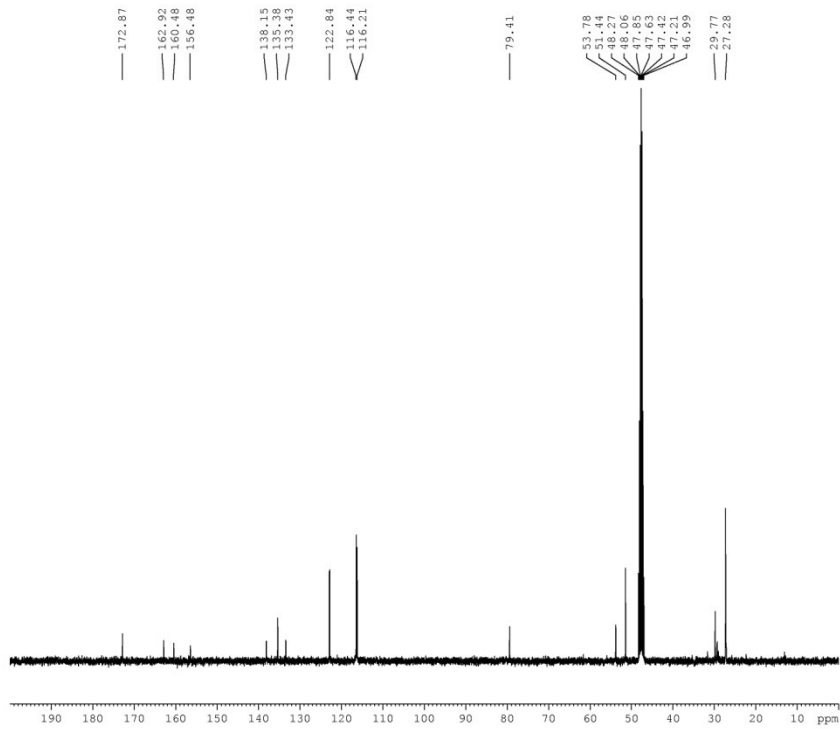
===== CHANNEL f1 =====
NUC1           13C
P1             9.50 usec
PL1            -1.00 dB
PL1W           44.90434265 W
SFO1           100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2       waltz16
NUC2           1H
PCPD2          80.00 usec
PL2            -2.00 dB
PL12           14.33 dB
PL13           18.33 dB
PL2W           14.80958652 W
PL12W          0.34478071 W
PL13W          0.13725966 W
SFO2           400.1316005 MHz
SI             32768
SF            100.6127690 MHz
WDW            EM
SSB            0
LB             1.00 Hz
GB             0
PC             1.40

```

**N- $\alpha$ -Boc-1-(4-fluorophenyl)-L-histidine methyl ester (2l)**





```

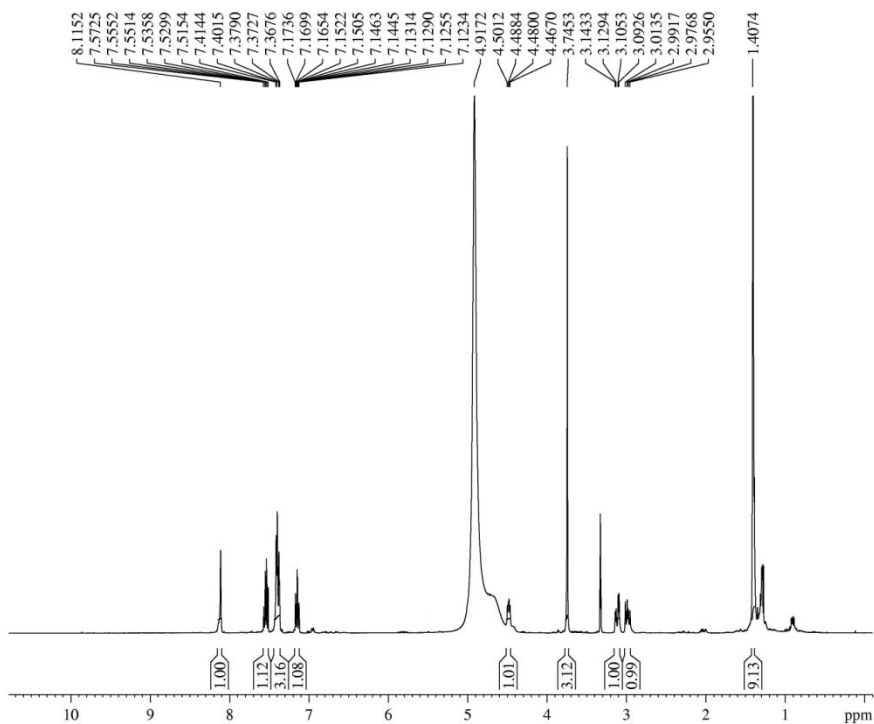
NAME          kks-592
EXPNO         11
PROCNO        1
Date_         20150917
Time          11.58
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zgpg30
TD            65536
SOLVENT       MeOD
NS            512
DS            4
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631988 sec
RG            203
DW            20.800 usec
DE            6.50 usec
TE            298.4 K
D1            2.0000000 sec
D11           0.0300000 sec
TDO           1

===== CHANNEL f1 =====
NUC1          13C
P1            9.50 usec
PL1           -1.00 dB
PL1W          44.90434265 W
SF01          100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2       waltz16
NUC2          1H
PCPD2         80.00 usec
PL2           -2.00 dB
PL12          14.33 dB
PL13          18.33 dB
PL1W          14.80958652 W
PL12W         0.34478071 W
PL13W         0.13725966 W
SF02          400.1316005 MHz
SI            32768
SF            100.6127690 MHz
WDW           EM
SSB           0
LB            1.00 Hz
GB            0
PC            1.40

```

***N*- $\alpha$ -Boc-1-(3-fluorophenyl)-L-histidine methyl ester (2m)**



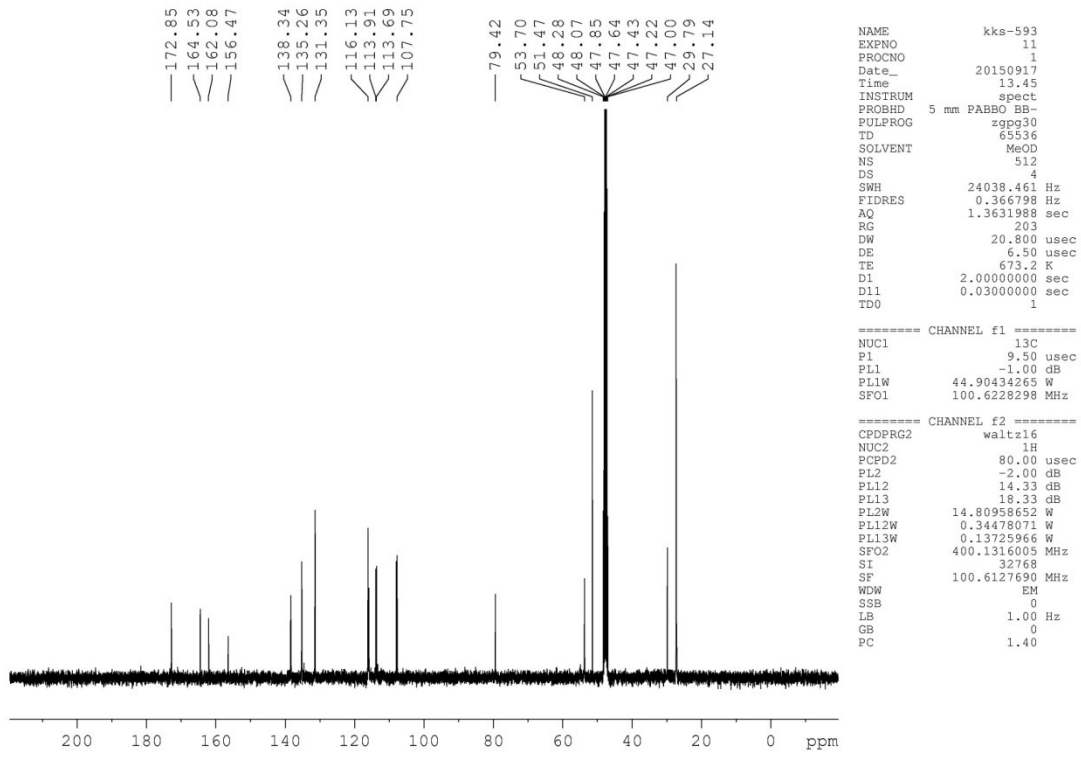
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NAME          kks-593
EXPNO         10
PROCNO        1
Date_         20150917
Time          11.11
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ           3.9846387 sec
RG            64
DW           60.800 usec
DE           6.50 usec
TE           297.2 K
D1           1.00000000 sec
TD0           1

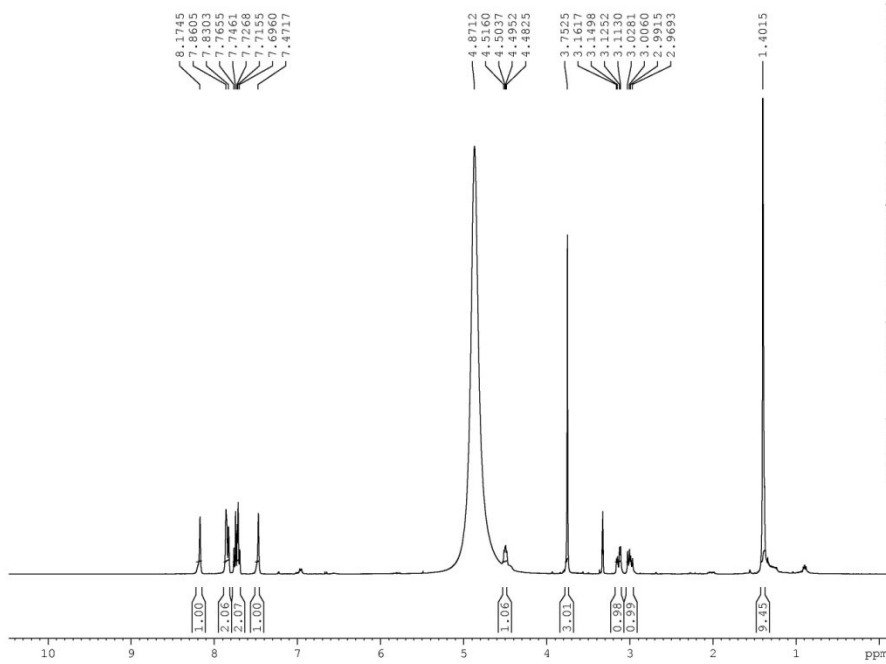
===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1          -2.00 dB
PL1W         14.80958652 W
SFO1         400.1324710 MHz
SI           32768
SF           400.1300000 MHz
WDW          EM
SSB          0
LB           0.30 Hz
GB           0
PC           1.40

```





***N*- $\alpha$ -Boc-1-(3-trifluoromethylphenyl)-L-histidine methyl ester (2n)**

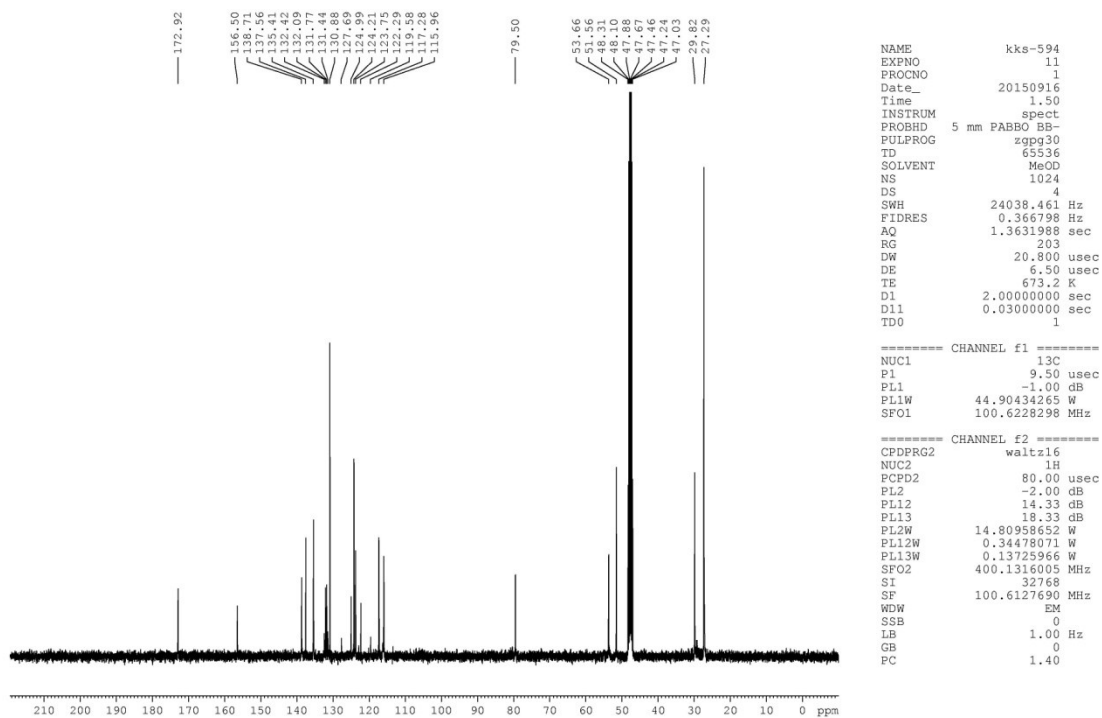


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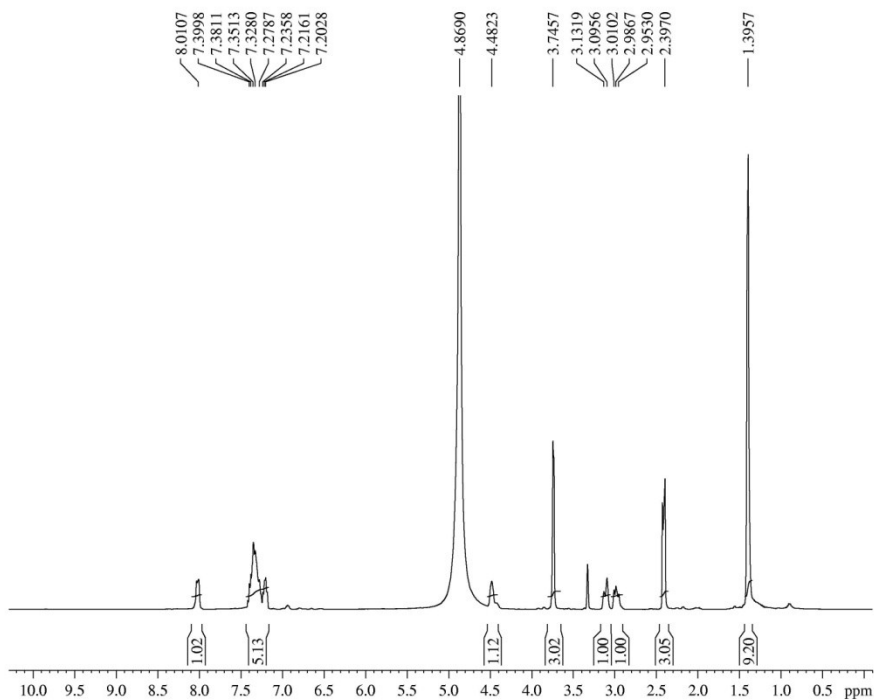
NAME          kks-594
EXPNO         10
PROCNO        1
Date_         20150915
Time          16.12
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            50.8
DW            60.800 usec
DE            6.50 usec
TE            673.2 K
D1            1.00000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1           -2.00 dB
PL1W         14.80958652 W
SFO1         400.1324710 MHz
SI            32768
SF            400.1300000 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.40

```



***N*- $\alpha$ -Boc-1-(3-methylphenyl)-L-histidine methyl ester (2o)**

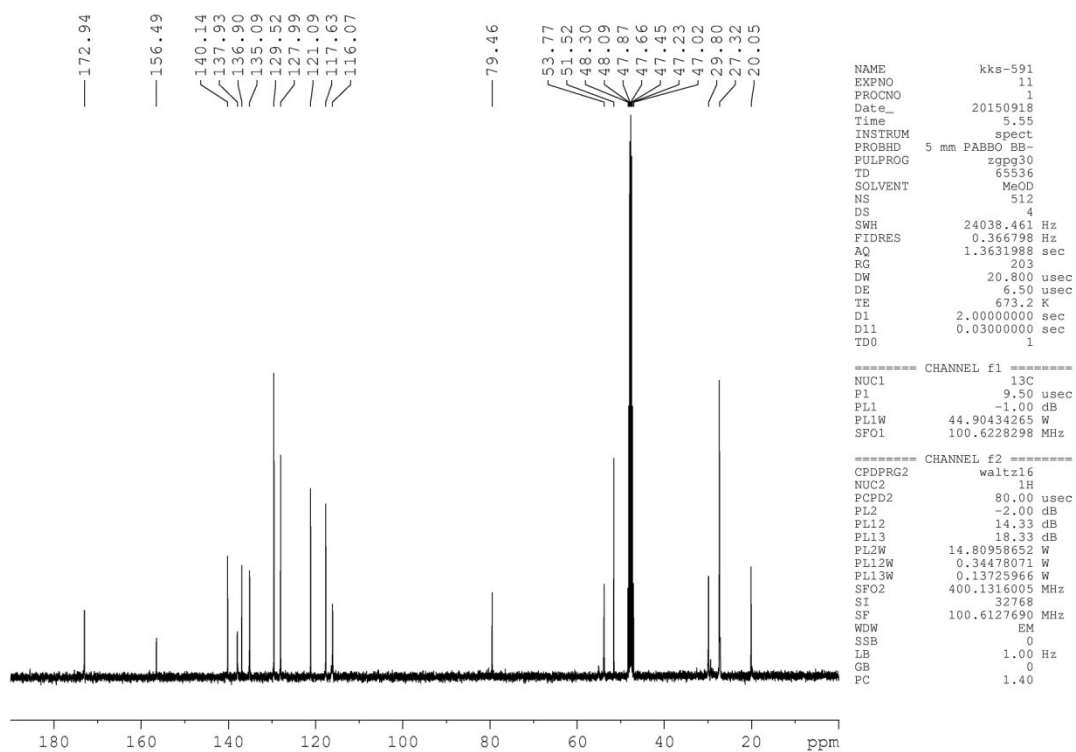


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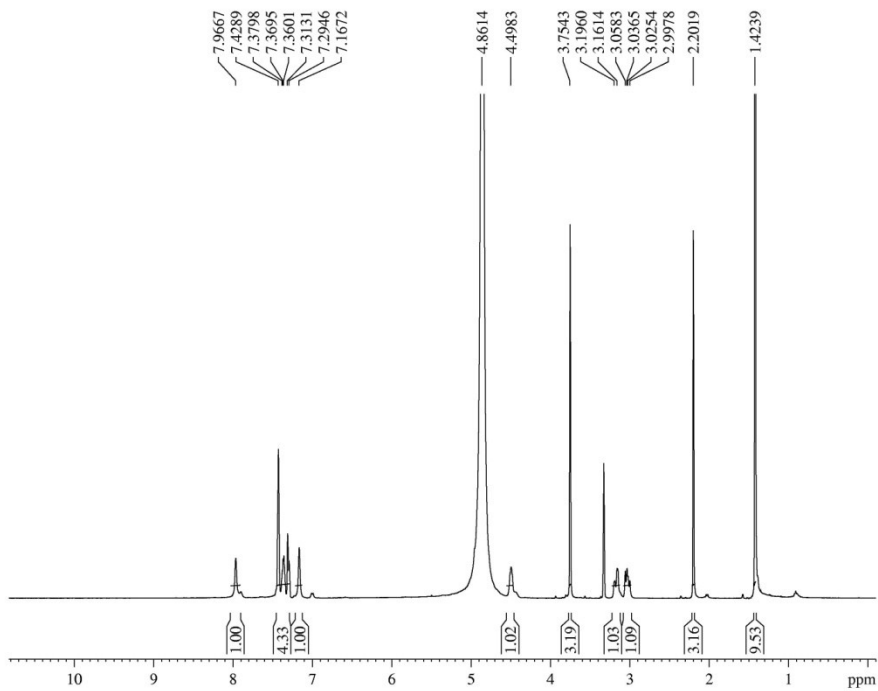
NAME          kks-591
EXPNO         10
PROCNO        1
Date_         20150917
Time          16.28
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            50.8
DW            60.800 usec
DE            6.50 usec
TE            673.2 K
D1            1.00000000 sec
TDO           1

===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1           -2.00 dB
PLLW         14.80958652 W
SFO1         400.1324710 MHz
SI           32768
SF           400.1300000 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.40

```



***N*- $\alpha$ -Boc-1-(2-methylphenyl)-L-histidine methyl ester (2p)**

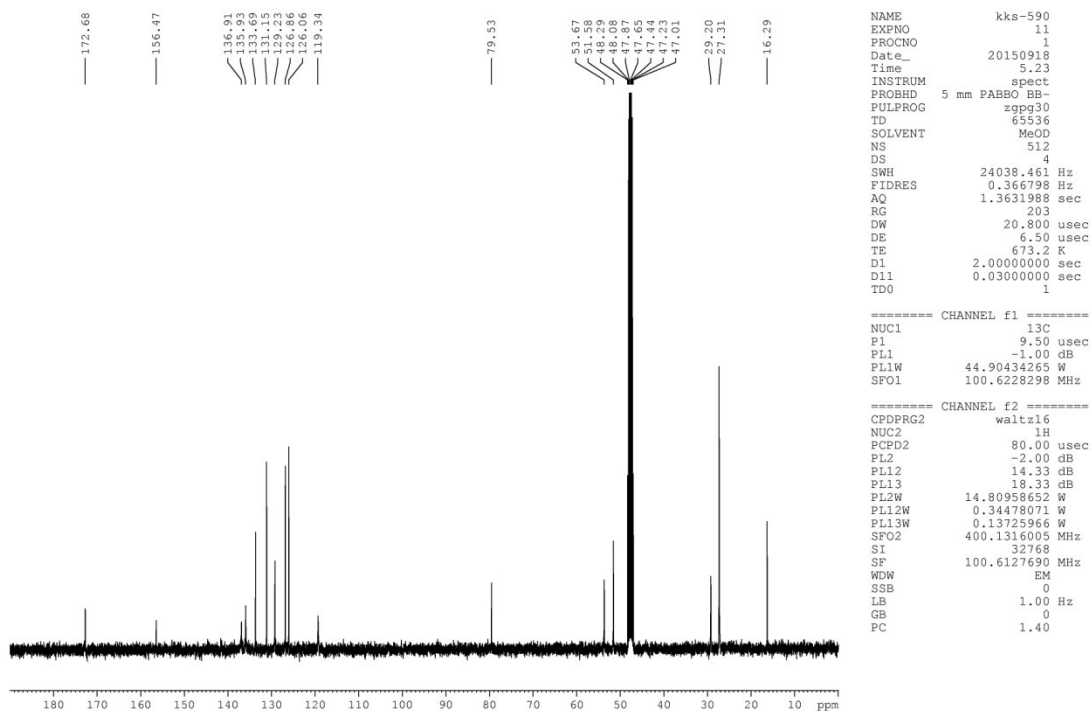


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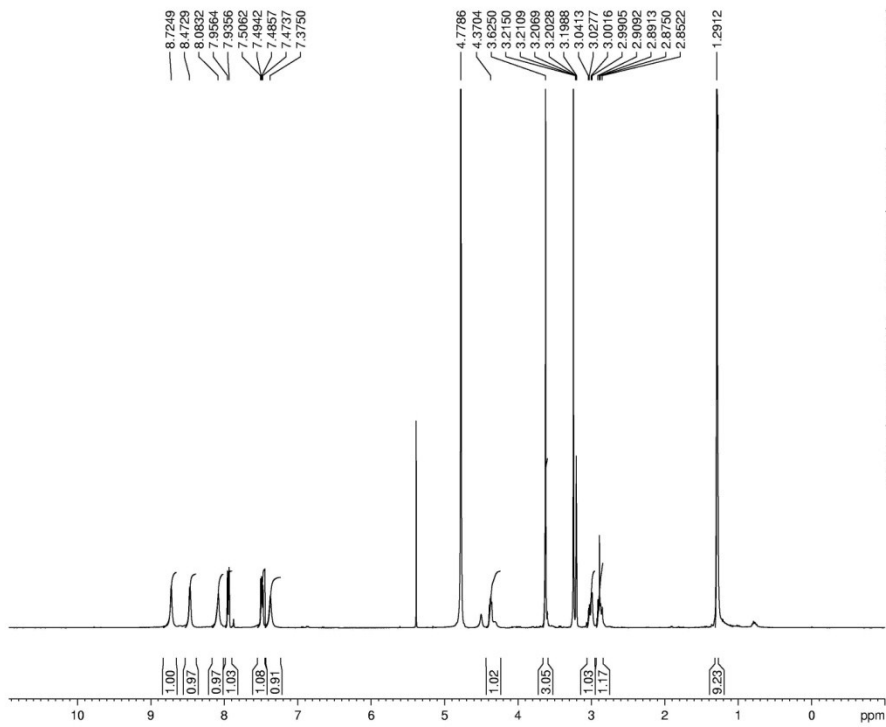
NAME          kks-590
EXPNO         10
PROCNO        1
Date_         20150917
Time          16.23
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            64
DW            60.800 usec
DE            6.50 usec
TE            673.2 K
D1            1.00000000 sec
TDO           1

===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1           -2.00 dB
PLLW          14.80958652 W
SFO1          400.1324710 MHz
SI            32768
SF            400.1300000 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            5.00

```



***N*- $\alpha$ -Boc-1-(3-pyridyl)-L-histidine methyl ester (2q)**



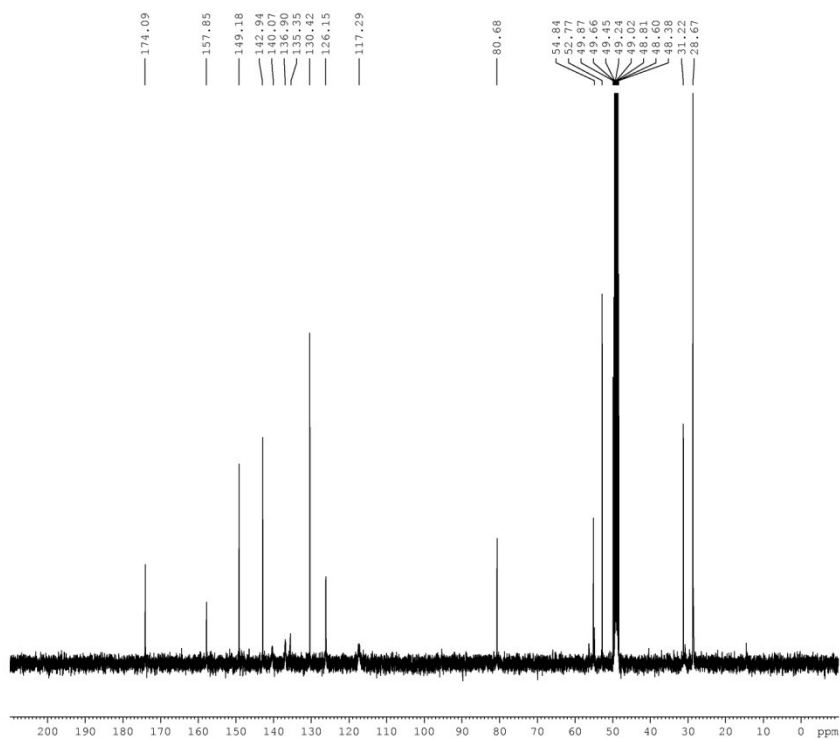
```

NAME          kks-644
EXPNO         10
PROCNO        1
Date_         20160317
Time          18.29
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            161
DW            60.800 usec
DE            6.50 usec
TE            295.9 K
D1            1.00000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1          -2.00 dB
PL1W         14.80958652 W
SFO1         400.1324710 MHz
SI           32768
SF           400.1300487 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.40

```





```

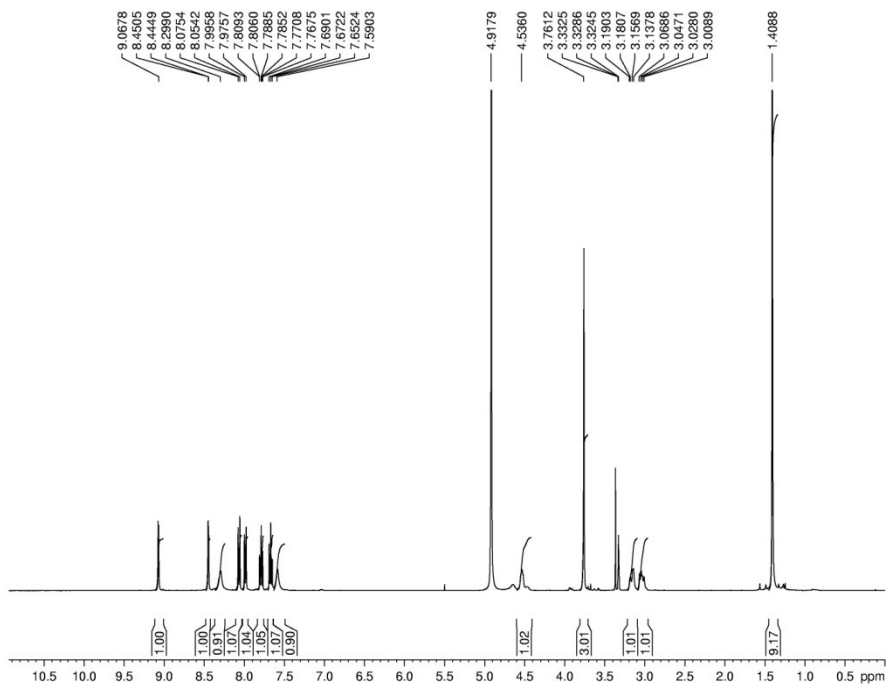
NAME          kks-644
EXPNO         11
PROCNO        1
Date_         20160317
Time_         19.28
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zgpg30
TD            65536
SOLVENT       MeOD
NS            1024
DS            4
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631988 sec
RG            203
DW            20.800 usec
DE            6.50 usec
TE            296.6 K
D1            2.0000000 sec
D11           0.0300000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          13C
P1            9.50 usec
PL1           -1.00 dB
PL1W          44.90434265 W
SFO1          100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2       waltz16
NUC2          1H
PCPD2         80.00 usec
PL2           -2.00 dB
PL12          14.33 dB
PL13          18.33 dB
PL2W          14.80958652 W
PL12W         0.34478071 W
PL13W         0.13725966 W
SFO2          400.1316005 MHz
SI            32768
SF            100.6126261 MHz
WDW           EM
SSB           0
LB            1.00 Hz
GB            0
PC            1.40

```

***N*- $\alpha$ -Boc-1-(3-quinolinyl)-L-histidine methyl ester (2r)**

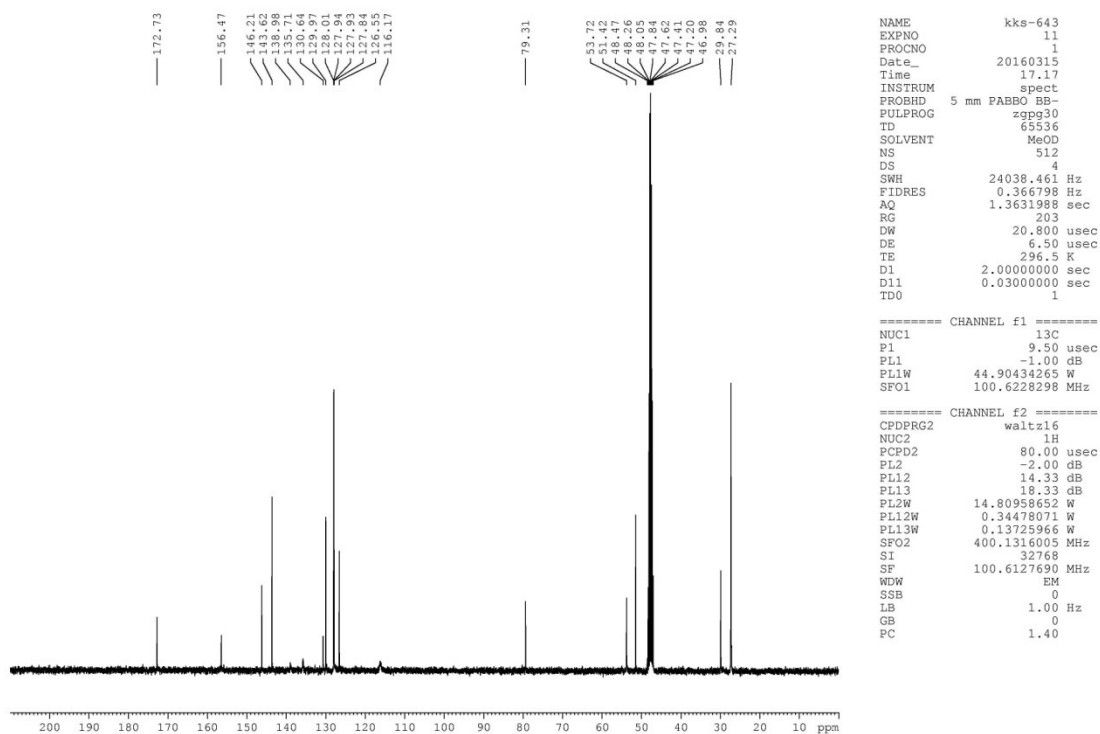


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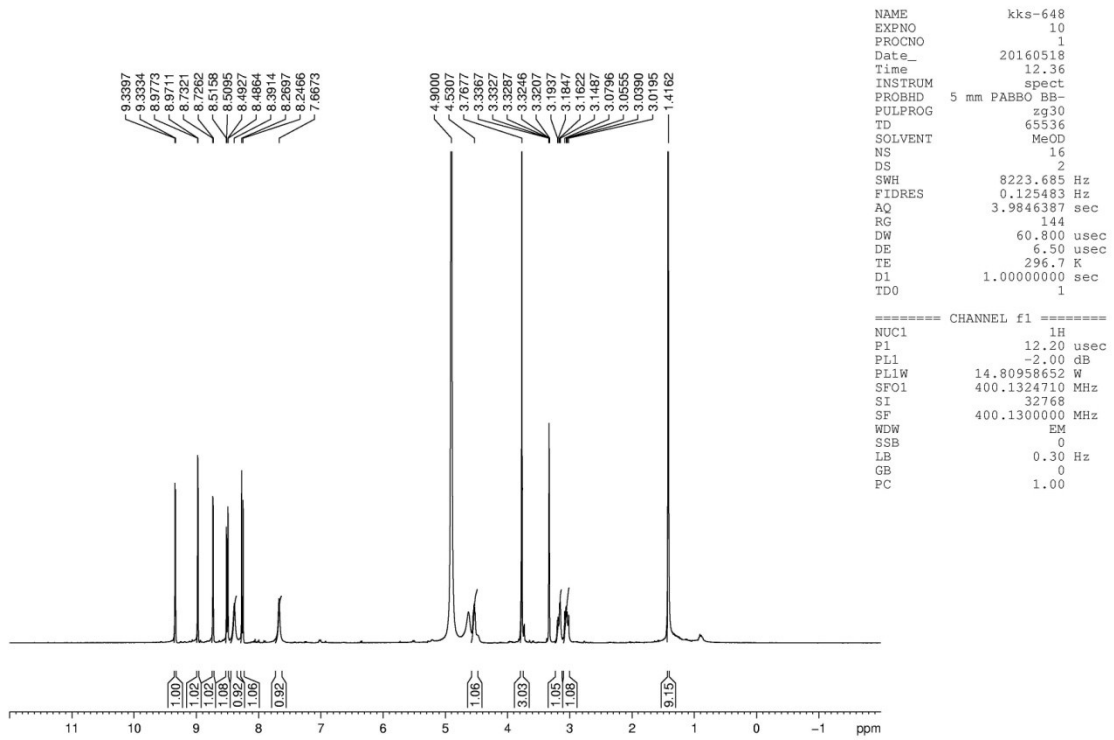
NAME          kks-643
EXPNO         10
PROCNO        1
Date_         20160315
Time          16.40
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES       0.125483 Hz
AQ           3.9846387 sec
RG            71.8
DW           60.800 usec
DE            6.50 usec
TE            295.6 K
D1           1.00000000 sec
TD0           1

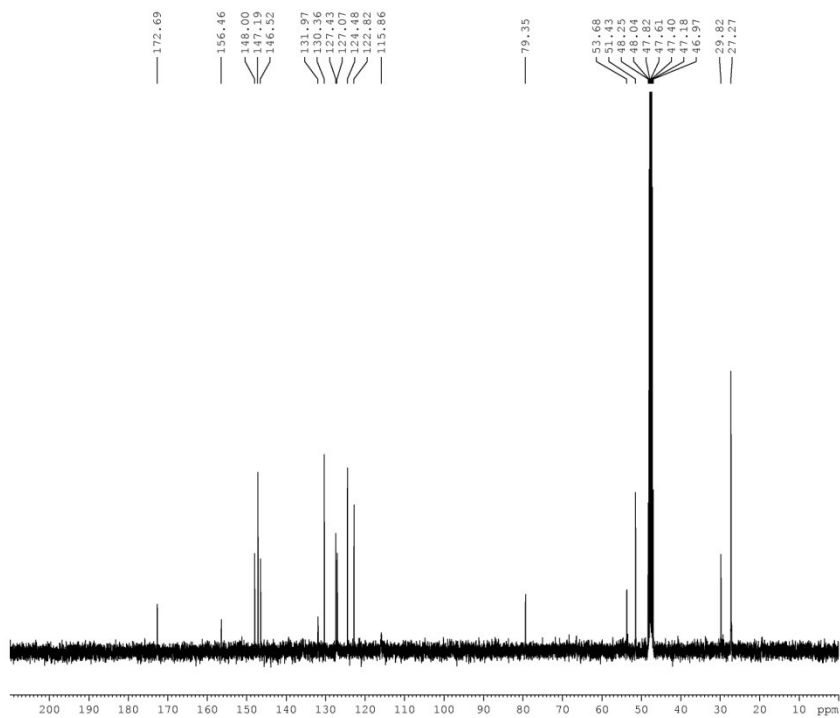
===== CHANNEL f1 =====
NUC1          1H
P1            12.20 usec
PL1           -2.00 dB
PL1W         14.80958652 W
SF01         400.1324710 MHz
SI            32768
SF           400.1300000 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.40

```

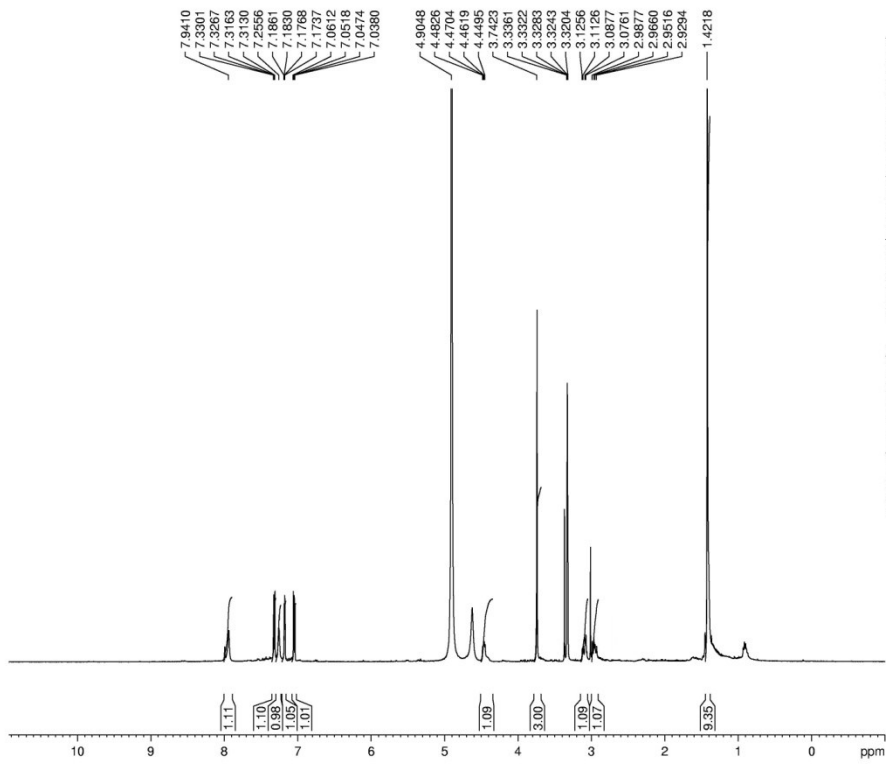


***N*-α-Boc-1-(6-nitro-3-quinolinyl)-L-histidine methyl ester (2s)**





***N*- $\alpha$ -Boc-1-(2-thiophenyl)-L-histidine methyl ester (2t)**

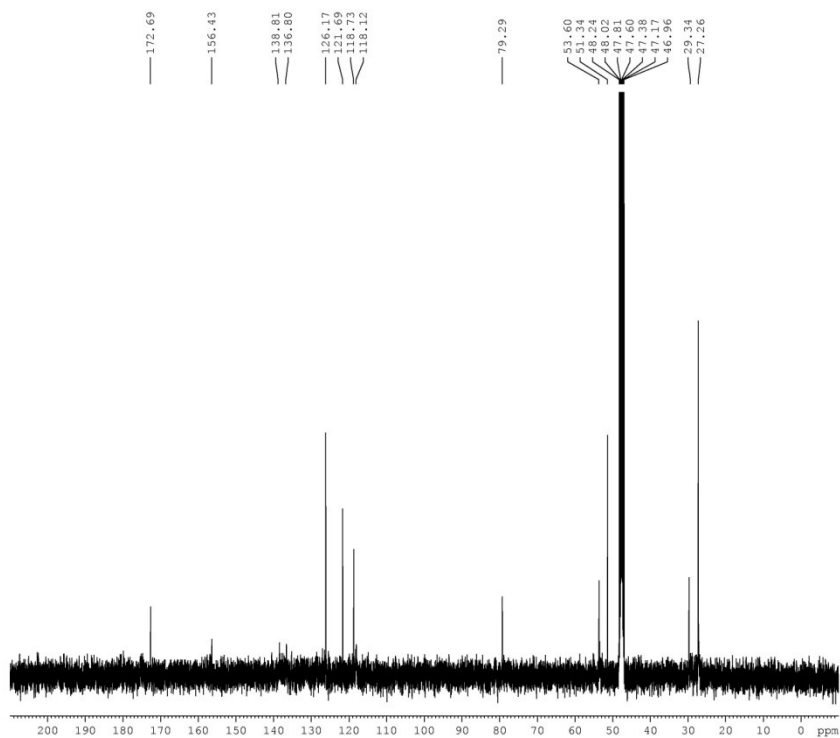


```

NAME          kks-645
EXPNO         10
PROCNO        1
Date_         20160322
Time          16.27
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zg30
TD            65536
SOLVENT       MeOD
NS            16
DS            2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9846387 sec
RG            203
DW            60.800 usec
DE            6.50 usec
TE            296.0 K
D1            1.00000000 sec
TD0           1

----- CHANNEL f1 -----
NUC1           1H
P1             12.20 usec
PL1            -2.00 dB
PLLW          14.80958652 W
SFO1          400.1324710 MHz
SI             32768
SF            400.1300000 MHz
WDW            EM
SSB            0
LB             0.30 Hz
GB             0
PC             1.40

```



```

NAME          kks-645
EXPNO         11
PROCNO        1
Date_         20160322
Time          23.21
INSTRUM       spect
PROBHD        5 mm PABBO BB-
PULPROG       zgpg30
TD            65536
SOLVENT       MeOD
NS            1024
DS            4
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631988 sec
RG            203
DW            20.800 usec
DE            6.50 usec
TE            297.1 K
D1            2.0000000 sec
D11           0.0300000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          13C
P1            9.50 usec
PL1           -1.00 dB
PL1W          44.90434265 W
SFO1          100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2       waltz16
NUC2          1H
PCPD2         80.00 usec
PL2           -2.00 dB
PL12          14.33 dB
PL13          18.33 dB
PL2W          14.80958652 W
PL12W         0.34478071 W
PL13W         0.13725966 W
SFO2          400.1316005 MHz
SI            32768
SF            100.6127690 MHz
WDW           EM
SSB           0
LB            1.00 Hz
GB            0
PC            1.40

```

### 3. Chiral HPLC study

Compound **2a**, Boc-D-His(1-phenyl)-OMe and Boc-DL-His(1-phenyl)-OMe were synthesized under optimized reaction conditions, and subjected to full deprotection under 7N HCl at 100 °C for 12 h. The compounds L-His(1-phenyl)-2HCl, D-His(1-phenyl)-2HCl and DL-His(1-phenyl)-2HCl were analyzed by chiral HPLC.

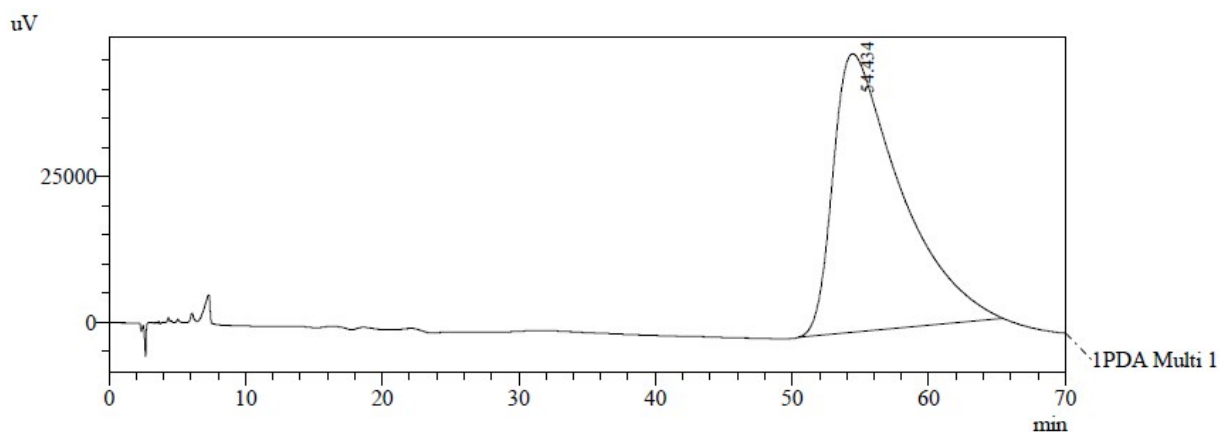


Figure 1. Chiral HPLC chromatogram of L-His(1-phenyl)-2HCl

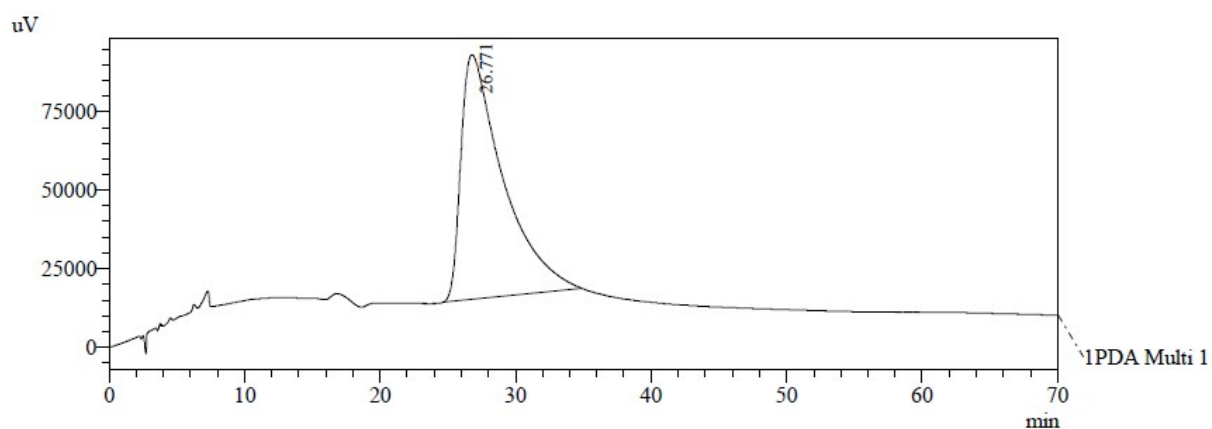
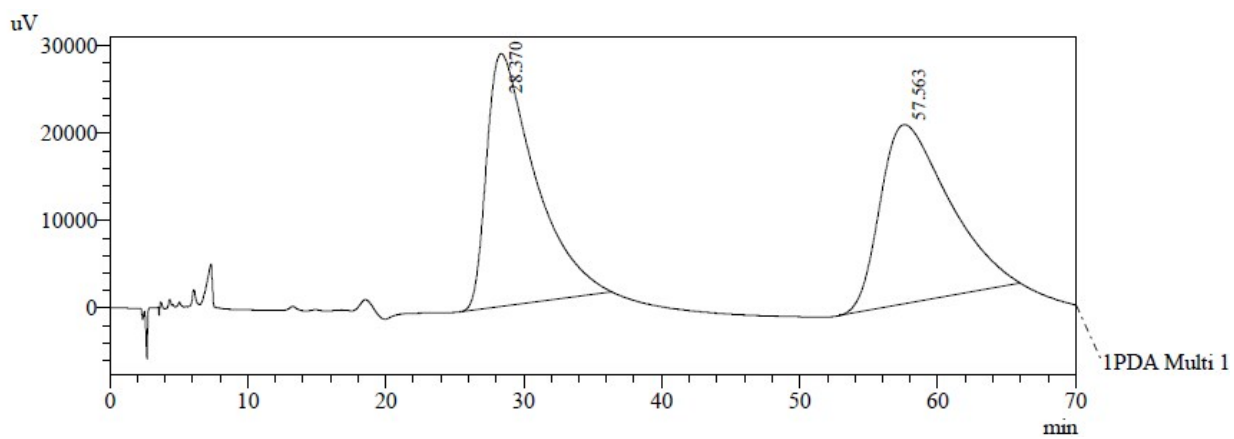


Figure 2. Chiral HPLC chromatogram of D-His(1-phenyl)-2HCl





**Figure 3. Chiral HPLC chromatogram of DL-His(1-phenyl)-2HCl**