



## Supporting Information

for

### Exploring the scope of DBU-promoted amidations of 7-methoxycarbonylpterin

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### General procedures, characterization data, and copies of NMR spectra

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### **General information:**

All reagents used were of commercial quality and obtained from Aldrich Chemical Co. and used as received. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded in DMSO-*d*<sub>6</sub> (or methanol-*d*<sub>4</sub> for NMR kinetics) with a Bruker spectrometer using the solvent as the reference. Chemical shifts are given in parts per million (ppm). IR data were collected with a NEXUS 670 FT-IR. Purity was assessed on a Waters UPLC with a QDa detector. High resolution mass spectrometry was performed with a Varian 9.4T QFT-ESI ICR system. Filtrations were performed by aid of reduced pressure. Amidation reactions were run using an Anton-Paar MonoWave50<sup>TM</sup> reactor, operated without microwave irradiation and simply worked as a controlled heating block.<sup>1</sup>

### **Synthesis**

**7-Methoxycarbonylpterin (1):** Compound **1** was prepared by our previously reported acyl-radical insertion reaction.<sup>2</sup>

#### **General method for the DBU-assisted amidation:**

Compound **1** (50 mg, 0.23 mmol) was suspended in 1.0 mL of anhydrous MeOH in an oven-dried borosilicate reaction vessel (Anton-Paar), and stirred to create a slurry. To this was added DBU (68 μL, 0.45 mmol, 2 equiv) which resulted in full dissolution of **1**. To this was added the amine (2 equiv). (**Note:** for amines containing an acidic functional group, e.g. Gly/Ser/Ala, 4 equiv DBU were used to ensure basic conditions). The reaction vessel was then fitted with a silicone cap containing a PTFE seal. The tube was placed in a MonoWave50<sup>TM</sup> reactor and irradiated for the time and temperature indicated. Once the reaction was complete, the mixture was diluted with 1 mL of DI water, and acidified by the dropwise addition of 3 M HCl, resulting in a yellow precipitate. The product was isolated by filtration, rinsed several times with water and MeOH, and dried over P<sub>2</sub>O<sub>5</sub> in a vacuum oven.

**(2-Amino-4-oxo-3,4-dihydropteridine-7-carbonyl)glycine (2):** Compound **2** was synthesized by the general method above, using 34 mg glycine and 4 equiv DBU, resulting in 59 mg (99%) **2**. MP > 300°C. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ(ppm)= 12.72 (br, 1H),

11.61 (s, 1H), 9.04 (t,  $J = 5.6$  Hz, 1H), 8.88 (s, 1H), 7.03 (br, 2H), 3.99 (d,  $J = 6.0$  Hz);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta(\text{ppm}) = 171.2, 163.5, 160.8, 156.5, 154.9, 147.6, 136.9, 132.4, 41.5$ ; HRMS-ESI ( $m/z$ )  $[\text{M}-\text{H}]^-$  calc. for  $(\text{C}_9\text{H}_7\text{N}_6\text{O}_4)^-$  263.0534; found 263.0533. This is consistent with that reported in the literature.<sup>3</sup>

**2-Amino-N-(4-nitrophenethyl)-4-oxo-3,4-dihydropteridine-7-carboxamide (3):**

Compound **3** was synthesized by the general method, using 91 mg of 4-nitrophenethylamine hydrochloride and 4 equiv DBU, resulting in 77 mg (96%) of **3**. MP  $> 300^\circ\text{C}$ .  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta(\text{ppm}) = 11.58$  (s, 1H), 8.98 (t,  $J = 6$  Hz, 1H), 8.83 (s, 1H), 8.15 (d,  $J = 8.8$  Hz, 2H), 7.54 (d,  $J = 8.8$  Hz, 2H), 6.98 (br, 2H), 3.62 (q,  $J = 6.8$  Hz, 2H), 3.04 (t,  $J = 7$  Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta(\text{ppm}) = 163.3, 160.8, 156.5, 154.8, 148.3, 148.1, 146.6, 137.0, 132.1, 130.5, 123.9, 40.8, 35.1$ ; IR ( $\text{cm}^{-1}$ ): 3414, 3216, 1722, 1637, 1514, 1342; HRMS-ESI ( $m/z$ )  $[\text{M}+\text{H}]^+$  calc. for  $(\text{C}_{15}\text{H}_{14}\text{N}_7\text{O}_4)^+$  356.1102; found 356.1101

**2-Amino-N-benzyl-4-oxo-3,4-dihydropteridine-7-carboxamide (4):**

Compound **4** was synthesized by the general method, using 50  $\mu\text{L}$  of benzylamine and 2 equiv DBU, resulting in 64 mg (91%) of **4**. MP  $> 300^\circ\text{C}$ .  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta(\text{ppm}) = 11.63$  (s, 1H), 9.41 (t,  $J = 6.3$  Hz, 1H), 8.88 (s, 1H), 7.35-7.2 (m, 5H), 7.01 (br, 2H), 4.57 (d,  $J = 6$  Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta(\text{ppm}) = 163.4, 160.8, 156.6, 154.8, 148.3, 139.6, 137.2, 132.1, 128.7$  (2C), 127.8 (2C), 127.3, 42.9; IR ( $\text{cm}^{-1}$ ): 3434, 3321, 3189, 1713, 1635, 1518, 1222, 772; HRMS-ESI ( $m/z$ )  $[\text{M}+\text{H}]^+$  calc. for  $(\text{C}_{14}\text{H}_{13}\text{N}_6\text{O}_2)^+$  297.1094; found 297.1095

**(2-Amino-4-oxo-3,4-dihydropteridine-7-carbonyl)serine (5):**

Compound **5** was synthesized by the general method above, using 48 mg serine and 4 equiv DBU, resulting in 58 mg (88%) **5**. MP  $> 300^\circ\text{C}$ .  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta(\text{ppm}) = 13.02$  (br, 1H), 11.65 (s, 1H), 8.89 (s, 1H), 8.68 (d,  $J = 7.9$  Hz, 1H), 7.05 (br, 2H), 5.27 (br. s, 1H), 4.50 (dt,  $J = 7.9, 3.6$  Hz, 1H), 3.93-3.79 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta(\text{ppm}) = 171.9, 162.7, 160.8, 156.4, 155.0, 147.2, 136.7, 132.6, 61.5, 55.2$ ; HRMS-ESI ( $m/z$ )  $[\text{M}-\text{H}]^-$  calc. for  $(\text{C}_{10}\text{H}_9\text{N}_6\text{O}_5)^-$  293.0640; found 293.0638. This is consistent with that reported in the literature.<sup>3</sup>

**2-Amino-4-oxo-N-propyl-3,4-dihydropteridine-7-carboxamide (6):**

Compound **6** was synthesized by the general method, using 37  $\mu\text{L}$  of 1-propylamine and 2 equiv DBU, resulting in 49 mg (87%) of **6**. MP  $> 300^\circ\text{C}$ .  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta(\text{ppm}) = 11.68$  (s, 1H), 8.86 (s, 1H), 8.82 (t,  $J = 6$  Hz, 1H), 7.05 (br, 2H), 3.28 (q,  $J = 7.2$  Hz, 2H), 1.57 (sext.,  $J = 7.2$  Hz, 2H), 0.88 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta(\text{ppm}) = 163.2, 160.9, 156.3, 154.8, 148.4, 137.1, 132.0, 41.1, 22.8, 11.8$ ; IR ( $\text{cm}^{-1}$ ): 3260, 3130, 2964, 1705, 1644, 1518, 1397; HRMS-ESI ( $m/z$ )  $[\text{M}+\text{H}]^+$  calc. for  $(\text{C}_{10}\text{H}_{13}\text{N}_6\text{O}_2)^+$  249.1094; found 249.1095

**2-Amino-N-(2-hydroxypropyl)-4-oxo-3,4-dihydropteridine-7-carboxamide (7):**

Compound **7** was synthesized by the general method, using 35  $\mu\text{L}$  of 1-amino-2-propanol and 2 equiv DBU, resulting in 51 mg (85%) of **7**. MP  $> 300^\circ\text{C}$ .  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta(\text{ppm}) = 11.59$  (s, 1H), 8.87 (s, 1H), 8.61 (t,  $J = 5.6$  Hz, 1H), 7.02 (br, 2H), 4.88 (d,  $J = 4.8$  Hz, 1H), 3.82 (quint.,  $J = 6.4$  Hz, 1H), 3.36 (m, 1H), 3.21 (m, 1H), 1.08 (d,  $J = 6.4$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta(\text{ppm}) = 163.0, 160.9, 156.4, 154.9, 148.0, 136.9, 132.2, 65.3, 46.9, 21.6$ ; IR ( $\text{cm}^{-1}$ ): 3400-3100 (broad/overlapping), 2933, 1728, 1679, 1631, 1518, 1230; HRMS-ESI ( $m/z$ )  $[\text{M}+\text{H}]^+$  calc. for  $(\text{C}_{10}\text{H}_{13}\text{N}_6\text{O}_3)^+$  265.1044; found 265.1043

**2-Amino-N-(4-aminophenethyl)-4-oxo-3,4-dihydropteridine-7-carboxamide (8):**

Compound **8** was synthesized by the general method above, using 59  $\mu\text{L}$  4-(2-aminoethyl)aniline and 2 equiv DBU, which provided 56 mg (76%) of **8**. mp > 300°C.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta(\text{ppm})$ = 11.59 (s, 1H), 8.85 (s, 1H), 8.74 (t,  $J$  = 5.6 Hz, 1H), 7.03 (br, 2H), 6.89 (d,  $J$  = 8 Hz, 2H), 6.51 (d,  $J$  = 8 Hz, 2H), 5.46 (br, 2H), 3.47 (q,  $J$  = 6.8 Hz, 2H), 2.69 (t,  $J$  = 7.2 Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta(\text{ppm})$ = 162.9, 160.8, 154.9, 148.2, 146.9, 137.0, 132.1, 129.4 (2C), 126.7, 121.2, 114.7 (2C), 41.3, 34.7; IR ( $\text{cm}^{-1}$ ): 3413, 3340, 3195, 1731, 1655, 1530, 1426; HRMS-ESI ( $m/z$ )  $[\text{M}+\text{H}]^+$  calc. for  $(\text{C}_{15}\text{H}_{16}\text{N}_7\text{O}_2)^+$  326.1360; found 326.1358

**2-Amino-N-(2-hydroxyethyl)-N-methyl-4-oxo-3,4-dihydropteridine-7-carboxamide**

**(9):** Compound **9** was synthesized by the general method above, using 37  $\mu\text{L}$  *N*-methylaminoethanol and 2 equiv DBU. This resulted in 43 mg (71%) of **9** which exists as a 2:1 mixture of the *s-cis* and *s-trans* rotamers. MP > 300°C.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta(\text{ppm})$  = {two rotamers}<sup>4</sup> 8.41 (s, 1H) {8.45 minor rotamer}, 7.07 (br, 2H) {overlapping minor rotamer}, 4.71 (t,  $J$  = 5.2 Hz, 1H) {4.84 minor rotamer}, 3.51 (q,  $J$  = 5.2 Hz, 2H) {3.65 minor rotamer}, 3.41 (t,  $J$  = 5.6 Hz, 2H) {3.55 minor rotamer}, 3.05 (s, 3H) {3.01 minor rotamer};  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta(\text{ppm})$ = {two rotamers} 167.0 {1.66.2 minor rotamer}, 161.2, 156.2, 155.1, 154.1 {153.9 minor rotamer}, 138.3 {137.6 minor rotamer}, 129.5 {129.8 minor rotamer}, 58.8 {58.7 minor rotamer}, 52.5 {50.2 minor rotamer}, 33.6 {37.9 minor rotamer}; IR ( $\text{cm}^{-1}$ ): 3395, 3259, 3126, 2734, 1697, 1613, 1520, 1405, 1234; HRMS-ESI ( $m/z$ )  $[\text{M}+\text{H}]^+$  calc. for  $(\text{C}_{10}\text{H}_{13}\text{N}_6\text{O}_3)^+$  265.1044; found 265.1044

**2-Amino-4-oxo-N-(2-(pyridin-2-yl)ethyl)-3,4-dihydropteridine-7-carboxamide (10):**

Compound **10** was synthesized by the general method, using 54  $\mu\text{L}$  2-(2-aminoethyl)pyridine and 2 equiv DBU, which provided 46 mg (66%) of **10**. mp > 300°C.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta(\text{ppm})$ = 11.63 (s, 1H), 8.95 (t,  $J$  = 6 Hz, 1H), 8.85 (s, 1H), 8.54 (d,  $J$  = 4 Hz, 1H), 7.78 (t,  $J$  = 7.2 Hz, 1H), 7.35 (d,  $J$  = 7.6 Hz, 1H), 7.29 (t,  $J$  = 6 Hz, 1H), 7.02 (br, 2H), 3.71 (q,  $J$  = 6.4 Hz, 2H), 3.07 (t,  $J$  = 6.8 Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta(\text{ppm})$ = 165.5, 163.2, 160.9, 159.1, 154.8, 148.8, 148.1, 137.9, 137.0, 132.1, 124.0, 122.3, 39.1, 37.0; IR ( $\text{cm}^{-1}$ ): 3126, 2973, 1672, 1609, 1436, 1134, 767; HRMS-ESI ( $m/z$ )  $[\text{M}+\text{H}]^+$  calc. for  $(\text{C}_{14}\text{H}_{14}\text{N}_7\text{O}_2)^+$  312.1203; found 312.1203

**2-Amino-N-isopropyl-4-oxo-3,4-dihydropteridine-7-carboxamide (11):**

Compound **11** was synthesized by the general method, using 40  $\mu\text{L}$  of 2-propylamine and 2 equiv DBU, resulting in 37 mg (66%) of **11**. MP > 300°C.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta(\text{ppm})$ = 11.59 (s, 1H), 8.85 (s, 1H), 8.48 (d,  $J$  = 8 Hz, 1H), 6.98 (br, 2H), 4.14 (oct,  $J$  = 6.8 Hz, 1H), 1.21 (d,  $J$  = 6.4 Hz, 6H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta(\text{ppm})$ = 165.5, 162.3, 160.9, 154.8, 148.5, 137.1, 131.9, 41.4, 22.5 (2C); IR ( $\text{cm}^{-1}$ ): 3141, 2974, 1695, 1633, 1515, 1386; HRMS-ESI ( $m/z$ )  $[\text{M}+\text{H}]^+$  calc. for  $(\text{C}_{10}\text{H}_{13}\text{N}_6\text{O}_2)^+$  249.1094; found 249.1093

**2-Amino-4-oxo-N-(1-phenylethyl)-3,4-dihydropteridine-7-carboxamide (12):**

Compound **12** was synthesized by the general method, using 59  $\mu\text{L}$  of  $\alpha$ -methylbenzylamine and 2 equiv DBU, resulting in 42 mg (60%) of **12**. MP > 300°C.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta(\text{ppm})$ = 11.65 (s, 1H), 9.07 (d,  $J$  = 8.4 Hz, 1H), 8.83 (s, 1H), 7.44 (d,  $J$  = 7.2 Hz, 2H), 7.34 (t,  $J$  = 7.2 Hz, 2H), 7.25 (t,  $J$  = 7.2 Hz, 1H), 7.03 (br, 2H), 5.19 (quint,  $J$  = 7.6 Hz, 1H), 1.54 (d,  $J$  = 7.2 Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta(\text{ppm})$ = 162.6, 161.0, 156.5, 154.9, 148.4, 144.5, 137.2, 132.1, 128.8 (2C), 127.3, 126.7 (2C), 48.9,

22.3; IR (cm<sup>-1</sup>): 3405, 3141, 1643, 1515, 1397, 773, 693; HRMS-ESI (m/z) [M+H]<sup>+</sup> calc. for (C<sub>15</sub>H<sub>15</sub>N<sub>6</sub>O<sub>2</sub>)<sup>+</sup> 311.1251; found 311.1252

**(2-Amino-4-oxo-3,4-dihydropteridine-7-carbonyl)alanine (13):** Compound **13** was synthesized by the general method above, using 41 mg alanine and 4 equiv DBU, resulting in 31 mg (49%) **13**. MP > 300°C. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ(ppm)= 12.90 (br, 1H), 11.67 (s, 1H), 8.86 (s, 1H), 8.83 (d, *J* = 8 Hz, 1H), 7.04 (br, 2H), 4.48 (quint, *J* = 7.2 Hz, 1H), 1.45 (d, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ(ppm)= 173.9, 165.6, 162.8, 160.8, 154.9, 147.6, 136.9, 132.4, 48.3, 17.7; HRMS-ESI (m/z) [M-H]<sup>-</sup> calc. for (C<sub>10</sub>H<sub>9</sub>N<sub>6</sub>O<sub>4</sub>)<sup>-</sup> 277.0691; found 277.0689. This is consistent with that reported in the literature.<sup>3</sup>

**Methyl 5-((2-amino-4-oxo-3,4-dihydropteridine-7-carboxamido)methyl)furan-2-carboxylate (14):** Compound **14** was synthesized by the general method above, using 69 mg methyl 5-(aminomethyl)-furan-2-carboxylate<sup>5</sup> and 2 equiv DBU. This resulted in a mixture of the product and 7-carboxy-pterin, which was sonicated in a dilute aqueous solution of NaHCO<sub>3</sub> to dissolve the acid and the product was isolated by filtration, resulting in 37 mg (47%) **14** after drying. MP > 300°C. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ(ppm)= 11.62 (s, 1H), 9.45 (t, *J* = 6 Hz, 1H), 8.88 (s, 1H), 7.24 (d, *J* = 3.6 Hz, 1H), 7.02 (br, 2H), 6.5 (d, *J* = 3.2 Hz, 1H), 4.56 (d, *J* = 6 Hz, 2H), 3.79 (s, 3H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ(ppm)= 163.5, 160.8, 158.7, 157.4, 156.2, 154.8, 147.9, 143.2, 137.2, 132.3, 119.8, 110.0, 52.1, 36.7; IR (cm<sup>-1</sup>): 3126, 1681, 1518, 1338, 1204, 1016, 761 HRMS-ESI (m/z) [M+H]<sup>+</sup> calc. for (C<sub>14</sub>H<sub>13</sub>N<sub>6</sub>O<sub>5</sub>)<sup>+</sup> 345.0942; found 345.0942

**2-Amino-7-(morpholine-4-carbonyl)pteridin-4(3H)-one (15):** Compound **15** was synthesized by the general method above, using 40 μL morpholine and 2 equiv DBU. Initially this resulted in a 1:1 mixture of the product and 7-carboxy-pterin, which was sonicated in a dilute aqueous solution of NaHCO<sub>3</sub> to dissolve the carboxylate, and the product was collected by filtration, resulting in 28 mg (44%) **15** after drying. MP > 300°C. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ(ppm)= 11.64 (s, 1H), 8.49 (s, 1H), 7.07 (br, 2H), 3.68 (m, 4H), 3.58 (m, 2H), 3.49 (m, 2H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ(ppm)= 164.9, 161.2, 156.3, 155.2, 152.8, 137.9, 130.1, 66.7, 66.4, 47.4, 42.5; IR (cm<sup>-1</sup>): 3438, 3336, 3084, 2986, 2934, 1720, 1632, 1595, 1204; HRMS-ESI (m/z) [M+H]<sup>+</sup> calc. for (C<sub>11</sub>H<sub>13</sub>N<sub>6</sub>O<sub>3</sub>)<sup>+</sup> 277.1044; found 277.1043

**2-Amino-*N*-benzyl-*N*-methyl-4-oxo-3,4-dihydropteridine-7-carboxamide (16):** Synthesis of **16** required a modified method, where 0.3 mL (10 equiv) of *N*-methylbenzylamine was added to the solution of 50 mg 7CMP (**1**) in 1 mL MeOH and 2 equiv of DBU. The reaction vessel was sealed and heated to 130 °C for 3 h. Work-up proceeded as described in the general method, providing 44 mg (63%) of **16**, existing as an equal mixture of the *s*-*cis* and *s*-*trans* rotamers. MP > 300°C. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ(ppm)= {two rotamers}<sup>4</sup> 11.57 {overlapping rotamer} (s, 1H), 8.53 {8.49} (s, 1H), 7.42-7.27 {overlapping rotamer} (m, 5H), 7.03 {overlapping rotamer} (br, 2H), 4.72 {4.58} (s, 2H), 2.91 {2.90} (s, 3H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ(ppm)= {two rotamers} 166.7 {166.5}, 161.1 {overlapping}, 155.2 {overlapping}, 153.6 {153.5}, 137.7 {137.6}, 137.2 {137.1}, 130.1 {130.0}, 129.1(2C) {129.0}, 128.9 {128.8}, 128.1(2C) {127.9}, 127.8 {overlapping}, 53.7 {50.4}, 36.6 {32.9}; IR (cm<sup>-1</sup>): 3150, 2744, 1696, 1658, 1512, 1407, 1334, 777, 637; HRMS-ESI (m/z) [M+H]<sup>+</sup> calc. for (C<sub>15</sub>H<sub>15</sub>N<sub>6</sub>O<sub>2</sub>)<sup>+</sup> 311.1251; found 311.1251

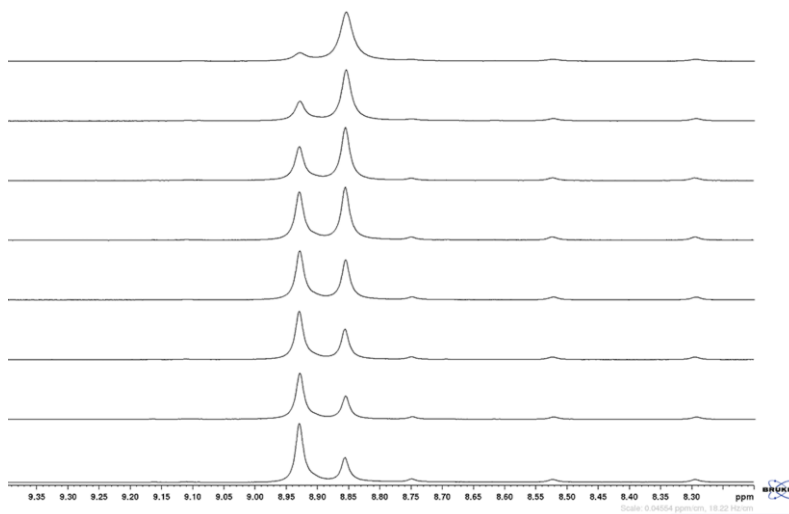
### **Pseudo-first order kinetics NMR data collection:**

Kinetics for the DBU-amidation was followed by  $^1\text{H}$  NMR for a representative set of amines. Pseudo-first order conditions were used, whereby the amine was in large excess and its change in concentration was negligible.<sup>5</sup> Therefore, the rate could be viewed as:

Rate =  $k_{\text{obs}}[7\text{-CMP}]$ , where  $k_{\text{obs}} = k[\text{Amine}]_0$

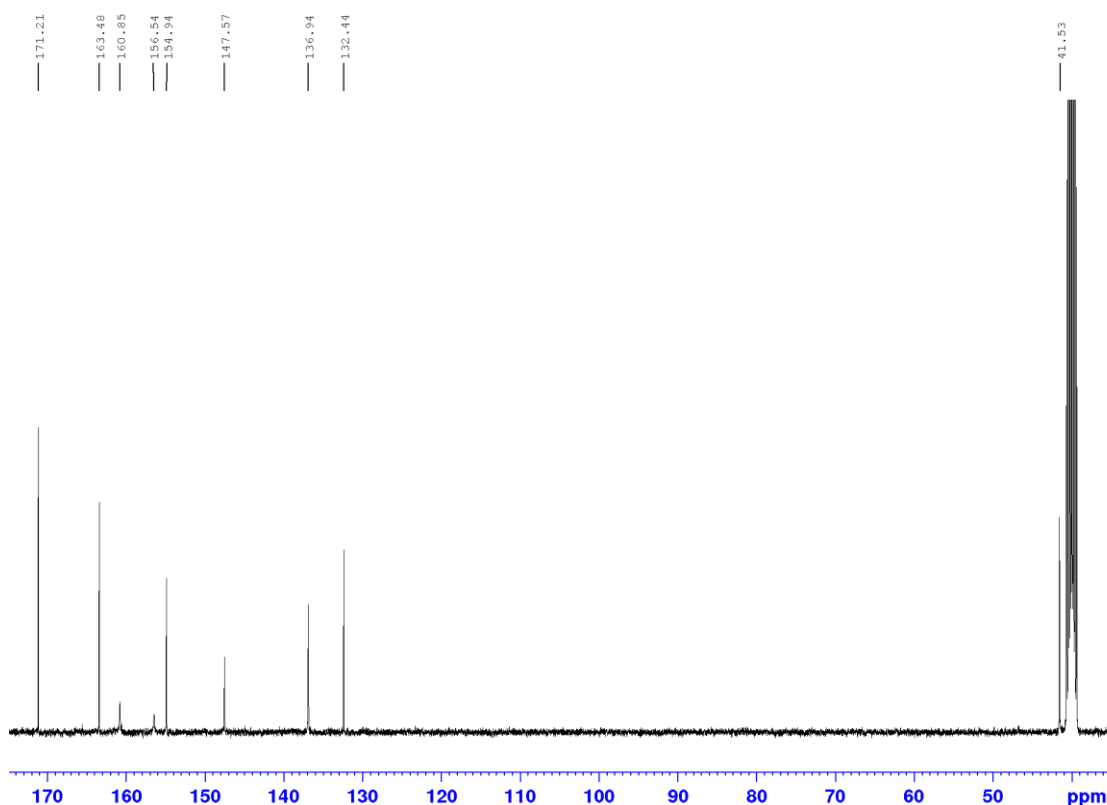
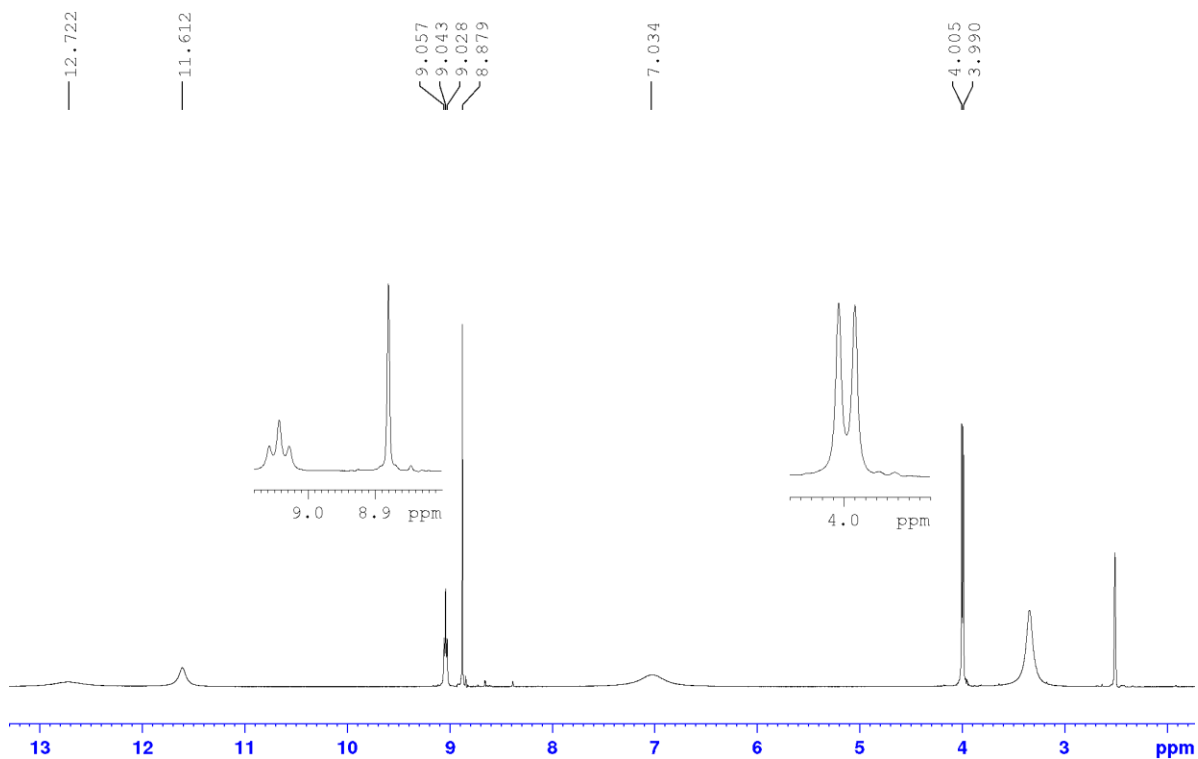
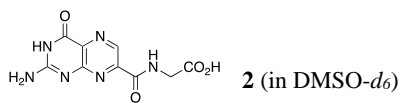
Therefore the integrated rate law becomes  $\ln[7\text{-CMP}]_t = \ln[7\text{-CMP}]_0 + k_{\text{obs}}t$ , and plotting  $\ln[7\text{-CMP}]$  vs  $t$  gives a slope of  $k_{\text{obs}}$ . The  $k$  value for the 2<sup>nd</sup> order rate is thus determined by dividing  $k_{\text{obs}}$  by the initial amine concentration.<sup>5</sup>

A typical  $^1\text{H}$  NMR experiment begins by suspending 7-CMP in anhydrous methanol- $d_4$ , followed by the addition of DBU and a large excess of the amine to provide a homogeneous solution. This solution is then transferred to an NMR tube, and a spectrum is collected every 60 min for 4–8 h. For faster reactions, data was collected every 20 min for the first hour. As glycine gave a particularly rapid reaction, data was collected every 10 min for the first 2 h. The disappearance of the aromatic  $\text{C}_6\text{-H}$  proton of 7-CMP (appears at 8.8 ppm in methanol- $d_4$ ) was coupled with the growth of the aromatic  $\text{C}_6\text{-H}$  proton for the amide product (typically appears between 8.91–8.95 ppm in methanol- $d_4$ ). Ratios of integrals were converted to % (7-CMP) and % (product), which was in turn converted to  $[7\text{-CMP}]_t$ .



**Figure S1:** Representative NMR data, showing the shift in the pterin  $\text{C}_6\text{-H}$  signal as 7-CMP reacts with glycine from  $t = 5$  min (top) to  $t = 75$  min (bottom) in methanol- $d_4$ .

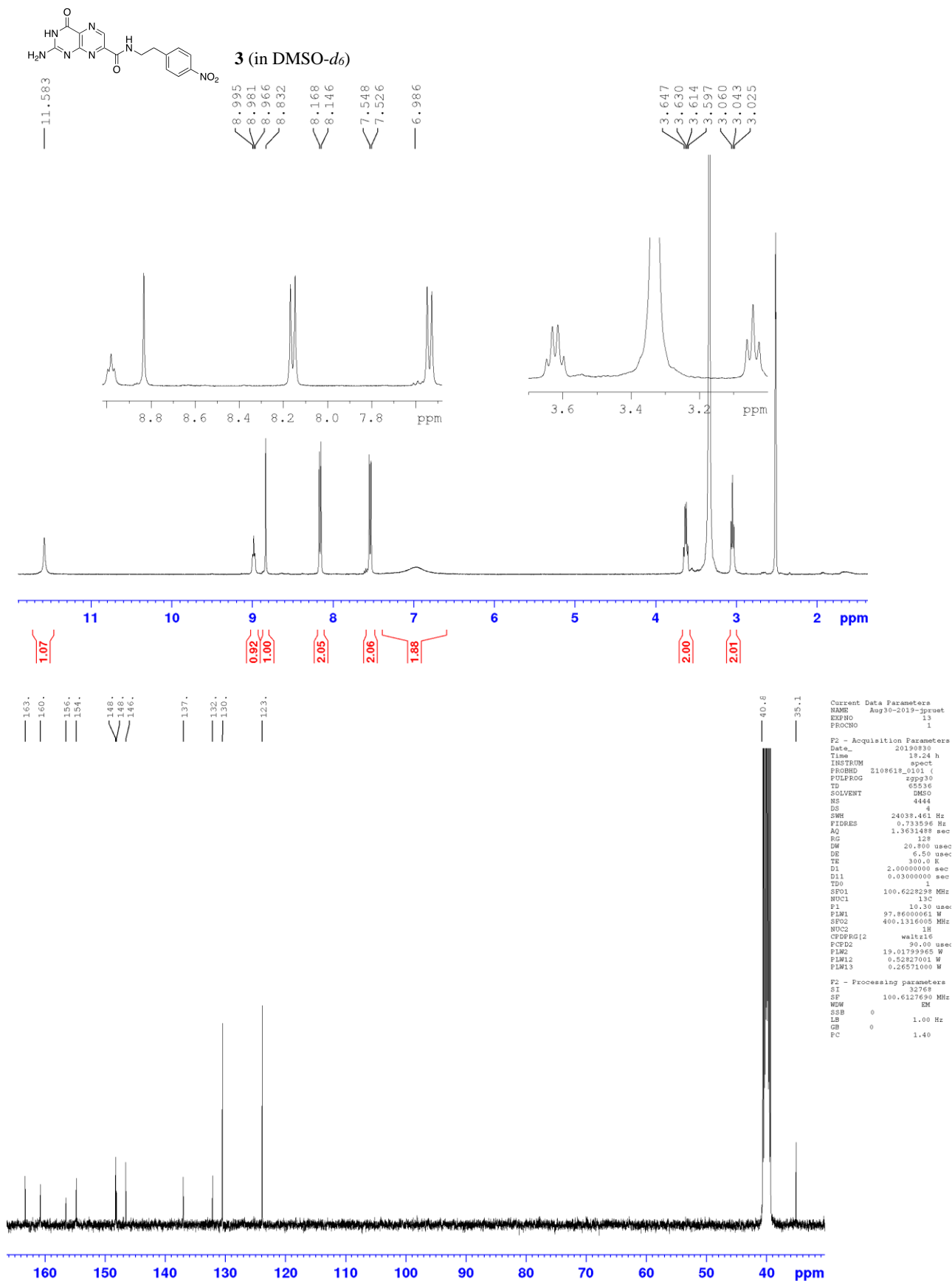
# Copies of $^1\text{H}$ and $^{13}\text{C}$ spectra:



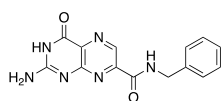
Current Data Parameters  
NAME Aug21-2019-jpawet  
EXPNO 10  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20190821  
Time 21.33 h  
INSTRUM spect  
PROBHD 5108618\_0101 (1  
PULPROG zgpg30  
TD 65536  
SOLVENT DMSO  
NS 5555  
DS 4  
SWH 24038.461 Hz  
FIDRES 0.733596 Hz  
AQ 1.963488 sec  
RG 128  
DW 20.800 usec  
DE 6.56 usec  
TE 300.0 K  
D1 2.00000000 sec  
D11 0.03000000 sec  
TD0 1  
SFO1 100.6281294 MHz  
NUC1 13C  
P1 10.35 usec  
PL1 97.86000061 W  
SFO2 400.1516005 MHz  
NUC2 1H  
PCPD02[2] waltz16  
F2PCG 90.00 usec  
PLM2 10.01799965 W  
PLM12 0.53837001 W  
PLM13 0.246571000 W

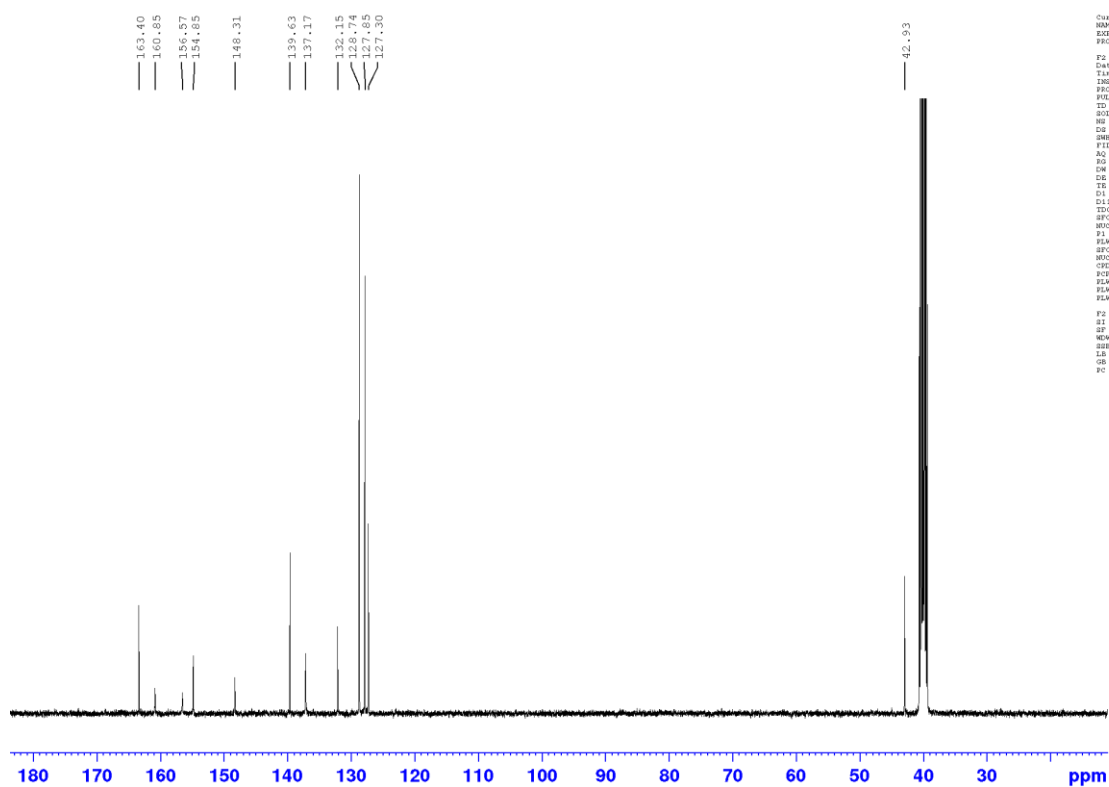
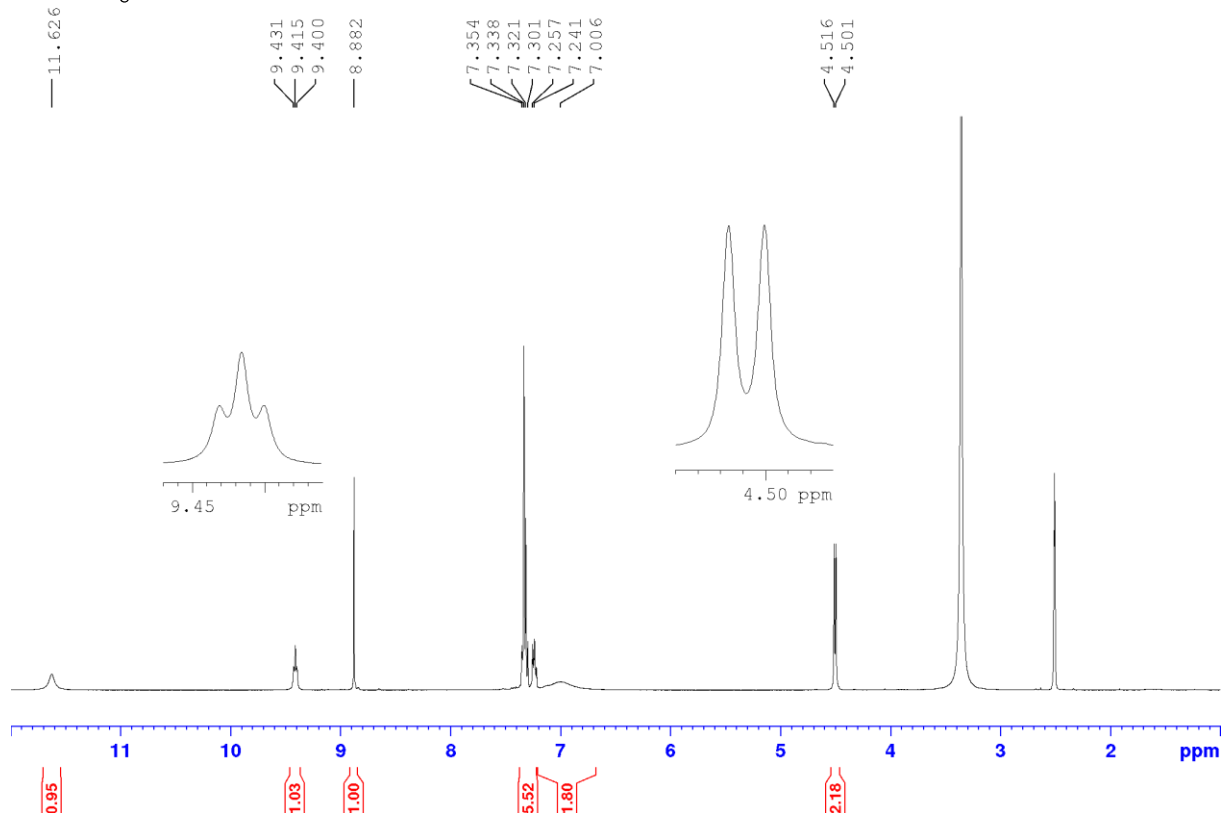
F2 - Processing parameters  
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SF 100.6127768 MHz  
WDW 0 EPI  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40



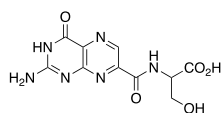




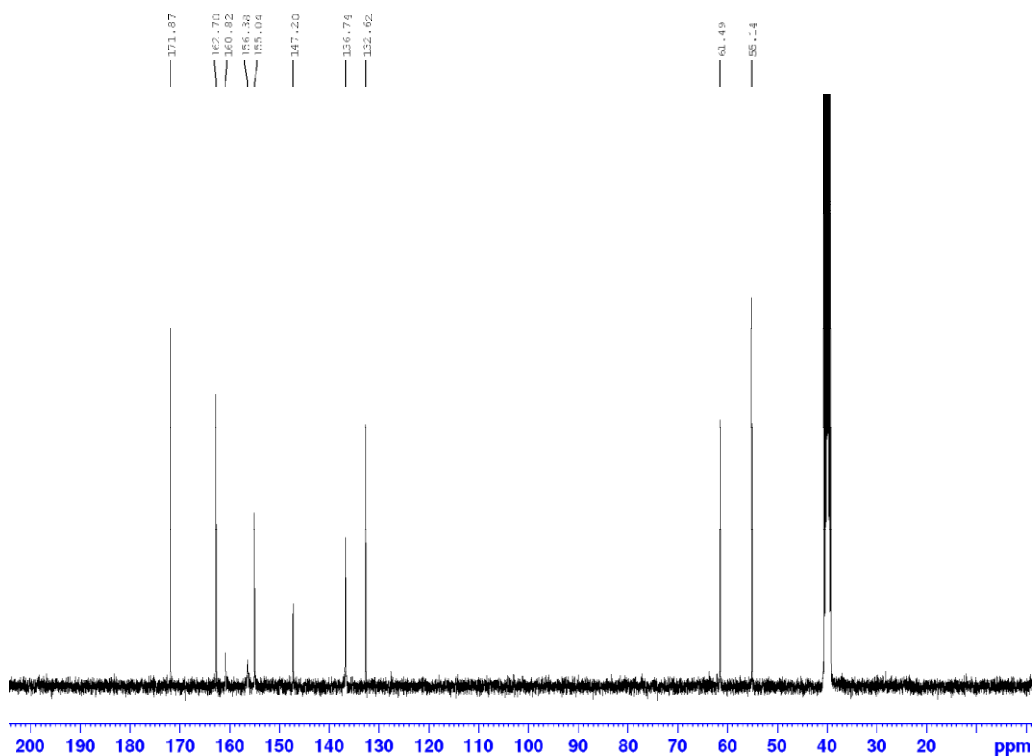
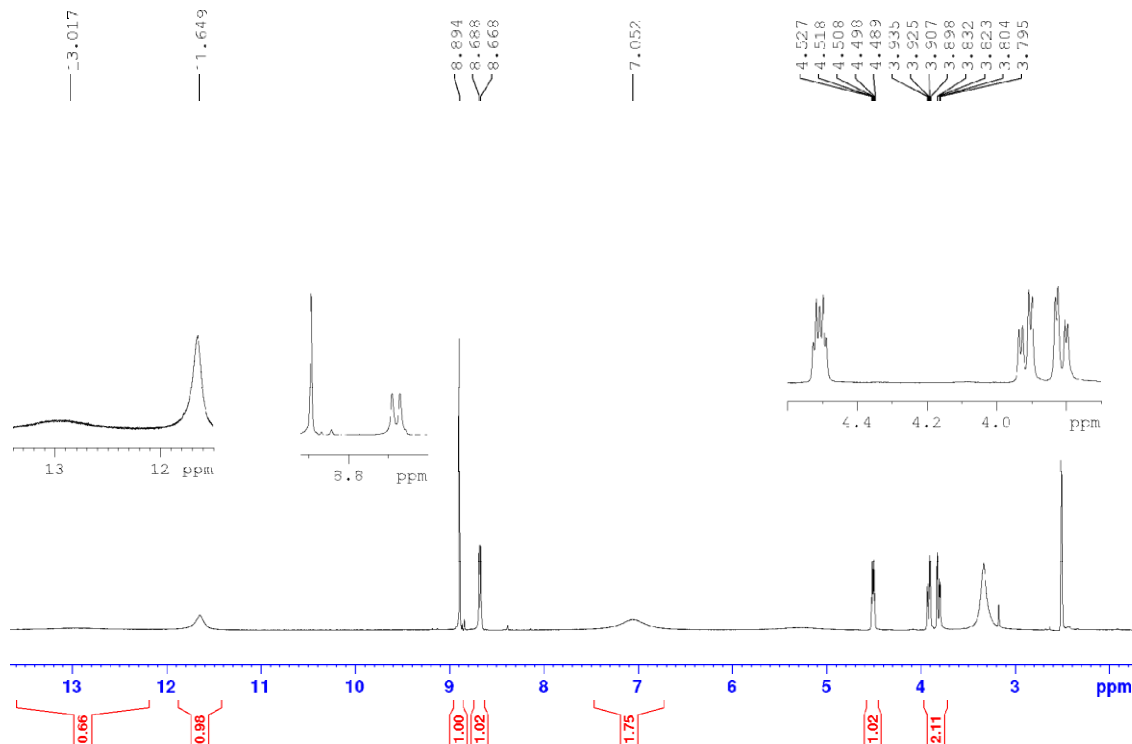
**4** (in DMSO-*d*<sub>6</sub>)



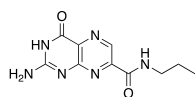
Current Data Parameters  
NAME Aug22-2019-190001  
EXPNO 1  
PROCNO 1  
F2 - Acquisition Parameters  
Date\_ 20190822  
Time 18.15 h  
INSTRUM spect  
PROBHD 5108618\_0101 (1  
PULPROG zgpg30  
TD 65536  
SOLVENT DMSO  
NS 4000  
DS 4  
SWH 24059.441 Hz  
FIDRES 0.775594 Hz  
AQ 1.3631488 sec  
RG 328  
CW 20.800 usec  
DE 6.50 usec  
TE 300.0 K  
D1 2.00000000 sec  
D11 0.03000000 sec  
TD0 100.6282838 MHz  
NUC1 13C  
P1 10.00 usec  
PLM1 97.86000000 W  
SFO2 400.1316000 MHz  
NUC2 1H  
CHOPROG2 waltz16  
P2 90.00 usec  
PLM2 19.01799965 W  
PLM12 0.52827000 W  
PLM13 0.24571000 W  
F2 - Processing parameters  
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SF 100.6127490 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40



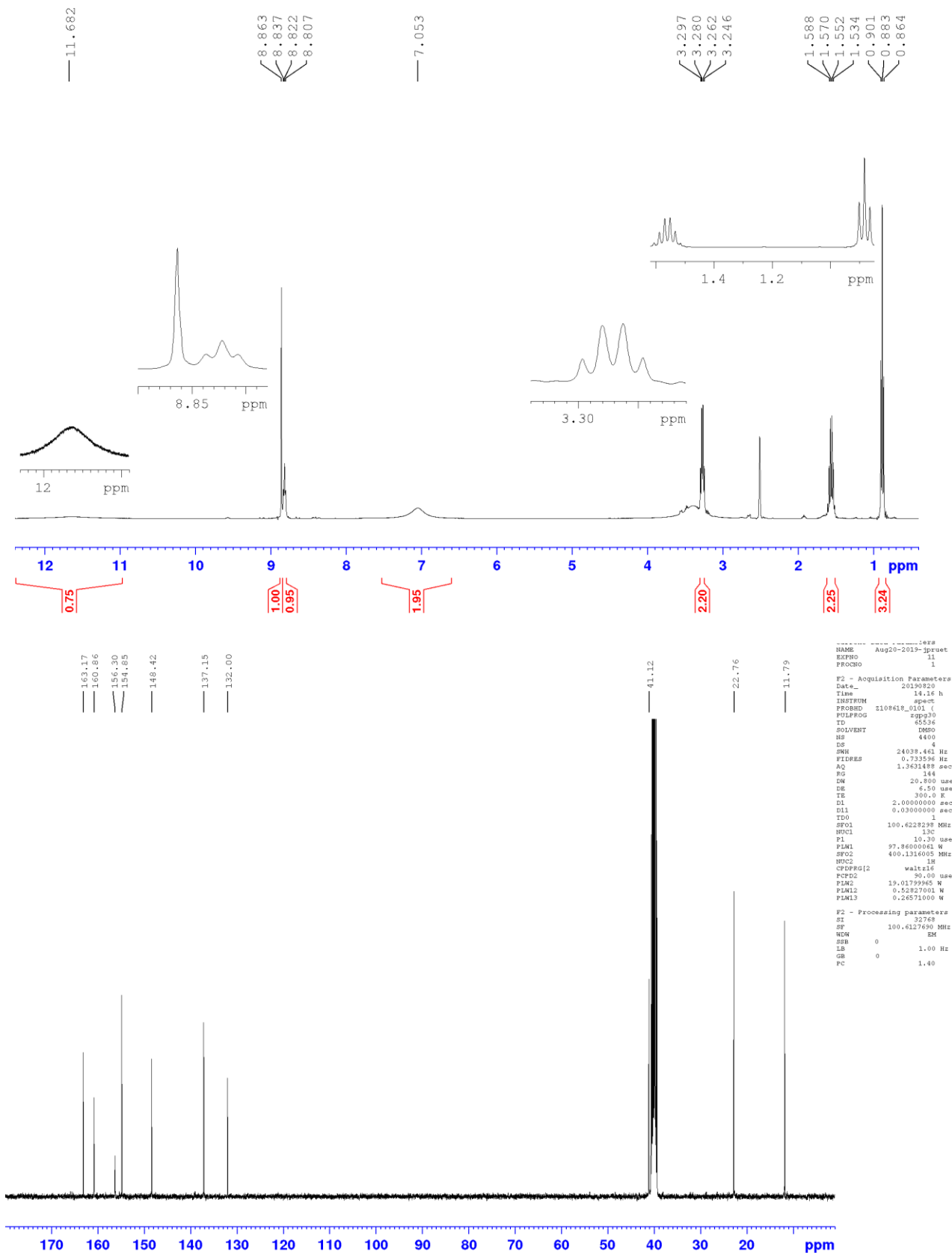
**5** (in DMSO-*d*<sub>6</sub>)

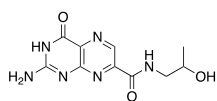


Current Data Parameters  
 NAME Aug11-2015-20000  
 EXPNO 12  
 PROCNO 1  
 F2 - Acquisition Parameters  
 Date\_ 20150822  
 Time 2.33 h  
 INSTRUM spect  
 PROBRG zgpg30  
 TD 65536  
 SOLVENT DMSO  
 NS 555  
 DS 4  
 SSB 24630.461 Hz  
 FIDRES 0.733596 Hz  
 AQ 1.563188 sec  
 RG 123  
 SW 20.899 MHz  
 LB 0.200 MHz  
 TR 300.0 s  
 D1 2.0000000 sec  
 D11 0.0300000 sec  
 TD0 103.6228208 MHz  
 FID1 130  
 F1 10.30 MHz  
 FID1 97.8600061 MHz  
 FID2 406.1316005 MHz  
 FID3 1.1  
 CDDG12 wait10  
 FID5 40.03 MHz  
 FID6 19.0722227 MHz  
 FID7 1.52327001 MHz  
 FID8 0.26571000 MHz  
 F2 - Processing parameters  
 AT 32768  
 SF 120.6127630 MHz  
 WDW EM  
 SSB 0  
 LB 1.30 Hz  
 GB 0  
 PC 1.40

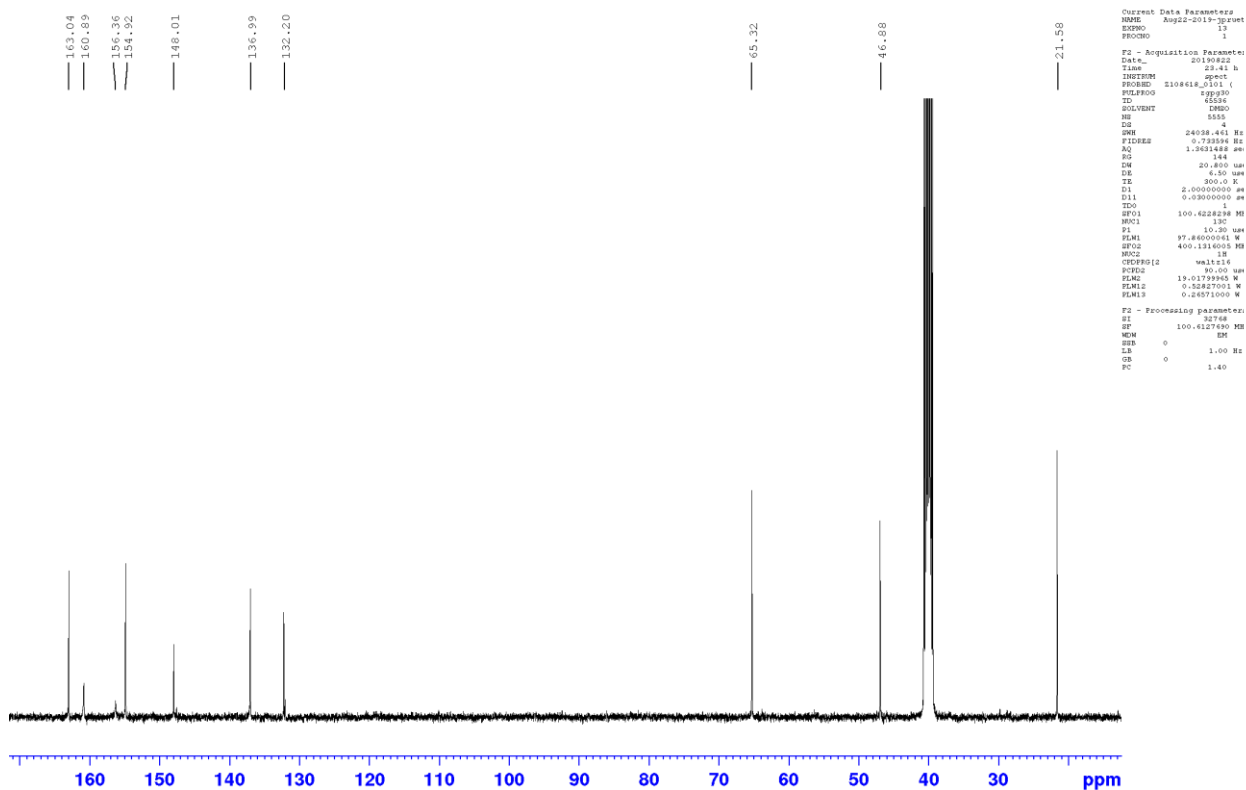
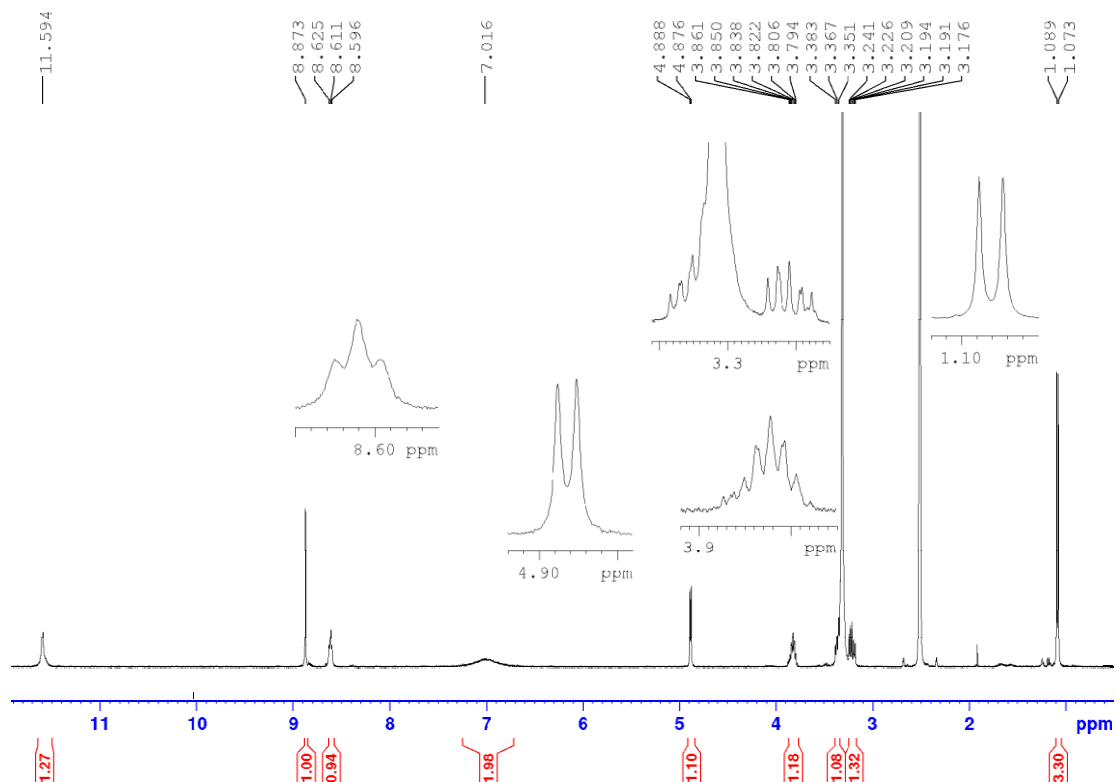


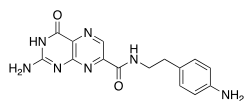
**6** (in DMSO-*d*<sub>6</sub>)



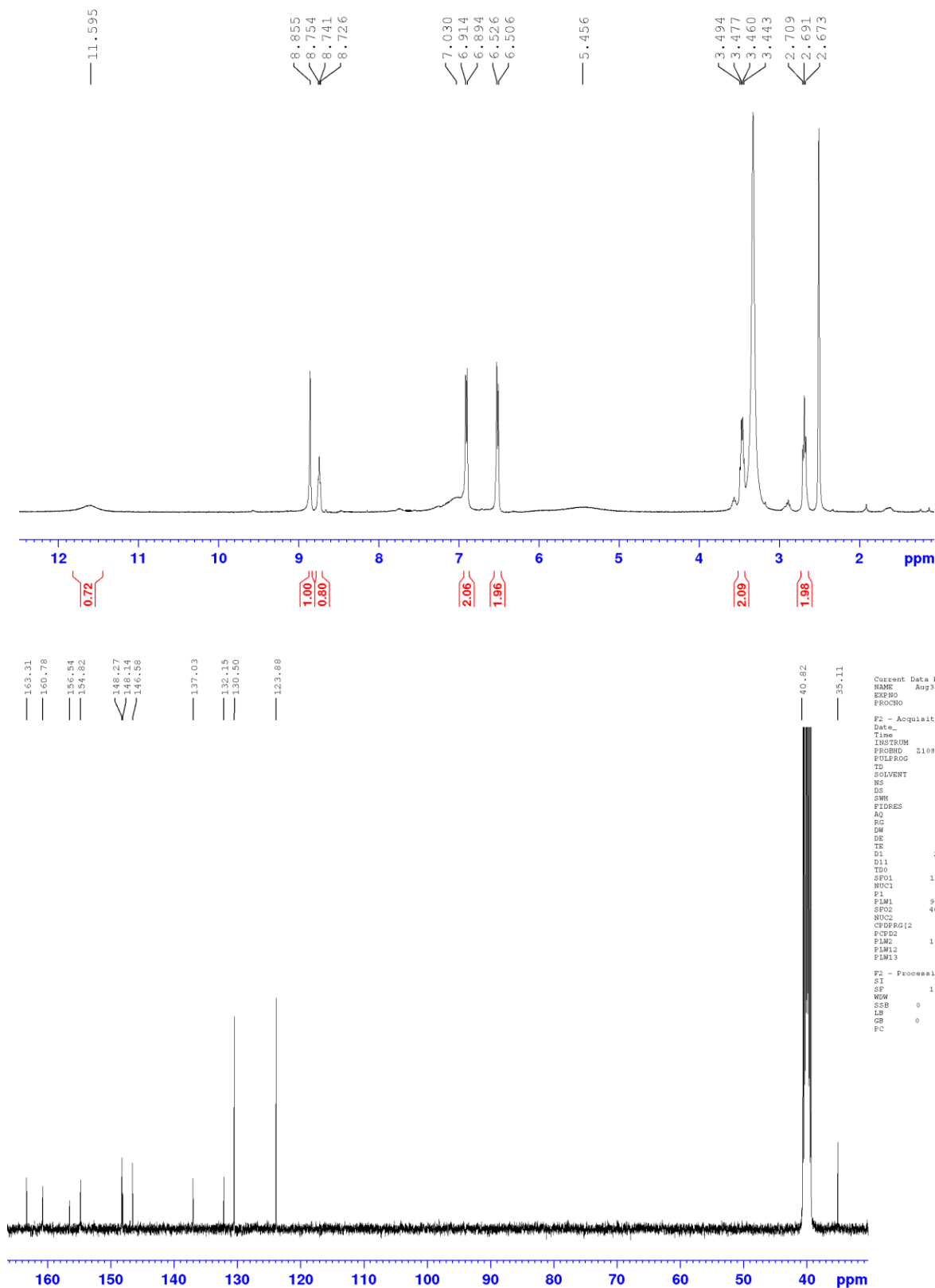


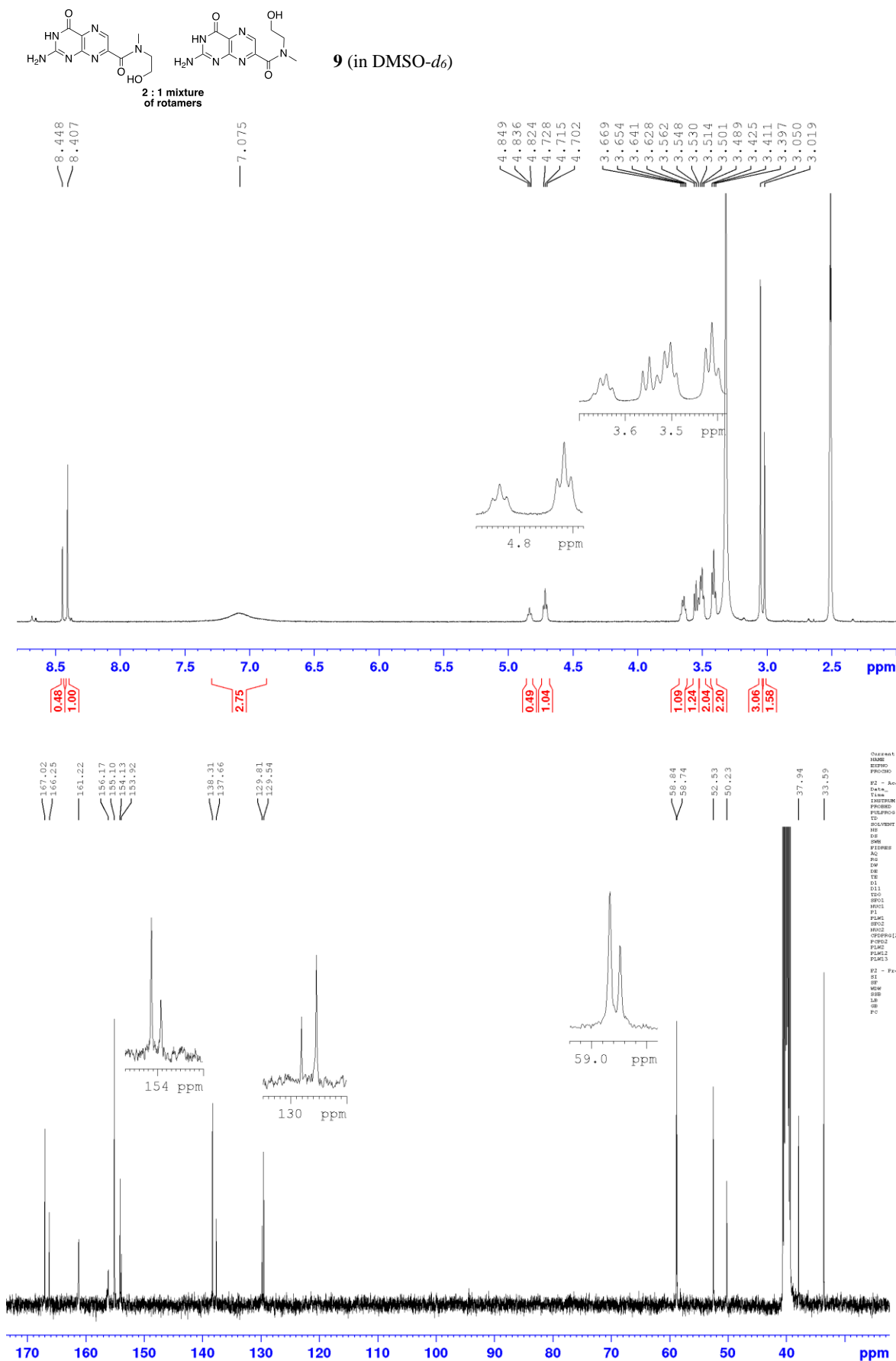
**7** (in DMSO-*d*<sub>6</sub>)

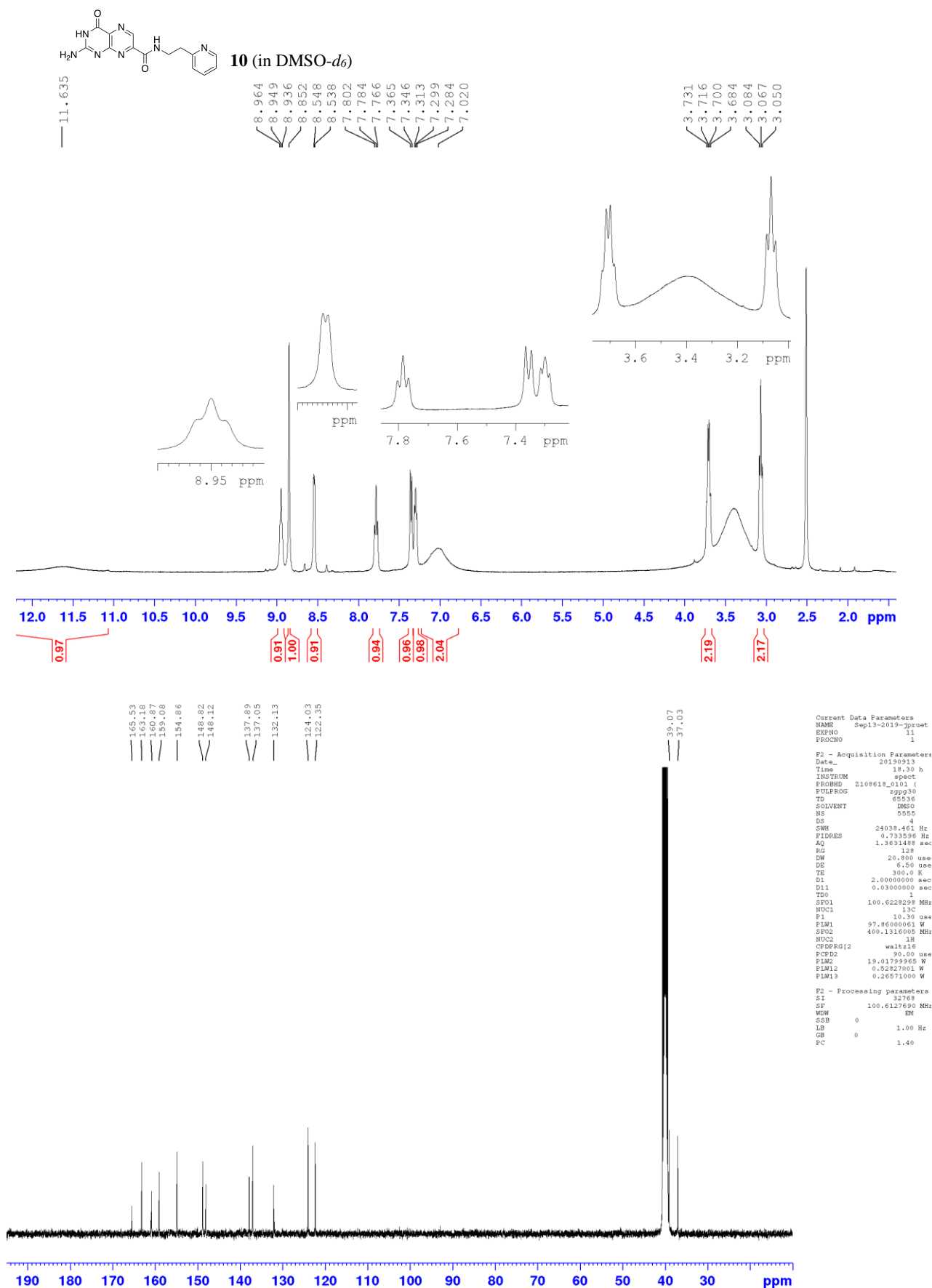


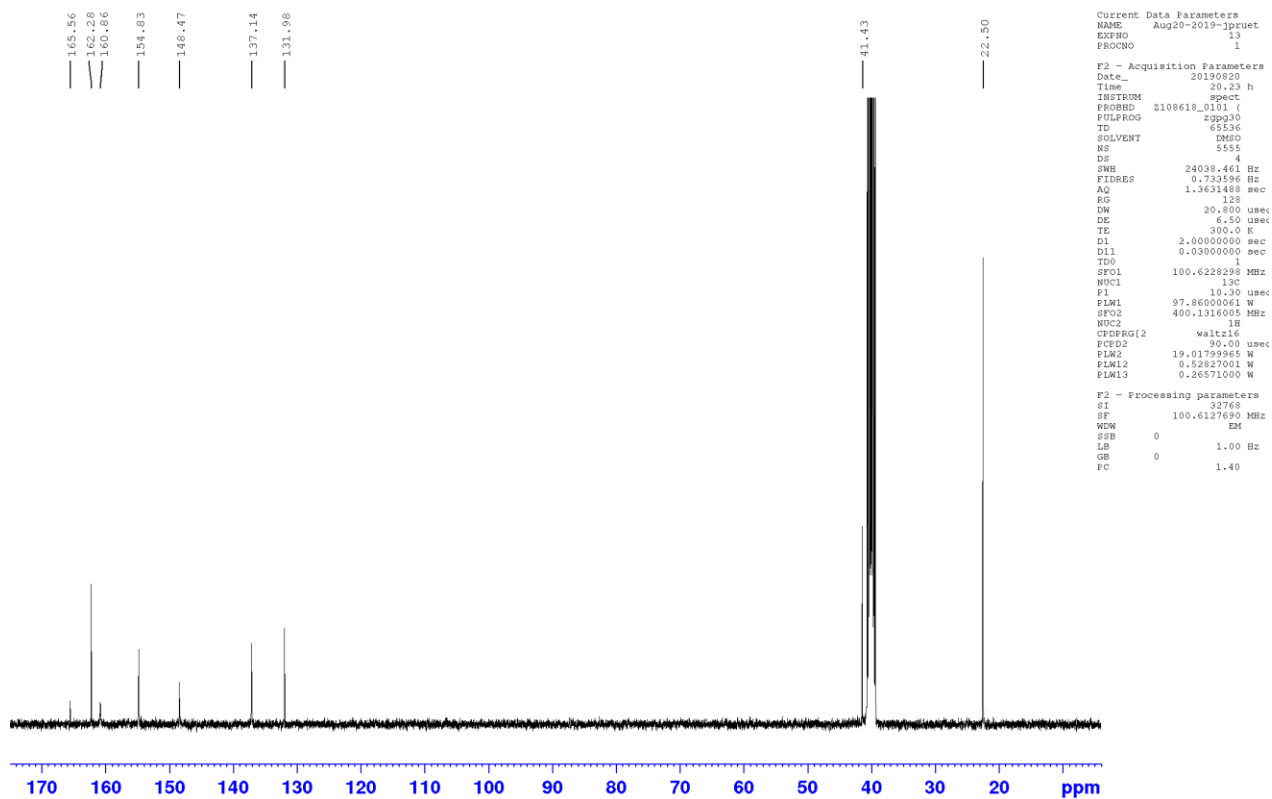
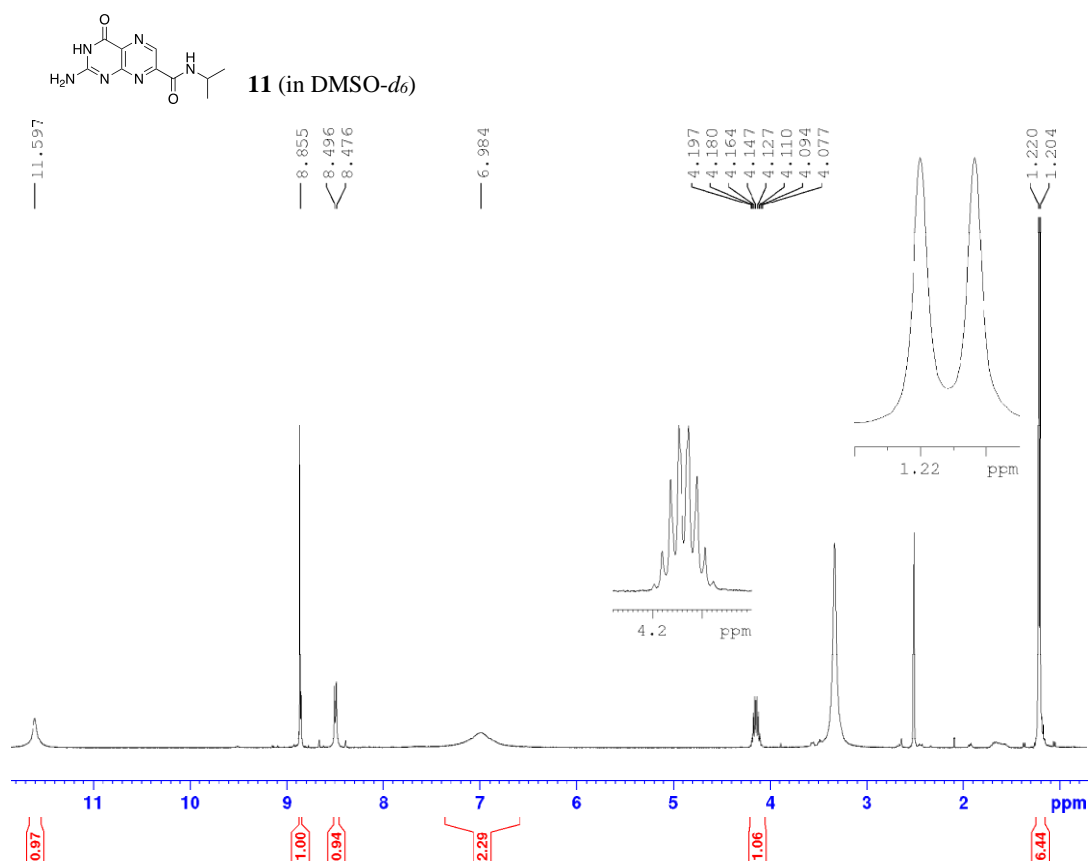


**8** (in DMSO-*d*<sub>6</sub>)

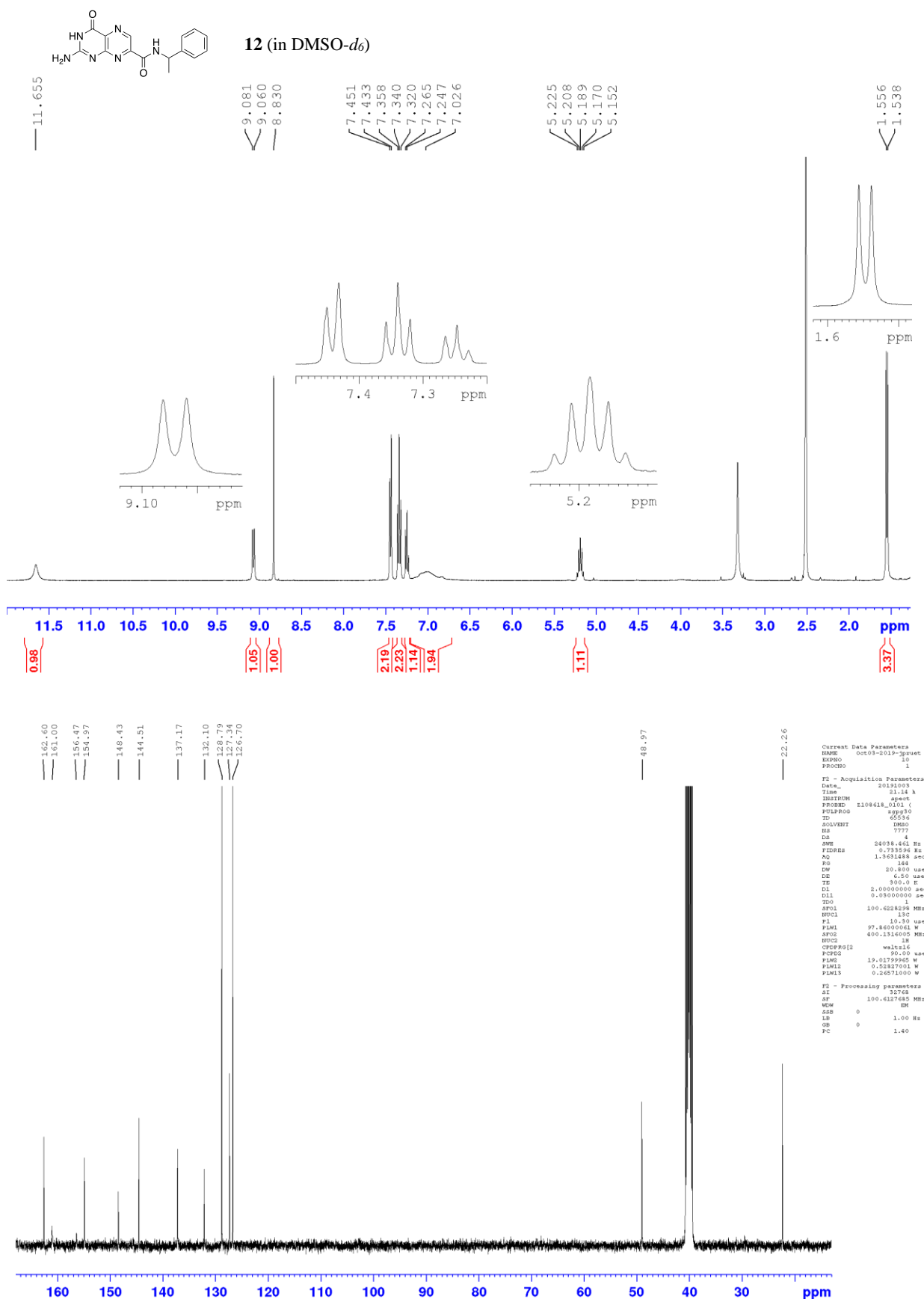


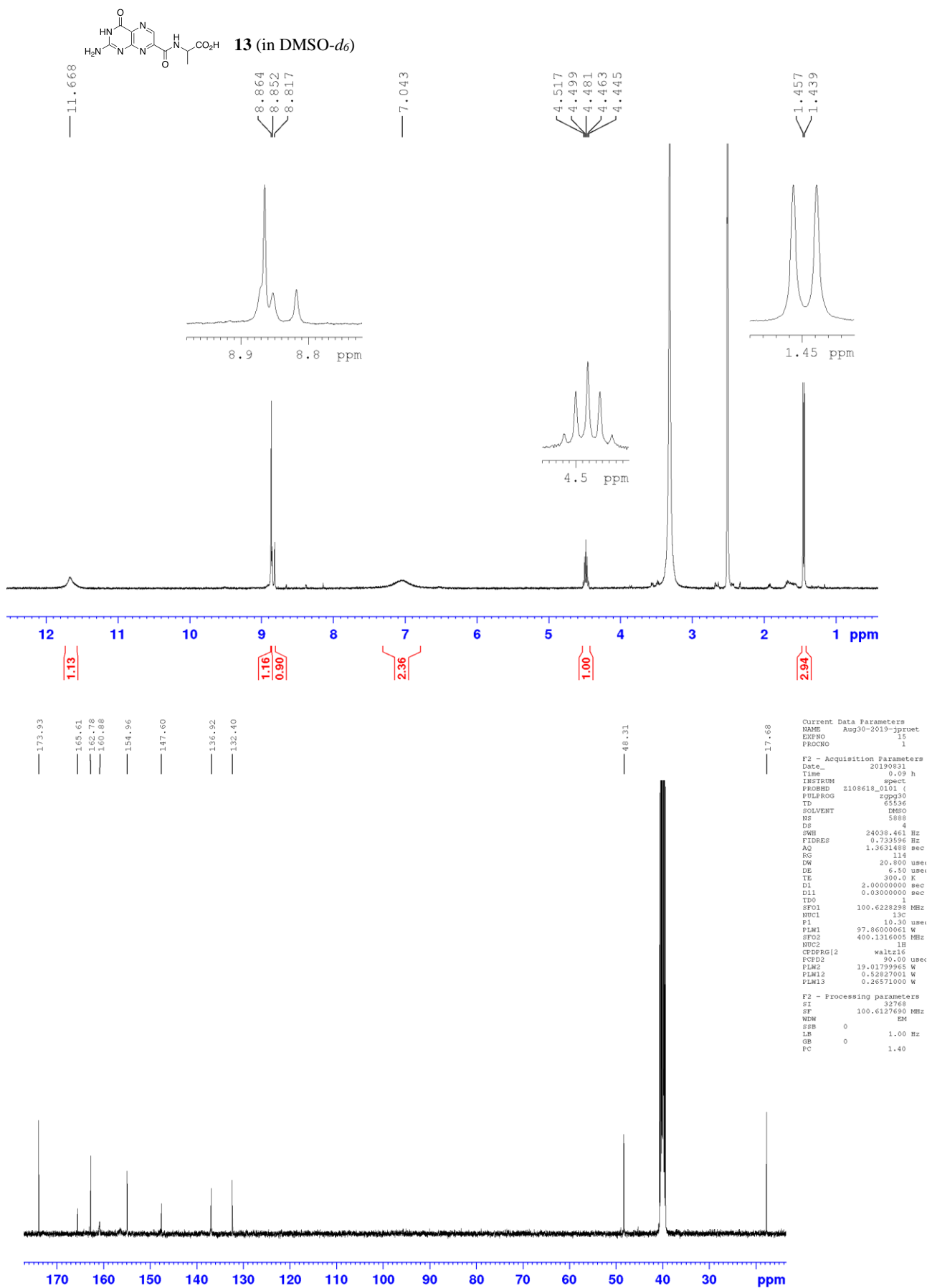


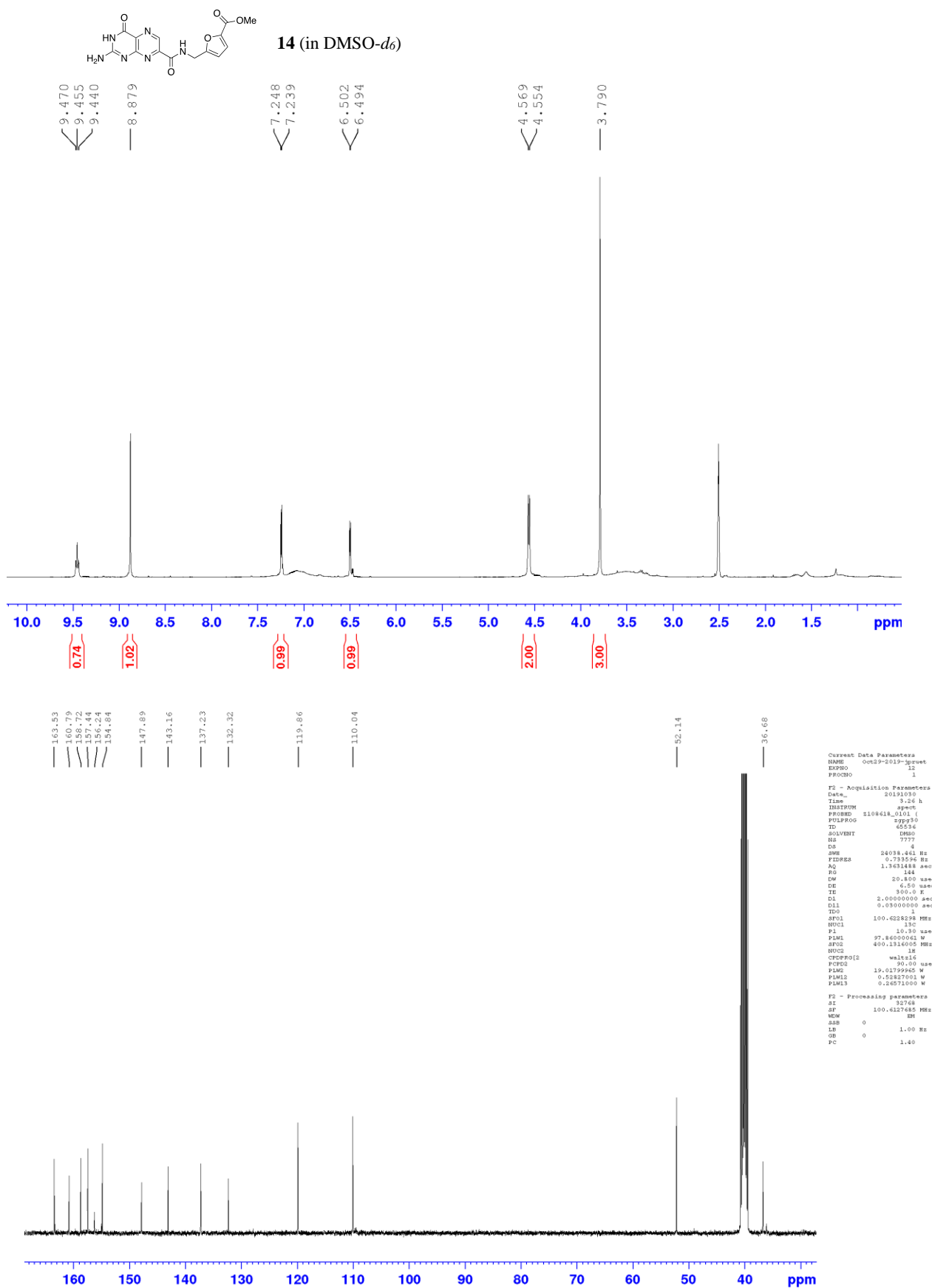


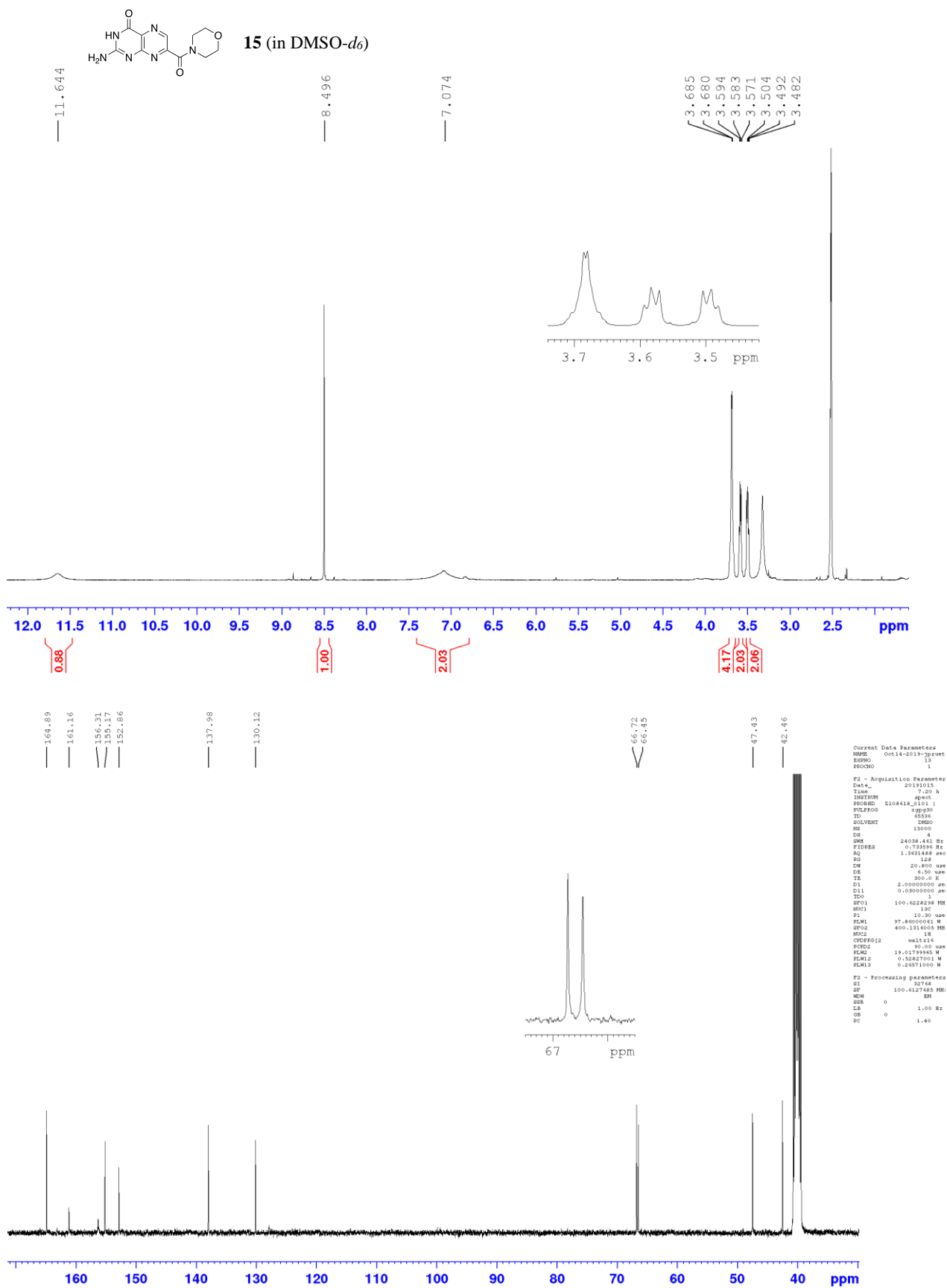


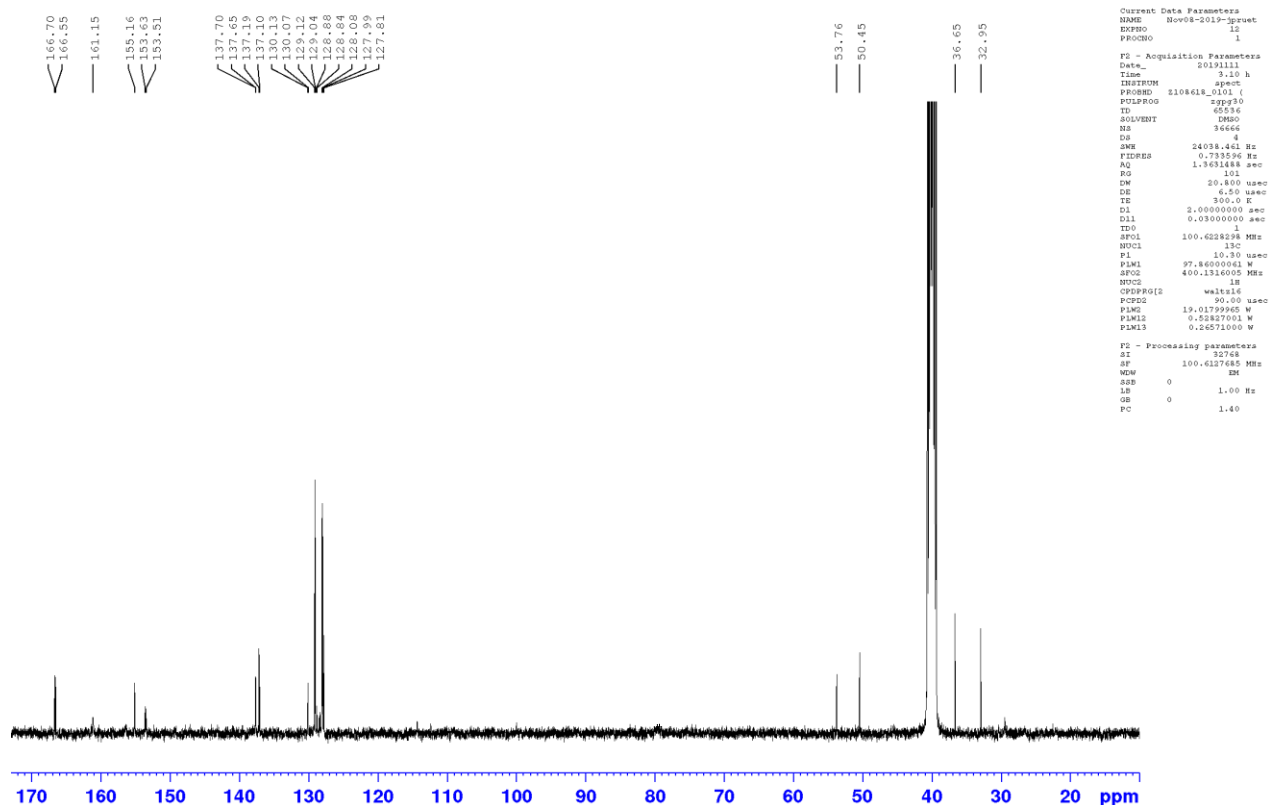
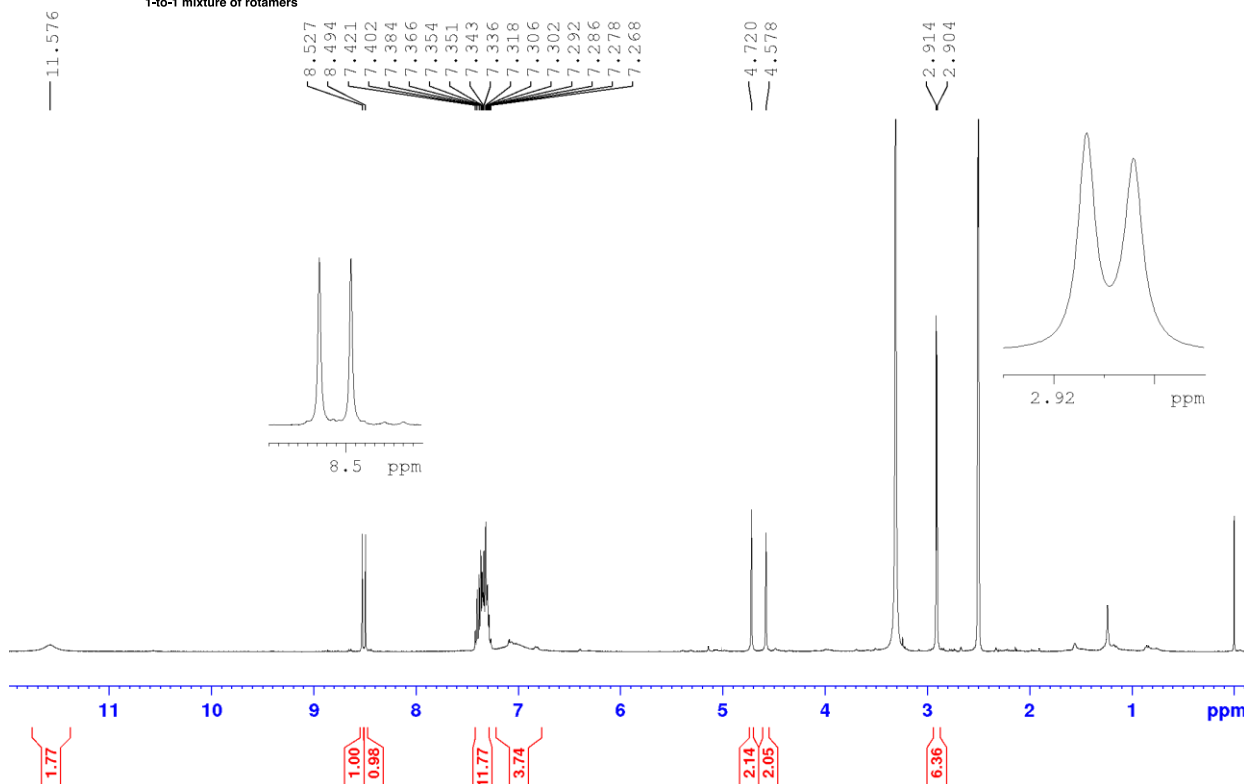
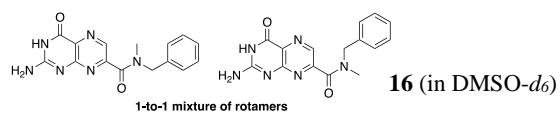












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