Supporting Information

Unveiling the choline chloride–thiourea (1 : 1) DES as a greener medium and reagent for pyrimidinethione synthesis from α,β-unsaturated carbonyl compounds

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General Considerations

All reactions were carried out in a 5 ml single-neck R.B. flask. The starting material chalcones were synthesized from corresponding acetophenones and benzaldehydes under basic conditions reported elsewhere in the literature. Acetophenones, benzaldehydes, ethanol, choline chloride, thiourea, and all other general laboratory chemicals were purchased from Sigma-Aldrich, Alfa Aesar, and other local suppliers. Reactions were monitored by thin layer chromatography (TLC) on pre-coated silica gel (Merck silica gel 60, F_{254}) plates and visualized under UV light.

Analytical Methods

NMR data were obtained on Jeol 400 MHz, Bruker 400 MHz and Bruker 500 MHz spectrometers. All compounds were characterized by ^{1}H, ^{13}C and ^{19}F NMR (399.78 MHz and 500 MHz, 100.5 MHz and 125 MHz, and 376.17 MHz respectively), and HRMS. HRMS (ESI) measurements were performed on an Agilent 6530 Accurate-Mass Q-TOF LC/MS. FT-IR spectrum was recorded on Thermo Scientific Nicolet iS50 FT-IR by ATR method. Copies of ^{1}H, ^{13}C and ^{19}F NMR spectra can be found at the end of the Supporting Information. All ^{1}H, ^{13}C and ^{19}F chemical shifts are reported in parts per million (PPM) and were measured relative to TMS or residual deuterated $CDCl_3$ and DMSO-D_6 as solvent. Yields are referred to the isolated compounds.

General Procedure for the Preparation of Choline chloride-Thiourea (CC:TU) DES

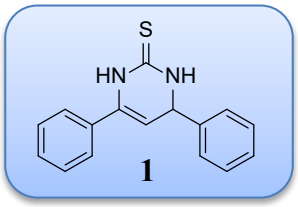
In a 100 mL single-neck R. B. flask was charged with choline chloride (10 g, 72 mmol, 1.0 equiv.) and thiourea (5.48 g, 72 mmol, 1.0 equiv.) and a magnetic stir bar. The flask was placed on a pre-heated oil bath at 75 ºC and stirred for 1.0 h to get CC:TU (1:1) DES as a clear colourless viscous liquid. The CC:TU was found to be a liquid DES at room temperature.[1]

General Procedure for the Preparation of Pyrimidinthione from Chalcones

In a 5.0 mL single-neck R. B. flask was charged with chalcones (0.5 mmol 1.0 equiv), thiourea (0.6 mmol, 1.2 equiv), CC:TU (1:1) DES, 1.5 mL, choline hydroxide base (45% in water) 0.2-0.3 mL, and a magnetic stir bar. The R. B. flask was then placed on a pre-heated oil bath at 75 ºC and stirred for 1 h to 26 h until all the starting material was consumed. Once the reaction was complete, judged by TLC, the reaction mixture was quenched in 25 mL of cold water and the precipitated solid was filtered and dried well, and no further purification was required.

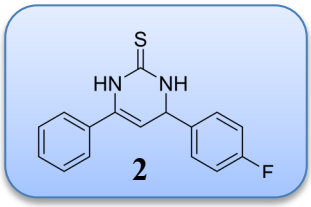
Analytical Data for the Synthesized Compounds

4,6-Diphenyl-3,4-dihydropyrimidine-2(1*H*)-thione (1)



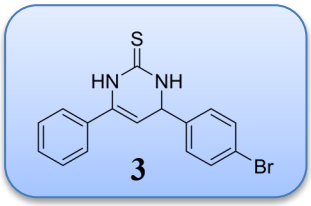
The general procedure described was followed to get the title compound from (*E*)-chalcone (104.1 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 2 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (84 mg, 63% yield, pale yellow): **^{1}H NMR (400 MHz, $CDCl_3$)** δ/ppm: 5.20 (s, 1H), 5.27 (s, 1H), 7.15 (s, 1H), 7.33-7.41 (m, 10H), 7.80 (s. 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ/ppm: 57.30, 100.79, 125.36, 127.04, 128.71, 129.12, 129.26, 129.67, 133.43, 134.12, 142.43, 175.37. **HRMS-ESI**: m/z calcd for **$C_{16}H_{14}N_2S$** $[M + H]^+$ 267.0956, found 267.0970, $[M + Na]^+$ 289.0770, found 289.0785.

4-(4-Fluorophenyl)-6-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione (2)



The general procedure described was followed to get the title compound from (*E*)-3-(4-fluorophenyl)-1-phenylprop-2-en-1-one (113.13 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 2 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (82.2 mg, 58% yield): **^{1}H NMR (500 MHz, DMSO-d$_6$)** δ/ppm: 4.14 (s, 1H), 4.39 (s, 1H), 6.23 (t, 2H, J = 4.5 Hz), 6.36-6.39 (m, 5H), 6.50 (m, b, 2H), 8.12 (s, 1H), 8.87 (s, 1H); **^{13}C NMR (125 MHz, DMSO-d$_6$)** δ/ppm: 53.97, 101.11, 115.57 (d, $J_{C\text{-}F}$ = 21.9 Hz), 125.99, 128.55, 128.61, 129.05, 133.31, 134.61, 140.35, 175.11; **^{19}F NMR (376 MHz, DMSO-d$_6$)** δ/ppm: -114.77 (m, 1F). **HRMS-ESI**: m/z calcd for **C$_{16}$H$_{13}$FN$_2$S** $[M + H]^+$ 285.0862, found 285.0859.

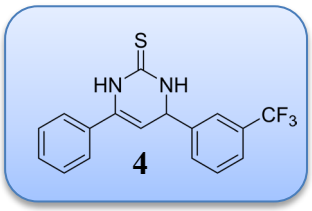
4-(4-Bromophenyl)-6-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione (3)



The general procedure described was followed to get the title compound from (*E*)-3-(4-bromophenyl)-1-phenylprop-2-en-1-one (143.5 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 1.5 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (149.1 mg, 88% yield): **^{1}H NMR (500 MHz, DMSO-d$_6$)** δ/ppm: 5.12-5.13 (m, b, 1H), 5.38 (d, 1H, J = 6.0 Hz), 7.28 (d, 2H, J = 10.5 Hz), 7.36-7.38 (m, 3H), 7.49-7.51 (m, 2H), 7.60 (d, 2H, J = 10.5 Hz), 9.15 (s, 1H), 9.93 (s, 1H); **^{13}C NMR (125 MHz, DMSO-d$_6$)** δ/ppm: 53.99, 100.74, 120.74, 126.00, 128.46, 128.67, 129.00, 131.67, 133.25, 134.69,

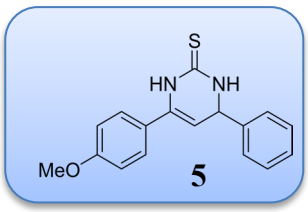
143.44, 175.24. **HRMS-ESI**: m/z calcd for **$C_{16}H_{13}BrN_2S$** $[M + H]^+$ 345.0056, found 345.0054, $[M + Na]^+$ 366.9875, found 366.9907.

6-Phenyl-4-(3-(trifluoromethyl)phenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (4)



The general procedure described was followed to get the title compound from (*E*)-1-phenyl-3-(3-(trifluoromethyl)phenyl)prop-2-en-1-one (138.13 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 3 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (101.5 mg, 61% yield): **^{1}H NMR (500 MHz, DMSO-d_6)** δ/ppm: 4.28 (d, 1H, *J* = 5.5 Hz), 4.48 (d, 1H, *J* = 5.5 Hz), 6.39-6.40 (m, 4H), 6.51-6.52 (m, 2H), 6.67 (b, 4H), 8.21 (s, 1H), 8.97 (s, 1H); **^{13}C NMR (125 MHz, DMSO-d_6)** δ/ppm: 54.09, 100.63, 122.91, 122.94, 124.47, 126.03, 128.57, 129.15, 130.09, 130.64, 133.18, 135.00, 145.40, 175.52; **^{19}F NMR (376 MHz, DMSO-d_6)** δ/ppm: -61.04 (s, 3F). **HRMS-ESI**: m/z calcd for **$C_{17}H_{13}F_3N_2S$** $[M + H]^+$ 335.0830, found 335.0835, $[M + Na]^+$ 357.0644, found 357.0657.

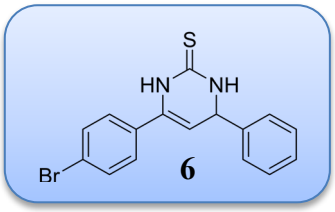
6-(4-Methoxyphenyl)-4-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione (5)



The general procedure described was followed to get the title compound from (*E*)-1-(4-methoxyphenyl)-3-phenylprop-2-en-1-one (119.1 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.0 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 26 h. The crude reaction mixture was quenched with 25 mL of water and the

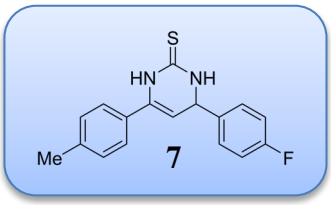
precipitated solid was filtered and dried (94.8 mg, 98% yield): **^{1}H NMR (400 MHz, $CDCl_3$)** δ/ppm: 3.76 (s, 3H), 5.05 (s, 1H), 5.20 (s, 1H), 6.60 (s, b, 1H), 6.84 (d, 2H, ^{3}J = 8.8 Hz), 7.27-7.34 (m, 7H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ/ppm: 55.56, 57.53, 99.43, 114.55, 126.64, 127.04, 128.80, 129.34, 133.64, 142.53, 160.76, 175.58. **HRMS-ESI**: m/z calcd for **$C_{17}H_{16}N_2OS$** $[M + H]^+$ 297.1056, found 296.1061, $[M + Na]^+$ 319.0876, found 319.0878.

6-(4-Bromophenyl)-4-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione (6)



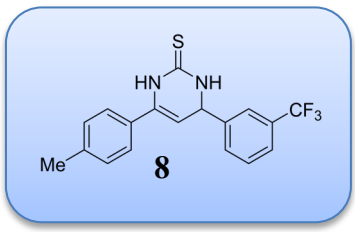
The general procedure described was followed to get the title compound from (*E*)-1-(4-bromophenyl)-3-phenylprop-2-en-1-one (143.45 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 7 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (134.3 mg, 79% yield): **^{1}H NMR (400 MHz, $CDCl_3$)** δ/ppm: 5.13 (s, b, 1H), 5.21 (s, b, 1H), 7.24 (d, 2H, *J* = 8.8 Hz), 7.28-7.30 (m, 4H), 7.33-7.36 (m, 3H), 7.46 (d, 2H, *J* = 8.4 Hz); **^{13}C NMR (100 MHz, $CDCl_3$)** δ/ppm: 57.42, 101.25, 126.90, 126.98, 128.92, 129.40, 132.40, 133.17, 142.14, 175.60. **HRMS-ESI**: m/z calcd for **$C_{16}H_{13}BrN_2S$** $[M + H]^+$ 345.0061, found 345.0058, $[M + Na]^+$ 366.9881, found 366.9854.

4-(4-Fluorophenyl)-6-(*p*-tolyl)-3,4-dihydropyrimidine-2(1*H*)-thione (7)



The general procedure described was followed to get the title compound from (*E*)-3-(4-fluorophenyl)-1-(p-tolyl)prop-2-en-1-one (112.14 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 7.5 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (78.7 mg, 94% yield): **^{1}H NMR (400 MHz, CDCl$_3$)** δ/ppm: 2.35 (s, 3H), 5.12 (s, 1H), 5.24 (d, 1H, *J* = 4.6 Hz), 7.05 (t, 2H, *J* = 8.4 Hz), 7.07 (s, 1H), 7.12 (s, 1H), 7.18 (d, 2H, *J* = 8.0 Hz), 7.29-7.34 (m, 4H), 7.76 (s, 1H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ/ppm: 21.27, 56.49, 99.73, 116.06 (d, $J_{C\text{-}F}$ = 21.9 Hz), 125.06, 128.79 (d, $J_{C\text{-}F}$ = 9.1 Hz), 129.72, 130.28, 134.06, 138.36 (d, $J_{C\text{-}F}$ = 3.1 Hz), 139.86, 162.7 (d, $J_{C\text{-}F}$ = 233 Hz), 175.09; **^{19}F NMR (376 MHz, DMSO-d$_6$)** δ/ppm: -114.81 (m, 1F). **HRMS-ESI**: m/z calcd for **$C_{17}H_{15}FN_2S$** $[M + H]^+$ 299.1018, found 299.102.

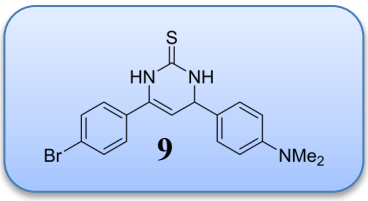
6-(*p*-Tolyl)-4-(3-(trifluoromethyl)phenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (8)



The general procedure described was followed to get the title compound from (*E*)-1-(*p*-tolyl)-3-(3-(trifluoromethyl)phenyl)prop-2-en-1-one (145.14 mg, 0.5 mmol, v), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 17.5 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered (119.6mg, 98% yield): **^{1}H NMR (400 MHz, CDCl$_3$)** δ/ppm: 2.37 (s, 3H), 5.16 (s, 1H), 5.36 (s, 1H), 6.82 (s, 1H), 7.21 (d, 2H, *J* = 8.0 Hz), 7.31 (d, 2H, *J* = 8.4 Hz), 7.53-7.63 (m, 4H),

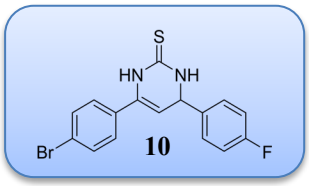
7.66 (s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ/ppm: 31.43, 57.41, 99.46, 124.05, 125.50, 130.27, 130.37, 130.57, 130.93, 134.90, 140.56, 143.78, 176.13; **^{19}F NMR (376 MHz, DMSO-d_6)** δ/ppm: -61.67 (s, 3F).**HRMS-ESI**: m/z calcd for **$C_{18}H_{15}F_3N_2S$** $[M + H]^+$ 349.0981, found 349.0991.

6-(4-Bromophenyl)-4-(4-(dimethylamino)phenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (9)



The general procedure described was followed to get the title compound from (*E*)-1-(4-bromophenyl)-3-(4-(dimethylamino)phenyl)prop-2-en-1-one (165.1 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 24 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (160.5 mg, 54% yield): **^{1}H NMR (400 MHz, $CDCl_3$)** δ/ppm: 2.96 (s, 6H), 5.16 (s, 2H), 6.72 (d, 2H, *J* = 8.8 Hz), 6.78 (s, 1H), 7.20 (d, 2H, *J* = 8.8 Hz), 7.29 (d, 2H, *J* = 8.4 Hz), 7.50 (d, 2H, *J* = 8.4 Hz), 7.66 (s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ/ppm: 40.67, 56.96, 101.91, 112.91, 123.65, 126.92, 128.09, 132.32, 132.59, 132.89, 150.83, 175.04. **HRMS-ESI**: m/z calcd for **$C_{18}H_{18}BrNS$** $[M + H]^+$ 388.0483 and 390.0463, found 388.0469 and 390.0450.

6-(4-Bromophenyl)-4-(4-fluorophenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (10)



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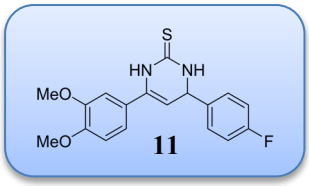
The general procedure described was followed to get the title compound from (*E*)-1-(4-bromophenyl)-3-(4-fluorophenyl)prop-2-en-1-one (152.5 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 °C for 2 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (180 mg, 90% yield): **^{1}H NMR (500 MHz, DMSO-d$_6$)** δ/ppm: 4.10 (d, 1H, *J* = 5.0 Hz), 4.39 (d, 1H, *J* = 5.0 Hz), 6.19 (t, 2H, *J* = 6.8 Hz), 6.31 (m, 2H), 6.42 (d, 2H, *J* = 8.5 Hz), 6.53 (d, 2H, *J* = 8.5 Hz), 8.09 (s, 1H), 8.91 (s, 1H); **^{13}C NMR (125 MHz, DMSO-d$_6$)** δ/ppm: 53.99, 101.78, 115.62 (d, $J_{C\text{-}F}$ = 69.6 Hz), 122.22, 128.24, 128.58, 128.64, 131.46, 132.58, 133.73, 140.20, 175.12; **^{19}F NMR (376 MHz, DMSO-d$_6$)** δ/ppm: -114.67 (m, 1F). **HRMS-ESI**: m/z calcd for **C$_{16}$H$_{12}$BrFN$_2$S** $[M + H]^+$ 362.9967 and 364.9946, found 362.9966 and 364.9948.

6-(3,4-Dimethoxyphenyl)-4-(4-fluorophenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (11)



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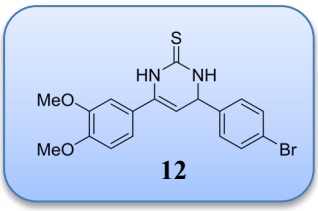
The general procedure described was followed to get the title compound from (*E*)-1-(3,4-dimethoxyphenyl)-3-(4-fluorophenyl)prop-2-en-1-one (143.1 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC-TU (1:1) DES 1.5 mL as solvent were heated at 75 °C for 3.5 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (122.5 mg, 76% yield): **^{1}H NMR (500 MHz, DMSO-d$_6$)** δ/ppm: 2.76 (s, 3H), 2.80 (s, 3H), 4.12 (s, 1H), 4.34 (s, 1H), 5.94 (d, 1H, *J* = 8.0 Hz), 6.06-6.08 (m,

2H), 6.23 (t, 2H, J = 8.8 Hz), 6.35-6.38 (m, 2H), 8.08 (s, 1H), 8.82(s, 1H); **^{13}C NMR (125 MHz, DMSO-d_6)** δ/ppm: 54.08, 55.61, 55.66, 99.73, 109.53, 111.53, 115.56 (d, J_{C-F} = 85 Hz), 115.65, 118.48, 125.85, 128.55 (d, J_{C-F} = 34 Hz), 134.30, 140.56, 148.45, 149.45, 175.03; **^{19}F NMR (376 MHz, DMSO-d_6)** δ/ppm: -114.82 (m, 1F). **HRMS-ESI**: m/z calcd for **$C_{18}H_{17}FN_2O_2S$** $[M + H]^+$ 345.1073, found 345.1075, $[M + Na]^+$ 367.0887, found 367.0898.

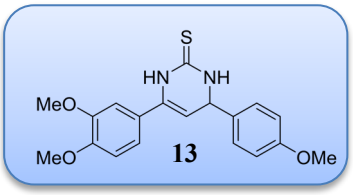
4-(4-Bromophenyl)-6-(3,4-dimethoxyphenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (12)



12

The general procedure described was followed to get the title compound from (*E*)-3-(4-bromophenyl)-1-(3,4-dimethoxyphenyl)prop-2-en-1-one (173.6 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 23 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (67.5 mg, 45% yield): **^{1}H NMR (400 MHz, $CDCl_3$)** δ/ppm: 3.82 (s, 6H), 5.00 (s, 1H), 5.17 (s, 1H), 6.81 (s, 2H), 6.91 (d, 1H , J = 8.4 Hz), 7.00 (s, 1H), 7.17 (d, 2H , J = 8.4 Hz), 7.46 (d, 2H , J = 8.4 Hz), 7.74 (s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ/ppm: 56.03, 56.11, 56.65, 99.05, 108.30, 111.22, 117.97, 122.66, 125.86, 128.61, 132.33, 134.06, 141.49, 149.35, 150.30, 175.27. **HRMS-ESI**: m/z calcd for **$C_{18}H_{17}BrN_2O_2S$** $[M + H]^+$ 405.0267 and 407.0247, found 405.0268 and 407.0257, $[M + Na]^+$ 427.0086, found 427.0153.

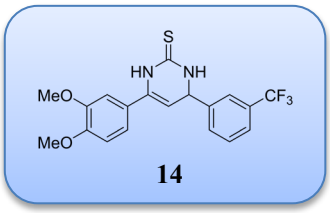
6-(3,4-Dimethoxyphenyl)-4-(4-methoxyphenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (13)



13

The general procedure described was followed to get the title compound from (*E*)-1-(3,4-dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (150.6 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 7 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (76 mg, 77% yield): **^{1}H NMR (400 MHz, CDCl$_3$)** δ/ppm: 3.73 (s, 3H), 3.82 (s, 6H), 5.012 (s, 1H), 5.15 (s, 1H), 6.79 (d, 2H, *J* = 7.8 Hz), 6.82 (d, 1H, *J* = 2.3 Hz), 6.84 (d, 2H, *J* = 8.1 Hz), 6.88 (s, 1H), 6.93 (dd, 1H, *J* = 6.20 Hz, *J* = 2.1 Hz), 7.22 (d, 2H, *J* = 8.7 Hz), 7.67 (s, 1H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ/ppm: 55.40, 56.01, 56.10, 56.72, 99.88, 108.30, 111.18, 114.46, 117.89, 126.15, 128.33, 133.66, 134.71, 149.29, 150.13, 159.82, 174.90. **HRMS-ESI**: m/z calcd for **C$_{19}$H$_{20}$N$_2$O$_3$S** $[M + H]^+$ 357.1273, found 357.1273.

6-(3,4-Dimethoxyphenyl)-4-(3-(trifluoromethyl)phenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (14)

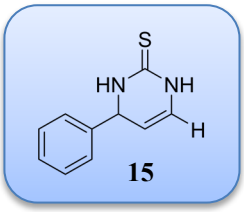


14

The general procedure described was followed to get the title compound from (*E*)-1-(3,4-dimethoxyphenyl)-3-(3-(trifluoromethyl)phenyl)prop-2-en-1-one (169.6 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 12 h. The crude reaction mixture was quenched with 25 mL

of water and the precipitated solid was filtered and dried (25 mg, 51% yield): **^{1}H NMR (400 MHz, $CDCl_3$)** δ/ppm: 3.88 (s, 6H), 5.08 (s, 1H), 5.34 (s, 1H), 6.842-6.847 (m, 3H), 6.99 (dd, 1H, *J* = 8.7 Hz, 2.4 Hz), 7.16 (s, 1H), 7.58 (s, 3H), 7.82 (s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ/ppm: 56.47, 56.55, 57.29, 99.18, 108.77, 110.34, 111.66, 118.50, 124.08 (q, J_{C-F} = 8.0 Hz), 125.94 (q, J_{C-F} = 7.2 Hz), 126.20, 130.31, 130.94, 131.91 (d, J_{C-F} = 33.1 Hz), 134.58, 143.84, 149.79, 150.80, 175.85; **^{19}F NMR (376 MHz, DMSO-d_6)** δ/ppm: -61.01 (m, 1F). **HRMS-ESI**: m/z calcd for **$C_{19}H_{17}F_3N_2O_2S$** $[M + H]^+$ 395.1041, found 395.1043.

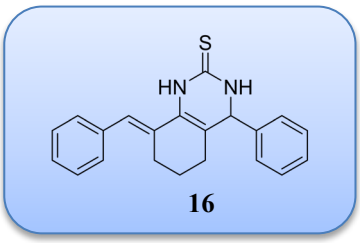
6-Phenyl-3,4-dihydropyrimidine-2(1*H*)-thione (15)



15

The general procedure described was followed to get the title compound from 1-phenylprop-2-en-1-one (66.08 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 21.5 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered, dried and obtained as isomeric mixture (45.6 mg, 99% yield): **^{1}H NMR (400 MHz, DMSO-d_6)** δ/ppm for predominant isomer: 3.42 (s, 1H), 4.20 (s, 1H), 6.19-6.25 (m, 5H), 6.28-6.33 (m, 3H), 7.21 (s, 1H), 7.29 (d, 1H, *J* = 6.9 Hz), 7.52 (s, 1H); **^{13}C NMR (100 MHz, DMSO-d_6)** δ/ppm: 51.86, 53.98, 126.66, 126.80, 128.15, 129.00, 129.03, 141.63, 176.93. **HRMS-ESI**: m/z calcd for **$C_{18}H_{17}BrN_2O_2S$** $[M + H]^+$ 191.0643, found 191.0640, $[M + Na]^+$ 213.0457, found 213.0459.

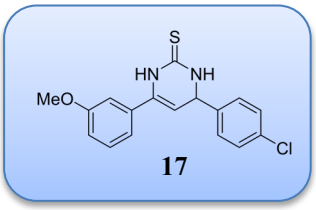
4-(4-Fluorophenyl)-6-(4-methoxyphenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (16)



16

The general procedure described was followed to get the title compound from 2,6-di((*E*)-benzylidene)cyclohexan-1-one (144.1 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 22 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (87.9 mg, 70% yield): **^{1}H NMR (400 MHz, $CDCl_3$)** δ/ppm: 1.52 (m, 2H), 1.55-1.61 (m, quint, 2H, *J* = 6.4 Hz), 1.76-1.94 (m, 2H), 2.39-2.66 (ttd, 2H, *J* = 5.6 Hz, *J* = 14.4 Hz), 4.86 (s, 1H), 6.50 (s, 1H), 6.85 (s, 1H), 7.17-7.20 (m, 3H), 7.24-7.33 (m, 7H), 7.60 (s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ/ppm: 22.37, 26.08, 26.70, 61.15, 113.58, 121.93, 126.57, 127.20, 127.30, 128.32, 128.76, 129.15, 129.32, 129.81, 136.30, 141.20, 174.04. **HRMS-ESI**: m/z calcd for **$C_{21}H_{20}N_2S$** $[M + H]^+$ 333.1420, found 333.1433, $[M + Na]^+$ 355.1239, found 355.1245.

4-(4-chlorophenyl)-6-(3-methoxyphenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (17)[2]

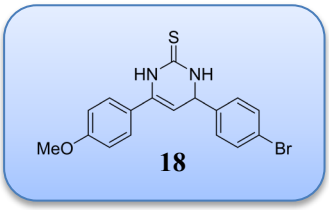


17

The general procedure described was followed to get the title compound from (*E*)-3-(4-chlorophenyl)-1-(3-methoxyphenyl)prop-2-en-1-one (136.3 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 20 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered, dried and obtained as isomeric mixture (73.3 mg, 65% yield):

^{1}H NMR (400 MHz, $CDCl_3$) δ/ppm: 3.75 (3.74, isomer peaks found in methoxy group, s, 3H), 5.10-5.11 (m, 1H), 5.17-5.20 (m, 1H), 6.80-6.82 (m, 1H), 6.85-6.88 (m, 2H), 6.92-6.94 (m, 1H), 7.22-7.24 (m, b, 2H), 7.29-732 (m, 3H), 7.70 (s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ/ppm: 55.46 (55.40), 57.16 (56.58), 101.02 (100.25), 112.64 (110.89), 115.32 (113.96), 119.05 (117.53), 128.28 (126.60), 129.40 (129.29), 130.36 (130.24), 133.11 (131.74), 134.55 (134.15), 135.60 (134.59), 143.60 (140.80), 160.29 (160.08), 175.43 (175.38). **HRMS-ESI**: m/z calcd for **$C_{17}H_{15}ClN_2OS$** $[M + H]^+$ 331.0666, found 331.0659.

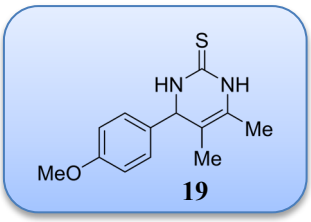
4-(4-bromophenyl)-6-(4-methoxyphenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (18)[2]



18

The general procedure described was followed to get the title compound from (*E*)-3-(4-bromophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (158.5 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 18 h. The crude reaction mixture was quenched with 25 mL of water and the precipitated solid was filtered and dried (126.4 mg, 94% yield): **^{1}H NMR (400 MHz, $CDCl_3$)** δ/ppm: 3.76 (s, 1H), 4.99-5.01 (p, J = 4 Hz, 1H), 5.16-5.17 (dd, J = 5.2 Hz, J = 2 Hz, 1H), 6.81 (b, 1H), 6.84 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 7.58 (s, b, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ/ppm: 55.43, 56.70, 98.72, 114.46, 122.66, 125.50, 126.56, 128.57, 132.33, 133.87, 141.49, 160.73, 175.45. **HRMS-ESI**: m/z calcd for **$C_{17}H_{15}BrN_2OS$** $[M + H]^+$ 375.0162 and 377.0141, found 375.0149 and 377.1032.

4-(4-methoxyphenyl)-5,6-dimethyl-3,4-dihydropyrimidine-2(1H)-thione (19)

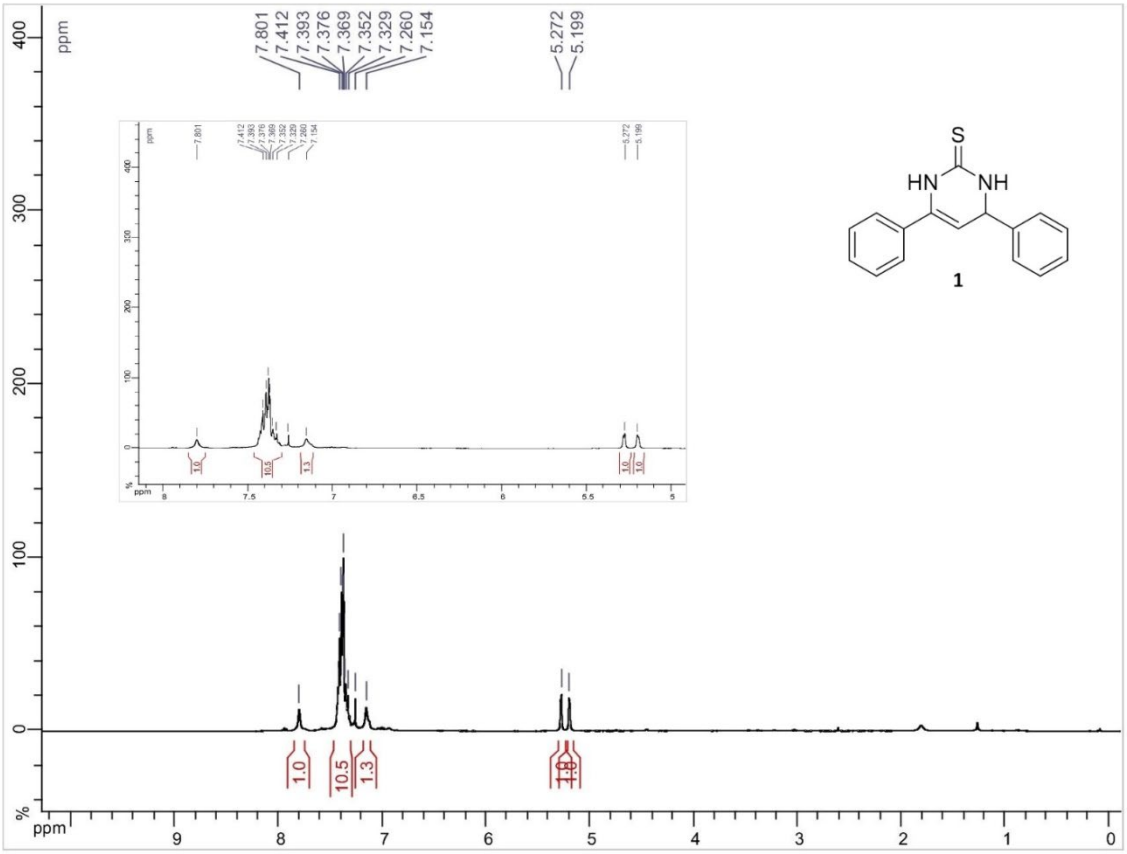


19

The general procedure described was followed to get the title compound from (*E*)-4-(4-methoxyphenyl)-3-methylbut-3-en-2-one[3] (95.12 mg, 0.5 mmol, 1.0 equiv.), thiourea (45.6 mg, 0.6 mmol, 1.2 equiv.), choline hydroxide (0.25 mL) in CC:TU (1:1) DES 1.5 mL as solvent were heated at 75 ºC for 5 h. The crude reaction mixture was quenched with 25 mL of water and the product was separated by solvent extraction using ethyl acetate and drying yielded off-white semi-solid (70 mg, 56% yield): **^{1}H NMR (400 MHz, $CDCl_3$)** δ/ppm: 1.37 (s, 3H), 1.76 (s, 3H), 3.73 (s, 3H), 4.69 (s, 1H), 6.81 (d, *J* = 8.8 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ/ppm: 14.52, 15.35, 55.36, 61.02, 105.91, 114.32, 124.08, 128.46, 133.94, 159.78, 173.29.

References

1. E. A. Golysheva, N. A. Maslennikova, D. S. Baranov and S. A. Dzuba, Structural properties of supercooled deep eutectic solvents: choline chloride-thiourea compared to reline, *Phys. Chem. Chem. Phys.*, 2022, **24**, 5974–5981.
2. S. El-Meligie, A. T. Taher, A. M. Kamal and A. Youssef, Design, synthesis and cytotoxic activity of certain novel chalcone analogous compounds, *Eur. J. Med. Chem.*, 2017, **126**, 52–60.
3. S. M. Lu, C. Bolm, Highly enantioselective synthesis of optically active ketones by iridium-catalyzed asymmetric hydrogenation, *Angew. Chem. Int. Ed*. 2008, **47**, 8920-8923.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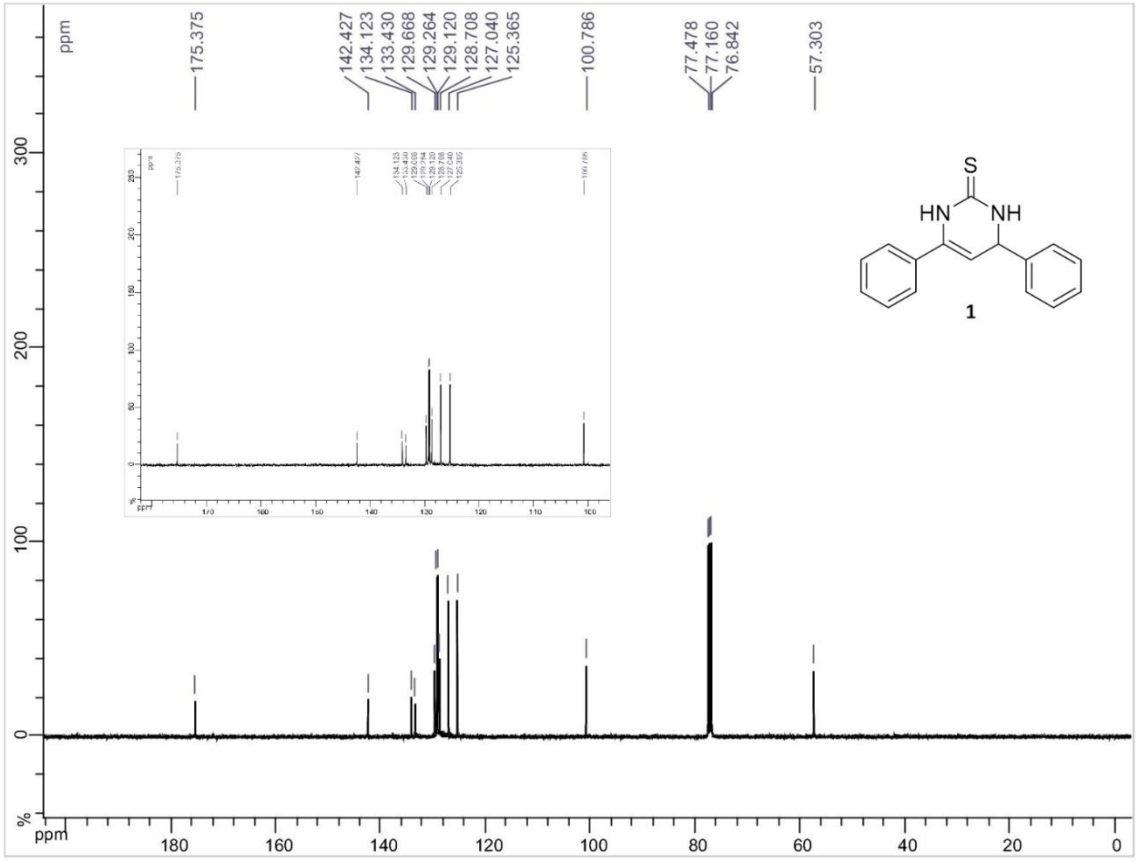
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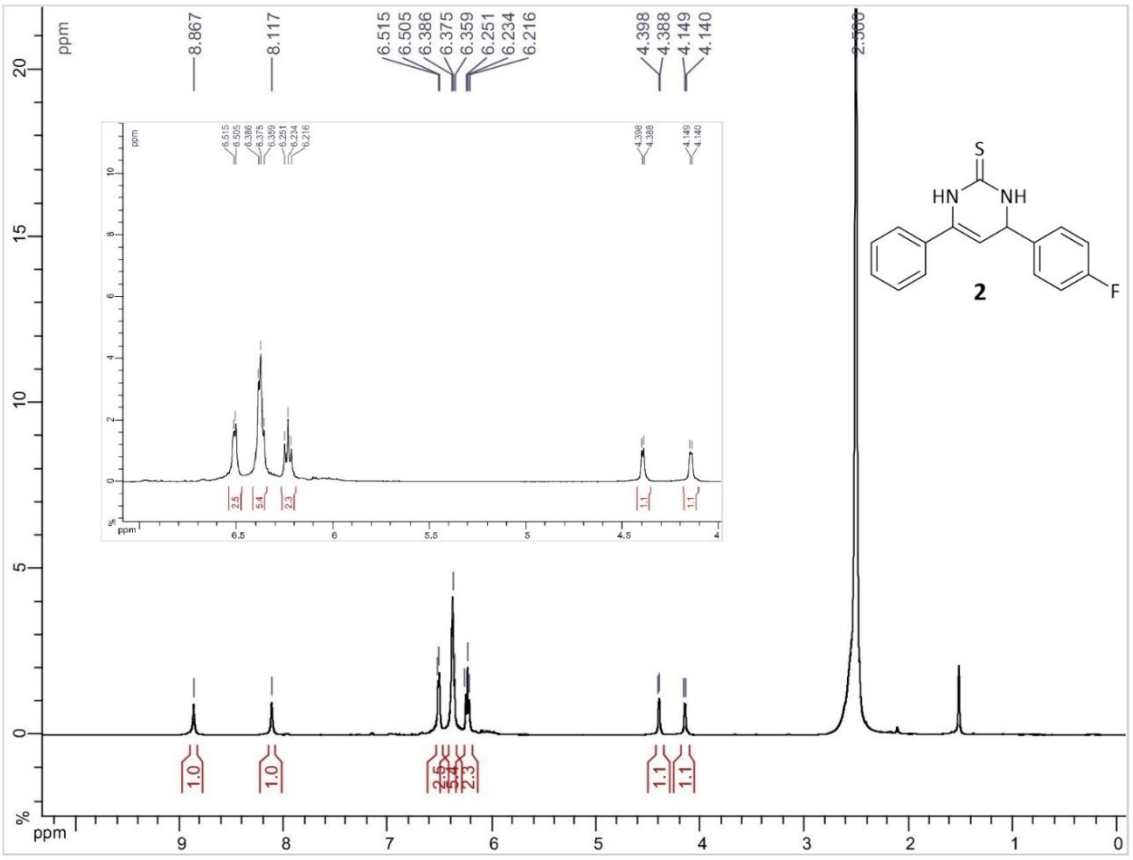
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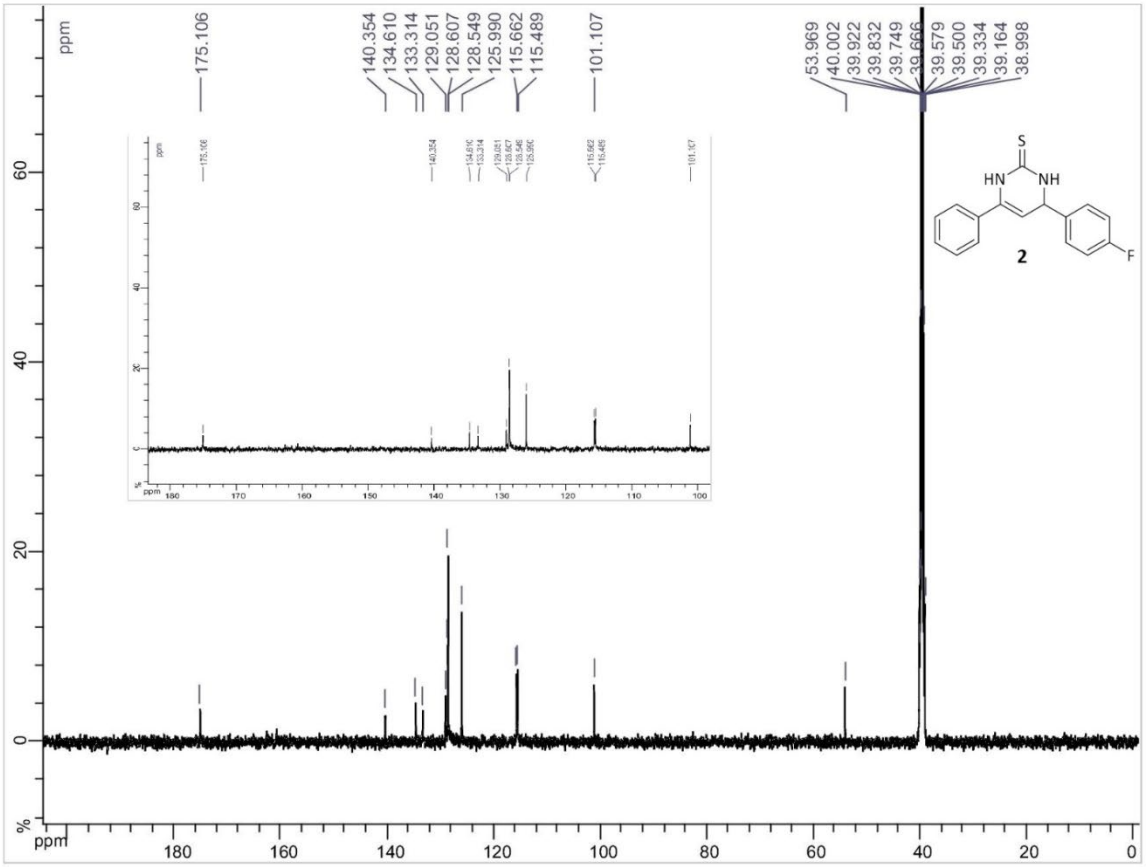
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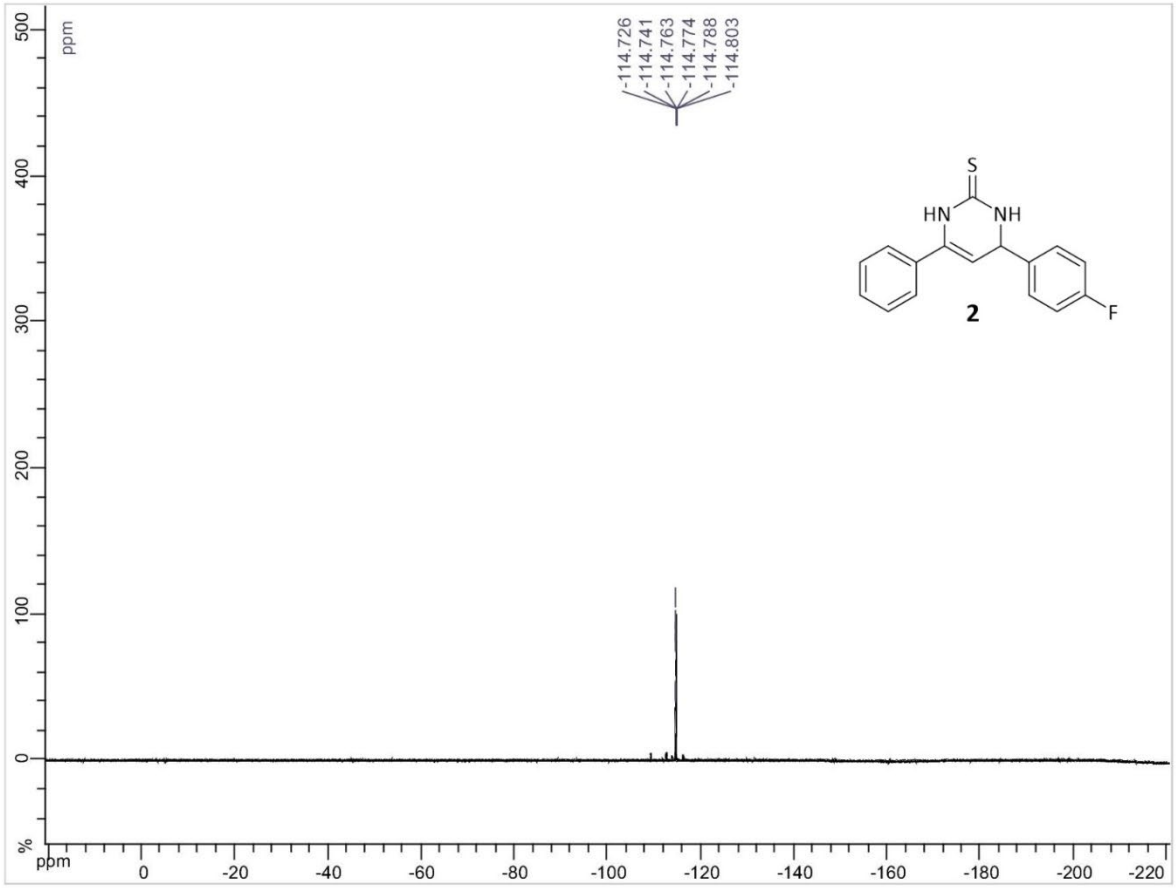
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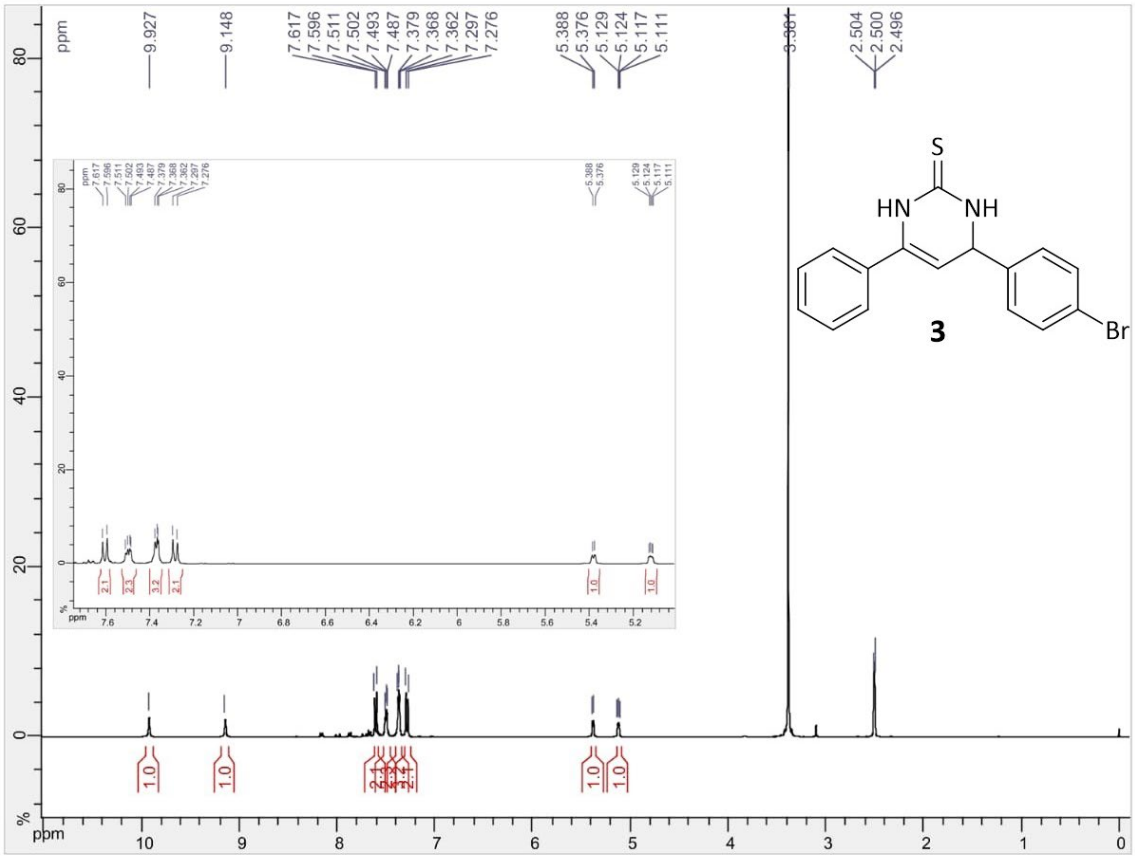
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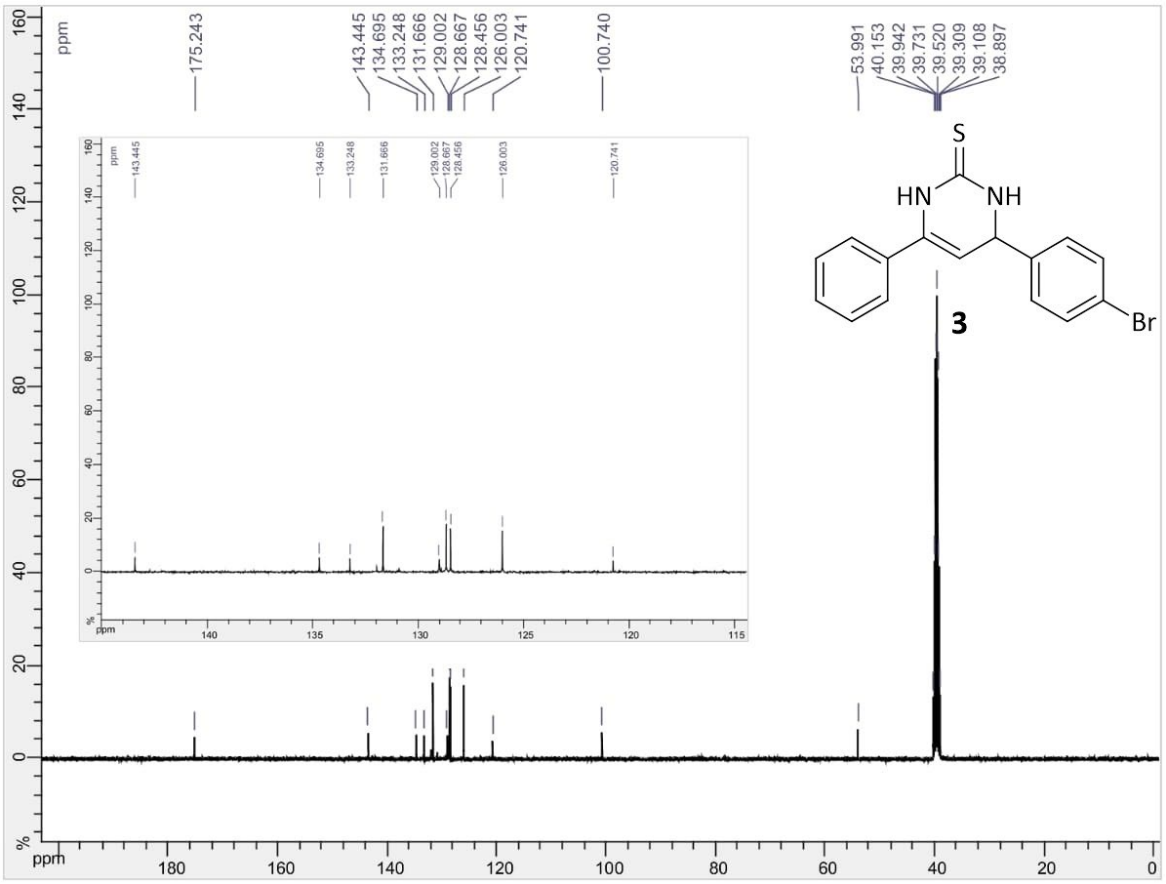
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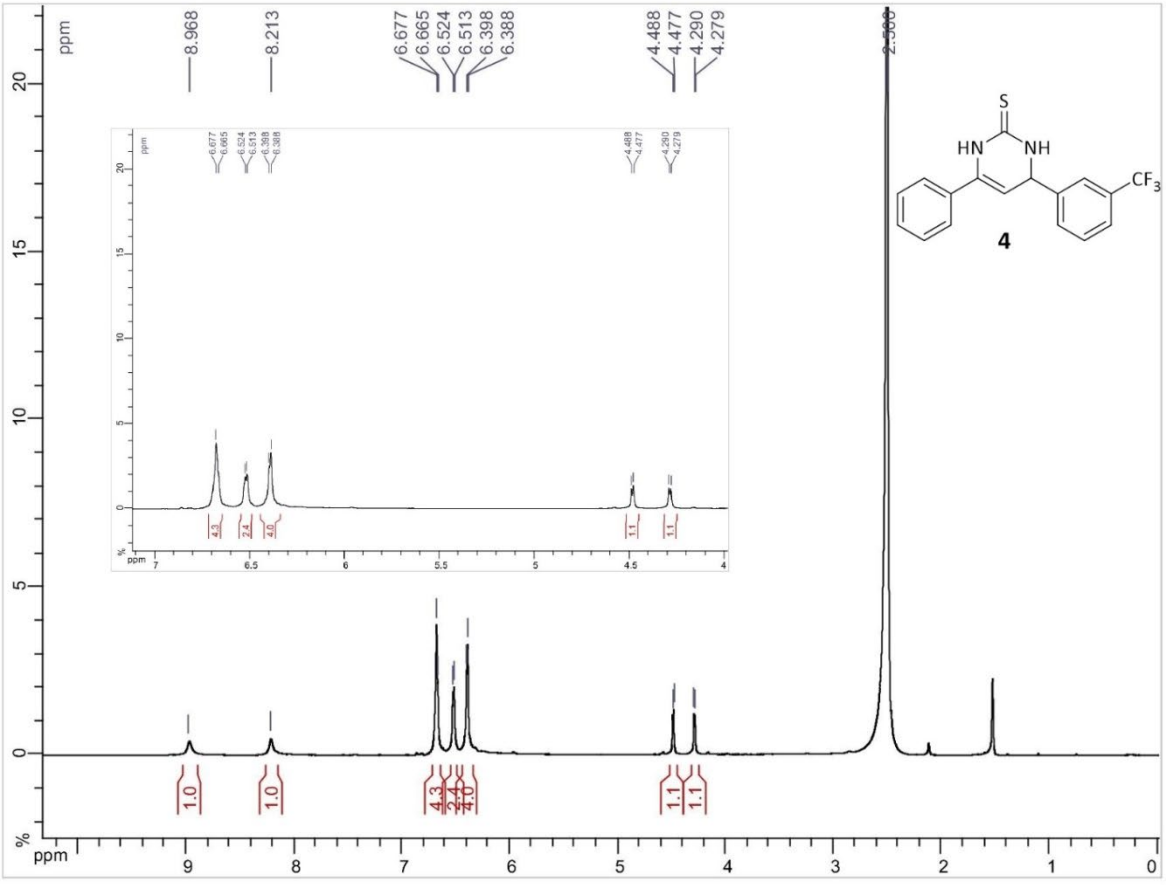
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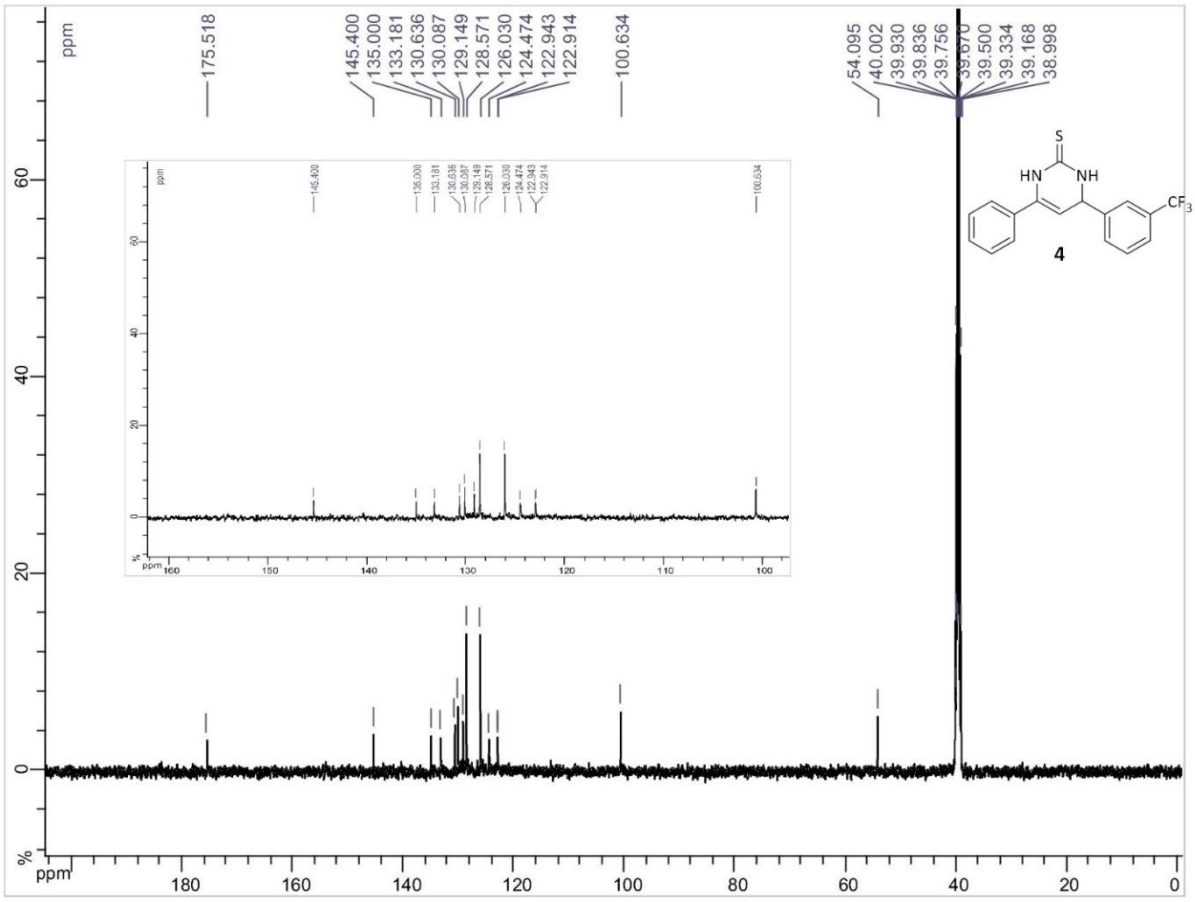
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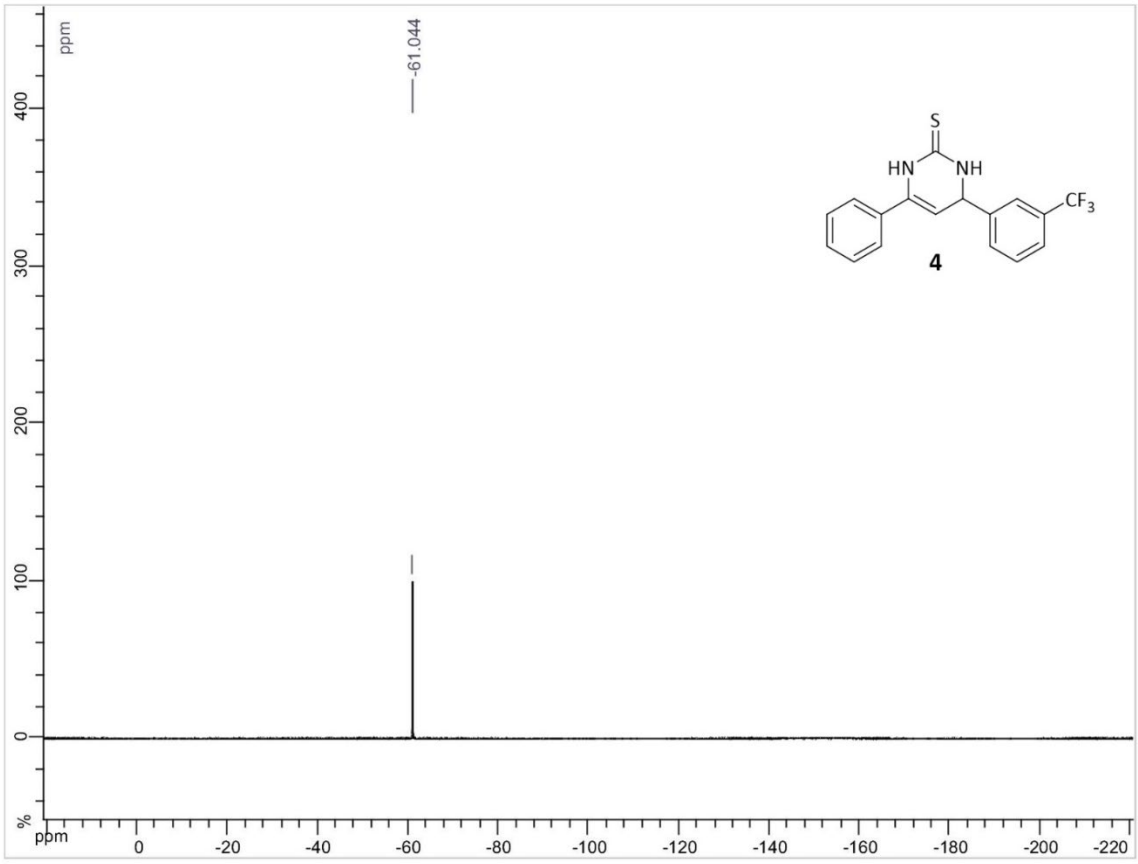
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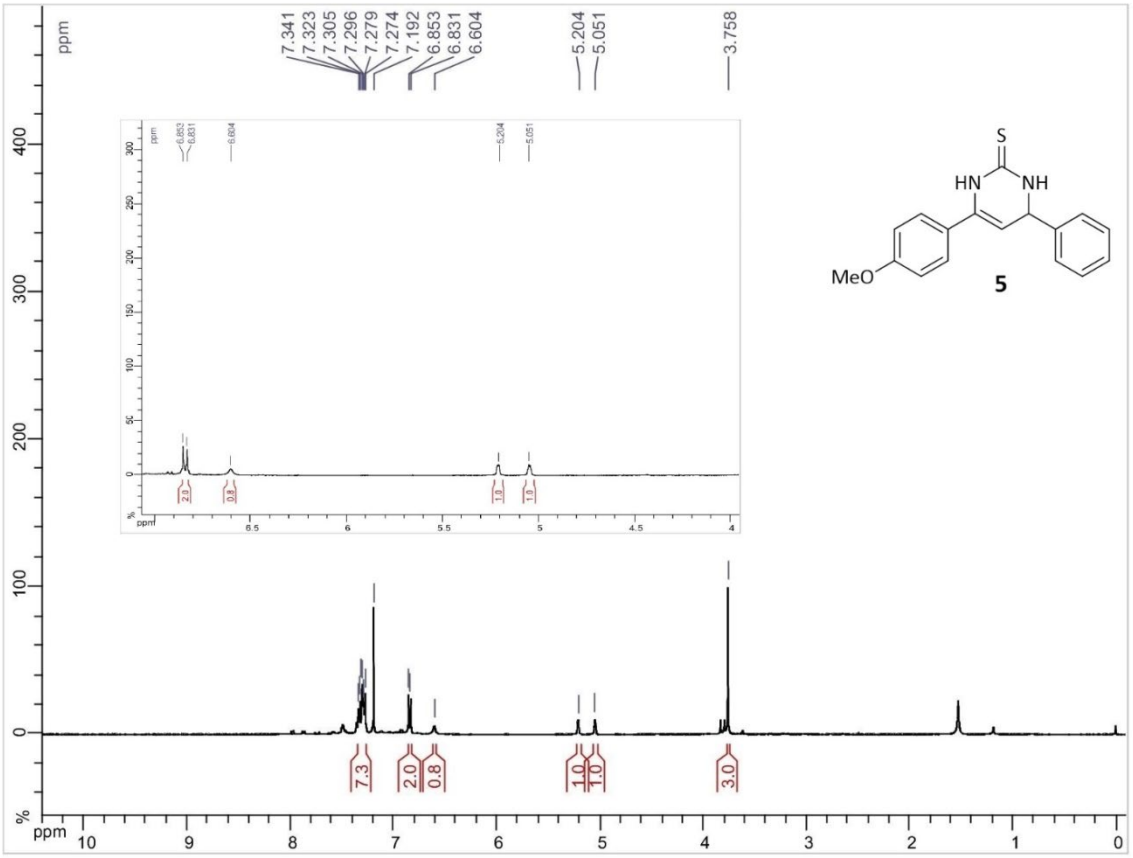
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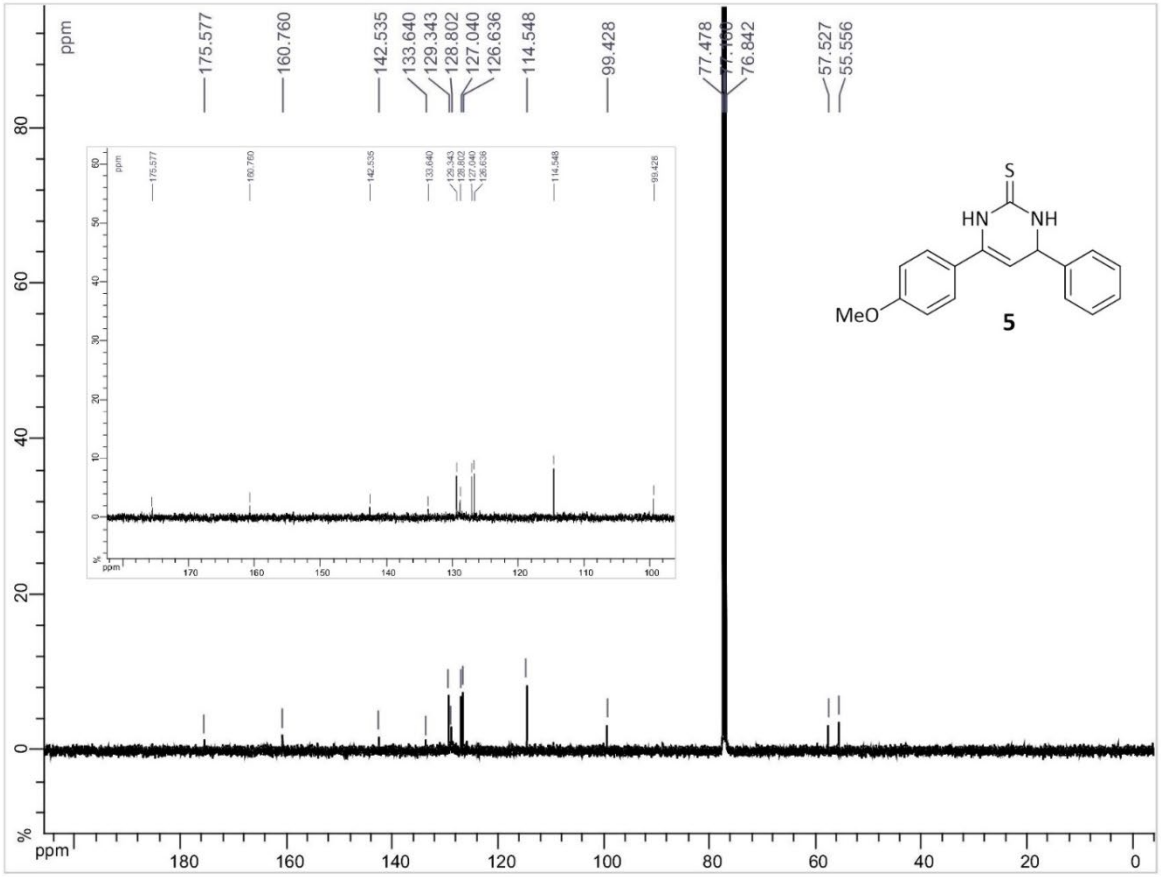
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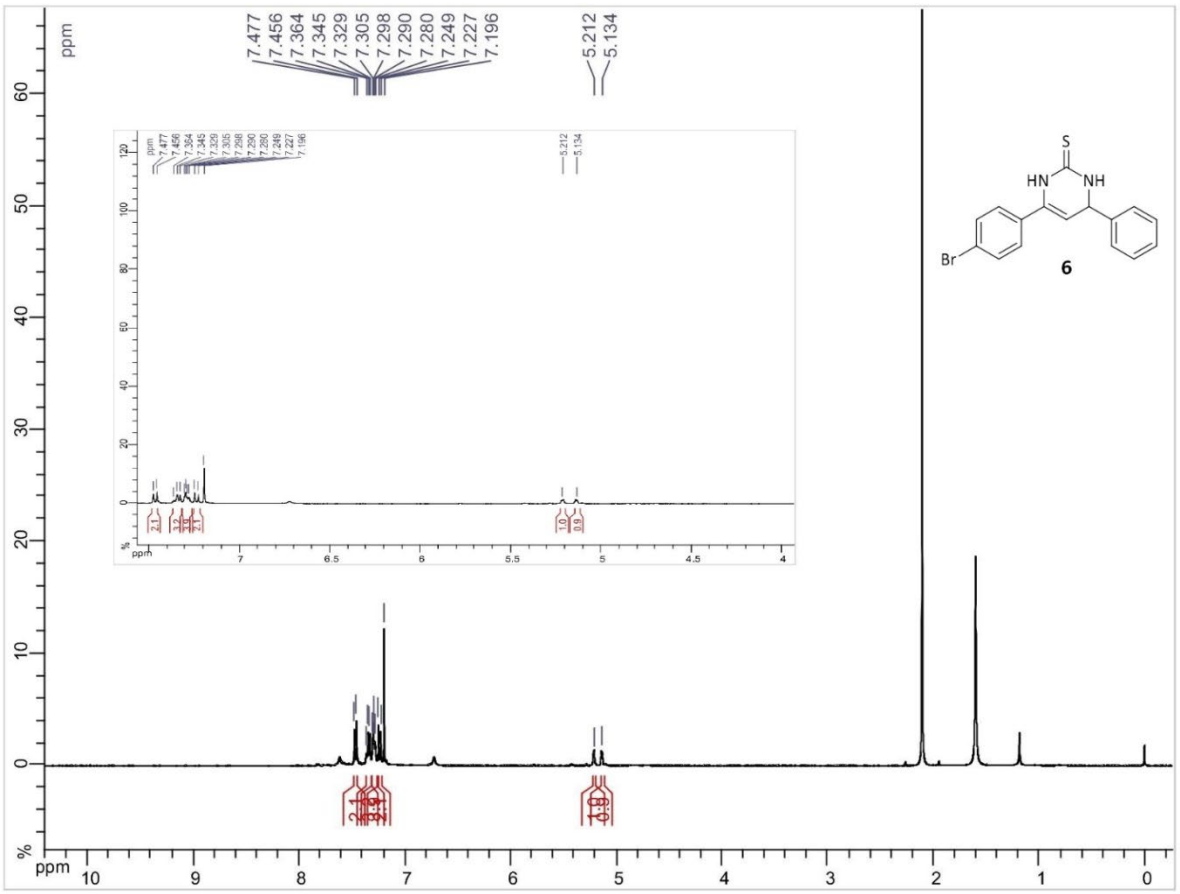
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7.249
7.227
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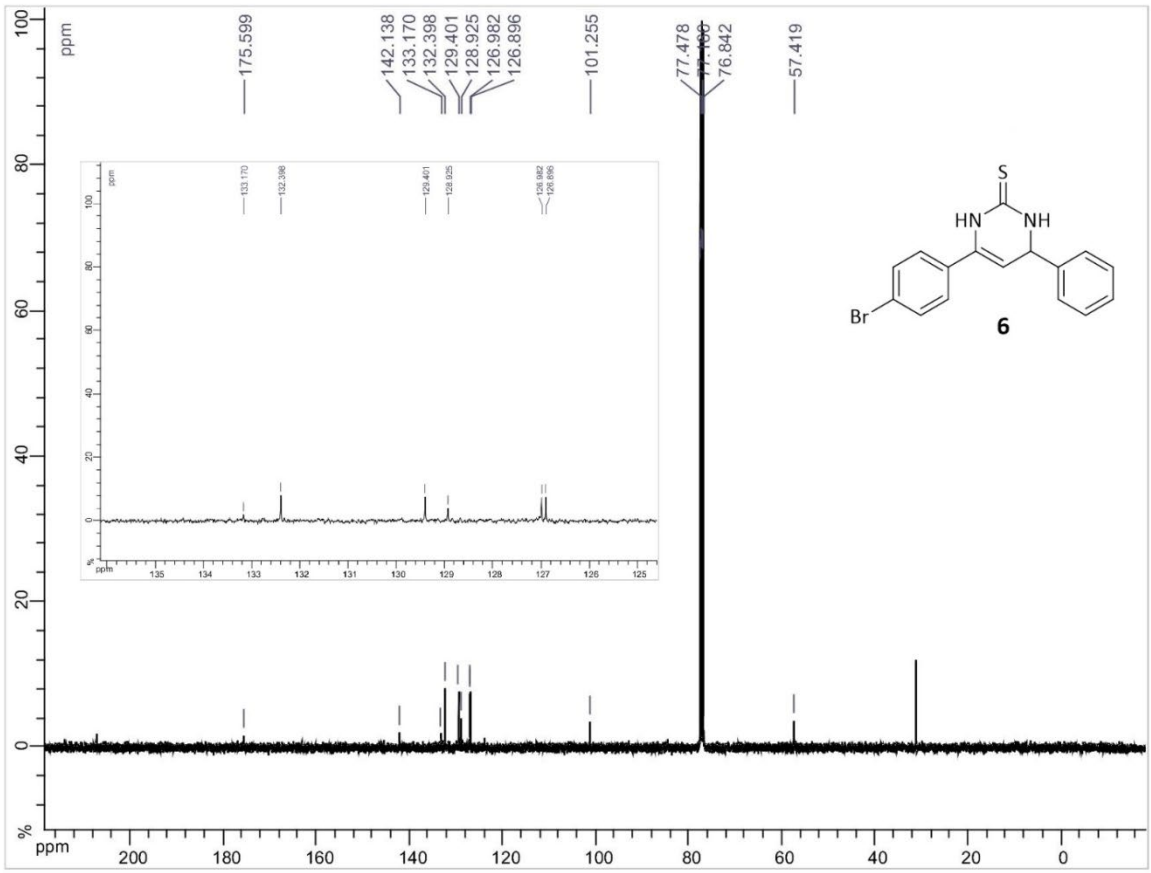
HN
NH
Br
6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133.170
132.398
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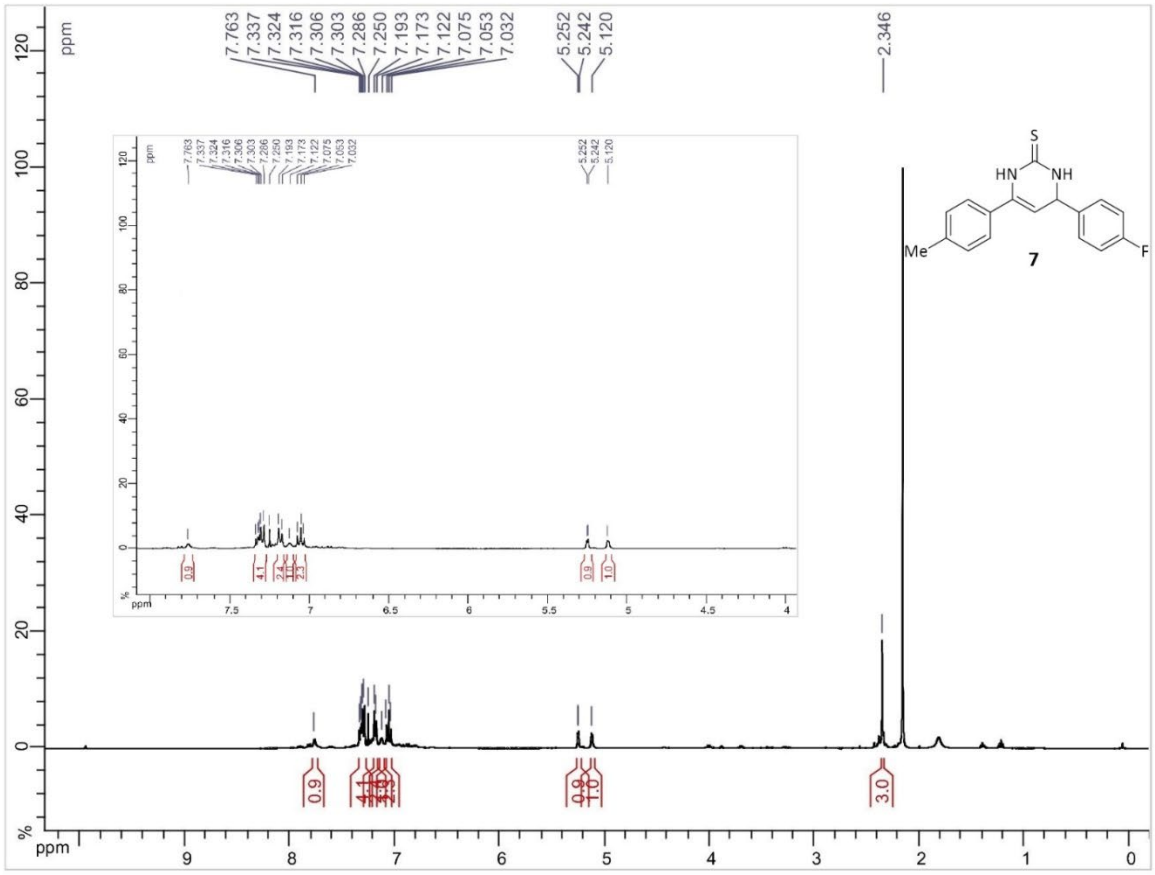
77.478
77.160
76.842
57.419
S
HN
NH
Br
6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7.303
7.286
7.250
7.193
7.173
7.122
7.075
7.053
7.032
5.252
5.242
5.120
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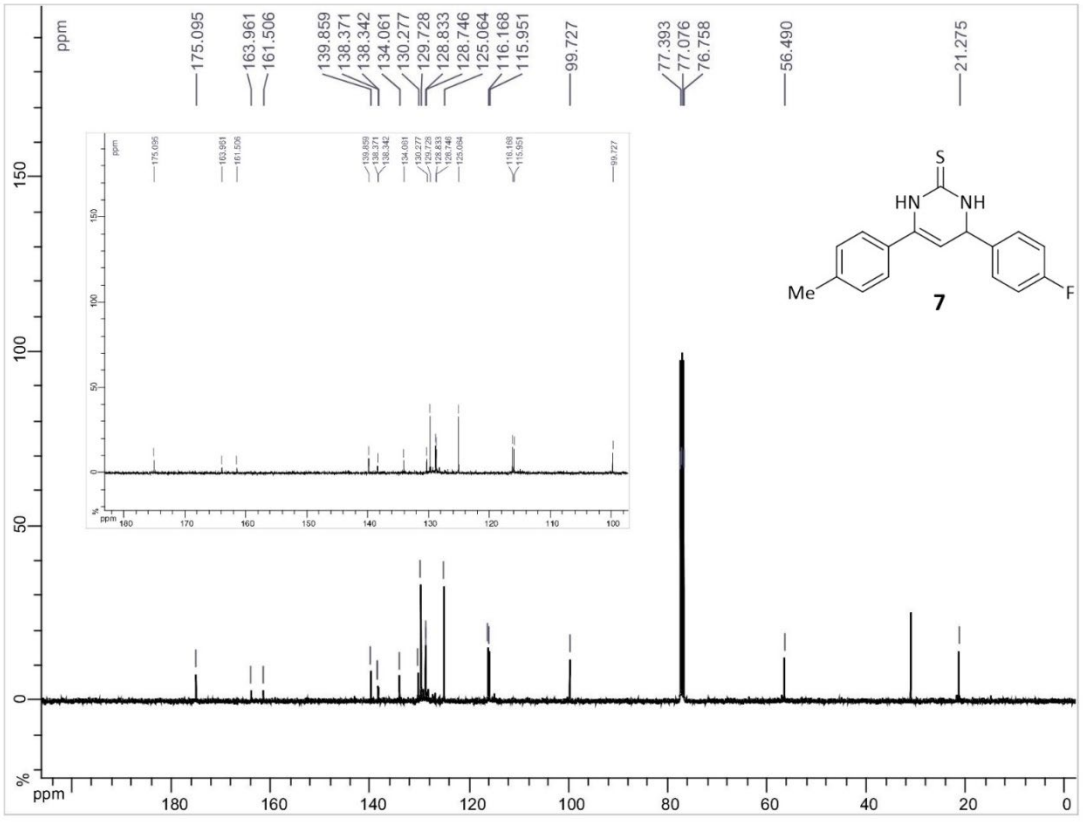
2.4
2.3
0.9
1.0
3.0
S
HN
NH
Me
F
7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129.728
128.833
128.746
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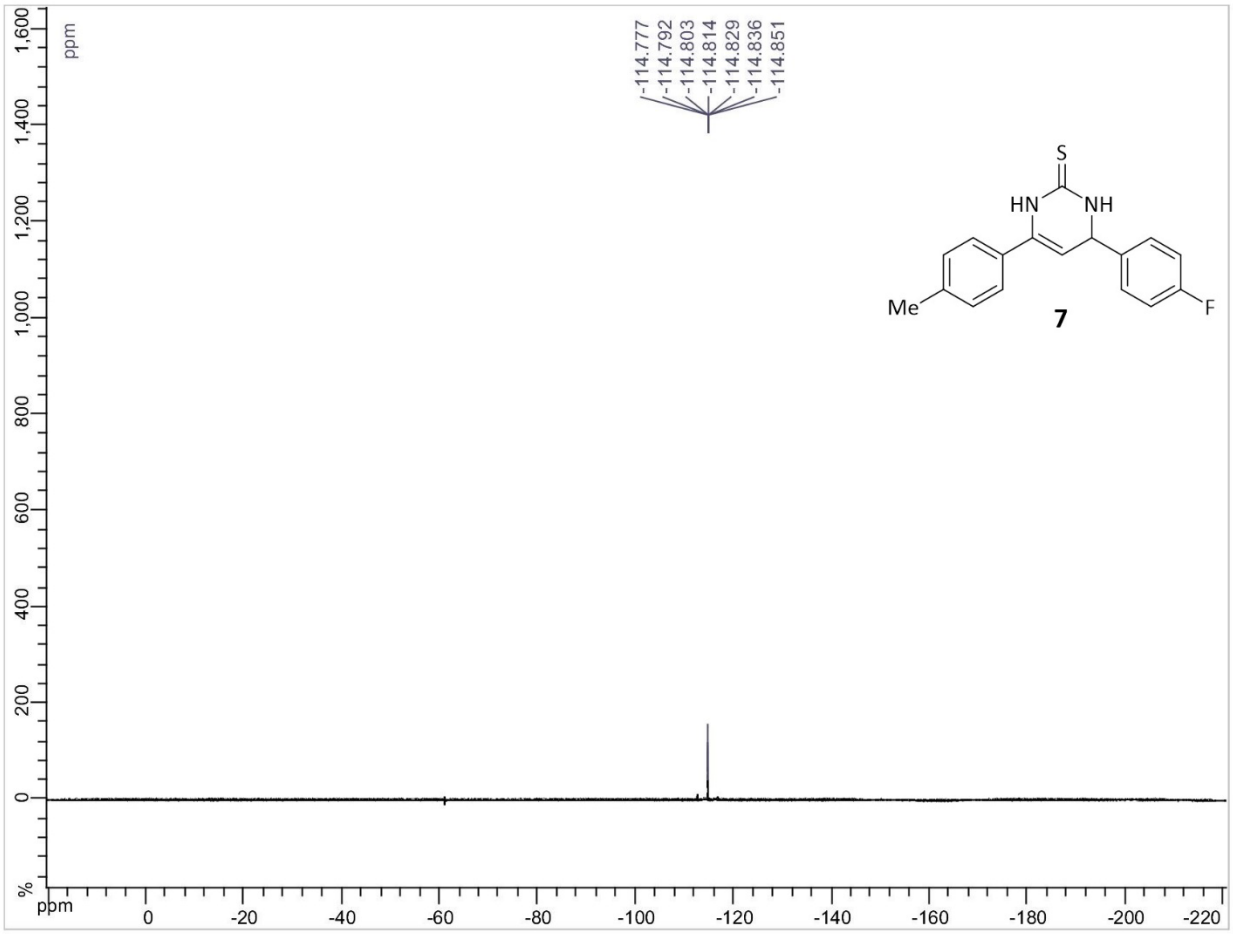
99.727
77.393
77.076
76.758
56.490
21.275
S
HN
NH
Me
F
7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HN
NH
Me
F
7
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1,400
1,200
1,000
800
600
400
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0
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ppm
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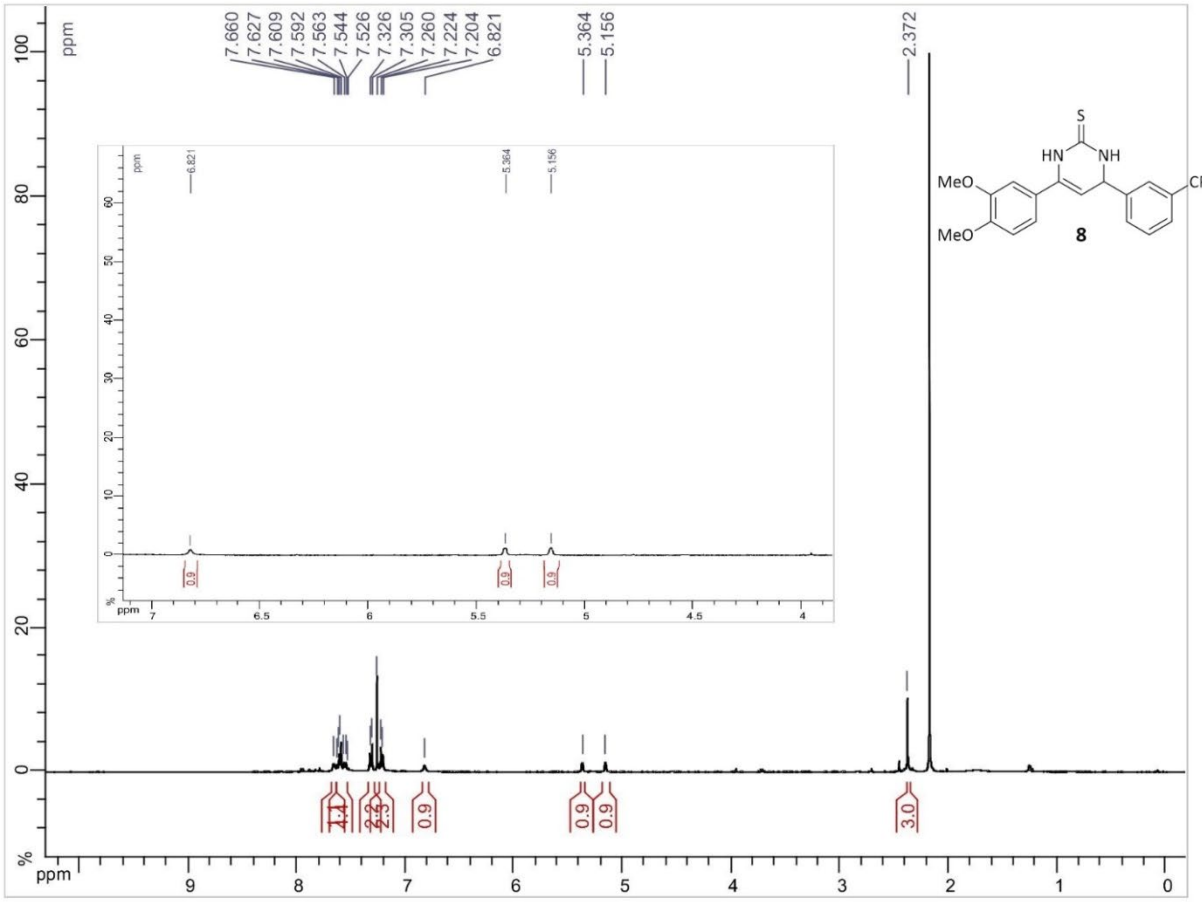
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7.260
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6.821
5.364
5.156
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S
MeO
MeO
CF3
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1.3
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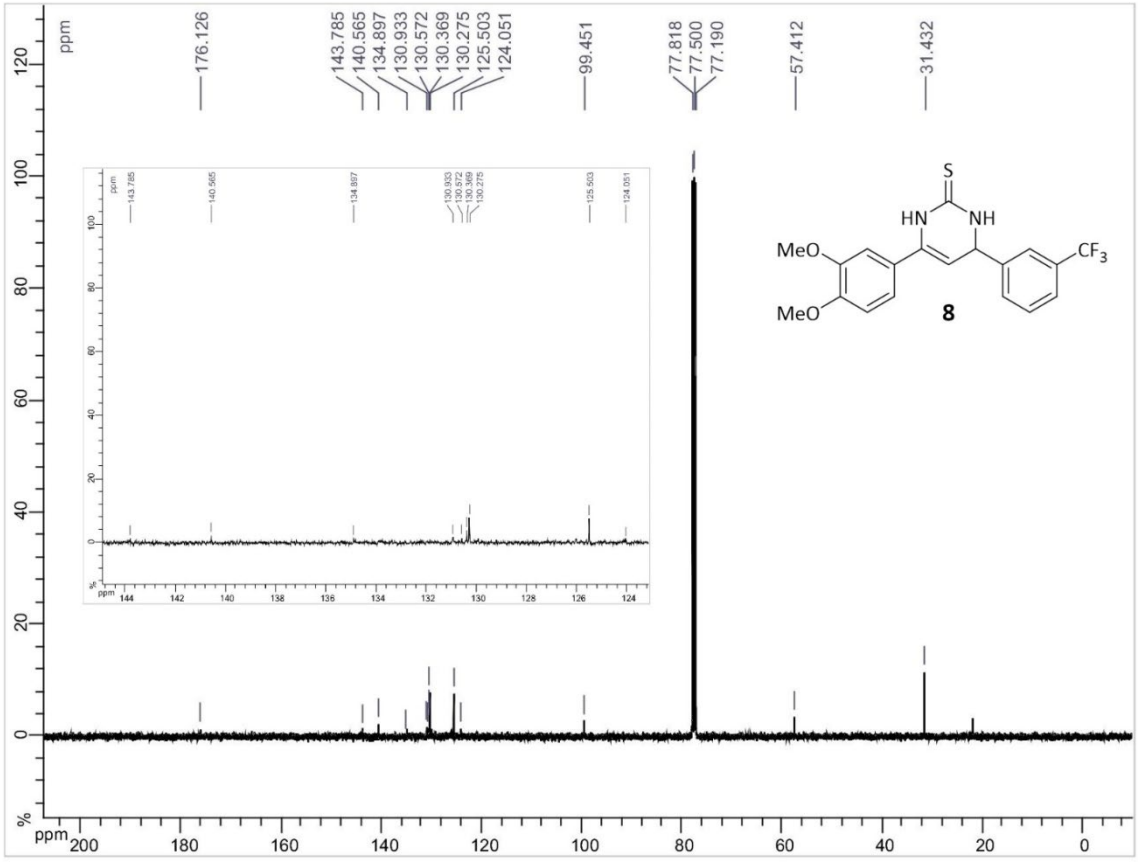
3.0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130.369
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77.190
57.412
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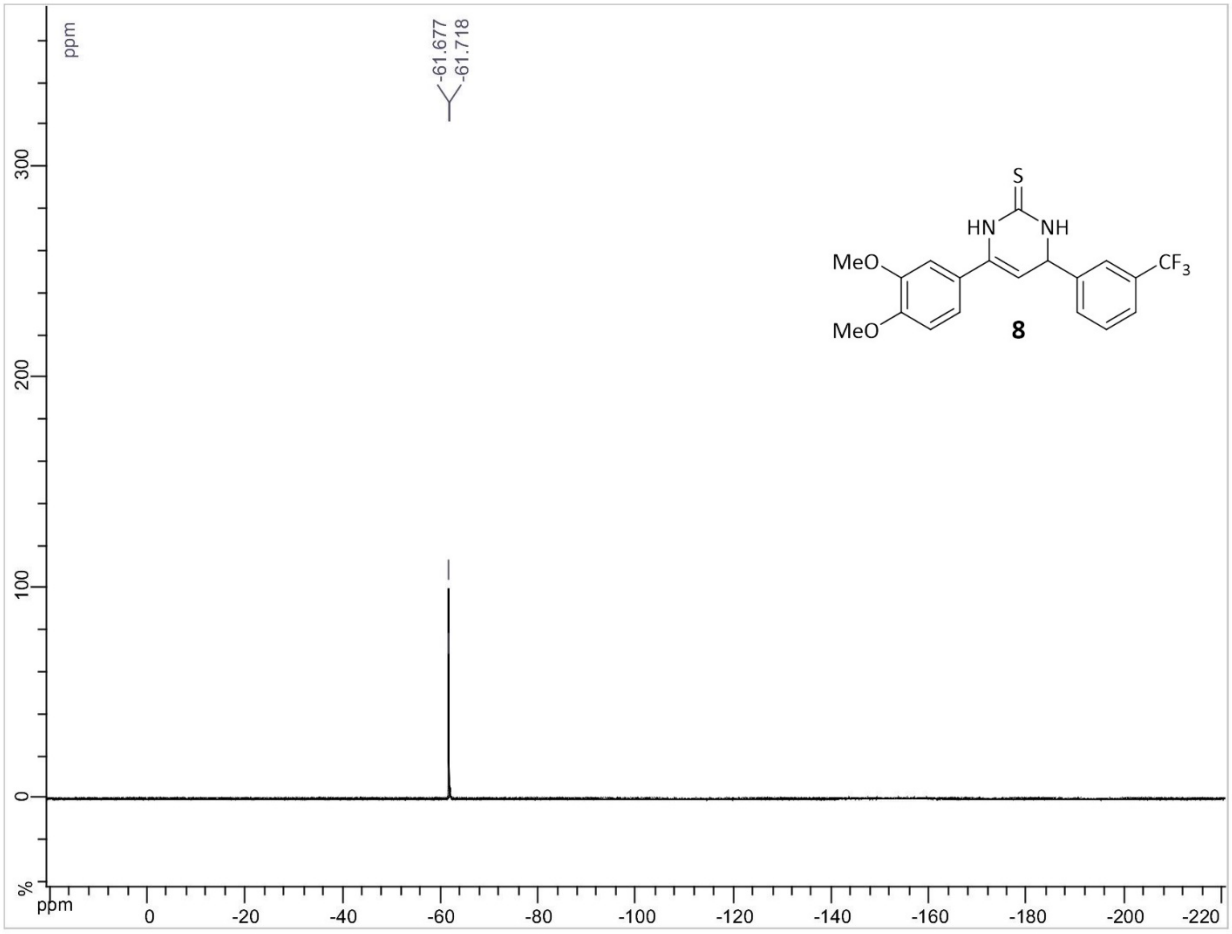
S
MeO
MeO
CF3
8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%
ppm
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-20
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-120
-140
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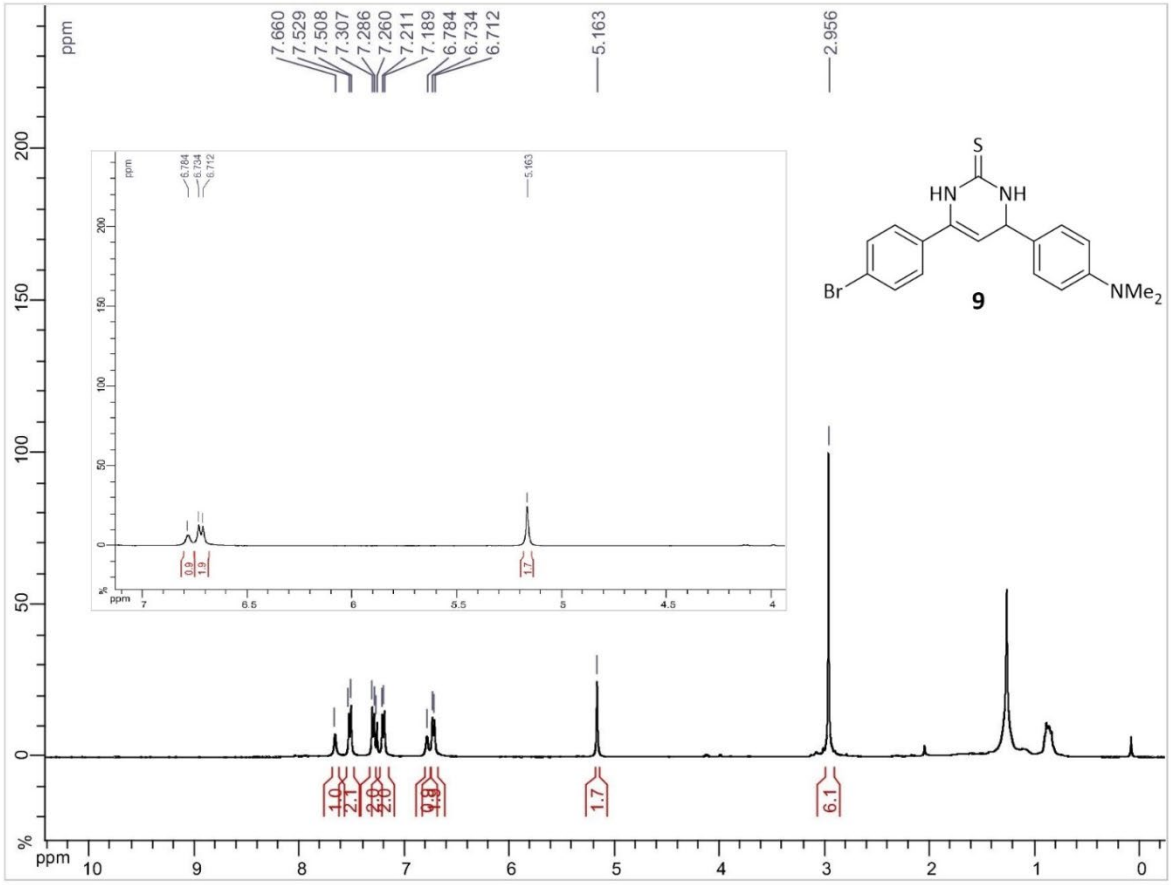
-180
-200
-220
S
HN
NH
MeO
MeO
CF3
8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7.260
7.211
7.189
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6.734
6.712
5.163
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NH
Br
NMe2
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2.1
2.0
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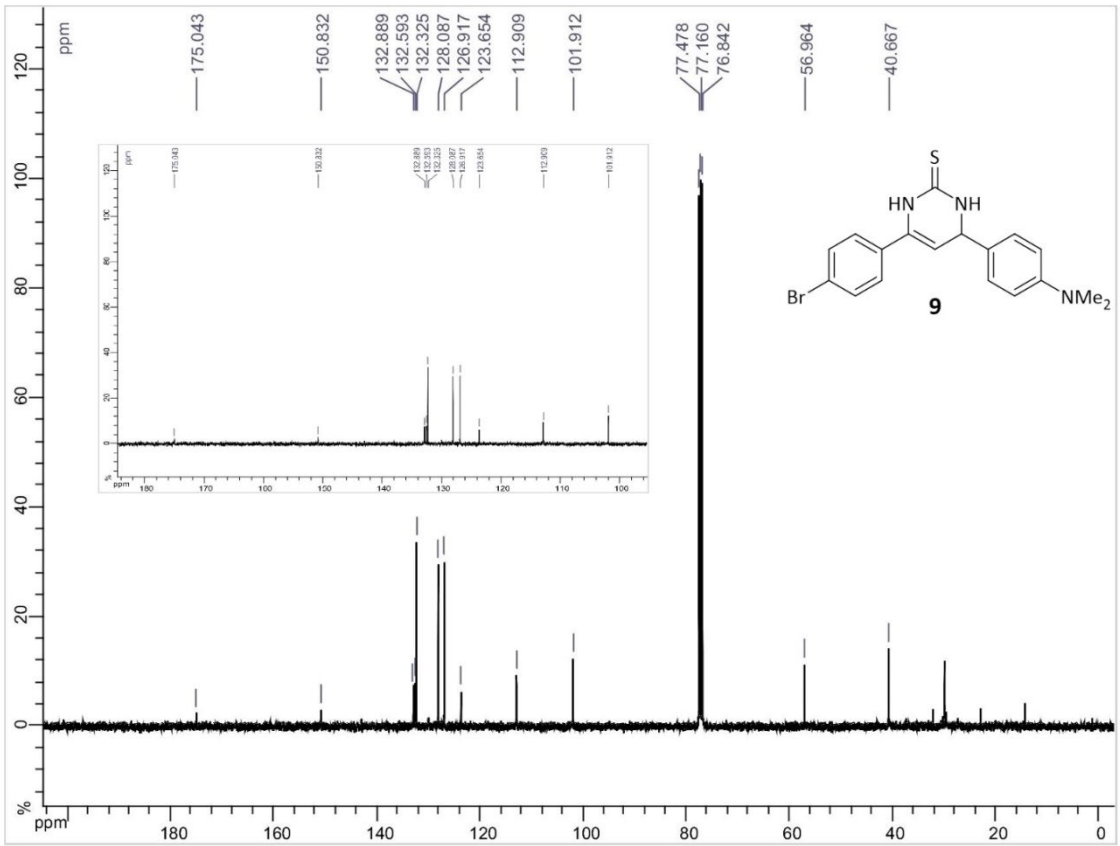
0.9
1.7
6.1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128.087
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56.964
40.667
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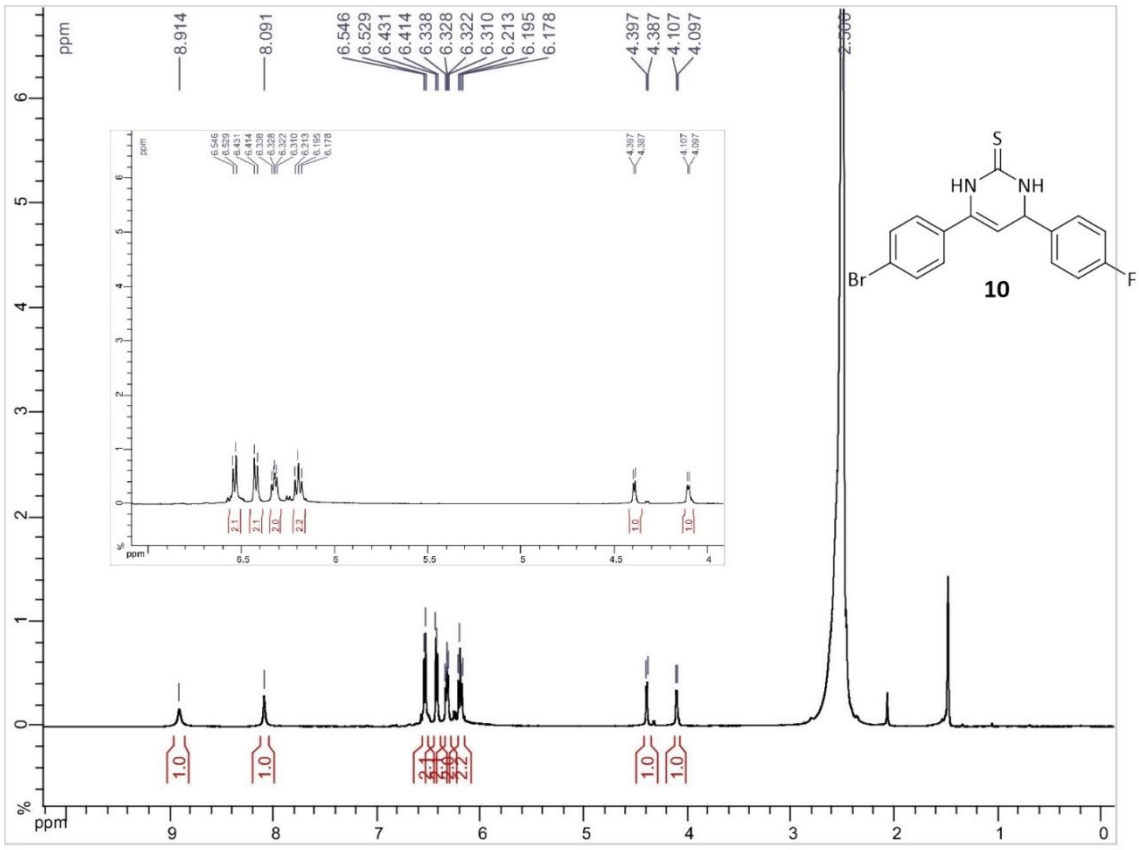
NH
Br
NMe2
9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6.529
6.431
6.414
6.338
6.328
6.322
6.310
6.213
6.195
6.178
4.397
4.387
4.107
4.097
2.508
S
HN
NH
Br
F
10
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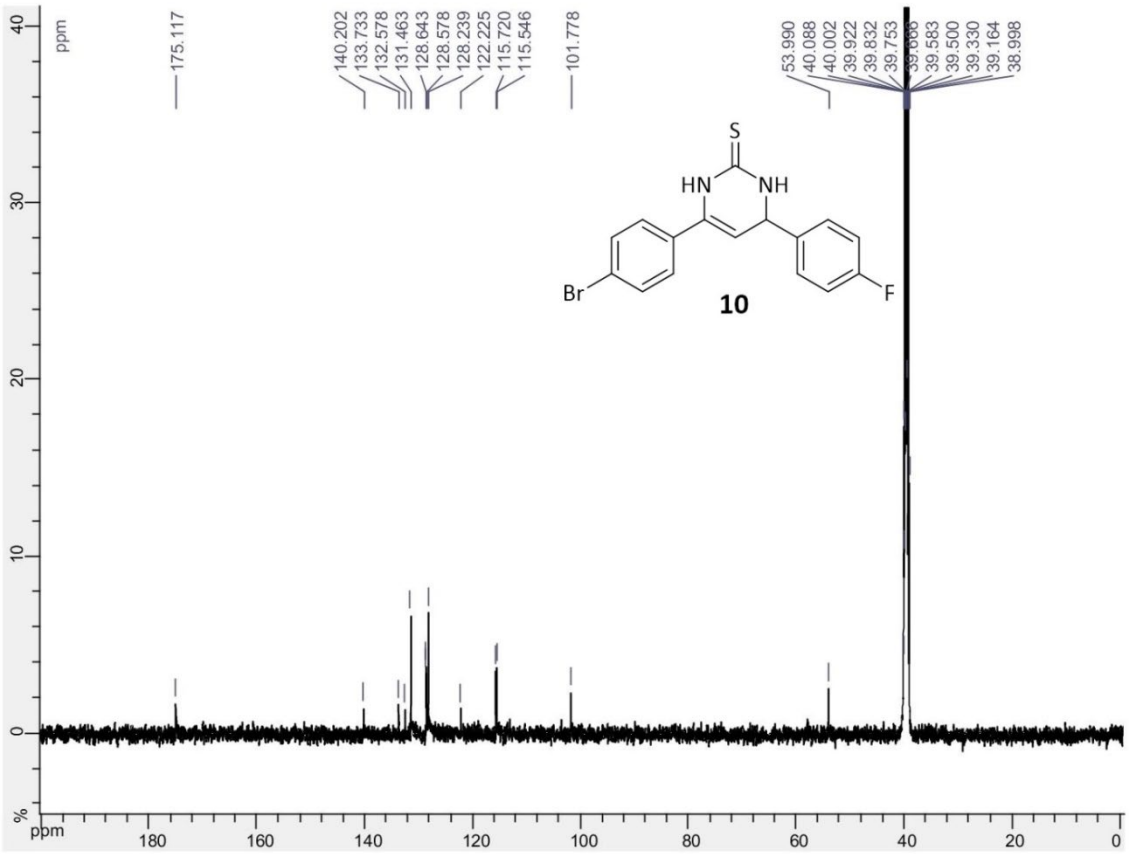
1.0
2.1
2.1
2.0
2.2
1.0
1.0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115.546
101.778
53.990
40.088
40.002
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39.753
39.583
39.500
39.330
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38.998
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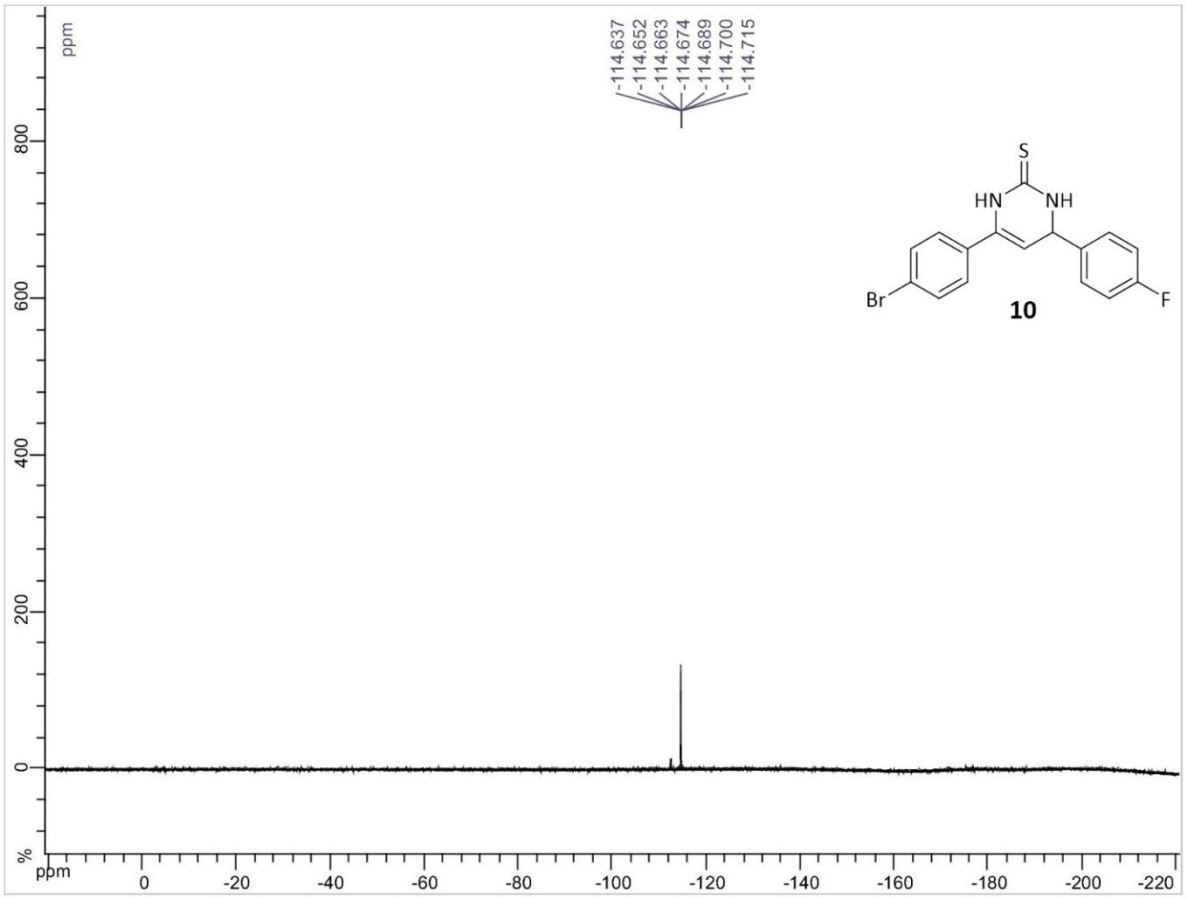
NH
Br
F
10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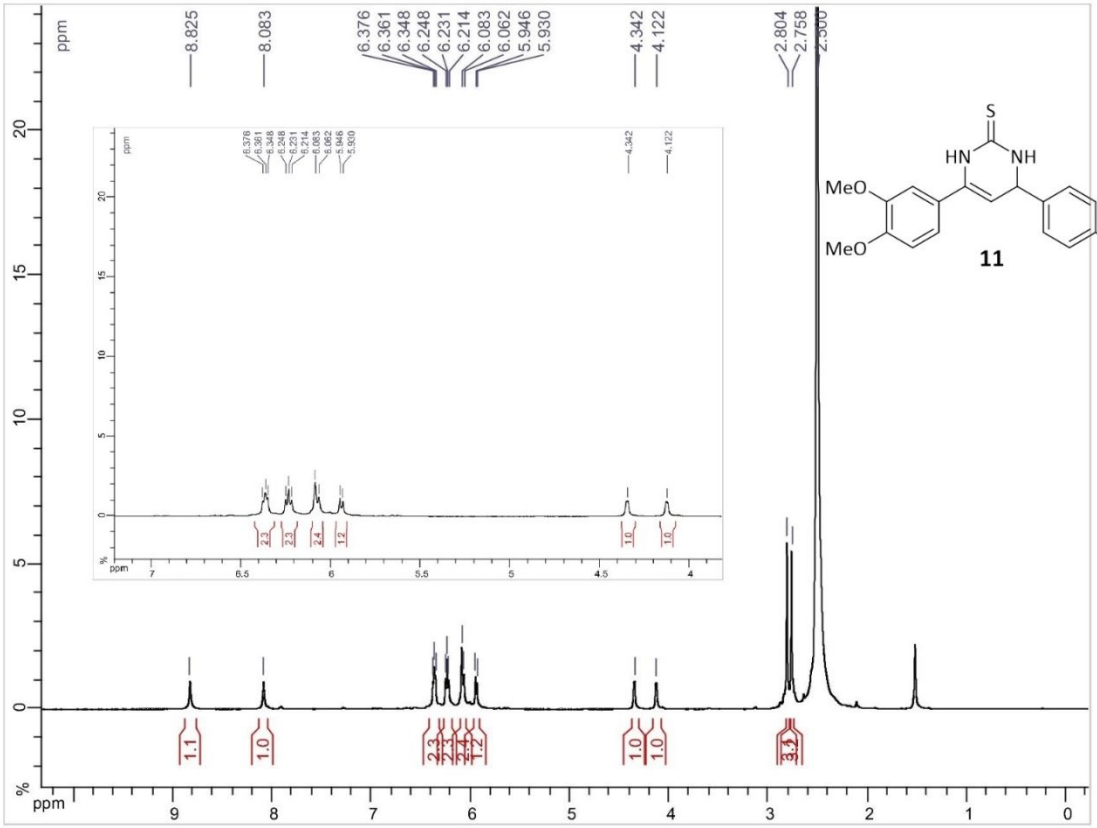
HN
NH
Br
F
10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8.083
6.376
6.361
6.348
6.248
6.231
6.214
6.083
6.062
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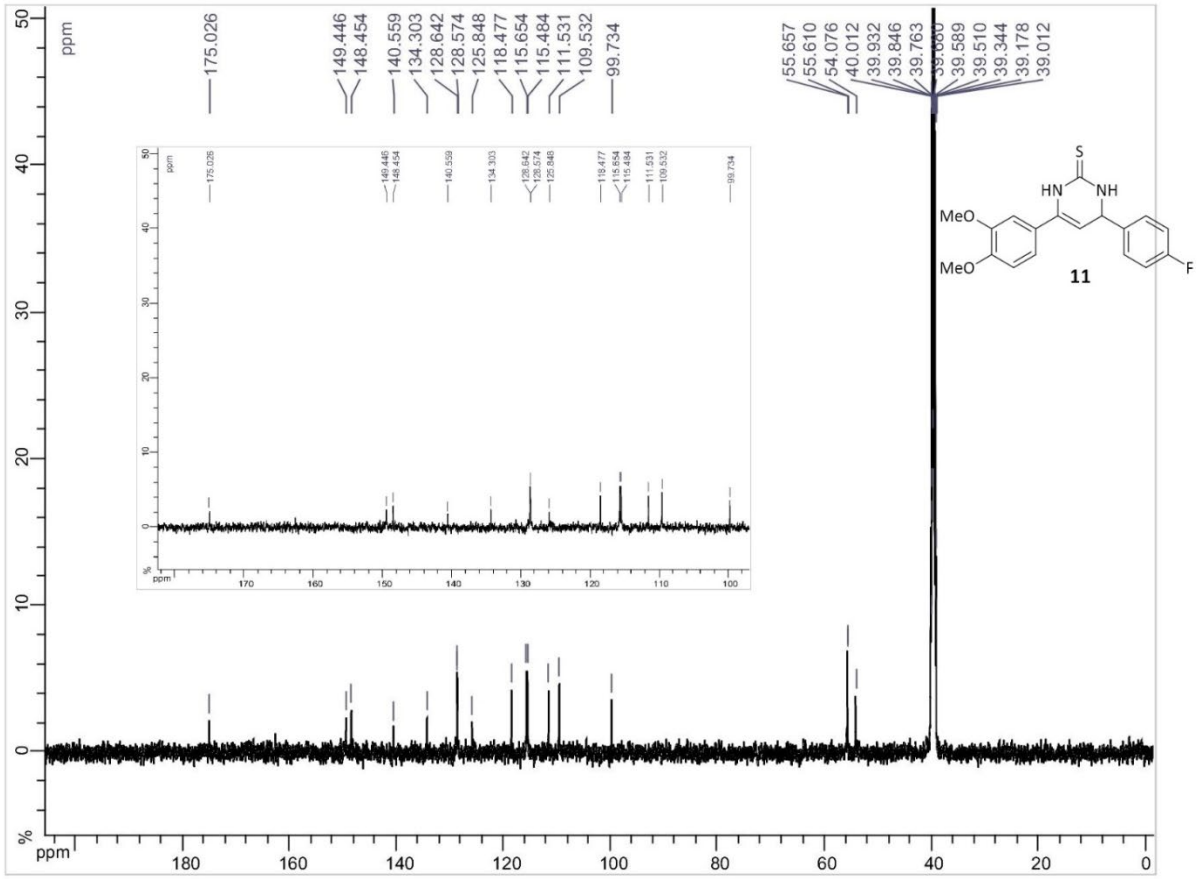
5.930
4.342
4.122
2.804
2.758
S
HN
NH
MeO
MeO
F
11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118.477
115.654
115.484
111.531
109.532
99.734
55.657
55.610
54.076
40.012
39.932
39.846
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39.589
39.510
39.344
39.178
39.012
S
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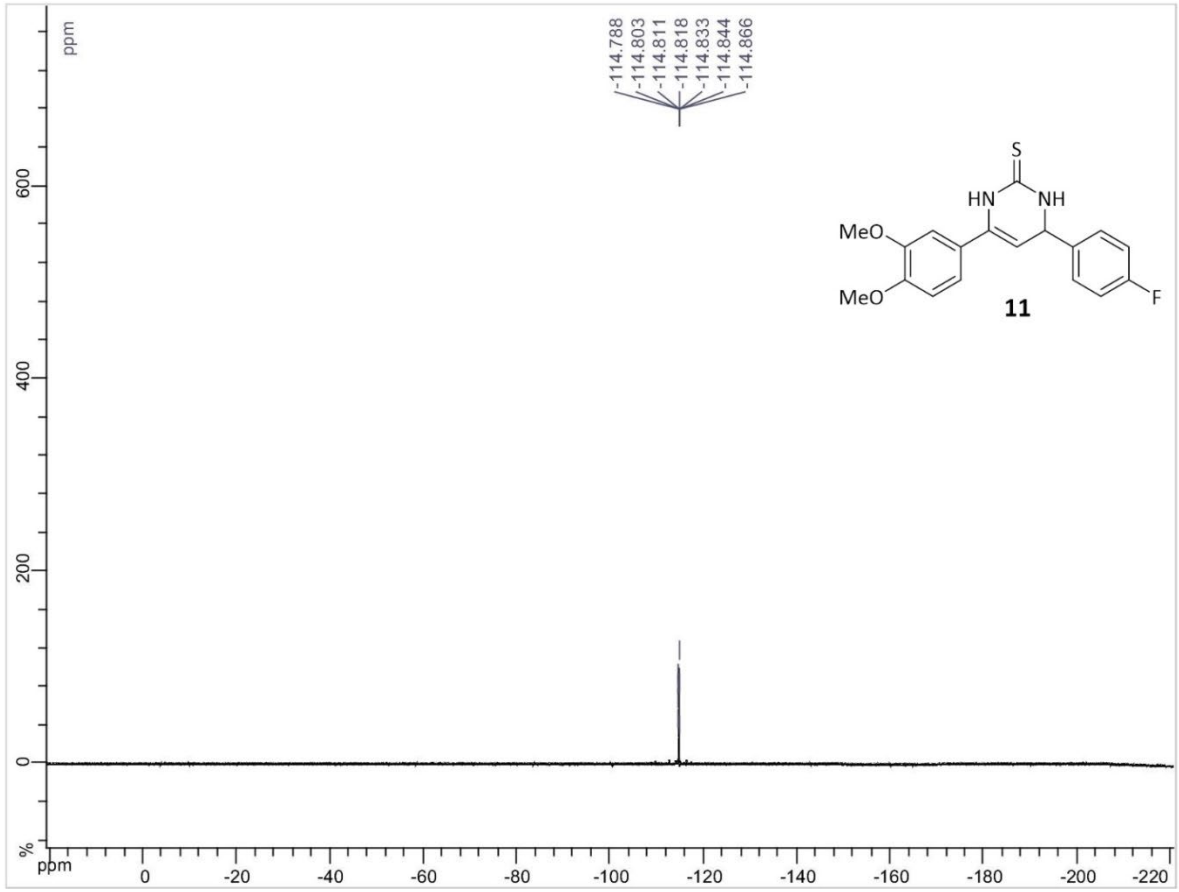
NH
MeO
MeO
F
11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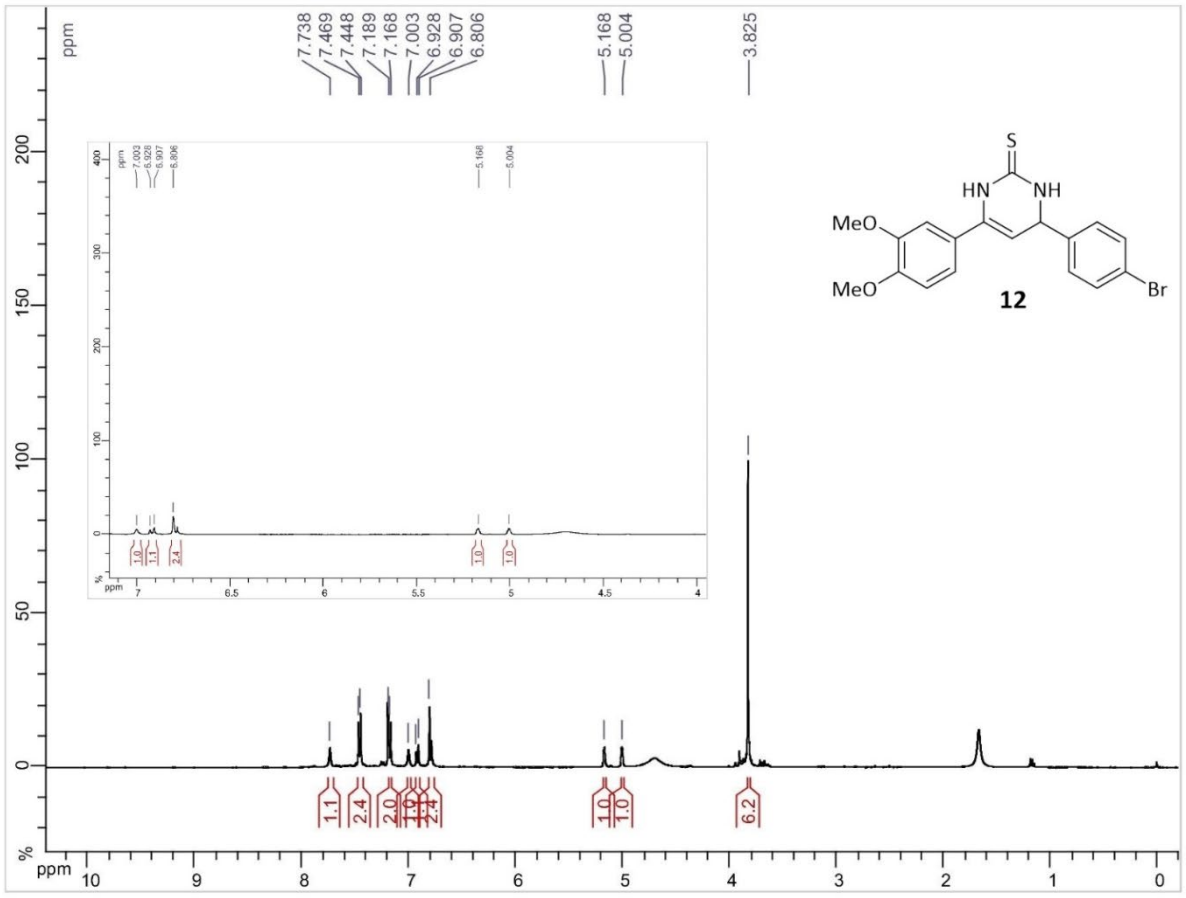
NH
MeO
MeO
F
11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6.806
5.168
5.004
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S
HN
NH
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MeO
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1.0
1.0
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1.0
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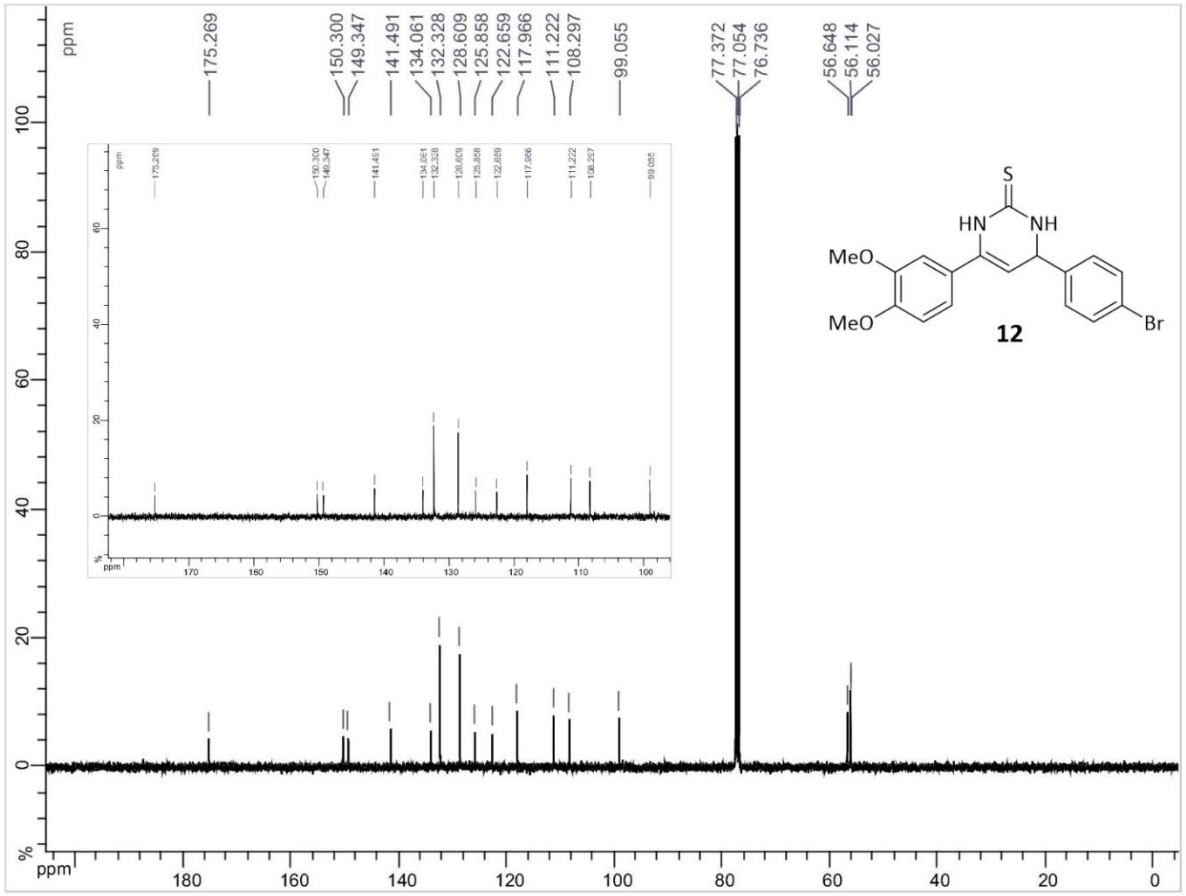
6.2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77.054
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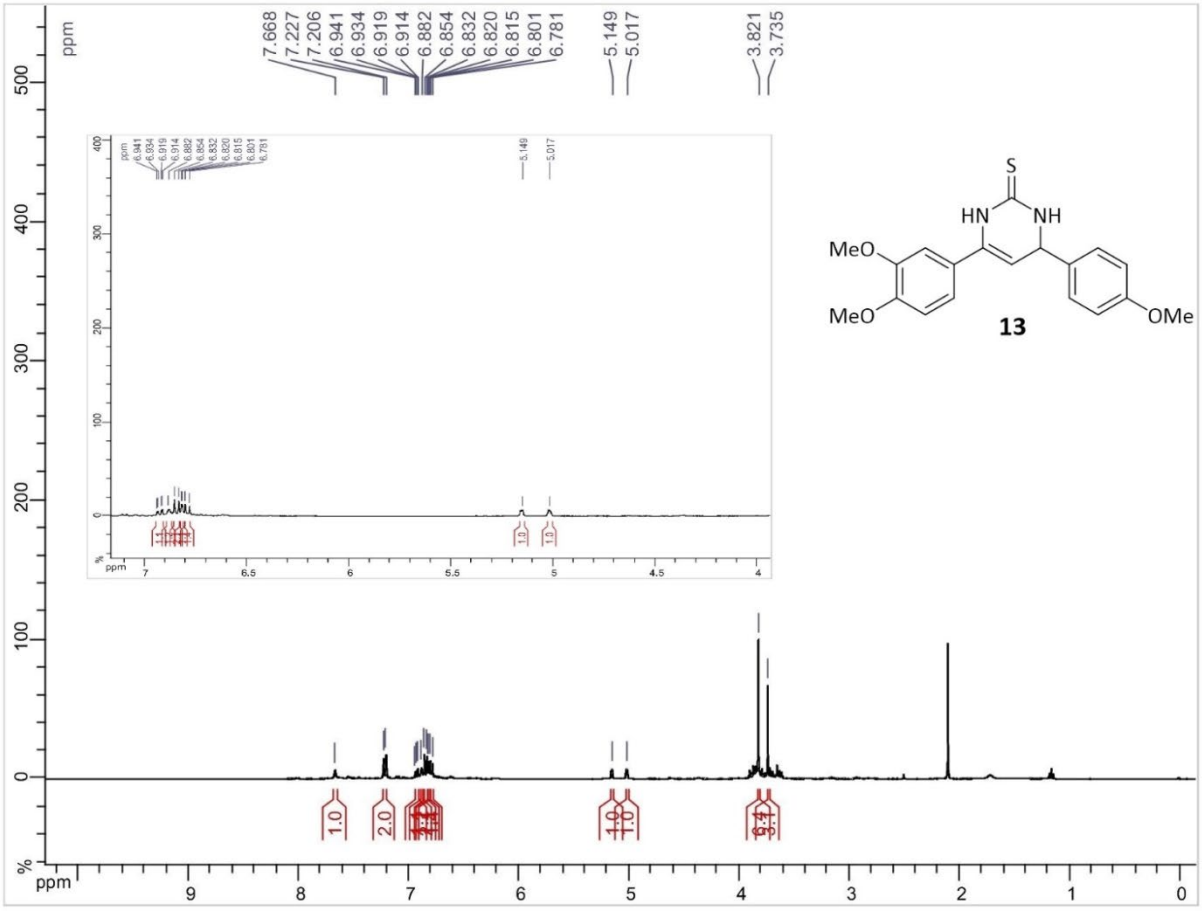
NH
MeO
MeO
Br
12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6.832
6.820
6.815
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5.149
5.017
3.821
3.735
ppm
S
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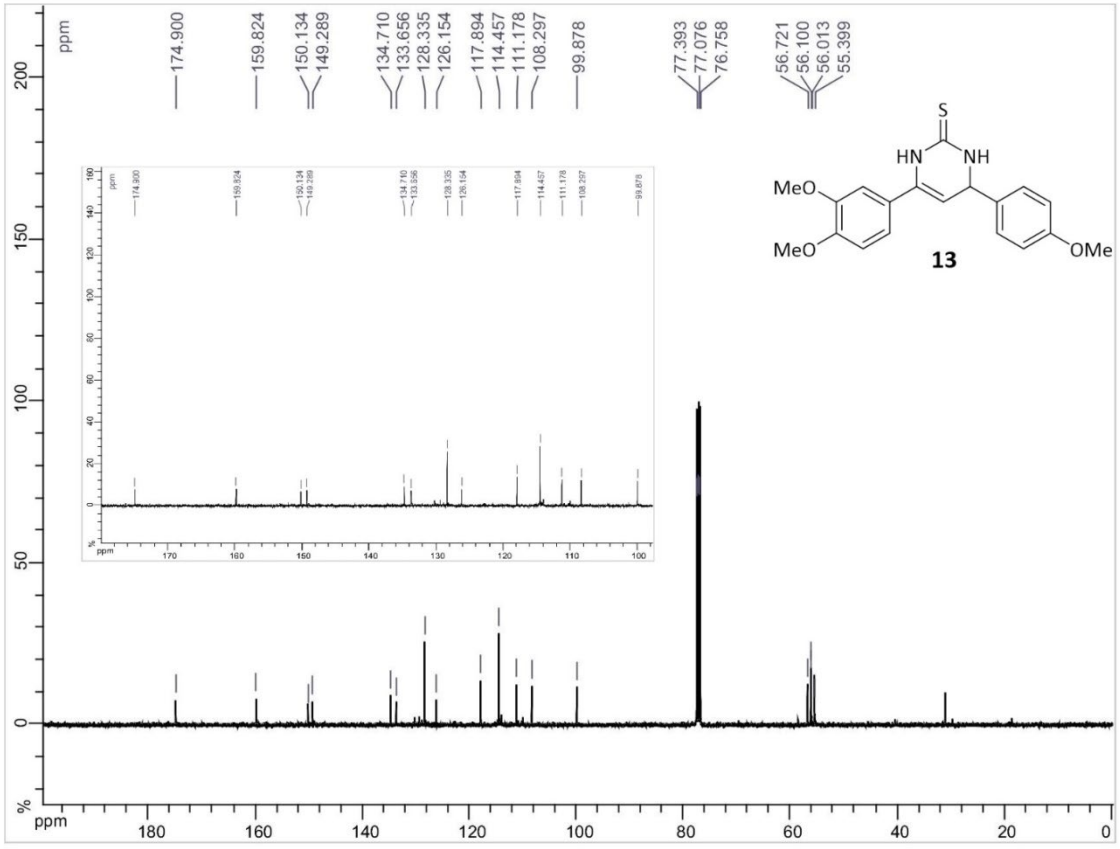
NH
MeO
MeO
OMe
13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117.894
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111.178
108.297
99.878
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77.076
76.758
56.721
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S
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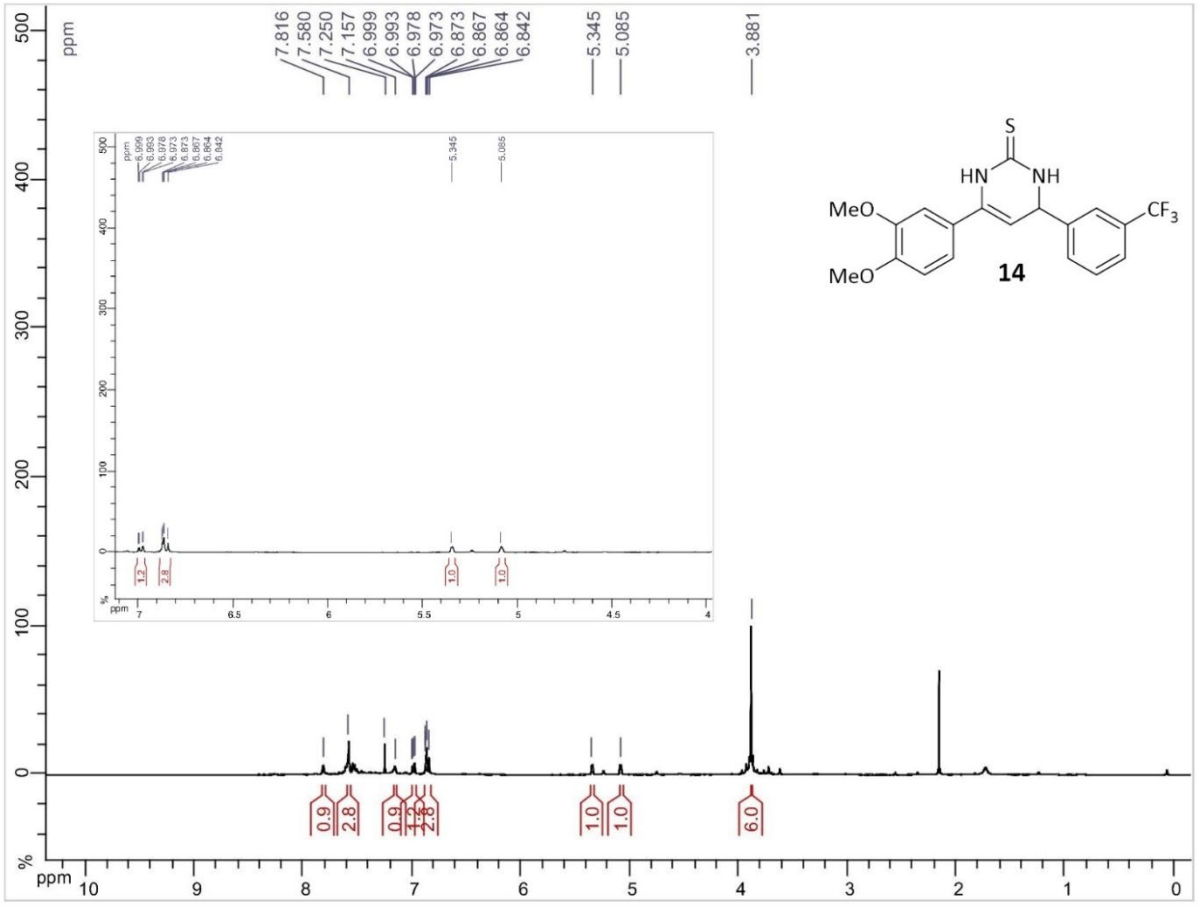
NH
MeO
MeO
OMe
13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6.864
6.842
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5.085
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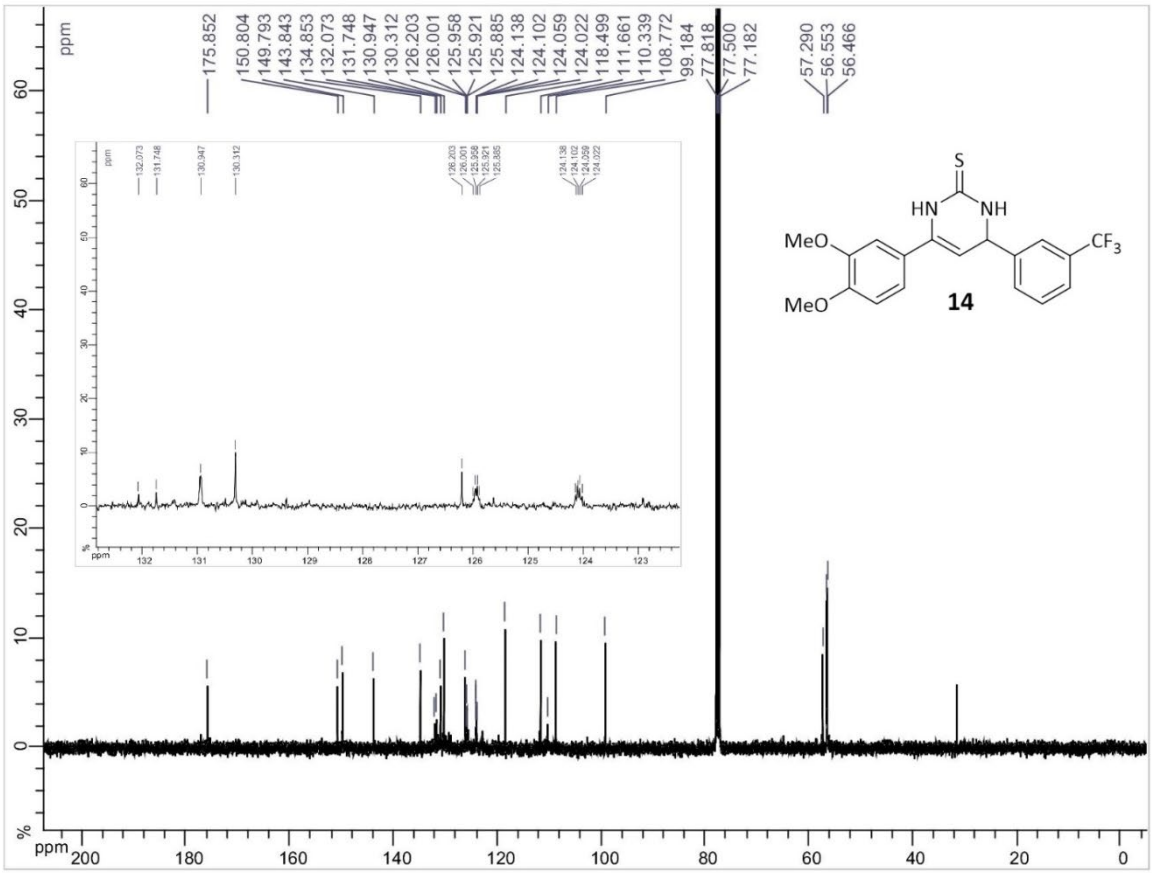
MeO
CF3
14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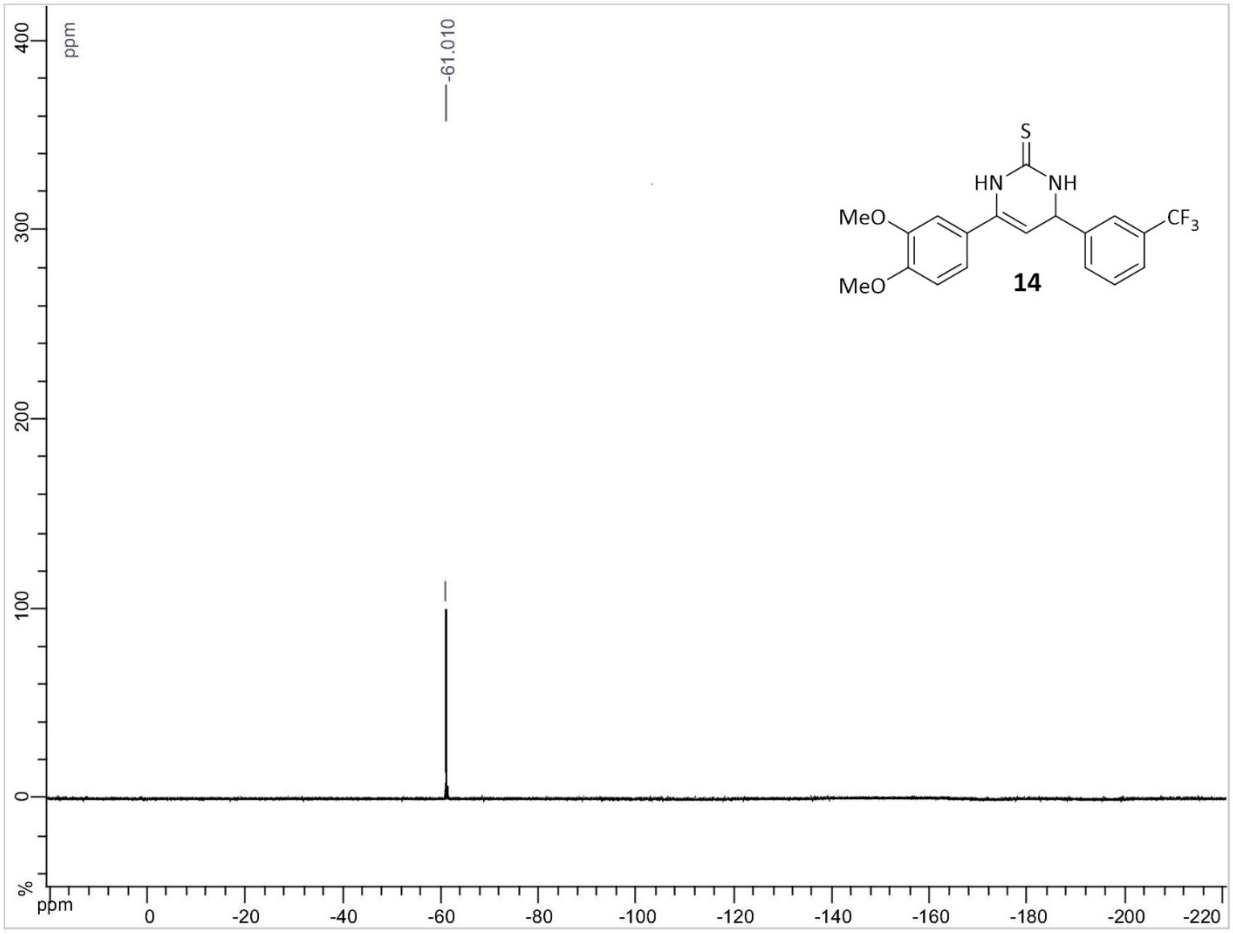
130.947
130.312
126.203
126.001
125.958
125.921
125.885
124.138
124.102
124.059
124.022
118.499
111.661
110.339
108.772
99.184
77.818
77.500
77.182
57.290
56.553
56.466
S
HN
NH
MeO
MeO
CF3
14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300
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100
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%
ppm
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-120
-140
-160
-180
-200
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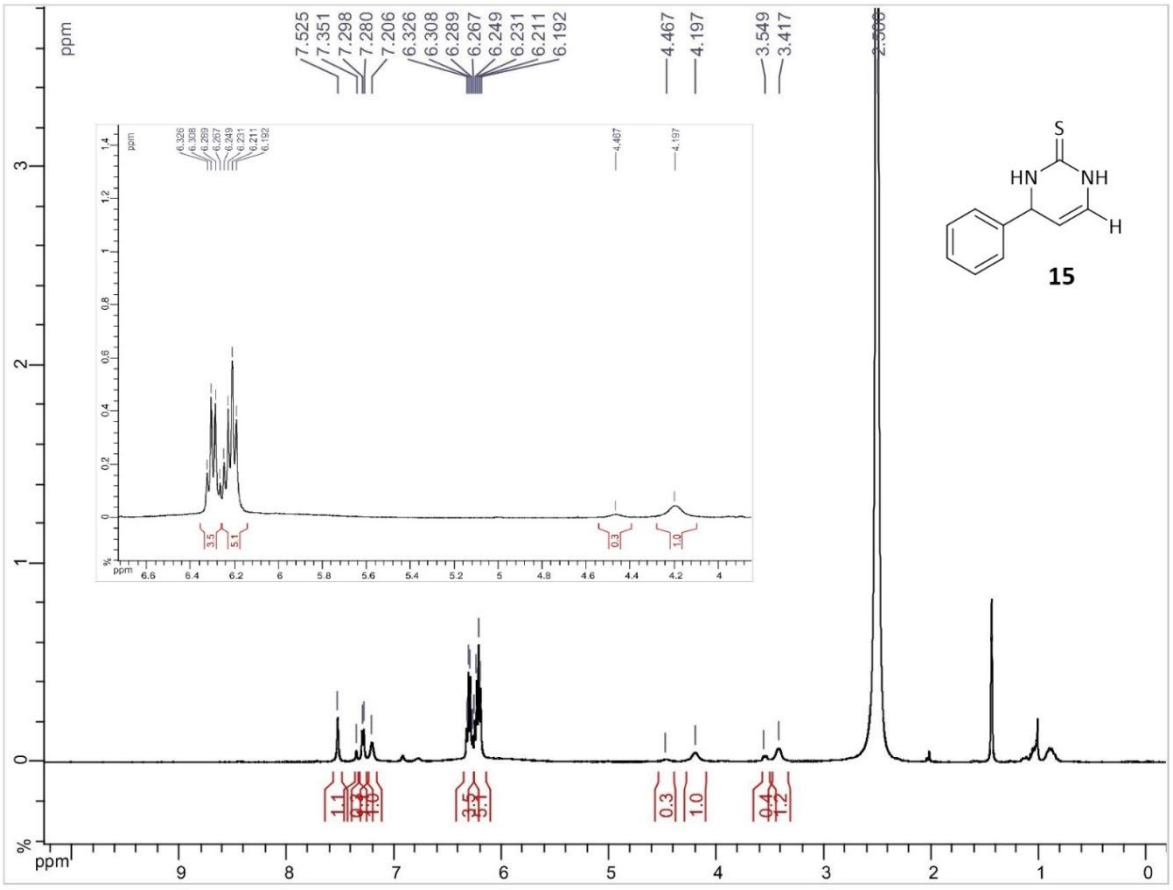
S
HN
NH
MeO
MeO
CF3
14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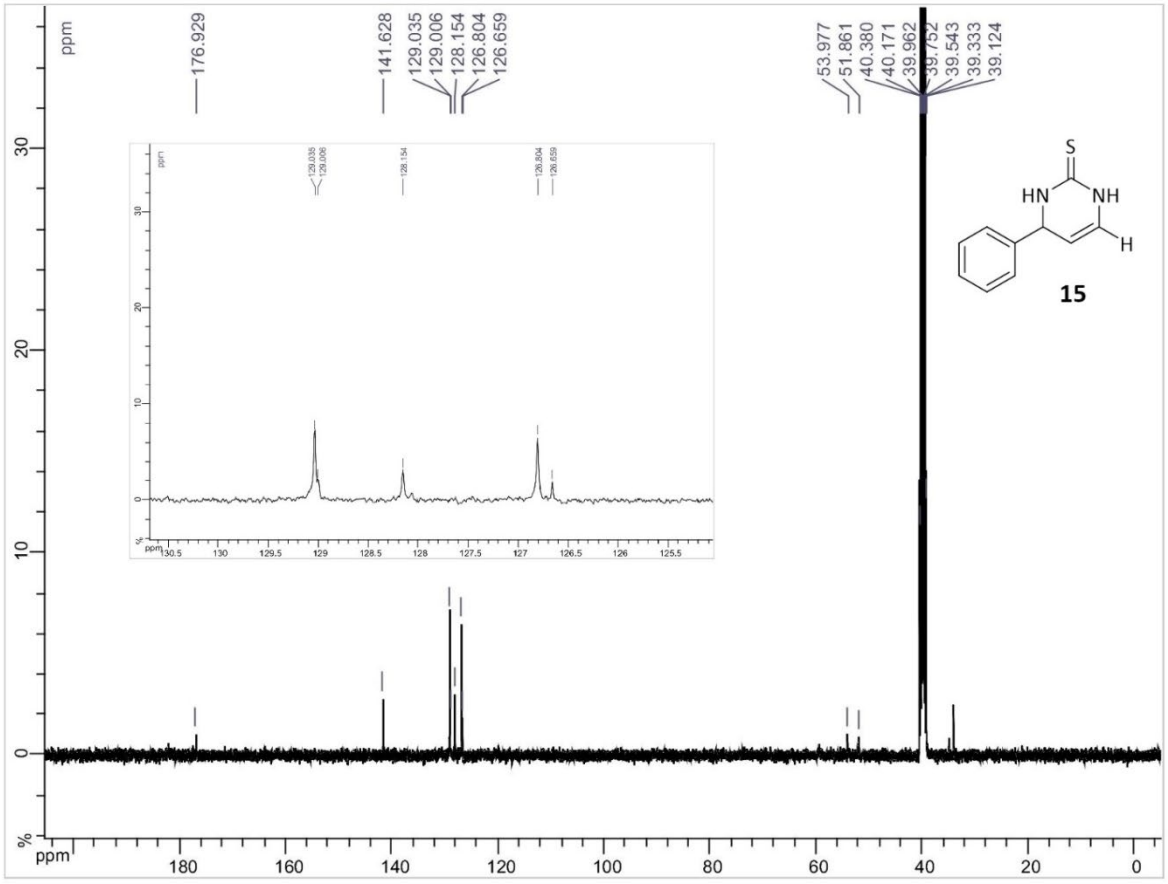
NH
H
15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39.333
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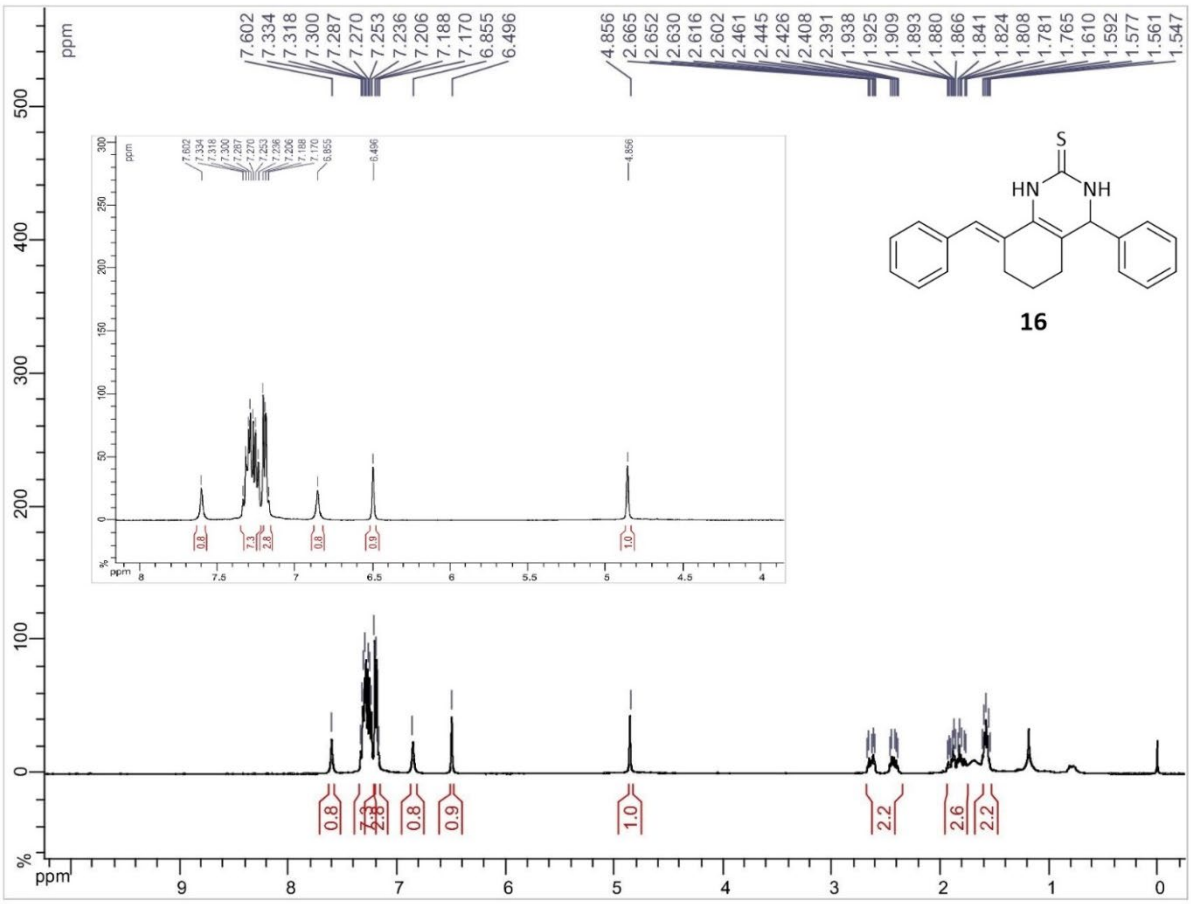
HN
NH
H
15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2.652
2.630
2.616
2.602
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2.445
2.426
2.408
2.391
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1.925
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1.880
1.866
1.841
1.824
1.808
1.781
1.765
1.610
1.592
1.577
1.561
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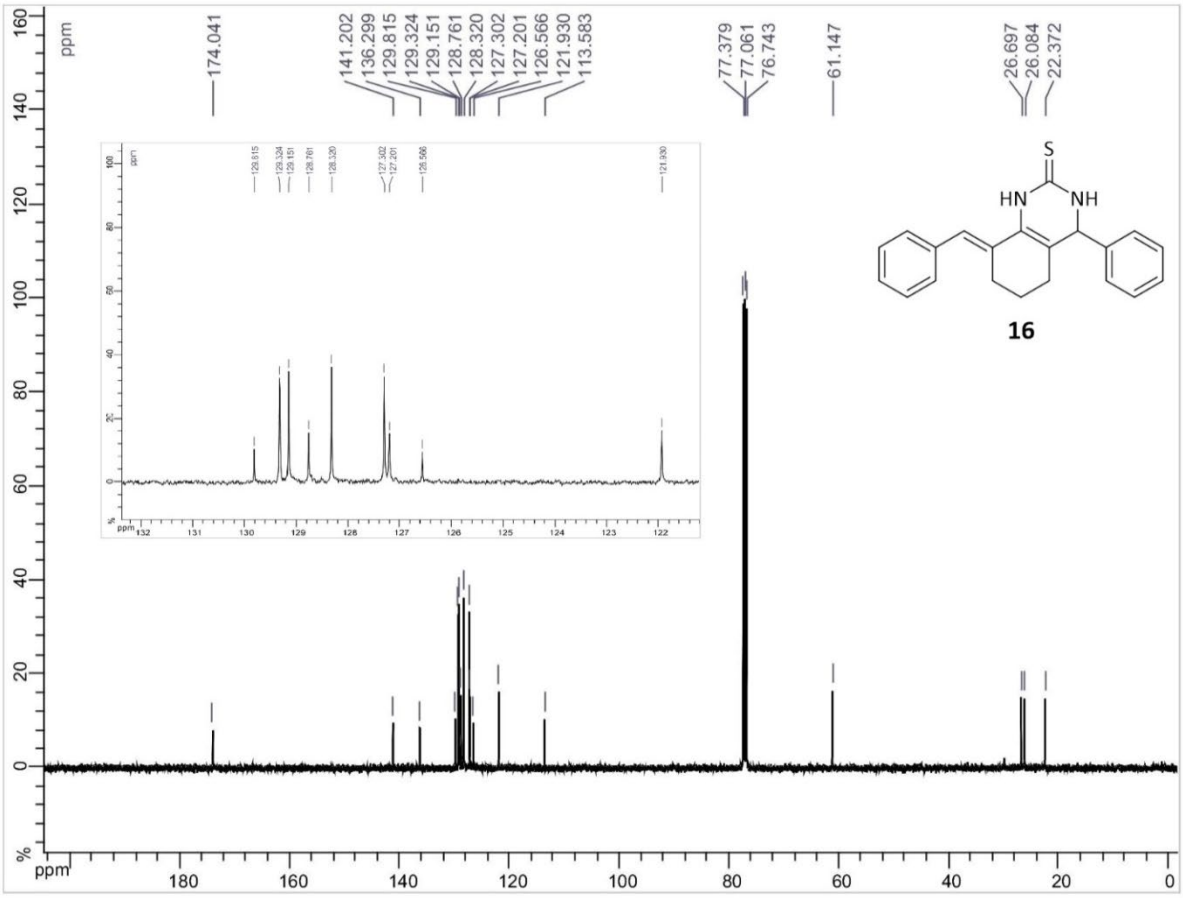
2.2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127.201
126.566
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77.379
77.061
76.743
61.147
26.697
26.084
22.372
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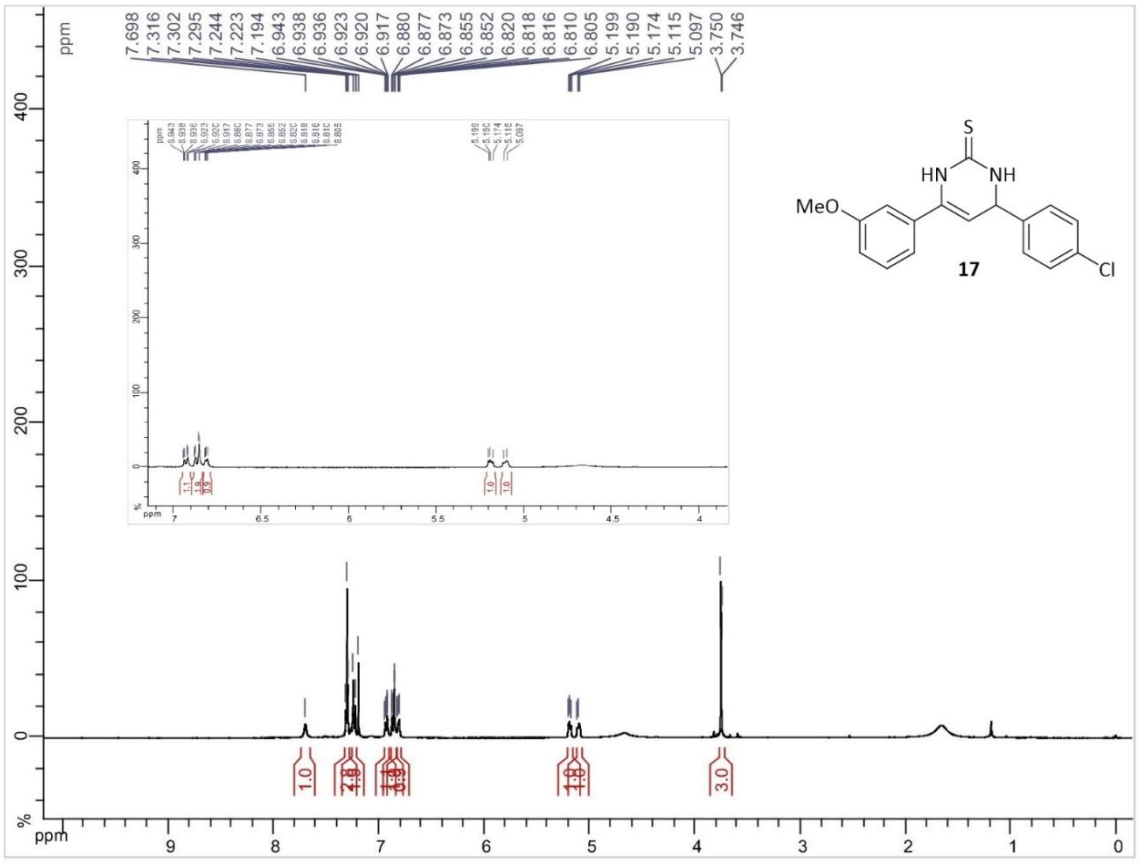
NH
16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6.917
6.880
6.877
6.873
6.855
6.852
6.820
6.818
6.816
6.810
6.805
5.199
5.190
5.174
5.115
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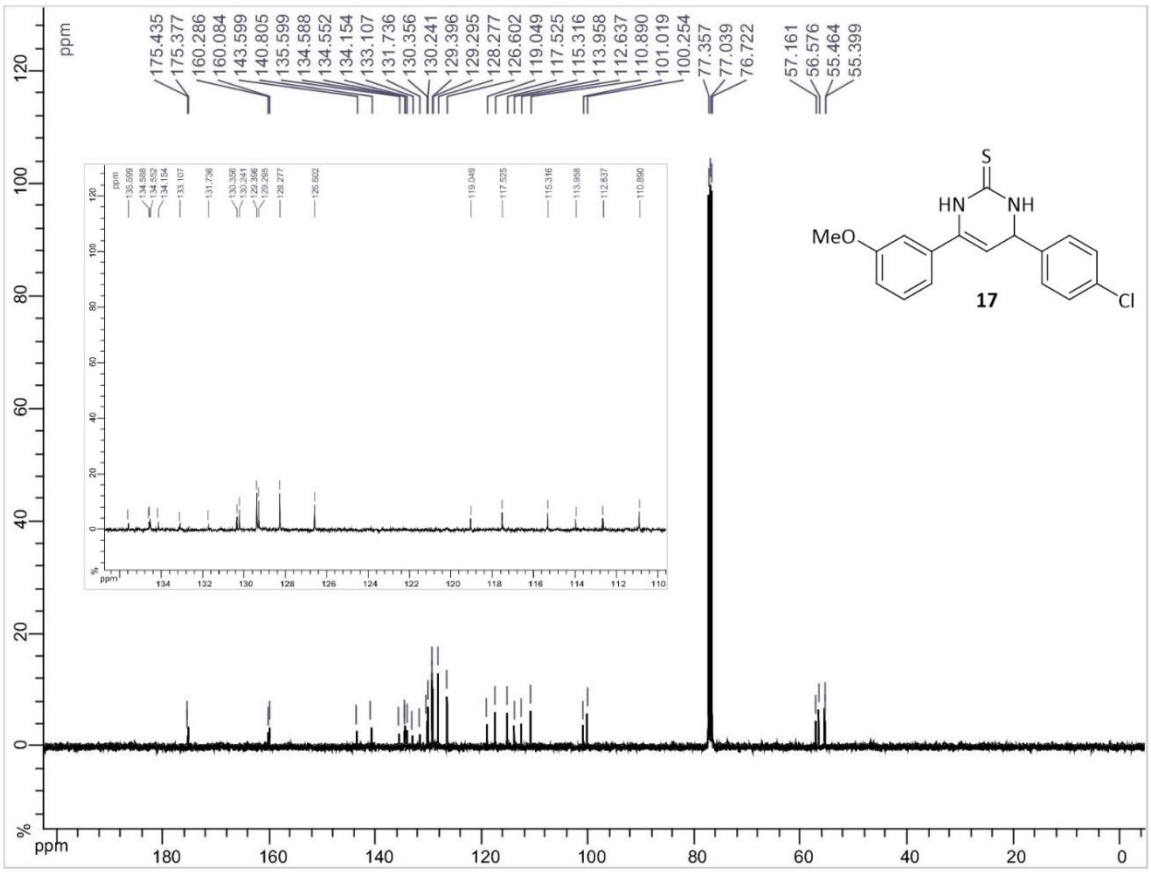
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128.277
126.602
119.049
117.525
115.316
113.958
112.637
110.890
101.019
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77.039
76.722
57.161
56.576
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55.399
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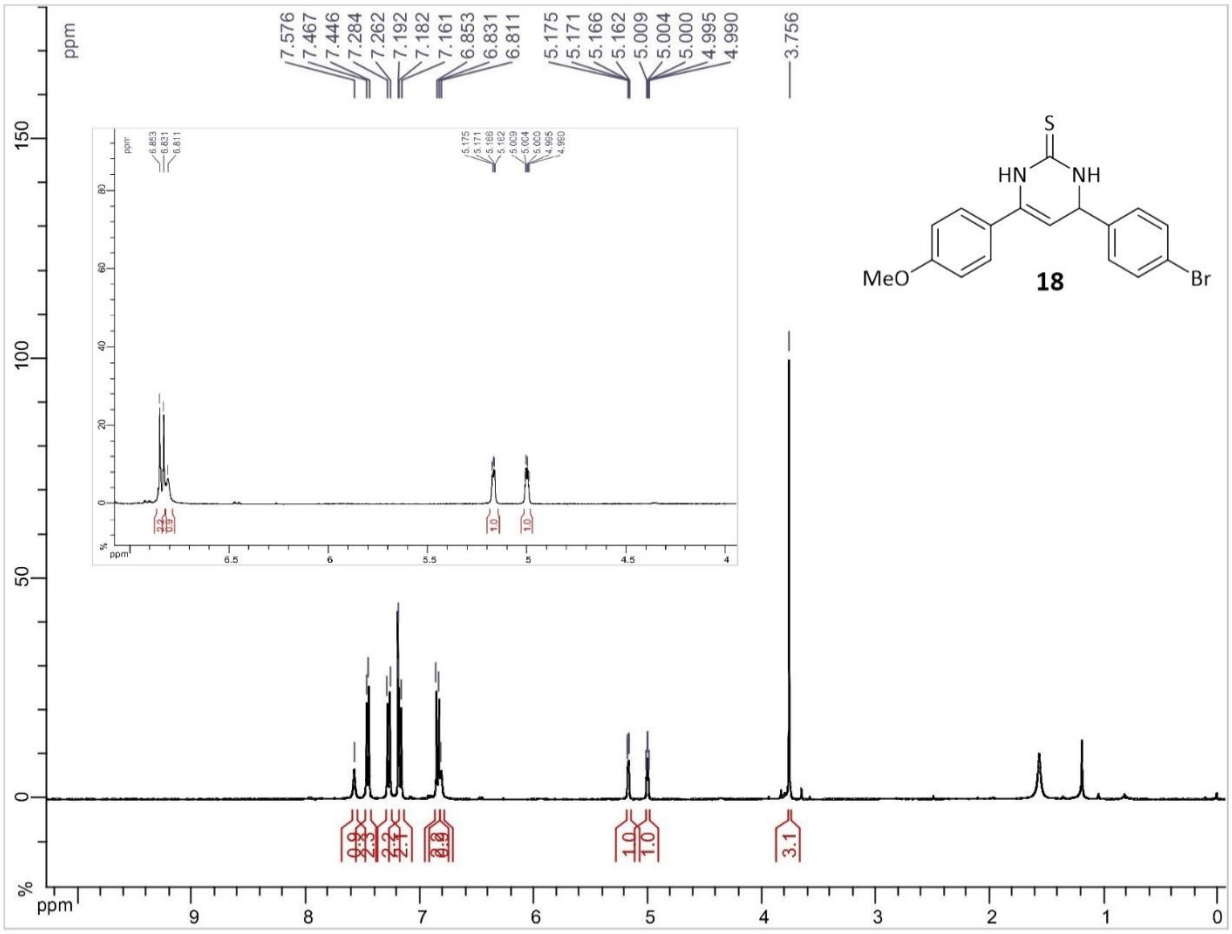
NH
MeO
Cl
17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6.811
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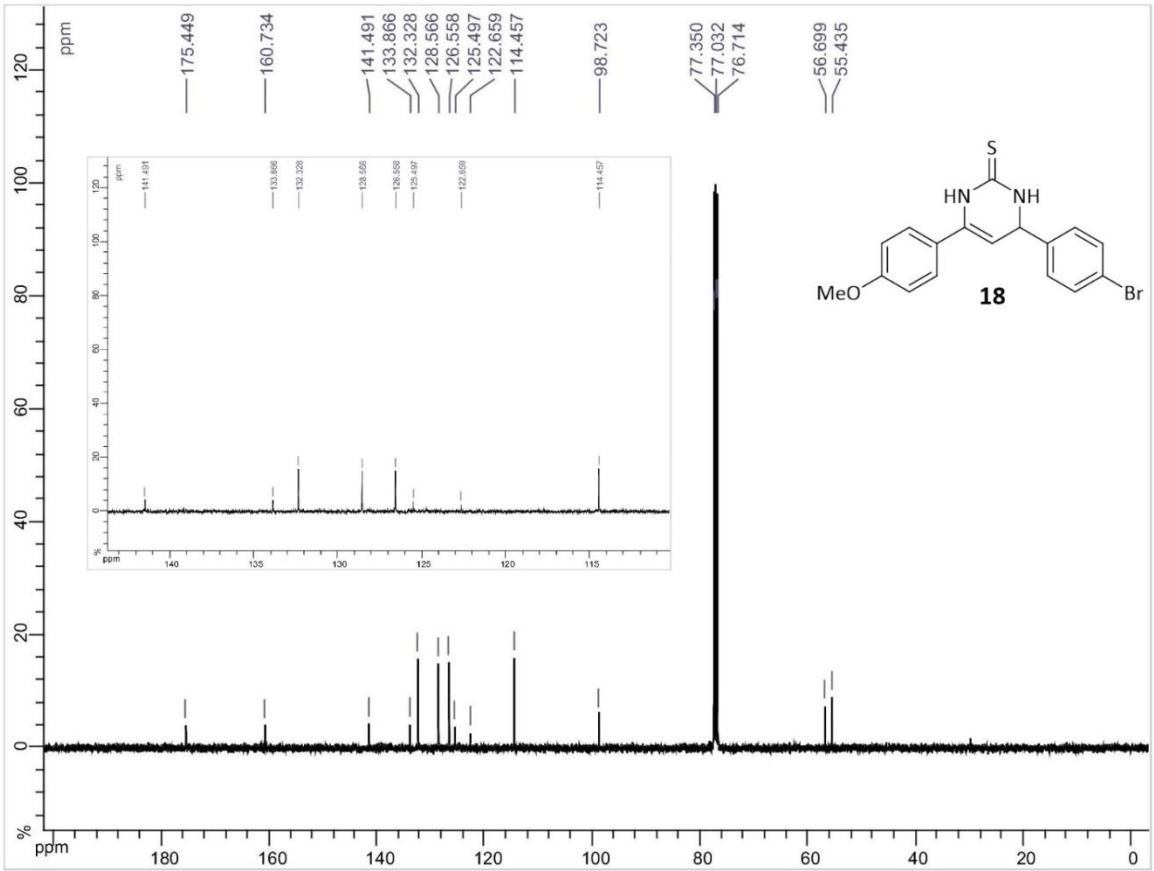
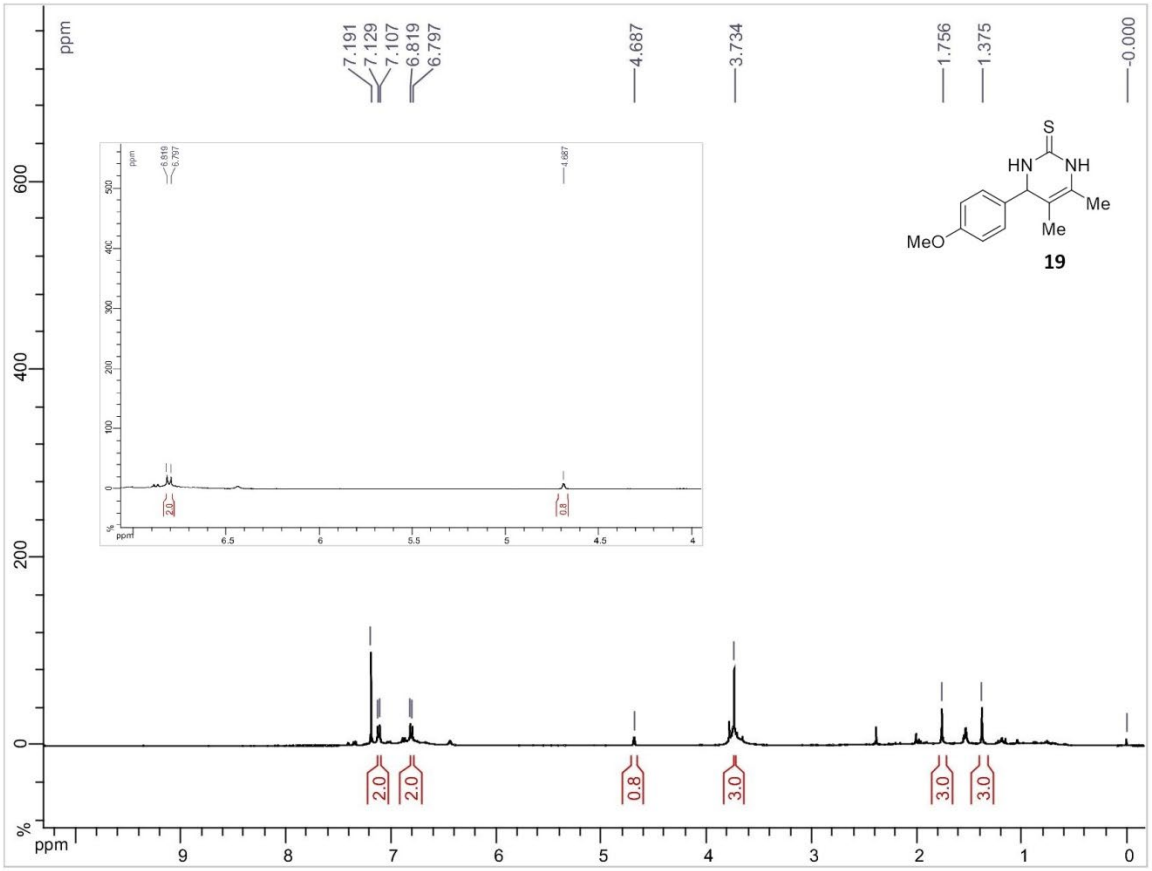
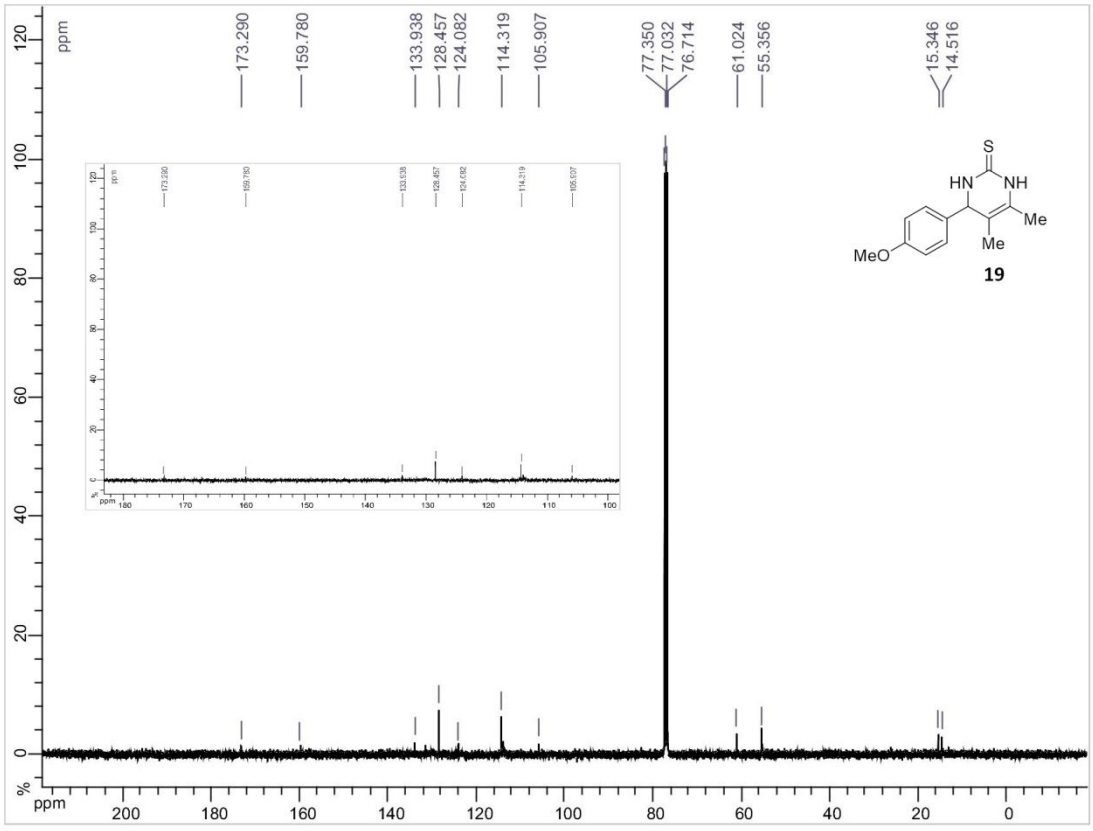
5.171
5.166
5.162
5.009
5.004
5.000
4.995
4.990
3.756
S
HN
NH
MeO
Br
18
ppm


ppm
175.449
160.734
141.491
133.866
132.328
128.566
126.558
125.497
122.659
114.457
98.723
77.350
77.032
76.714
56.699
55.435
S
HN
NH
MeO
Br
18
ppm


ppm
7.191
7.129
7.107
6.819
6.797
4.687
3.734
1.756
1.375
-0.000
S
HN
NH
Me
Me
MeO
19
2.0
2.0
0.8
3.0
3.0
3.0


ppm
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133.938
128.457
124.082
114.319
105.907
77.350
77.032
76.714
61.024
55.356
15.346
14.516
S
HN
NH
Me
Me
MeO
19