Electronic Supplementary Material (ESI) for RSC Advances.

SUPPORTING INFORMATION

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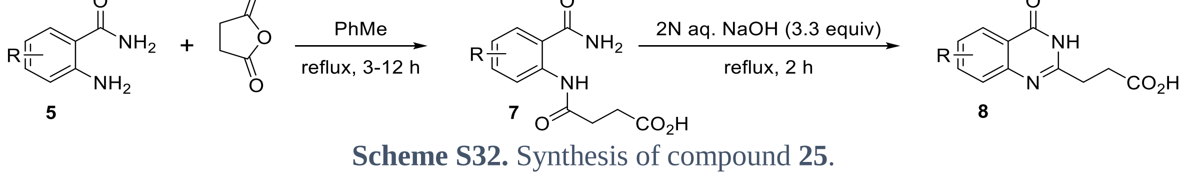
1. Experimental

1.1. General

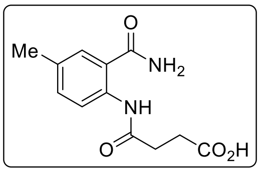
Solvents for solution phase reactions: methanol (MeOH), toluene (PhMe) were purchased in anhydrous grade from Sigma-Aldrich and used without further purification. Ethyl acetate (EtOAc), petroleum ether (PET), dichloromethane (CH_2Cl_2) and diethyl ether (Et_2O) were used as received. Reagents were purchased at the highest commercial quality and used without further purification unless otherwise stated. Evaporations were conducted under reduced pressure at temperatures less than 40 °C unless otherwise noted. Reactions were monitored by analytical thin layer chromatography (TLC) carried out on ALUGRAM Xtra SIL G/UV254, Macherey-Nagel silica gel plates. Compounds were visualized with a UV lamp (λ 254 nm) and stained with a solution of potassium permanganate. NMR spectra of samples in the indicated solvent were recorded on a Bruker Advance 400 or 500 MHz spectrometer and were calibrated using residual solvent as internal reference. The following abbreviations were used to indicate multiplicities: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, quint = quintuplet, m = multiplet, and AB = AB quartet. Low resolution (ESIMS) and/or high resolution mass spectrometric analyses (HRMS) were obtained by electrospray ionization on a on a Bruker Q-TOF Impact HD apparatus and performed either at the PLATeforme INstrumentale d'Analyses (PLATINA) mass spectrometry facility of the Institut de Chimie des Milieux et Matériaux de Poitiers (IC2MP, CNRS-UMR 7285, 86000 Poitiers, France).

1.2. Experiments for Scheme 1, thermal conditions.



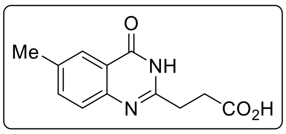
Scheme S32. Synthesis of compound **25**.

Compound 7b



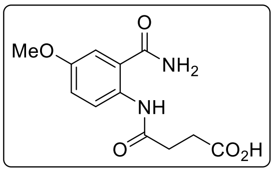
According to the procedure described in the literature,[1] in a flask equipped with a condenser, 2-amino-5-methylbenzamide (600 mg, 4 mmol, 1 equiv) and succinic anhydride (400 mg, 4 mmol, 1 equiv) were mixed in 5 ml of toluene. The suspension was vigorously refluxed for 3 h and then cooled to RT. The resulting white powder was filtered, washed with Et_2O and dried (945 mg, 95%). **R*f*** = 0.25 ($MeOH/CH_2Cl_2$ 10:90); **mp** 223-225 °C; **^{1}H NMR** (400 MHz, DMSO-*d_6*) *δ* (ppm): 12.16 (bs, 1H), 11.57 (s, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 8.21 (s, 1H), 6.67 (s, 1H), 7.62 (d, *J* = 1.5 Hz, 1H), 7.28 (dd, *J* = 8.5, 1.5 Hz, 1H), 2.56-2.53 (m, 4H), 2.28 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-*d_6*) *δ* (ppm): 173.7, 170.9, 169.7, 137.3, 132.6, 131.3, 128.9, 120.1, 119.5, 32.0, 28.8, 20.4; **HRMS** calcd for $C_{12}H_{15}N_2O_4$ $[M+H]^+$ 251.1032, found 251.1025.

Compound 8b



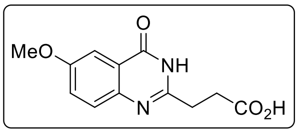
According to the procedure described in the literature,[1] in a flask equipped with a condenser, compound **E** (874 mg, 3.5 mmol, 1 equiv) was dissolved in an aqueous 2N NaOH solution (6 ml, 3.3 equiv). The resulting solution was refluxed for 1 h 30 and then cooled to RT. The pH was carefully adjusted to pH 5-6 with aqueous 3N HCl solution under vigorous stirring. The resulting white powder was filtered, washed with water and then dried (0.80 g, quant.). **R*f*** = 0.25 ($MeOH/CH_2Cl_2$ 15:85); **mp** 270-272 °C; **^{1}H NMR** (400 MHz, DMSO-*d_6*) *δ* (ppm): 12.13 (bs, 1H), 7.85 (s, 1H), 7.58 (d, *J* = 7.4 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 2.82 (t, *J* = 6.6 Hz, 2H), 2.73 (t, *J* = 6.5 Hz, 2H), 2.40 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-*d_6*) *δ* (ppm): 173.9, 161.9, 155.6, 146.8, 135.9, 135.9, 126.8, 125.3, 120.7, 30.1, 29.2, 21.0; **HRMS** calcd for $C_{12}H_{13}N_2O_3$ $[M+H]^+$ 233.0926, found 233.0917.

Compound 7c



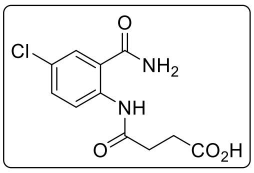
According to the procedure described in the literature,[1] in a flask equipped with a condenser, 2-amino-5-methoxybenzamide (2.49 g, 15 mmol, 1 equiv) and succinic anhydride (1.5 g, 15 mmol, 1 equiv) were mixed in 19 ml of toluene. The suspension was vigorously refluxed for 2 h and then cooled to RT. The resulting light grey powder was filtered, washed with Et_2O and dried (3.92 g, 98%). **R*f*** = 0.10 ($MeOH/CH_2Cl_2$ 5:95); **mp** 222-224 °C; **^{1}H NMR** (400 MHz, DMSO-*d_6*) *δ* (ppm): 12.16 (bs, 1H), 11.32 (s, 1H), 8.30 (d, *J* = 9.1 Hz, 1H), 8.24 (s, 1H), 7.72 (s, 1H), 7.31 (d, *J* = 2.9 Hz, 1H), 7.08 (dd, *J* = 9.1, 2.9 Hz, 1H), 3.77 (s, 3H), 2.52 (bs, 4H); **^{13}C NMR** (100 MHz, DMSO-*d_6*) *δ* (ppm): 173.7, 170.4, 169.5, 154.1, 132.8, 121.9, 121.3, 117.7, 113.4, 55.5, 31.9, 28.8; **HRMS** calcd for $C_{12}H_{14}N_2NaO_5$ $[M+Na]^+$ 289.0800, found 289.0789.

Compound 8c



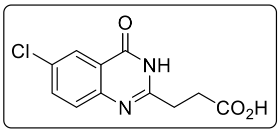
According to the procedure described in the literature,[1] in a flask equipped with a condenser, compound **E** (3.6 g, 13.5 mmol, 1 equiv) was dissolved in an aqueous 2N NaOH solution (22.3 ml, 3.3 equiv). The resulting solution was refluxed for 2 h and then cooled to RT. The pH was carefully adjusted to pH 5-6 with aqueous 3N HCl solution under vigorous stirring. The resulting white powder was filtered, washed with water and then dried (3.07 g, 91%). **R_f** = 0.23 (MeOH/CH_2Cl_2 10:90); **mp** 270-272 °C; **^{1}H NMR** (400 MHz, DMSO-*d_6*) δ (ppm): 12.19 (bs, 1H), 7.51 (d, *J* = 8.9 Hz, 1H), 7.46 (d, *J* = 2.7 Hz, 1H), 7.35 (d, *J* = 8.8, 2.7 Hz, 1H), 3.84 (s, 3H), 2.82 (t, *J* = 6.6 Hz, 2H), 2.72 (t, *J* = 6.6 Hz, 2H); **^{13}C NMR** (100 MHz, DMSO-*d_6*) δ (ppm): 173.7, 161.6, 157.3, 154.0, 143.2, 128.5, 123.7, 121.6, 105.8, 55.6, 30.0, 29.0; **HRMS** calcd for $C_{12}H_{13}N_2O_4$ $[M+H]^+$ 249.0875, found 249.0865.

Compound 7d



According to the procedure described in the literature,[1] in a flask equipped with a condenser, 2-amino-5-chlorobenzamide (1.7 g, 10 mmol, 1 equiv) and succinic anhydride (1 g, 10 mmol, 1 equiv) were mixed in 12.5 ml of toluene. The suspension was vigorously refluxed for 3 h and then cooled to RT. The resulting white solid was filtered, washed with Et_2O and dried (2.6 g, 96%). **R_f** = 0.10 (MeOH/CH_2Cl_2 5:95); **mp** 239-241 °C; **^{1}H NMR** (400 MHz, DMSO-*d_6*) δ (ppm): 12.18 (bs, 1H), 11.61 (s, 1H), 8.45 (d, *J* = 9.0 Hz, 1H), 8.36 (s, 1H), 7.86 (d, *J* = 2.4 Hz, 2H), 7.55 (dd, *J* = 9.0, 2.5 Hz, 1H), 2.57-2.53 (m, 4H); **^{13}C NMR** (100 MHz, DMSO-*d_6*) δ (ppm): 173.6, 170.2, 169.4, 138.5, 131.9, 128.2, 126.1, 121.8, 121.2, 32.1, 28.7; **HRMS** calcd for $C_{11}H_{12}ClN_2O_4$ $[M+H]^+$ 271.0486, found 271.0479.

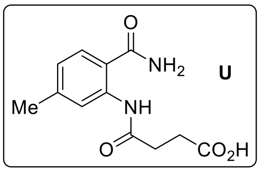
Compound 8d



According to the procedure described in the literature,[1] in a flask equipped with a condenser, compound **A** (2.48 g, 9.2 mmol, 1 equiv) was dissolved in an aqueous 2N NaOH solution (15 ml, 3.3 equiv). The resulting solution was refluxed for 2 h and then cooled to RT. The pH was carefully adjusted to pH 5-6 with aqueous 3N HCl solution under vigorous stirring. The resulting white powder was filtered, washed with water and then dried (2.31 g, 99.5). **R_f** = 0.30 (MeOH/CH_2Cl_2 15:85); **mp** 252-254 °C; **^{1}H NMR** (400 MHz, DMSO-*d_6*) δ (ppm): 12.40 (bs, 1H), 8.00 (d, *J* = 2.5 Hz, 1H), 7.79 (dd, J = 8.7, 2.5 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 2.87-2.83 (m, 2H), 2.75-2.72 (m, 2H); **^{13}C NMR** (100 MHz, DMSO-

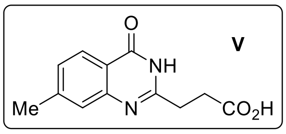
d_6) δ (ppm): 173.6, 160.8, 157.1, 147.4, 134.5, 130.3, 129.1, 124.8, 122.2, 29.8, 29.2; **HRMS** calcd for $C_{11}H_{10}ClN_2O_3$ $[M+H]^+$ 253.0380, found 253.0372.

Compound 7e



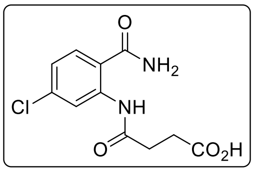
According to the procedure described in the literature,[1] in a flask equipped with a condenser, 2-amino-4-methylbenzamide (1.5 g, 10 mmol, 1 equiv) and succinic anhydride (1.0 g, 10 mmol, 1 equiv) were mixed in 12.5 ml of toluene. The suspension was vigorously refluxed for 3 h and then cooled to RT. The resulting yellow powder was filtered, washed with Et_2O and dried (2.3 g, 92%). **R_f** = 0.21 ($MeOH/CH_2Cl_2$ 10:90); **mp** 240-241 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm): 12.18 (bs, 1H), 11.88 (s, 1H), 8.33 (s, 1H), 8.20 (s, 1H), 7.70 (d, J = 8.0 Hz 1H), 7.64 (s, 1H), 6.91 (dd, J = 8.0, 1.0 Hz, 1H), 2.57-2.52 (m, 4H), 2.31 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ (ppm): 173.8, 170.9, 170.0, 142.5, 140.0, 128.6, 122.9, 120.2, 116.3, 32.2, 28.7, 21.5; **HRMS** calcd for $C_{12}H_{14}N_2NaO_4$ $[M+Na]^+$ 273.0851, found 273.0843.

Compound 8e



According to the procedure described in the literature,[1] in a flask equipped with a condenser, compound **E** (2.2 g, 8.8 mmol, 1 equiv) was dissolved in an aqueous 2N NaOH solution (14.5 ml, 3.3 equiv). The resulting solution was refluxed for 4 h and then cooled to RT. The pH was carefully adjusted to pH 5-6 with aqueous 3N HCl solution under vigorous stirring. The resulting light brown powder was filtered, washed with water and then dried (2.0 g, 97.9%). **R_f** = 0.31 ($MeOH/CH_2Cl_2$ 15:85); **mp** 241-243 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm): 12.12 (bs, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.38 (s, 1H), 7.28 (dd, J = 8.1, 1.1 Hz, 1H), 2.83 (t, J = 6.8 Hz, 2H), 2.73 (t, J = 6.4 Hz, 2H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ (ppm): 173.9, 162.0, 156.6, 148.9, 145.2, 127.8, 126.6, 125.9, 118.6, 30.1, 29.3, 21.6; **HRMS** calcd for $C_{12}H_{13}N_2O_3$ $[M+H]^+$ 233.0926, found 233.0923.

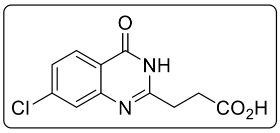
Compound 7f



According to the procedure described in the literature,[1] in a flask equipped with a condenser, 2-amino-4-chlorobenzamide (1.7 g, 10 mmol, 1 equiv) and succinic anhydride (1 g, 10 mmol, 1 equiv) were mixed in 12.5 ml of toluene. The suspension was vigorously refluxed for 3 h and then cooled to RT. The resulting white solid was filtered, washed with Et_2O and dried (2.54 g, 94%). **R_f** = 0.10 ($MeOH/CH_2Cl_2$ 10:90); **mp** 232-234 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm): 12.22 (bs, 1H), 11.90 (s, 1H), 8.57 (d, J = 2.2 Hz, 1H), 8.35 (s, 1H), 7.84 (s, 1H), 7.83 (d, J = 8.6

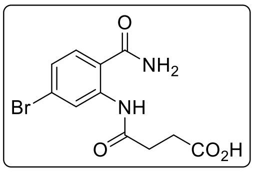
Hz, 1H), 7.20 (dd, *J* = 8.5, 2.2 Hz, 1H), 2.59-2.52 (m, 4H); **^{13}C NMR** (100 MHz, DMSO-*d_6*) *δ* (ppm): 173.6, 170.5, 170.0, 141.0, 136.7, 130.4, 122.0, 119.3, 117.7, 32.1, 28.6; **HRMS** calcd for $C_{11}H_{12}ClN_2O_4$ [M+H]$^+$ 271.0486, found 271.0483.

Compound 8f



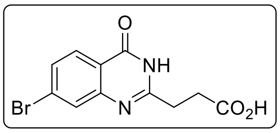
According to the procedure described in the literature,[1] in a flask equipped with a condenser, compound **M** (2.44 g, 9 mmol, 1 equiv) was dissolved in an aqueous 2N NaOH solution (15 ml, 3.3 equiv). The resulting solution was refluxed for 2 h and then cooled to RT. The pH was carefully adjusted to pH 5-6 with aqueous 3N HCl solution under vigorous stirring. The resulting orange powder was filtered, washed with water and then dried (2.28 g, quant.). **R*$_f$*** = 0.50 (MeOH/CH_2Cl_2 15:85); **mp** 268-270 °C; **^{1}H NMR** (400 MHz, DMSO-*d_6*) *δ* (ppm): 12.39 (bs, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.61 (s, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 2.84 (t, *J* = 6.8 Hz, 2H), 2.74 (t, *J* = 6.8 Hz, 2H); **^{13}C NMR** (100 MHz, DMSO-*d_6*) *δ* (ppm): 173.6, 161.2, 158.2, 149.8, 139.0, 127.9, 126.4, 126.0, 119.8, 29.8, 29.2; **HRMS** calcd for $C_{11}H_{10}ClN_2O_3$ [M+H]$^+$ 253.0380, found 253.0374.

Compound 7g



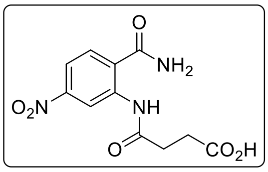
According to the procedure described in the literature,[1] in a flask equipped with a condenser, 2-amino-4-bromobenzamide (3.67 mmol, 1 equiv) and succinic anhydride (3.67 mmol, 1 equiv) were mixed in 4.6 ml of toluene. The suspension was vigorously refluxed for 12 h and then cooled to RT. The resulting white solid was filtered, washed with Et_2O and dried (1.07 g, 93%). **^{1}H NMR** (500 MHz, DMSO-*d_6*) *δ* (ppm): 12.27 (bs, 1H), 11.87 (s, 1H), 8.72 (s, 1H), 8.37 (s, 1H), 7.87 (s, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 1H), 2.59-2.51 (m, 4H); **^{13}C NMR** (100 MHz, DMSO-*d_6*) *δ* (ppm): 174.1, 171.0, 170.5, 141.4, 130.9, 126.0, 125.4, 122.6, 118.5, 32.5, 29.0.

Compound 8g



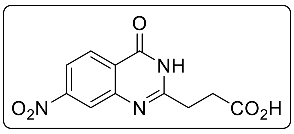
According to the procedure described in the literature,[1] in a flask equipped with a condenser, compound **7g** (0.5 g, 1.59 mmol, 1 equiv) was dissolved in an aqueous 2N NaOH solution (2.7 ml, 3.3 equiv). The resulting solution was refluxed for 2 h and then cooled to RT. The pH was carefully adjusted to pH 5-6 with aqueous 3N HCl solution under vigorous stirring. The resulting orange powder was filtered, washed with water and then dried (430mg, 91.2%). **R*$_f$*** = 0.50 (MeOH/CH_2Cl_2 15:85); **mp** 268-270 °C; **^{1}H NMR** (400 MHz, DMSO-*d_6*) *δ* (ppm): 12.39 (bs, 1H), 12.25 (bs, 1H), 7.99 (s, 1H), 7.77 (s, 1H), 7.63 (s, 1H), 2.85 (m, 2H), 2.74 (m, 2H);; **^{13}C NMR** (100 MHz, DMSO-*d_6*) *δ* (ppm): 174.0, 161.6, 158.4, 150.3, 129.6, 129.5, 128.7, 128.3, 120.5, 30.1, 29.6.

Compound 7h



According to the procedure described in the literature,[1] in a flask equipped with a condenser, 2-amino-4-chlorobenzamide (544 mg, 3 mmol, 1 equiv) and succinic anhydride (300 mg, 3 mmol, 1 equiv) were mixed in 4 ml of toluene. The suspension was vigorously refluxed for 2 days and then cooled to RT. The resulting yellow solid was filtered, washed with Et_2O and dried (2.54 g, 94%). **R*$_f$*** = 0.13 (MeOH/CH_2Cl_2 10:90); **mp** 207-209 °C; **^{1}H NMR** (400 MHz, DMSO-*d_6*) *δ* (ppm): 12.26 (bs, 1H), 11.61 (s, 1H), 9.28 (d, *J* = 2.3 Hz, 1H), 8.56 (s, 1H), 8.10 (s, 1H), 8.00 (d, *J* = 8.7 Hz, 1H), 7.95 (dd, *J* = 8.7, 2.3 Hz, 1H), 2.63 (t, *J* = 6.4 Hz, 2H), 2.55 (t, *J* = 6.4 Hz, 2H); **^{13}C NMR** (100 MHz, DMSO-*d_6*) *δ* (ppm): 173.6, 170.9, 169.1, 149.1, 140.1, 130.1, 125.1, 116.7, 114.4, 32.1, 28.6; **HRMS** calcd for $C_{11}H_{12}N_3O_6$ $[M+H]^+$ 282.0726, found 282.0723.

Compound 8h

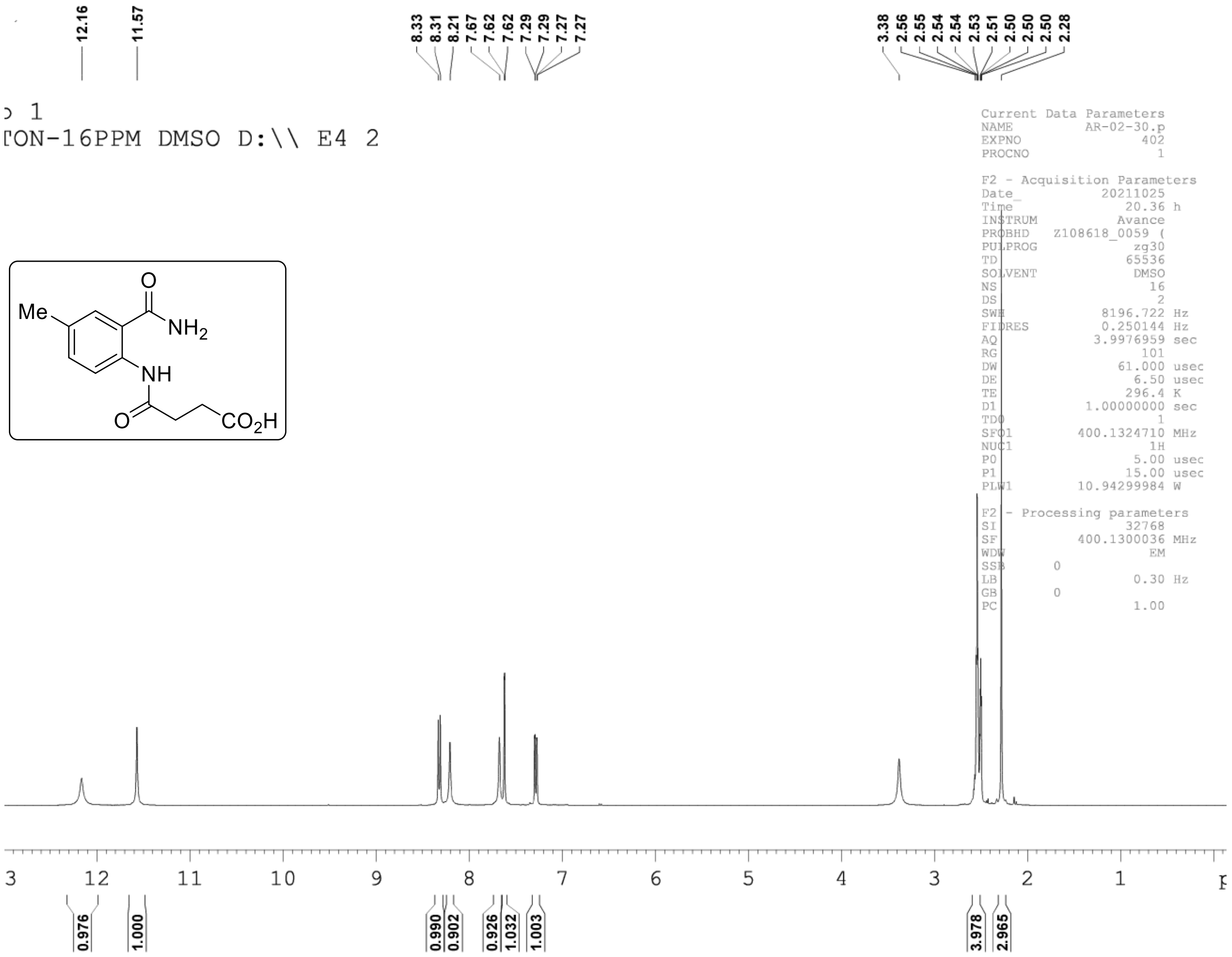


According to the procedure described in the literature,[1] in a flask equipped with a condenser, compound **Q** (655 mg, 2.3 mmol, 1 equiv) was dissolved in an aqueous 2N NaOH solution (4 ml, 3.3 equiv). The resulting solution was refluxed for 5 h and then cooled to RT. The pH was carefully adjusted to pH 5-6 with aqueous 3N HCl solution under vigorous stirring. The resulting orange powder was filtered, washed with water and then dried (527 mg, 86%). **R*$_f$*** = 0.50 (MeOH/CH_2Cl_2 15:85); **mp** 261-263 °C; **^{1}H NMR** (400 MHz, DMSO-*d_6*) *δ* (ppm): 12.61 (bs, 1H), 12.34 (bs, 1H), 8.24 (d, *J* = 8.6 Hz, 1H), 8.19 (d, *J* = 1.6 Hz, 1H), 8.13 (dd, *J* = 8.6, 1.8 Hz, 1H), 2.88 (t, *J* = 6.8 Hz, 2H), 2.76 (t, *J* = 6.7 Hz, 2H); **^{13}C NMR** (100 MHz, DMSO-*d_6*) *δ* (ppm): 173.8, 160.9, 159.2, 151.3, 149.2, 128.3, 125.3, 121.9, 119.9, 29.9, 29.4; **HRMS** calcd for $C_{11}H_{10}N_3O_5$ $[M+H]^+$ 264.0620, found 264.0619.

2. Additional references

[1] R. Ferreira de Freitas, R. J. Harding, I. Franzoni, M. Ravichandran, M. K. Mann, H. Ouyang, M. Lautens, V. Santhakumar, C. H. Arrowsmith, M. Schapira, *J. Med. Chem.* **2018**, *61*, 4517-4527.

3. ^{1}H and ^{13}C NMR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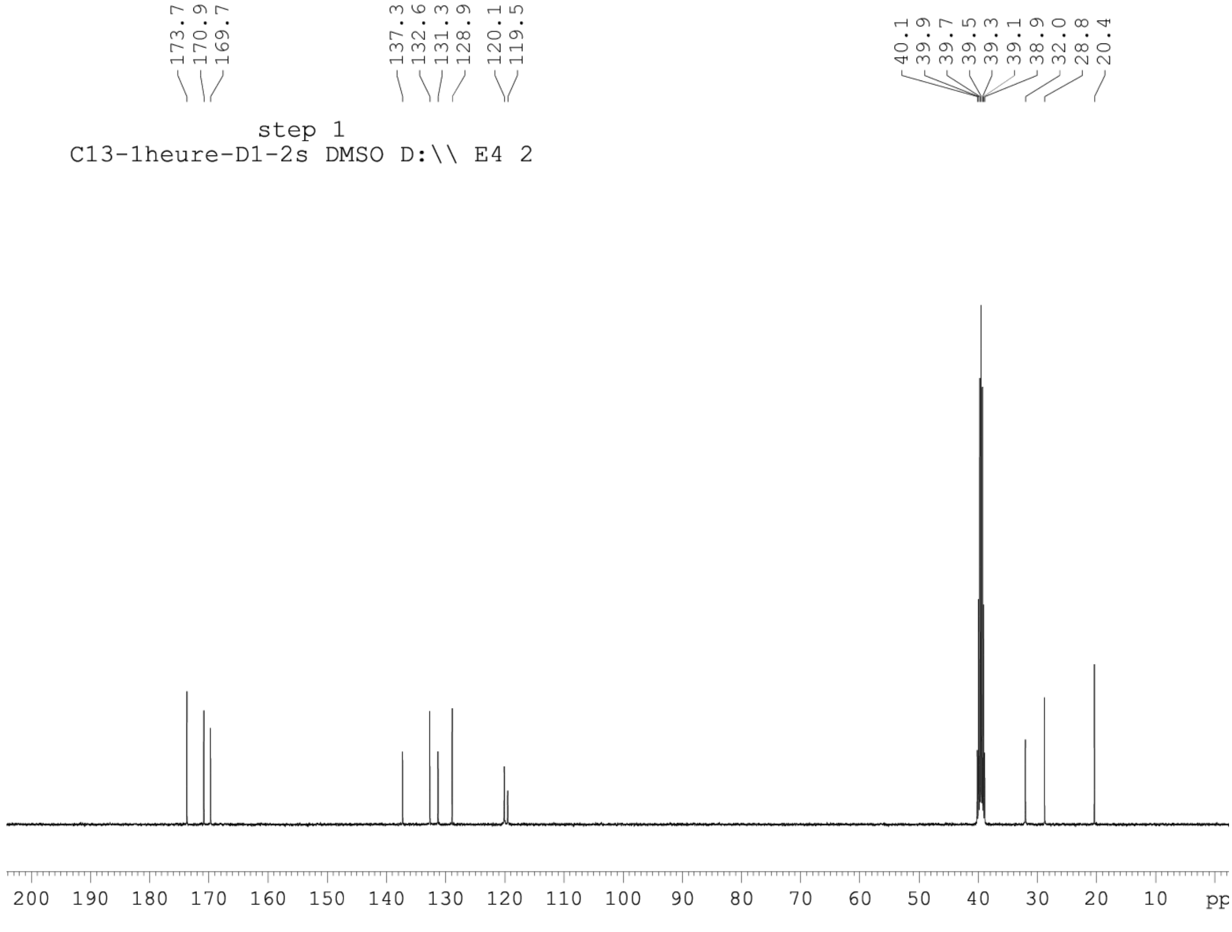
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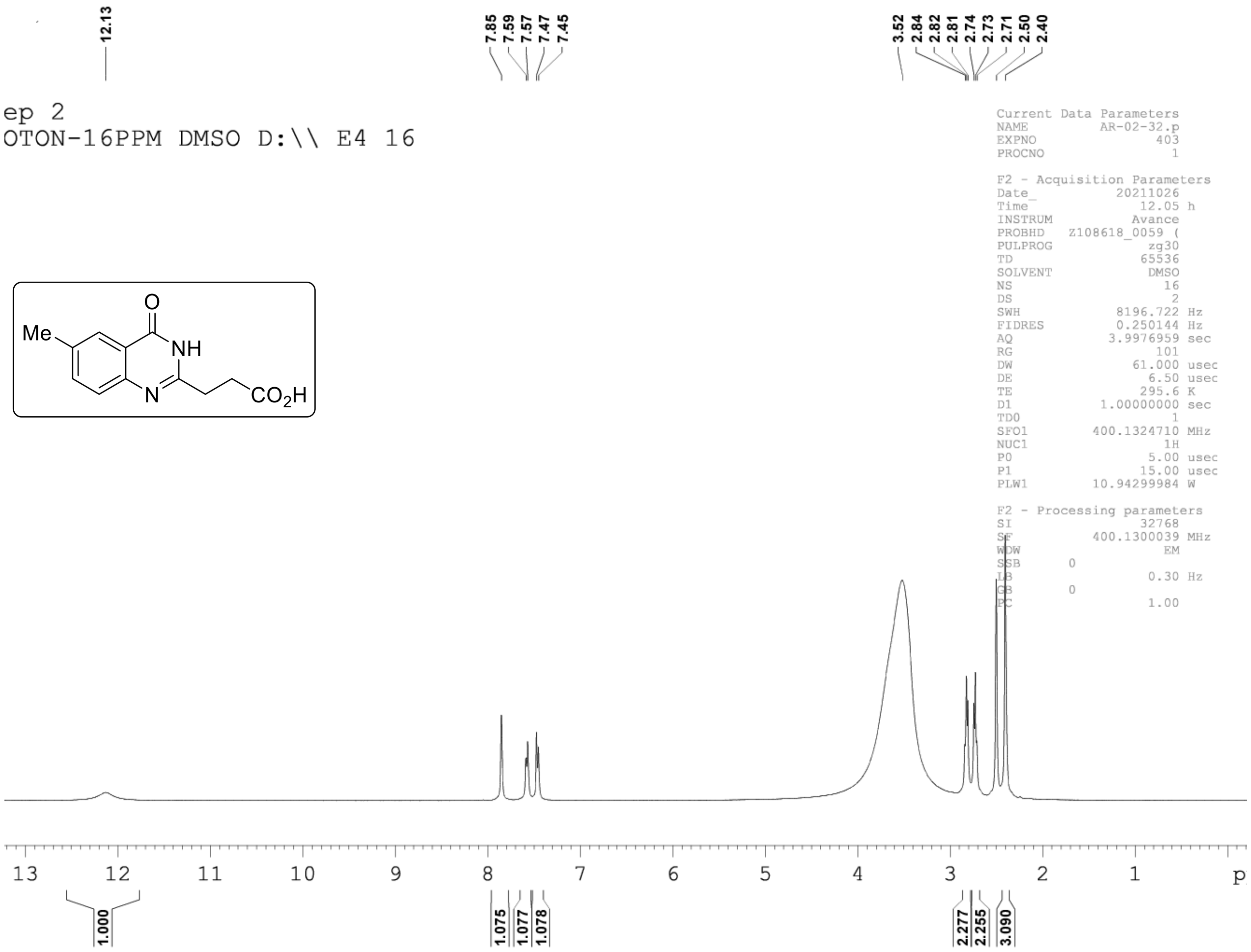
20.4
step 1
C13-1heure-D1-2s DMSO D:\\ E4 2
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
pp



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Current Data Parameters
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EXPNO                403
PROCNO                 1

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Time              12.05 h
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PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8196.722 Hz
FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG                   101
DW                61.000 usec
DE                  6.50 usec
TE                 295.6 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324710 MHz
NUC1                  1H
P0                  5.00 usec
P1                 15.00 usec
PLW1         10.94299984 W

F2 - Processing parameters
SI                 32768
SF           400.1300039 MHz
WDW                   EM
SSB      0
LB                  0.30 Hz
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PC                  1.00
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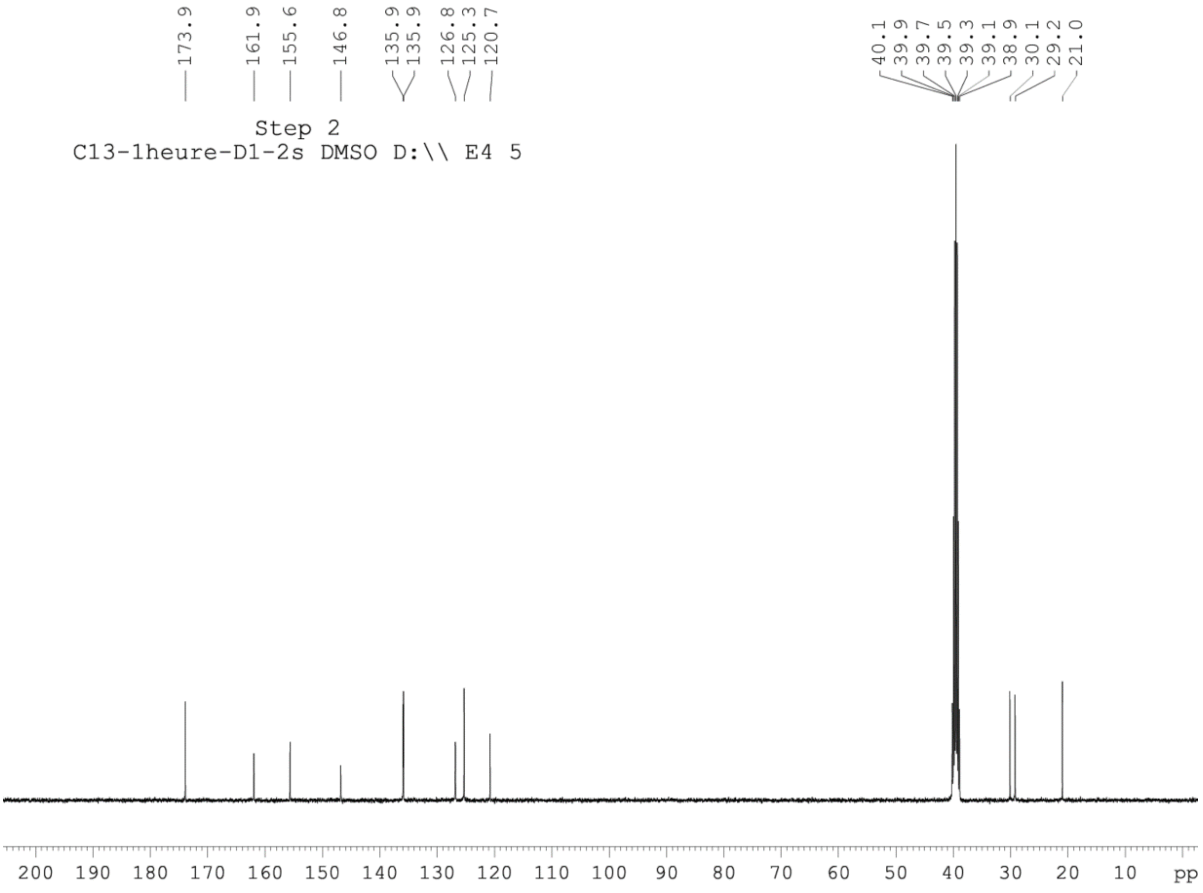

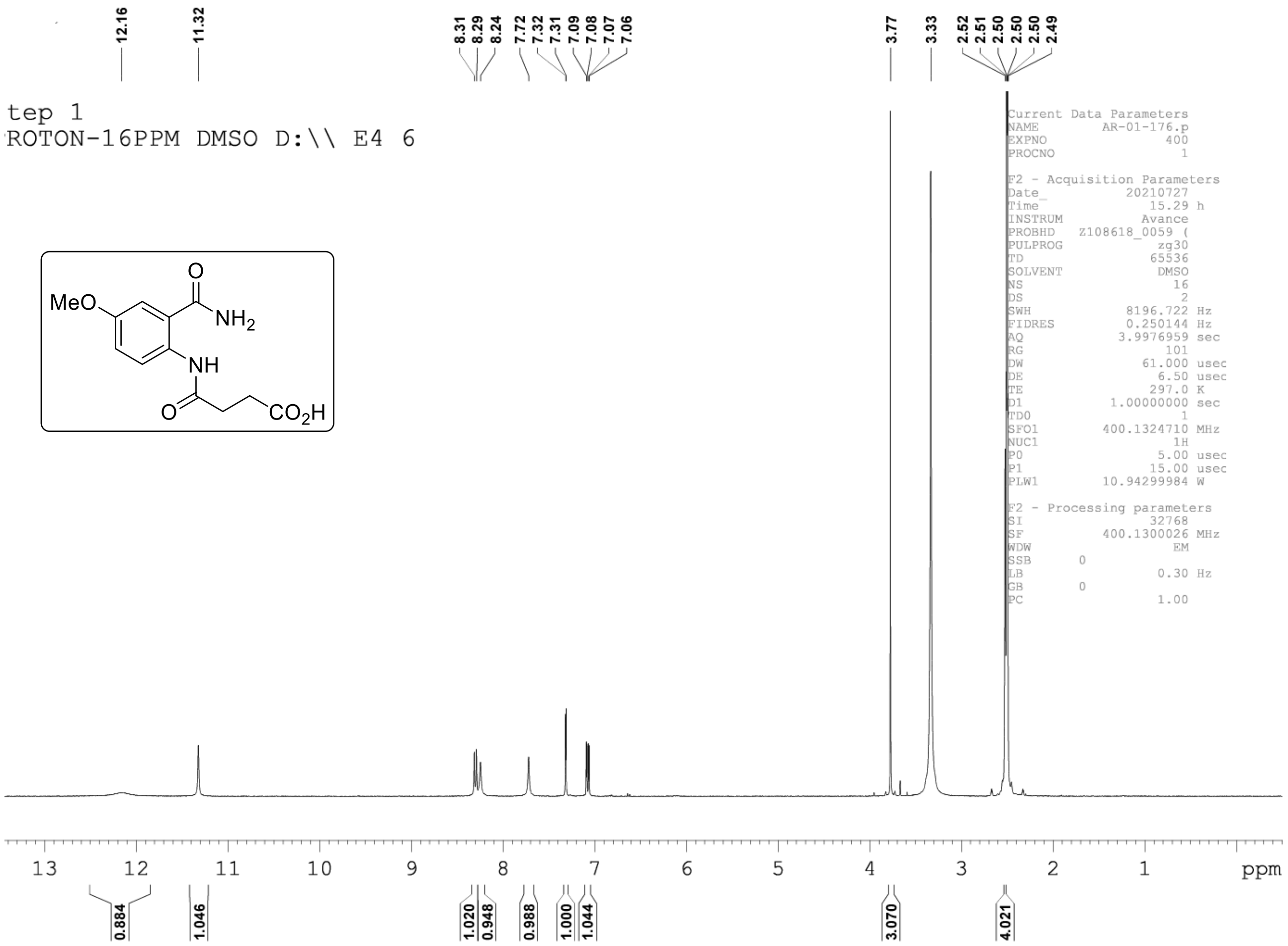
12.16
11.32
8.31
8.29
8.24
7.72
7.32
7.31
7.09
7.08
7.07
7.06
3.77
3.33
2.52
2.51
2.50
2.50
2.50
2.49
tep 1
ROTON-16PPM DMSO D:\\ E4 6
MeO
O
NH2
NH
O
CO2H
Current Data Parameters
NAME AR-01-176.p
EXPNO 400
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210727
Time 15.29 h
INSTRUM Avance
PROBHD Z108618_0059 (
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 6.50 usec
TE 297.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1324710 MHz
NUC1 1H
P0 5.00 usec
P1 15.00 usec
PLW1 10.94299984 W
F2 - Processing parameters
SI 32768
SF 400.1300026 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
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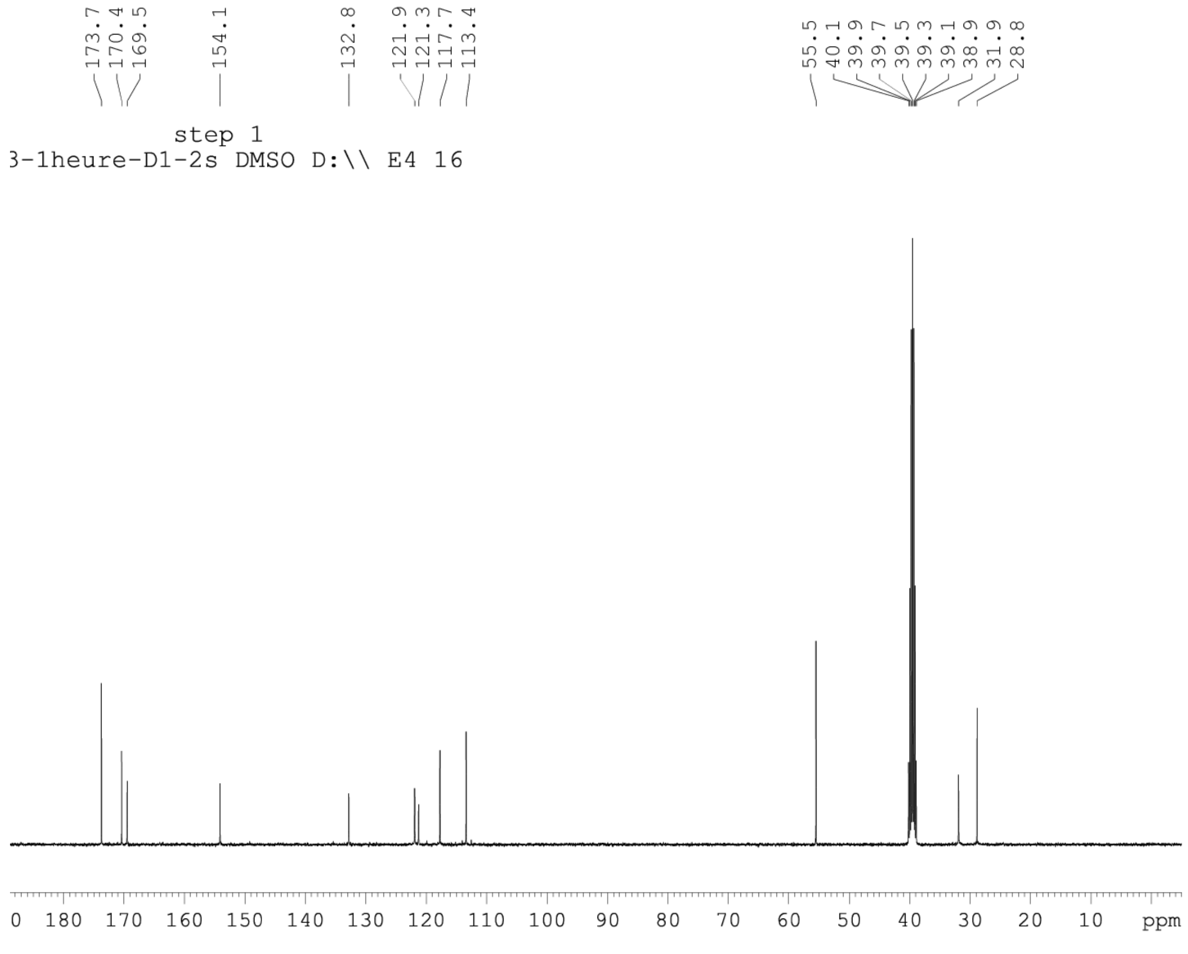
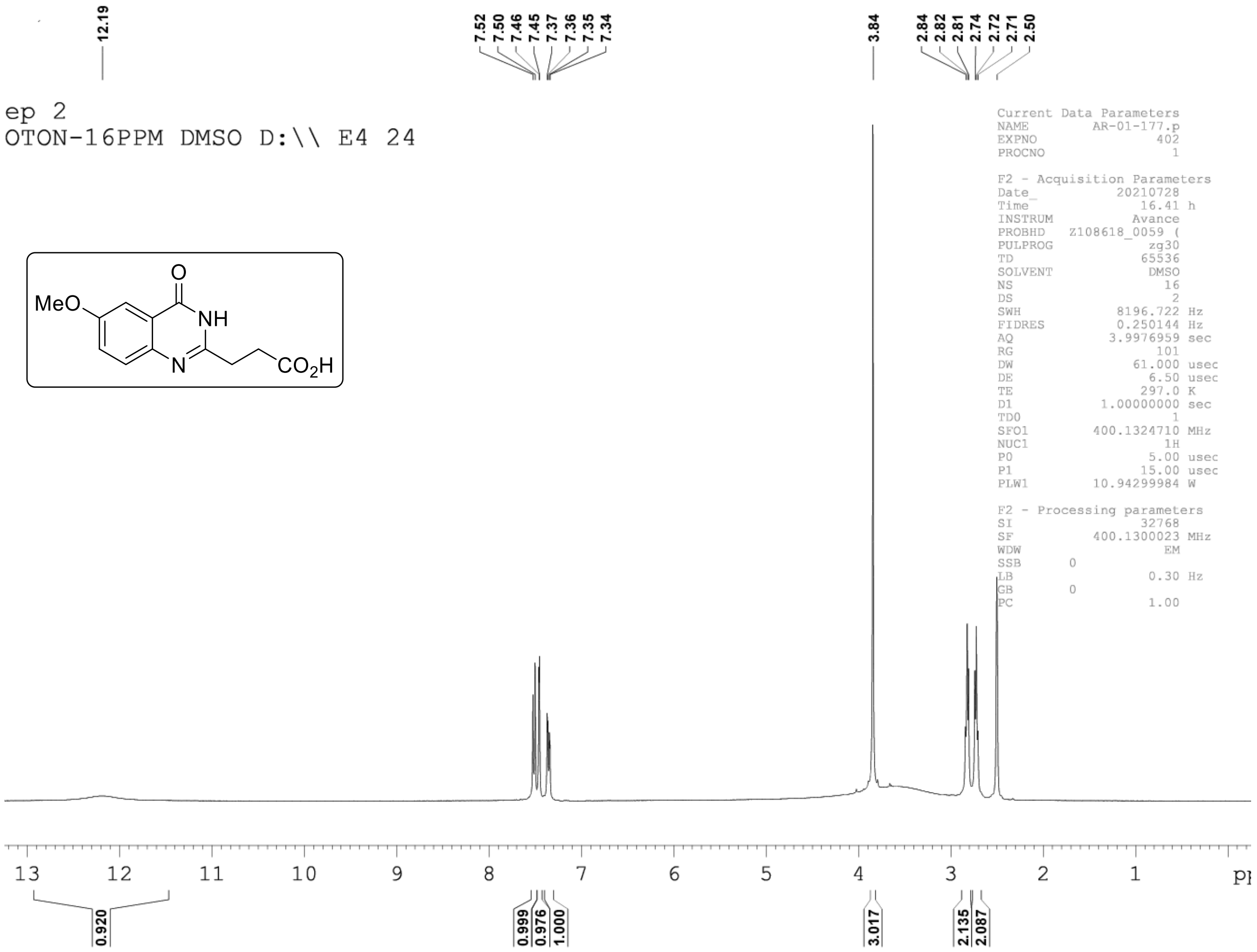
1.046
1.020
0.948
0.988
1.000
1.044
3.070
4.021


173.7
170.4
169.5
154.1
132.8
121.9
121.3
117.7
113.4
55.5
40.1
39.9
39.7
39.5
39.3
39.1
38.9
31.9
28.8
step 1
3-1heure-D1-2s DMSO D:\\ E4 16
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



```
Current Data Parameters
NAME          AR-01-177.p
EXPNO                 402
PROCNO                  1

F2 - Acquisition Parameters
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Time                16.41 h
INSTRUM            Avance
PROBHD   Z108618_0059 (
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH              8196.722 Hz
FIDRES           0.250144 Hz
AQ              3.9976959 sec
RG                    101
DW                 61.000 usec
DE                   6.50 usec
TE                  297.0 K
D1             1.00000000 sec
TD0                     1
SFO1          400.1324710 MHz
NUC1                   1H
P0                   5.00 usec
P1                  15.00 usec
PLW1          10.94299984 W

F2 - Processing parameters
SI                  32768
SF            400.1300023 MHz
WDW                    EM
SSB      0
LB                   0.30 Hz
GB       0
PC                   1.00
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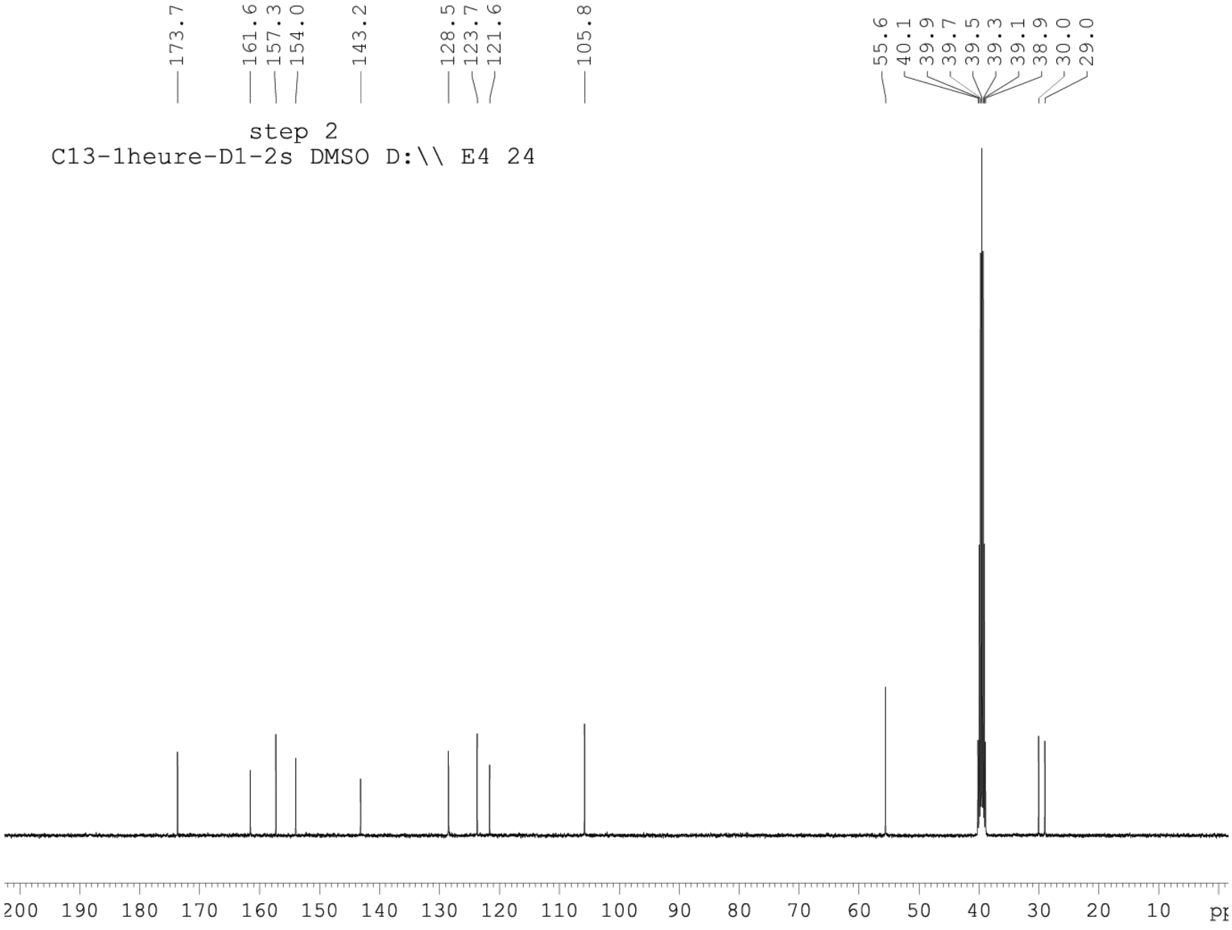

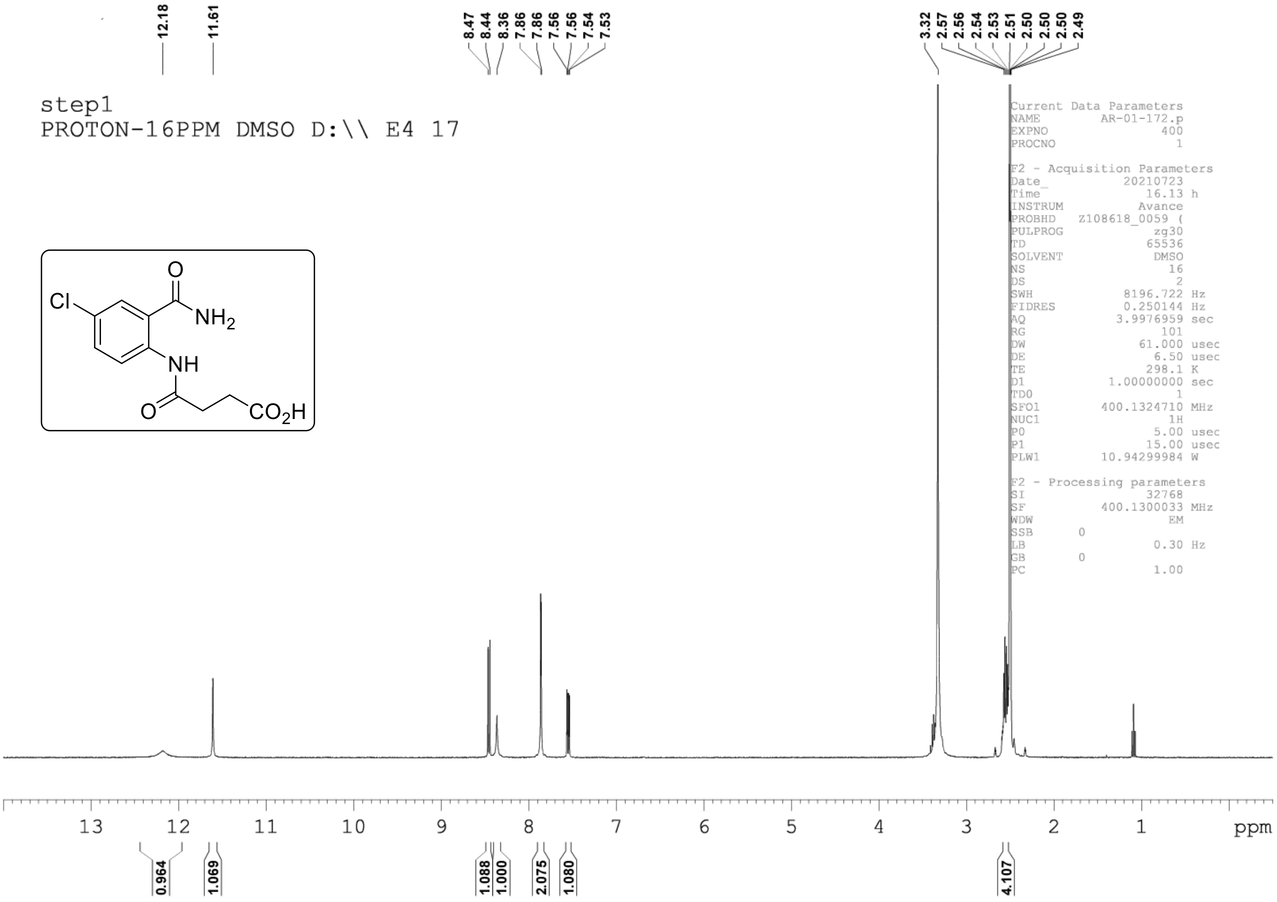

```
Current Data Parameters
NAME          AR-01-172.p
EXPNO                 400
PROCNO                  1

F2 - Acquisition Parameters
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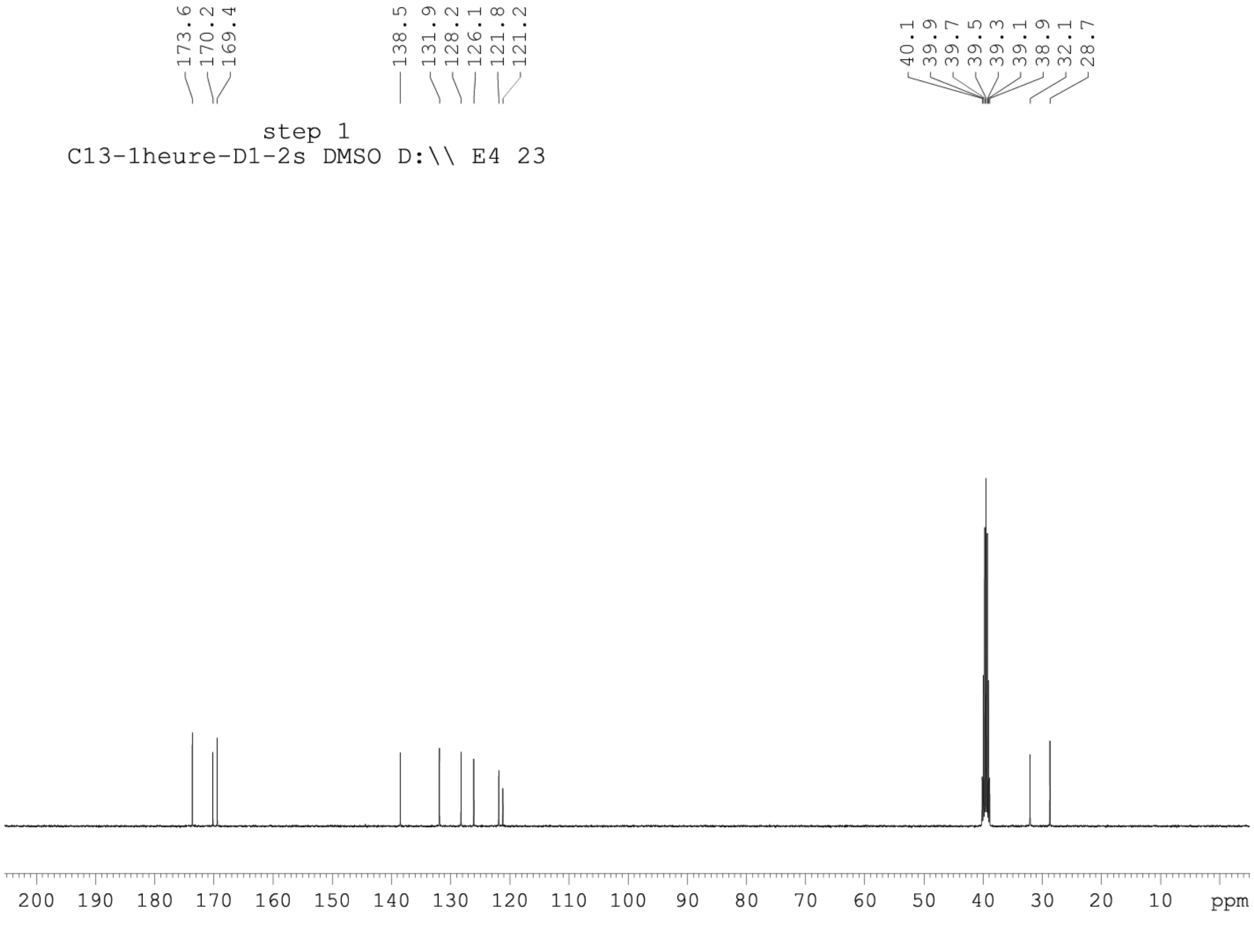
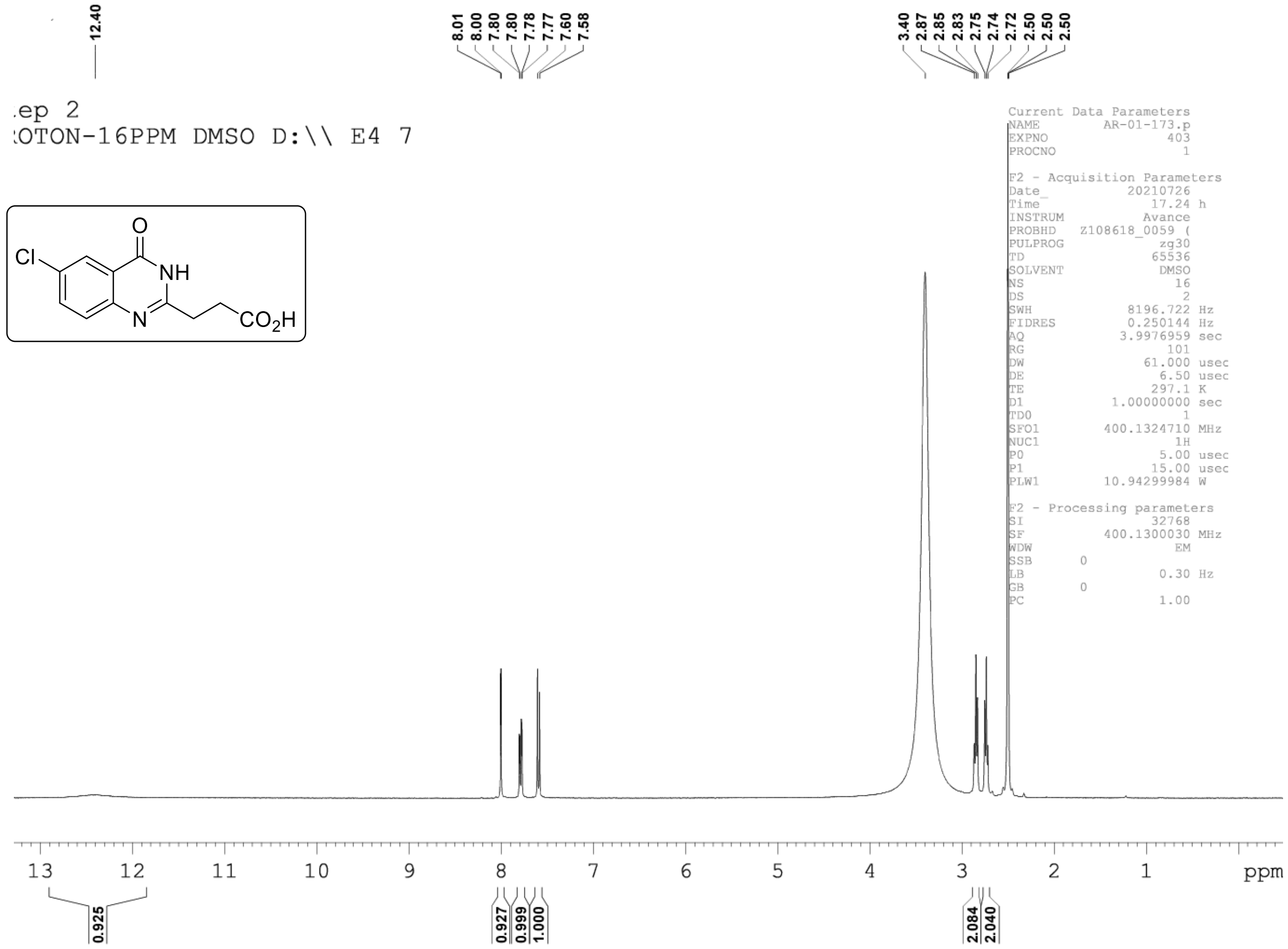
Time                16.13 h
INSTRUM            Avance
PROBHD   Z108618_0059 (
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH              8196.722 Hz
FIDRES           0.250144 Hz
AQ              3.9976959 sec
RG                    101
DW                 61.000 usec
DE                   6.50 usec
TE                  298.1 K
D1             1.00000000 sec
TD0                     1
SFO1          400.1324710 MHz
NUC1                   1H
P0                   5.00 usec
P1                  15.00 usec
PLW1          10.94299984 W

F2 - Processing parameters
SI                  32768
SF            400.1300033 MHz
WDW                    EM
SSB      0
LB                   0.30 Hz
GB       0
PC                   1.00
```





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Current Data Parameters
NAME          AR-01-173.p
EXPNO                 403
PROCNO                  1

F2 - Acquisition Parameters
Date_            20210726
Time                17.24 h
INSTRUM            Avance
PROBHD   Z108618_0059 (
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH              8196.722 Hz
FIDRES           0.250144 Hz
AQ              3.9976959 sec
RG                    101
DW                 61.000 usec
DE                   6.50 usec
TE                  297.1 K
D1             1.00000000 sec
TD0                     1
SFO1          400.1324710 MHz
NUC1                   1H
P0                   5.00 usec
P1                  15.00 usec
PLW1          10.94299984 W

F2 - Processing parameters
SI                  32768
SF            400.1300030 MHz
WDW                    EM
SSB      0
LB                   0.30 Hz
GB       0
PC                   1.00
```
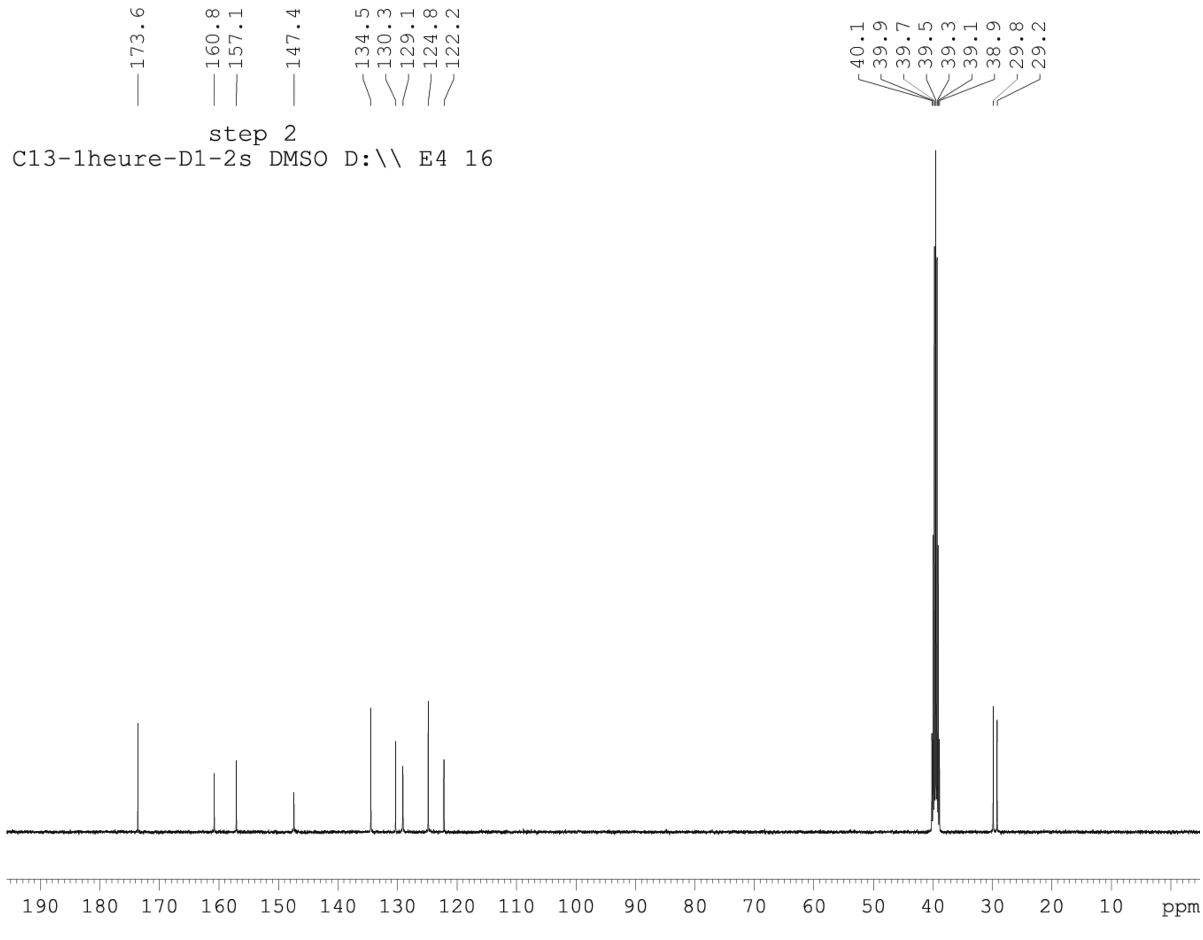
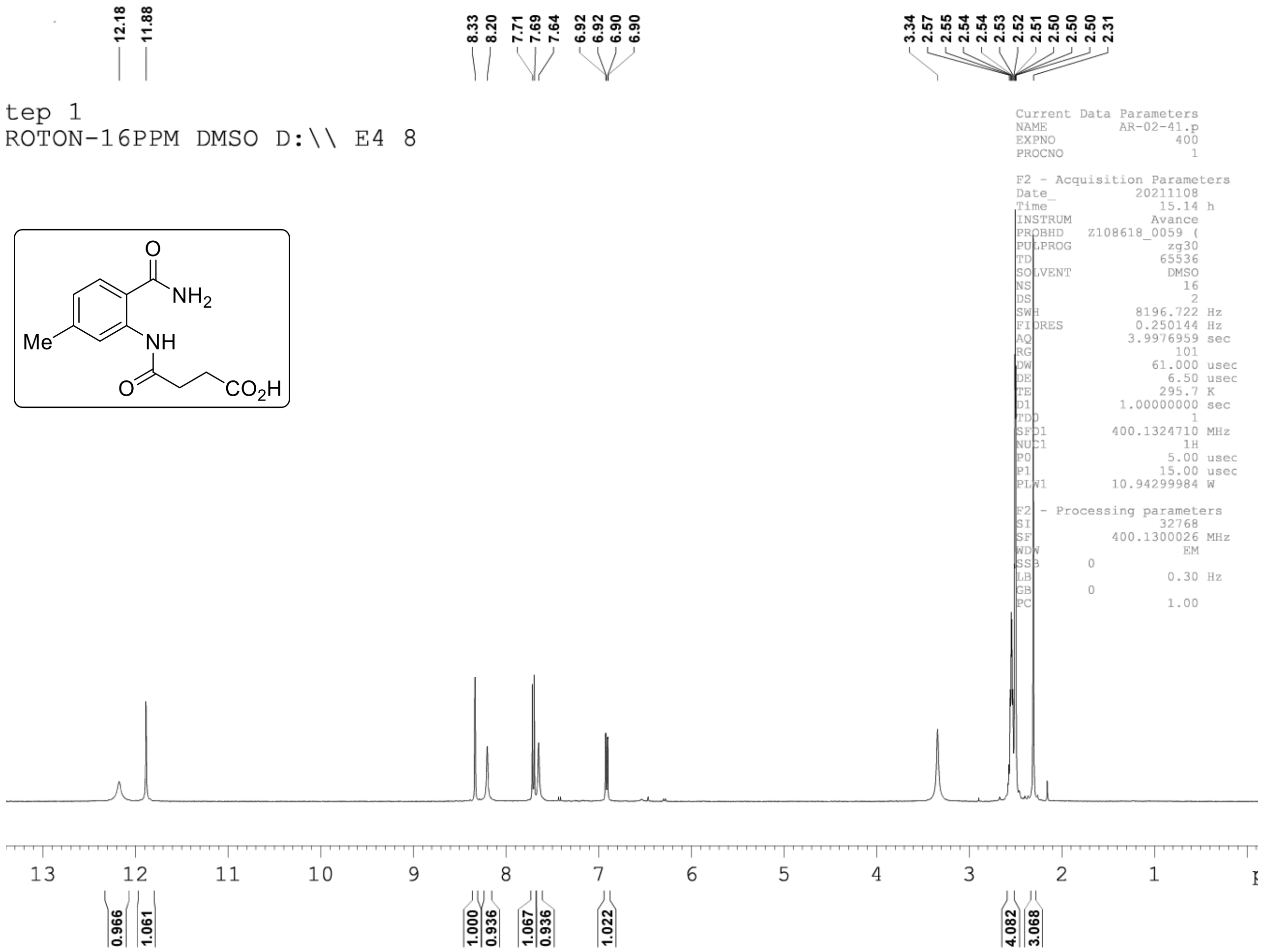
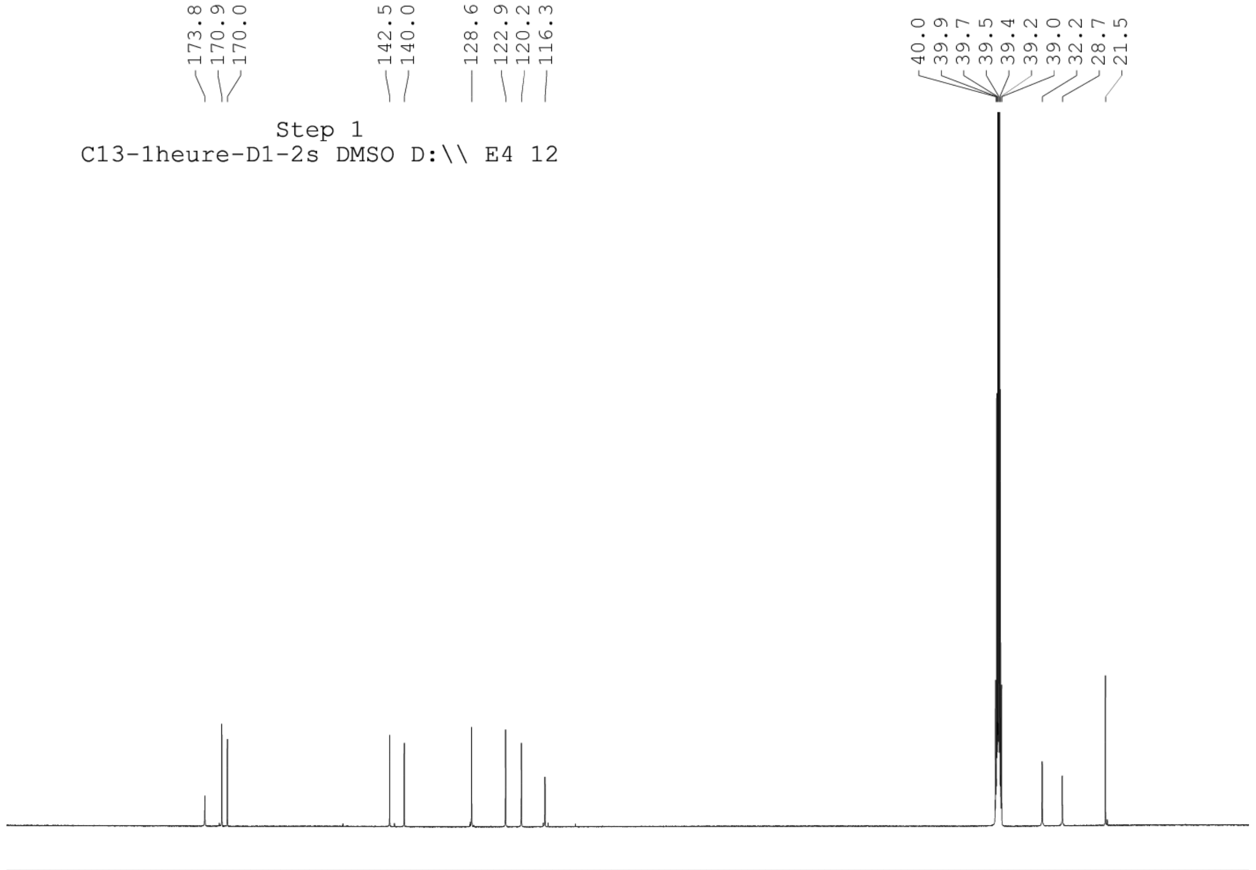




12.18
11.88
8.33
8.20
7.71
7.69
7.64
6.92
6.92
6.90
6.90
3.34
2.57
2.55
2.54
2.54
2.53
2.52
2.51
2.50
2.50
2.50
2.31
tep 1
ROTON-16PPM DMSO D:\\ E4 8
O
NH2
Me
NH
O
CO2H
Current Data Parameters
NAME AR-02-41.p
EXPNO 400
PROCNO 1
F2 - Acquisition Parameters
Date_ 20211108
Time 15.14 h
INSTRUM Avance
PROBHD Z108618_0059 (
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8196.722 Hz
FIDRES 0.250144 Hz
AQ 3.9976959 sec
RG 101
DW 61.000 usec
DE 6.50 usec
TE 295.7 K
D1 1.00000000 sec
TD0 1
SFO1 400.1324710 MHz
NUC1 1H
P0 5.00 usec
P1 15.00 usec
PLW1 10.94299984 W
F2 - Processing parameters
SI 32768
SF 400.1300026 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0.966
1.061
1.000
0.936
1.067
0.936
1.022
4.082
3.068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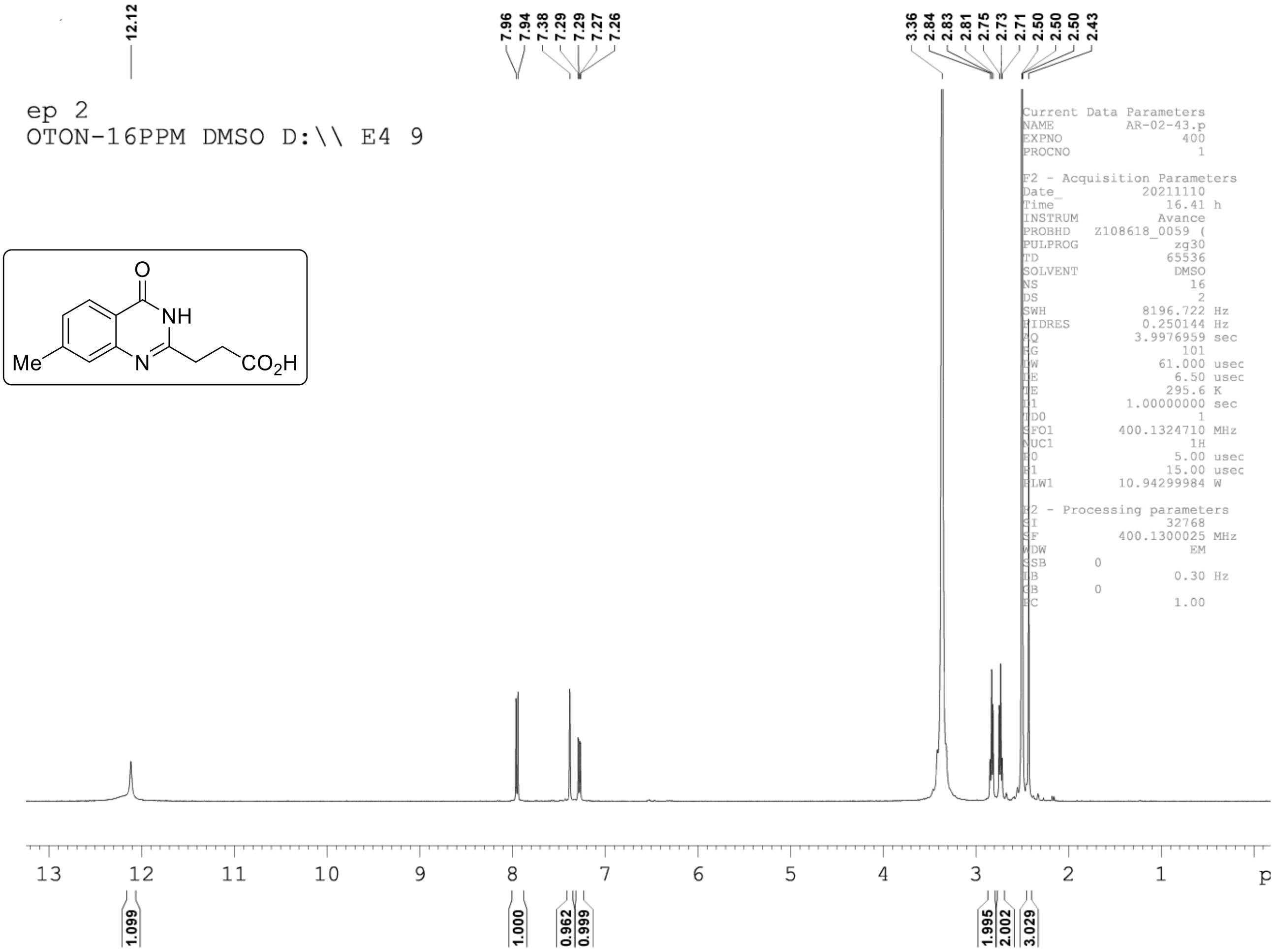
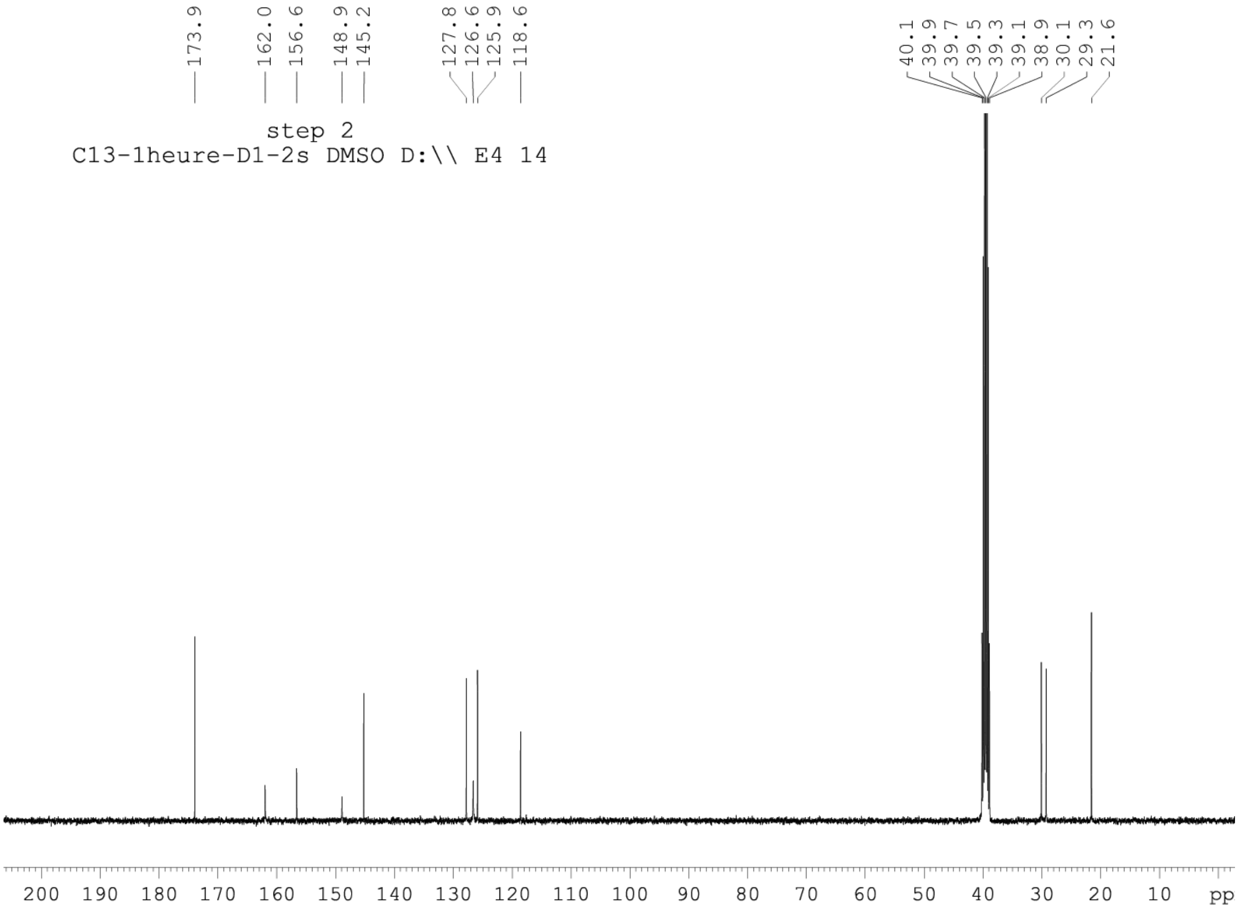
170.9
170.0
142.5
140.0
128.6
122.9
120.2
116.3
40.0
39.9
39.7
39.5
39.4
39.2
39.0
32.2
28.7
21.5
Step 1
C13-1heure-D1-2s DMSO D:\\ E4 12
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
pp

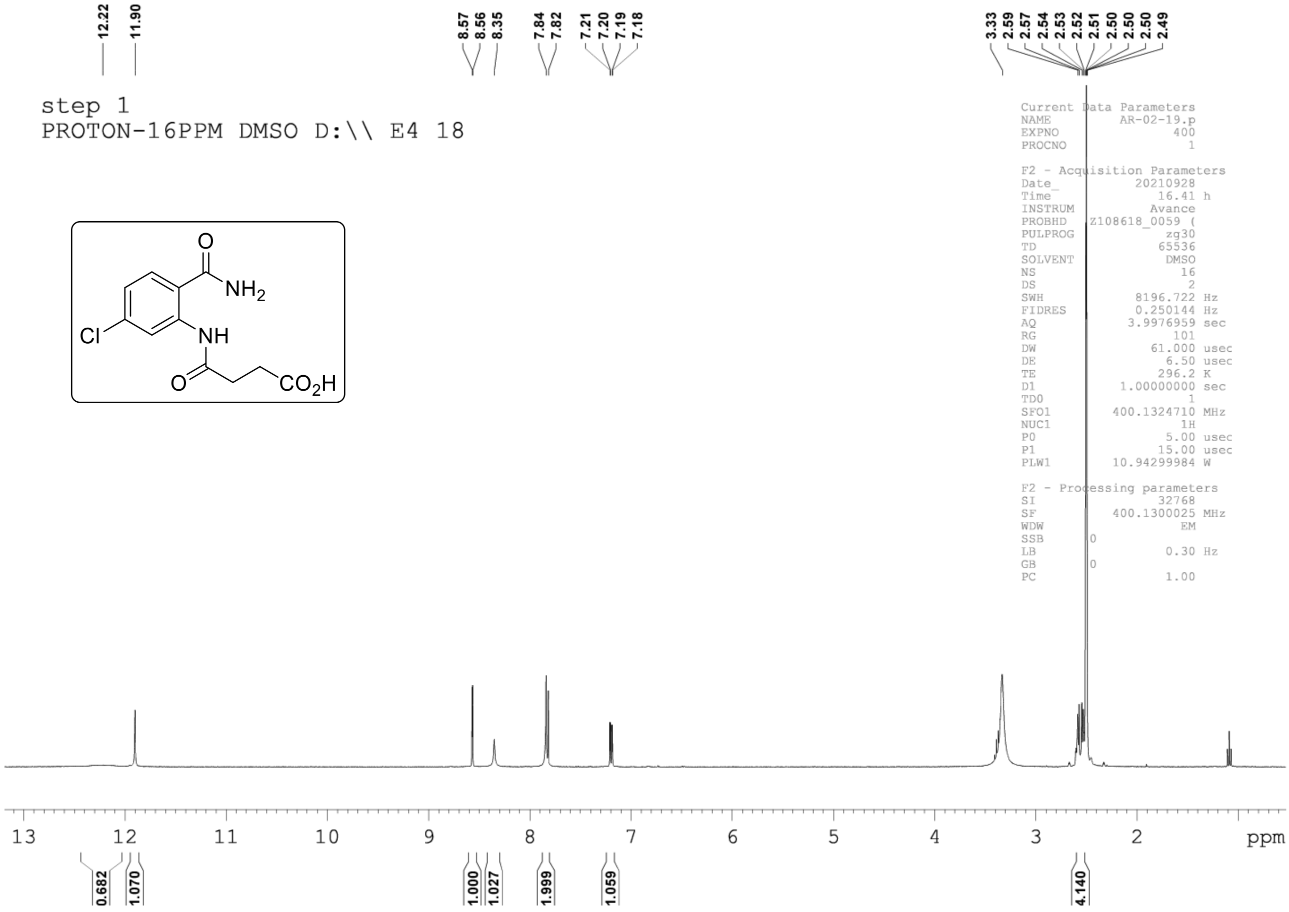


```
Current Data Parameters
NAME          AR-02-43.p
EXPNO                400
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211110
Time               16.41 h
INSTRUM           Avance
PROBHD   Z108618_0059 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8196.722 Hz
FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG                   101
DW                61.000 usec
DE                  6.50 usec
TE                 295.6 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324710 MHz
NUC1                  1H
P0                  5.00 usec
P1                 15.00 usec
PLW1         10.94299984 W

F2 - Processing parameters
SI                 32768
SF           400.1300025 MHz
WDW                   EM
SSB      0
LB                  0.30 Hz
GB       0
PC                  1.00
```



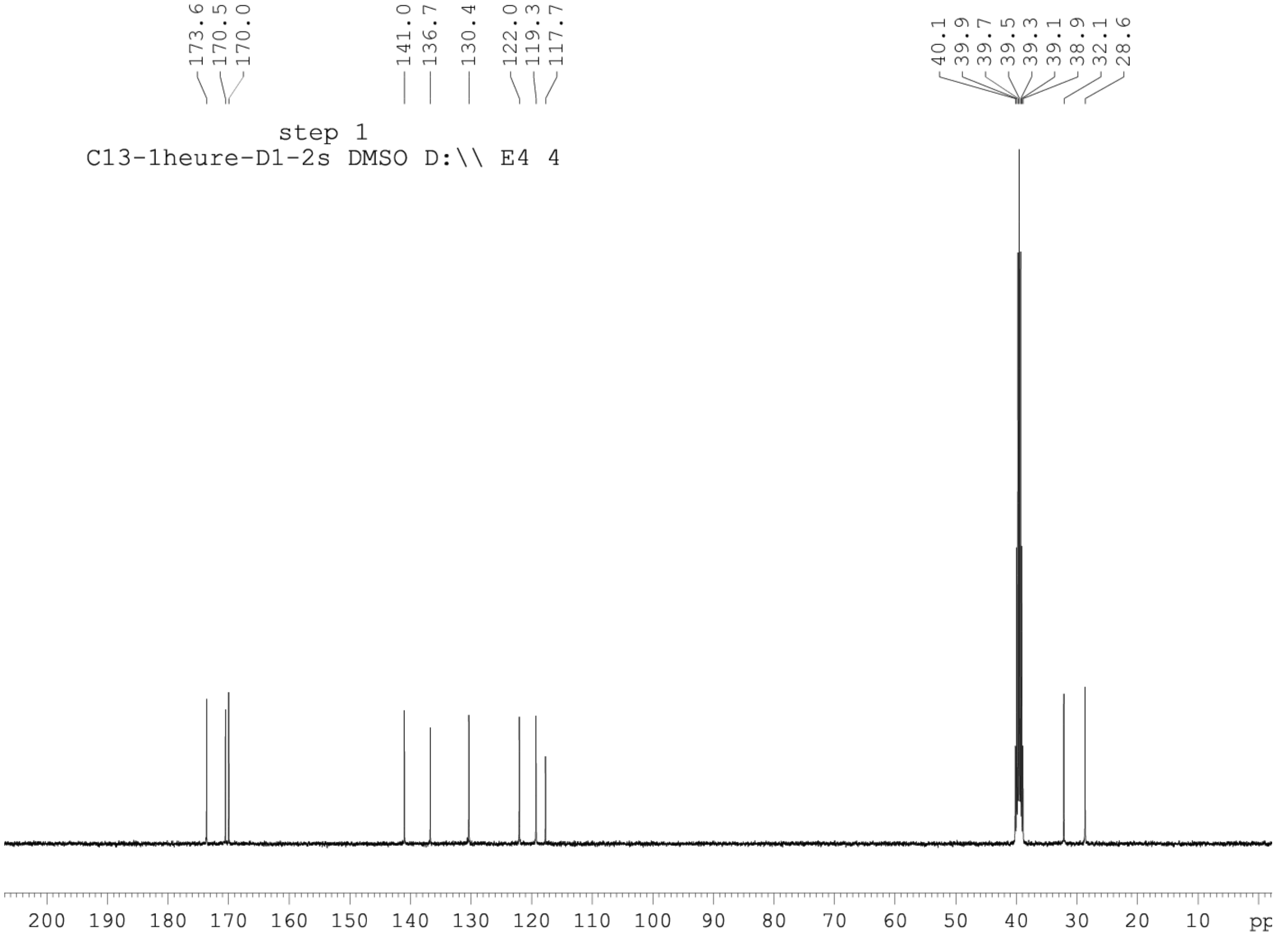


step 1
PROTON-16PPM DMSO D:\\ E4 18

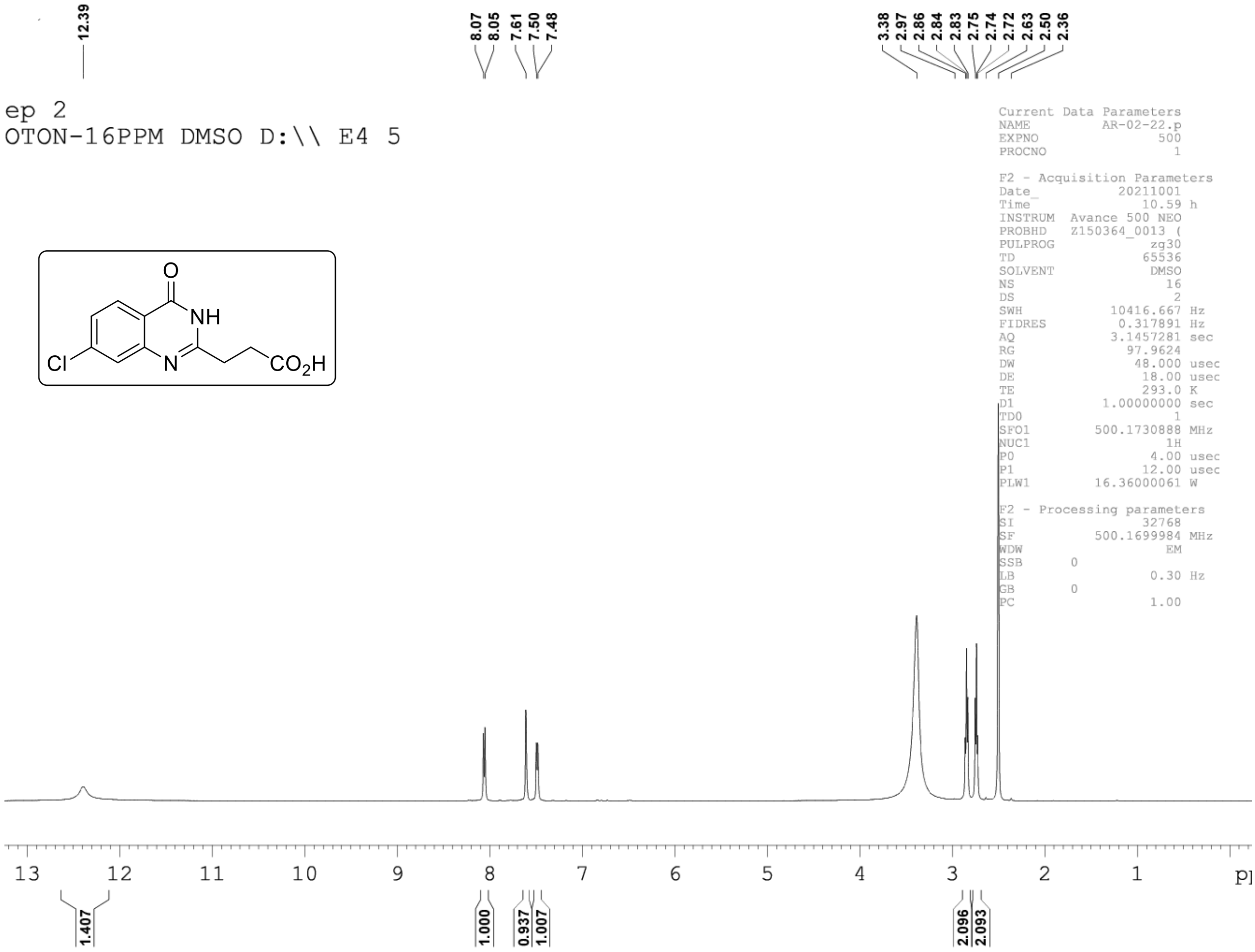
```
Current Data Parameters
NAME             AR-02-19.p
EXPNO                   400
PROCNO                    1

F2 - Acquisition Parameters
Date_              20210928
Time                  16.41 h
INSTRUM              Avance
PROBHD      Z108618_0059 (
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8196.722 Hz
FIDRES             0.250144 Hz
AQ                3.9976959 sec
RG                      101
DW                   61.000 usec
DE                     6.50 usec
TE                    296.2 K
D1               1.00000000 sec
TD0                       1
SFO1            400.1324710 MHz
NUC1                     1H
P0                     5.00 usec
P1                    15.00 usec
PLW1            10.94299984 W

F2 - Processing parameters
SI                    32768
SF              400.1300025 MHz
WDW                      EM
SSB         0
LB                     0.30 Hz
GB          0
PC                     1.00
```



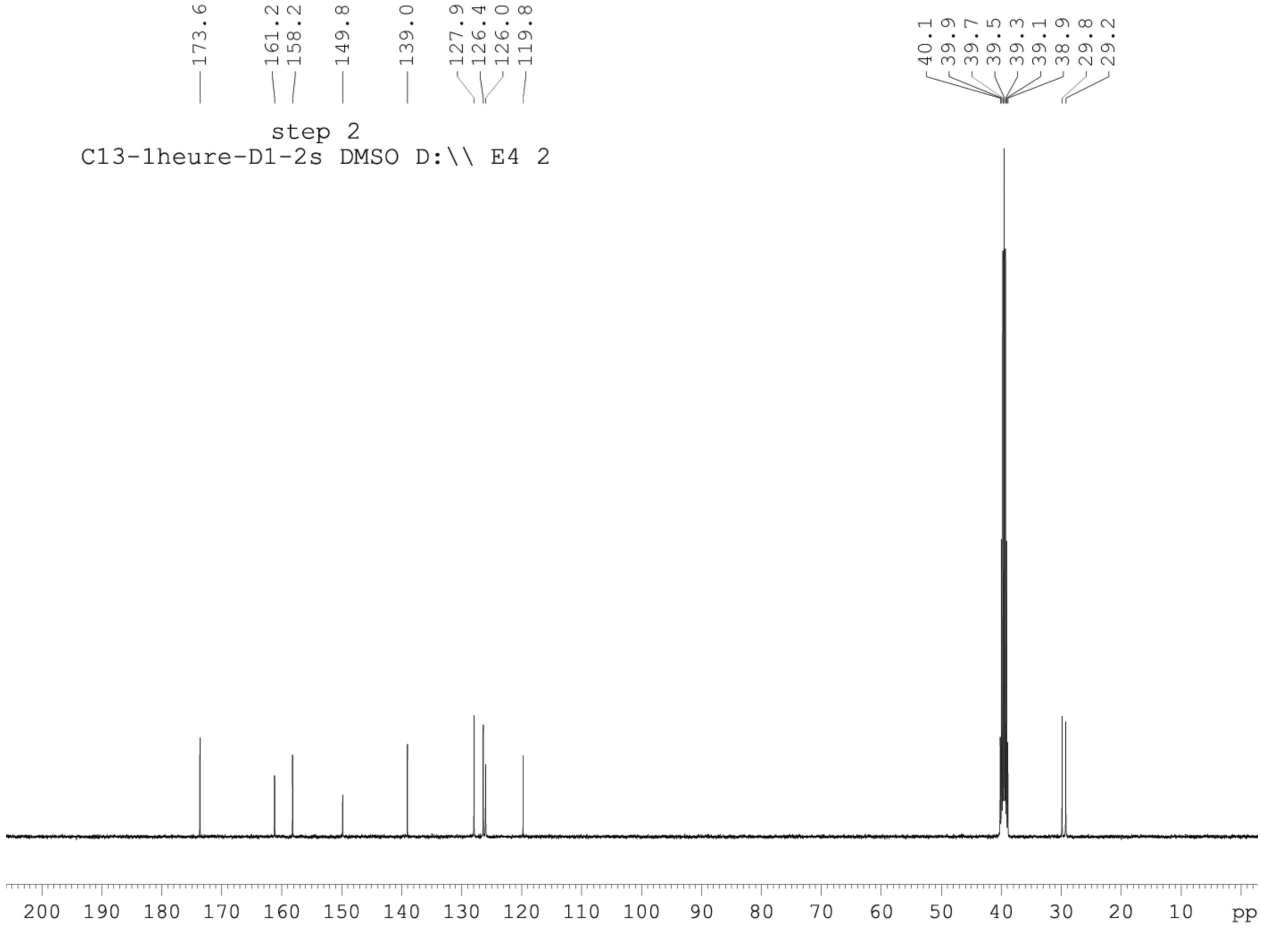
step 1
C13-1heure-D1-2s DMSO D:\\ E4 4

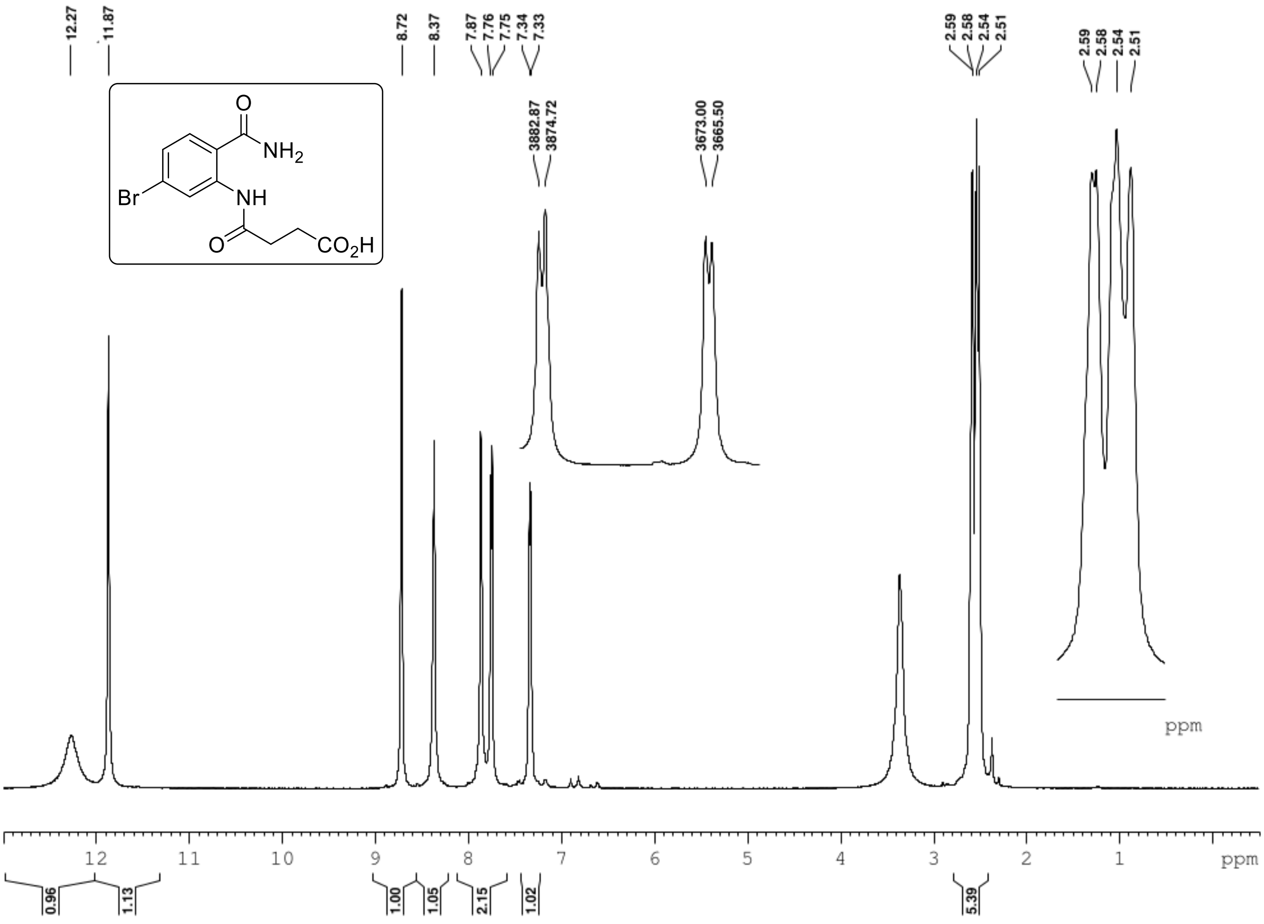


```
Current Data Parameters
NAME          AR-02-22.p
EXPNO                500
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211001
Time               10.59 h
INSTRUM  Avance 500 NEO
PROBHD   Z150364_0013 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH            10416.667 Hz
FIDRES          0.317891 Hz
AQ             3.1457281 sec
RG               97.9624
DW                48.000 usec
DE                 18.00 usec
TE                 293.0 K
D1            1.00000000 sec
TD0                    1
SFO1         500.1730888 MHz
NUC1                  1H
P0                  4.00 usec
P1                 12.00 usec
PLW1         16.36000061 W

F2 - Processing parameters
SI                 32768
SF           500.1699984 MHz
WDW                   EM
SSB      0
LB                  0.30 Hz
GB       0
PC                  1.00
```

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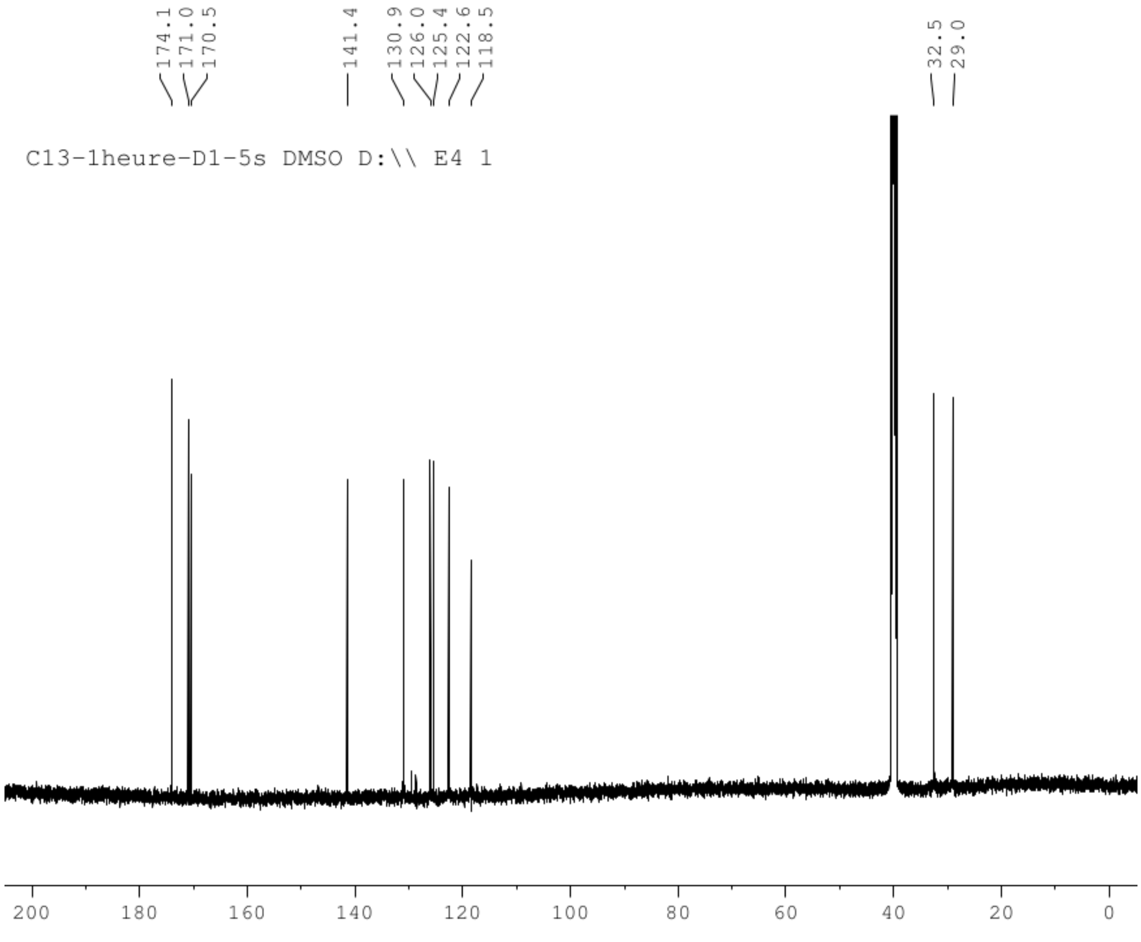
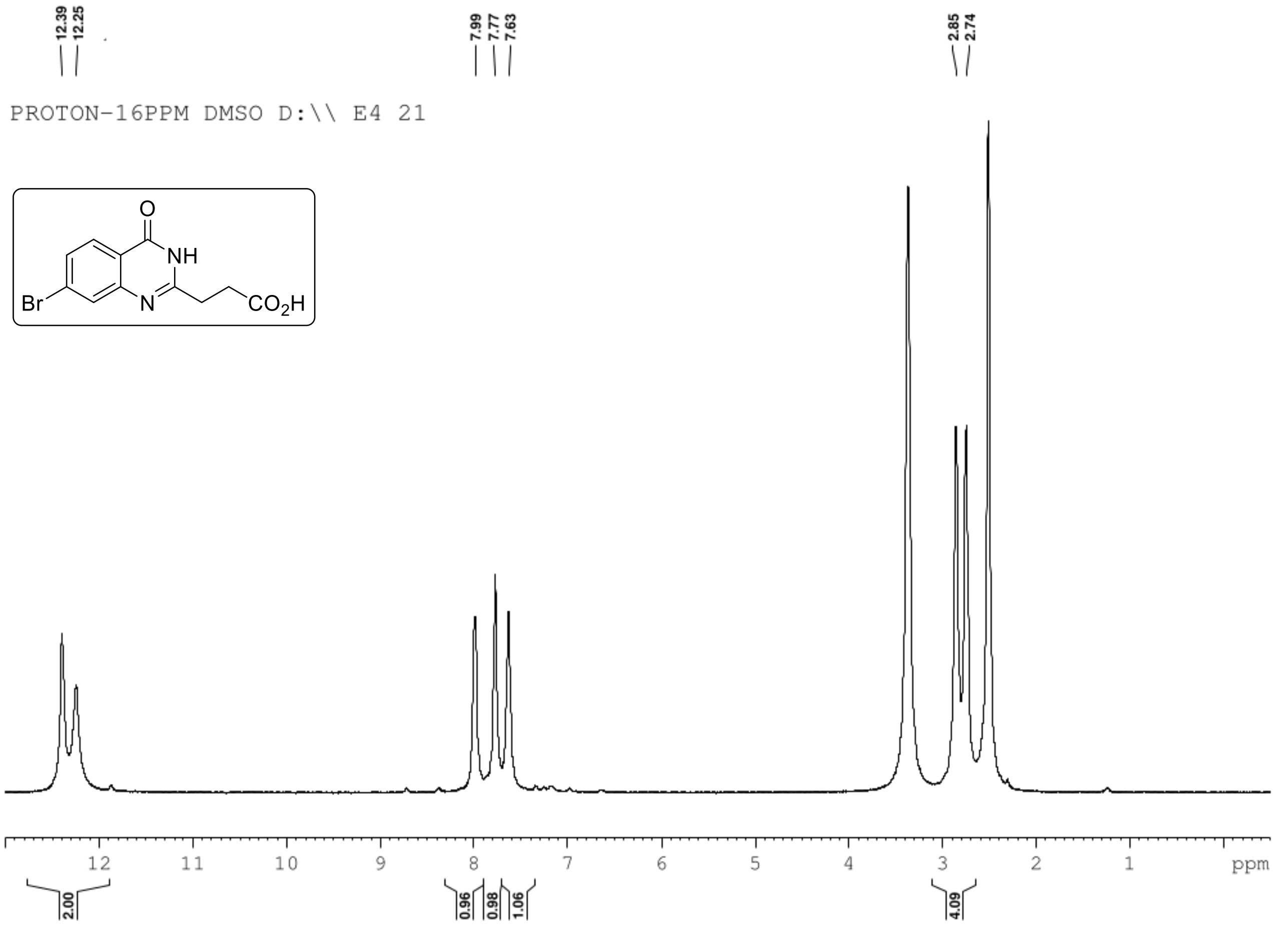
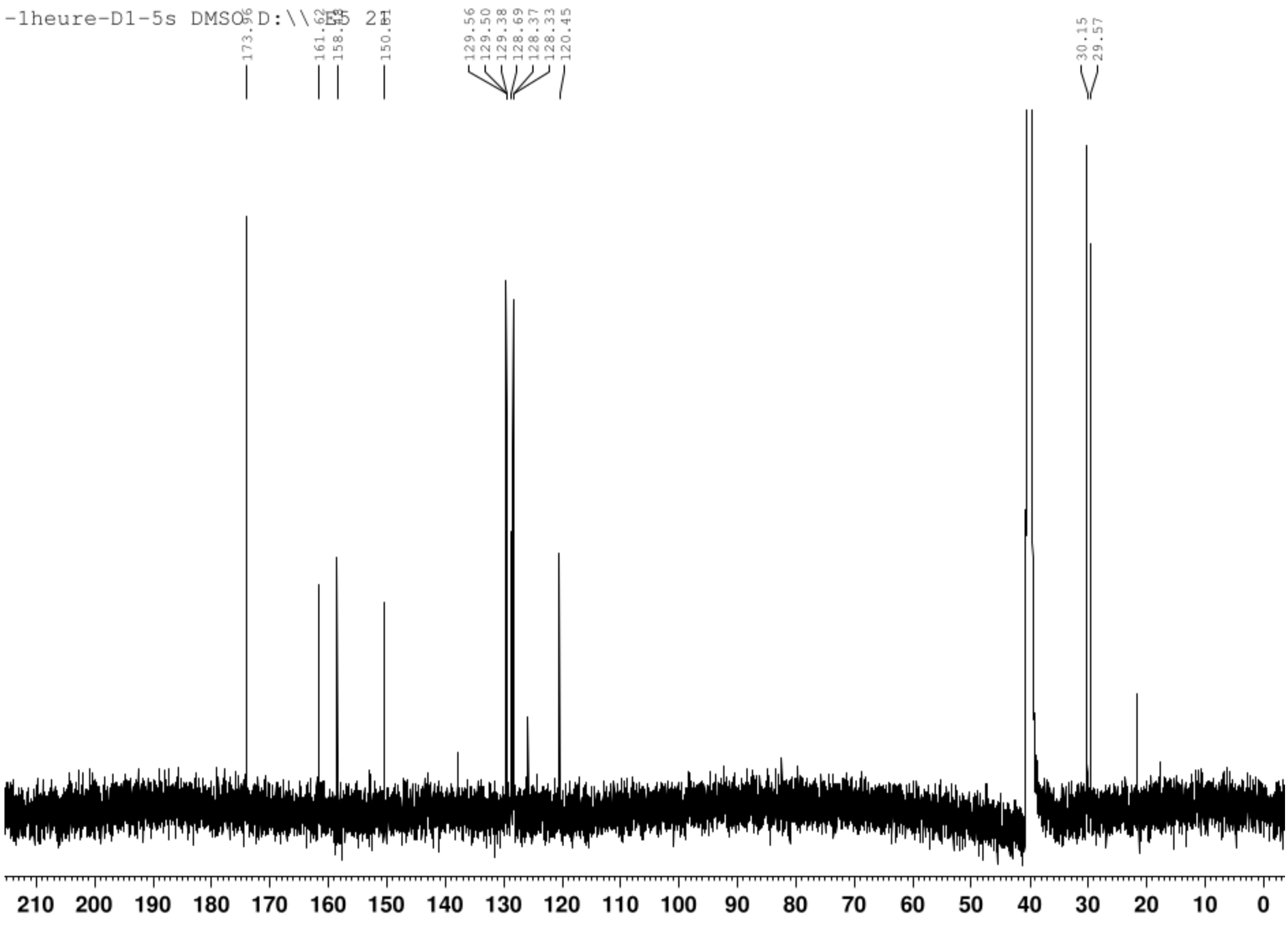
8.72
8.37
7.87
7.76
7.75
7.34
7.33
2.59
2.58
2.54
2.51
2.59
2.58
2.54
2.51
3882.87
3874.72
3673.00
3665.50
O
NH2
Br
NH
O
CO2H
ppm
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.96
1.13
1.00
1.05
2.15
1.02
5.39


174.1
171.0
170.5
141.4
130.9
126.0
125.4
122.6
118.5
32.5
29.0
C13-1heure-D1-5s DMSO D:\\ E4 1
200
180
160
140
120
100
80
60
40
20
0


12.39
12.25
7.99
7.77
7.63
2.85
2.74
PROTON-16PPM DMSO D:\\ E4 21
O
NH
Br
N
CO2H
12
11
10
9
8
7
6
5
4
3
2
1
ppm
2.00
0.96
0.98
1.06
4.09


-1heure-D1-5s DMSO D:\\ E5 21
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161.62
158.
150.
129.56
129.50
129.38
128.69
128.37
128.33
120.45
30.15
29.57
210
200
190
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70
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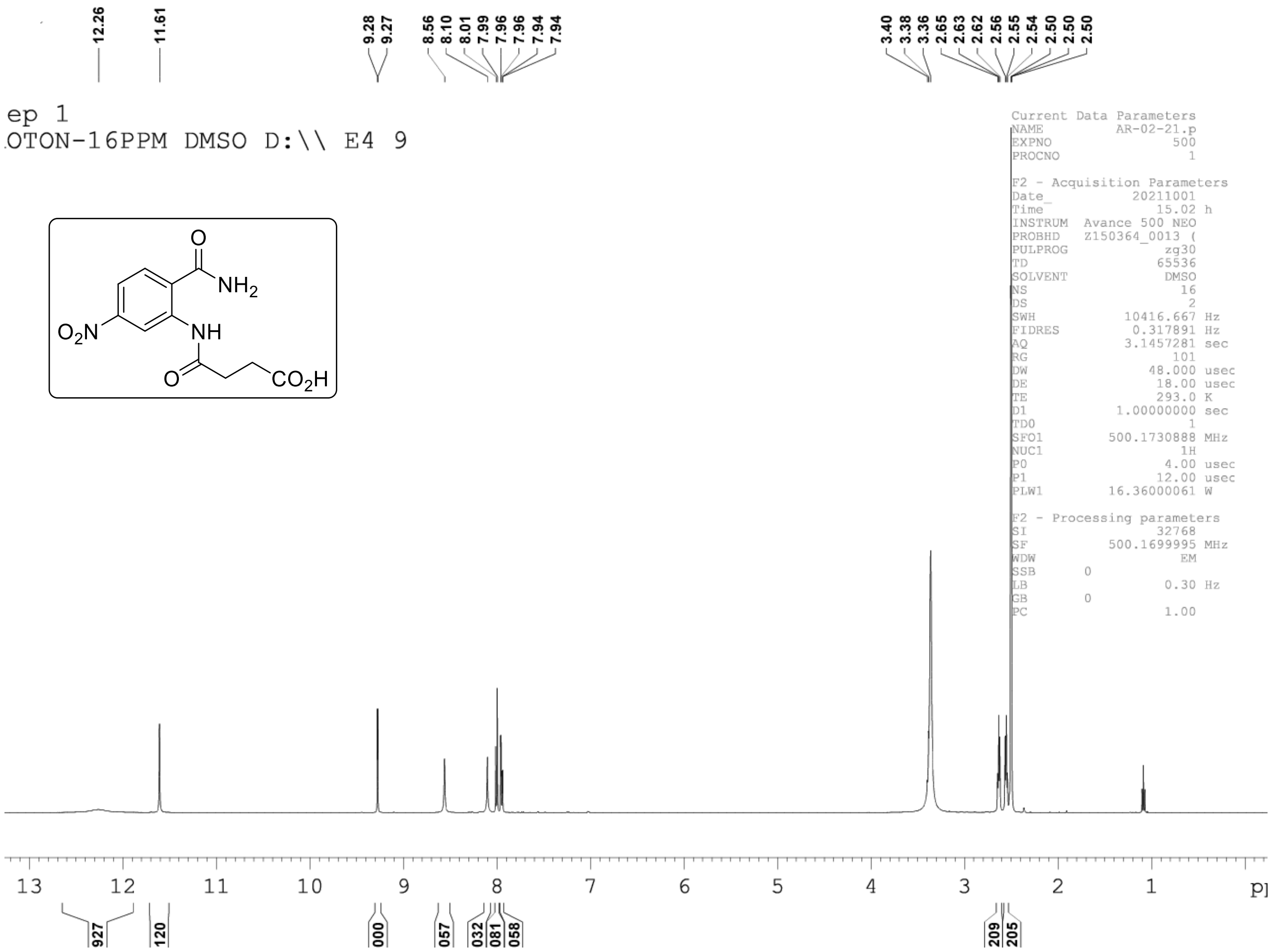
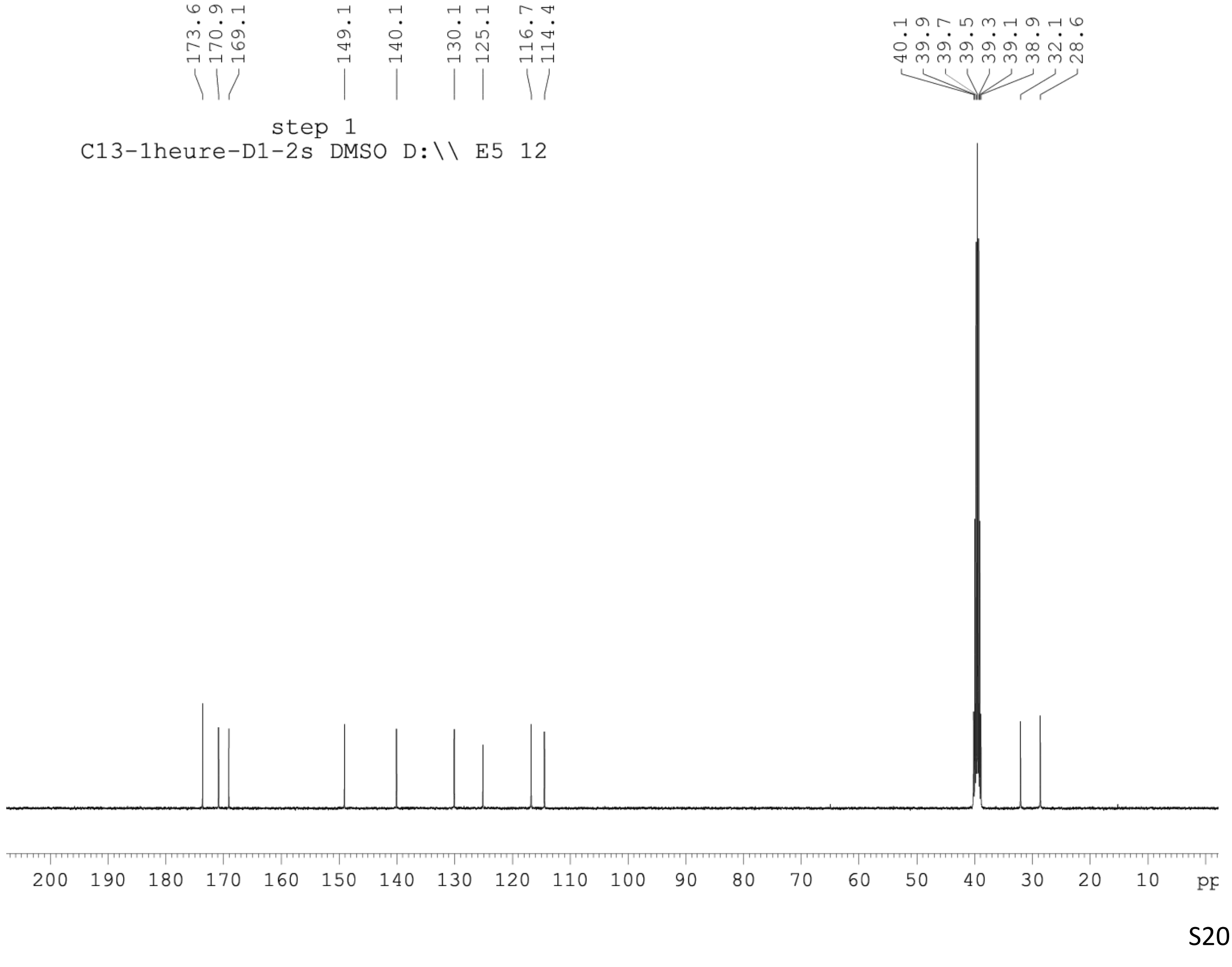
50
40
30
20
10
0

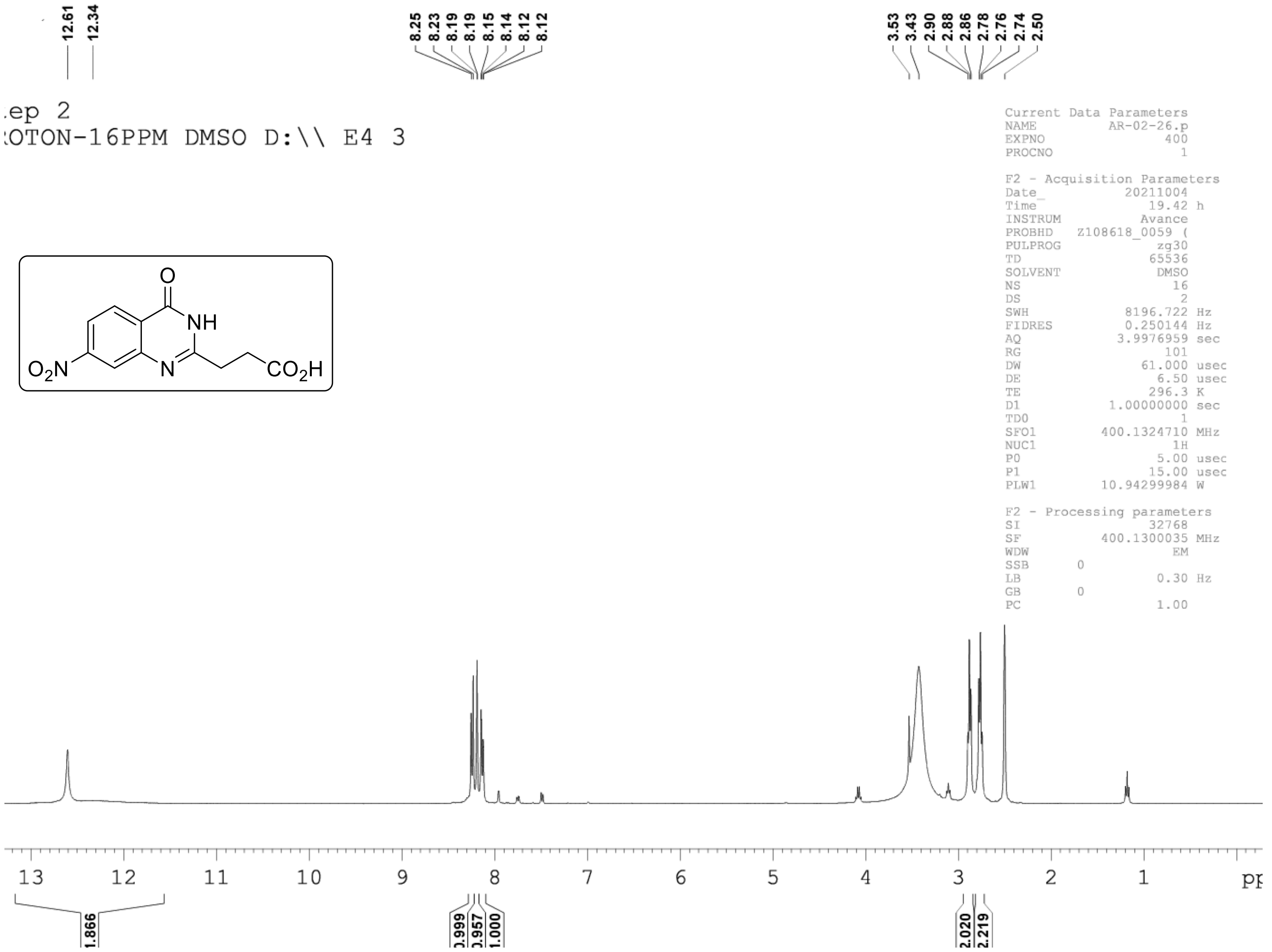


```
Current Data Parameters
NAME            AR-02-21.p
EXPNO                  500
PROCNO                   1

F2 - Acquisition Parameters
Date_             20211001
Time                 15.02 h
INSTRUM   Avance 500 NEO
PROBHD    Z150364_0013 (
PULPROG               zg30
TD                   65536
SOLVENT               DMSO
NS                      16
DS                       2
SWH              10416.667 Hz
FIDRES            0.317891 Hz
AQ               3.1457281 sec
RG                     101
DW                  48.000 usec
DE                   18.00 usec
TE                   293.0 K
D1              1.00000000 sec
TD0                      1
SFO1           500.1730888 MHz
NUC1                    1H
P0                    4.00 usec
P1                   12.00 usec
PLW1           16.36000061 W

F2 - Processing parameters
SI                   32768
SF             500.1699995 MHz
WDW                     EM
SSB      0
LB                    0.30 Hz
GB       0
PC                    1.00
```



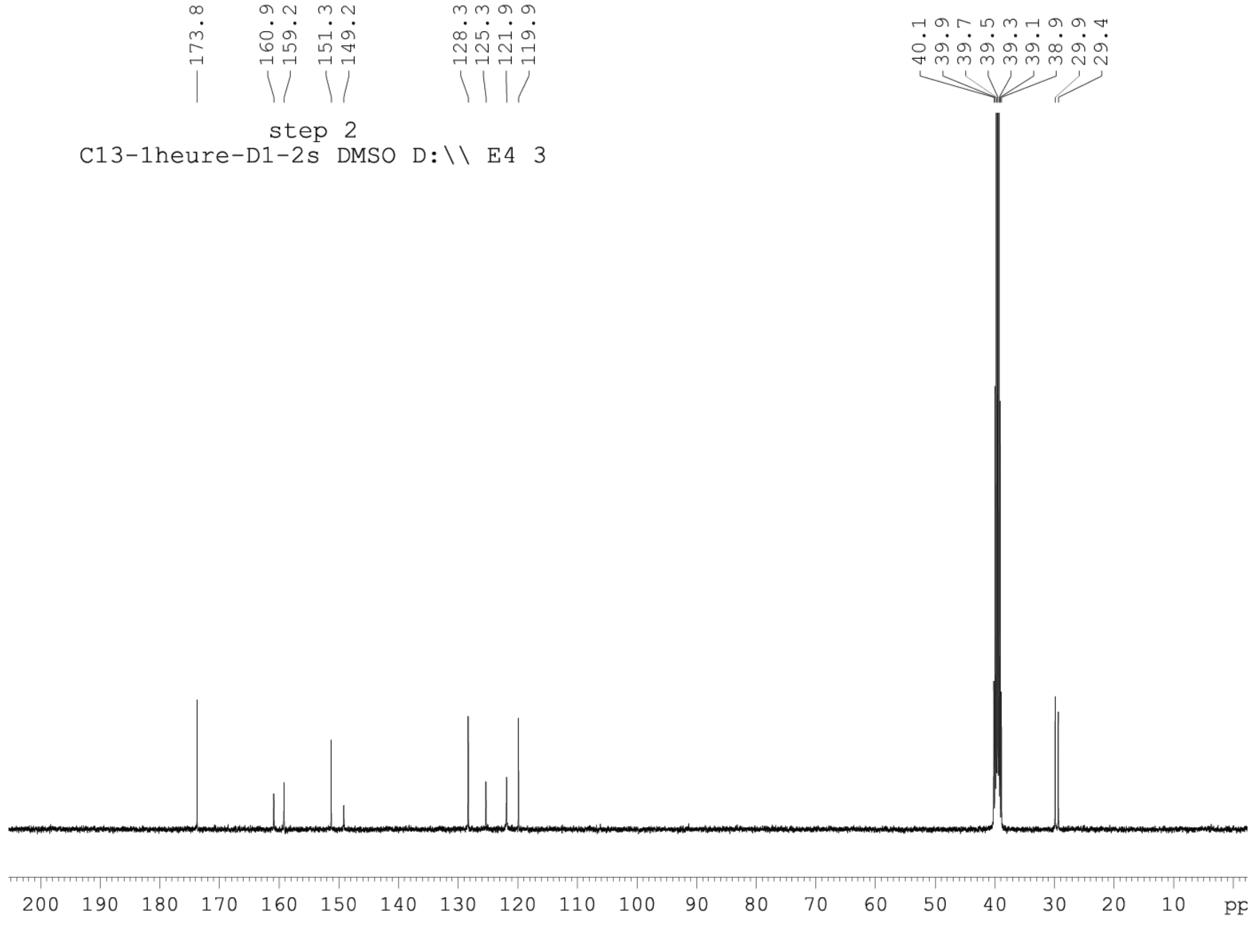


.ep 2
:OTON-16PPM DMSO D:\\ E4 3

```
Current Data Parameters
NAME             AR-02-26.p
EXPNO                   400
PROCNO                    1

F2 - Acquisition Parameters
Date_              20211004
Time                  19.42 h
INSTRUM              Avance
PROBHD   Z108618_0059 (
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8196.722 Hz
FIDRES             0.250144 Hz
AQ                3.9976959 sec
RG                      101
DW                   61.000 usec
DE                     6.50 usec
TE                    296.3 K
D1               1.00000000 sec
TD0                       1
SFO1            400.1324710 MHz
NUC1                     1H
P0                     5.00 usec
P1                    15.00 usec
PLW1            10.94299984 W

F2 - Processing parameters
SI                    32768
SF              400.1300035 MHz
WDW                      EM
SSB      0
LB                     0.30 Hz
GB       0
PC                     1.00
```



step 2
C13-1heure-D1-2s DMSO D:\\ E4 3

4. ^{1}H NMR spectra of crude reaction experiments

The figures S1 and S2 show the crude result of experiments performed at different temperatures, powers or times.

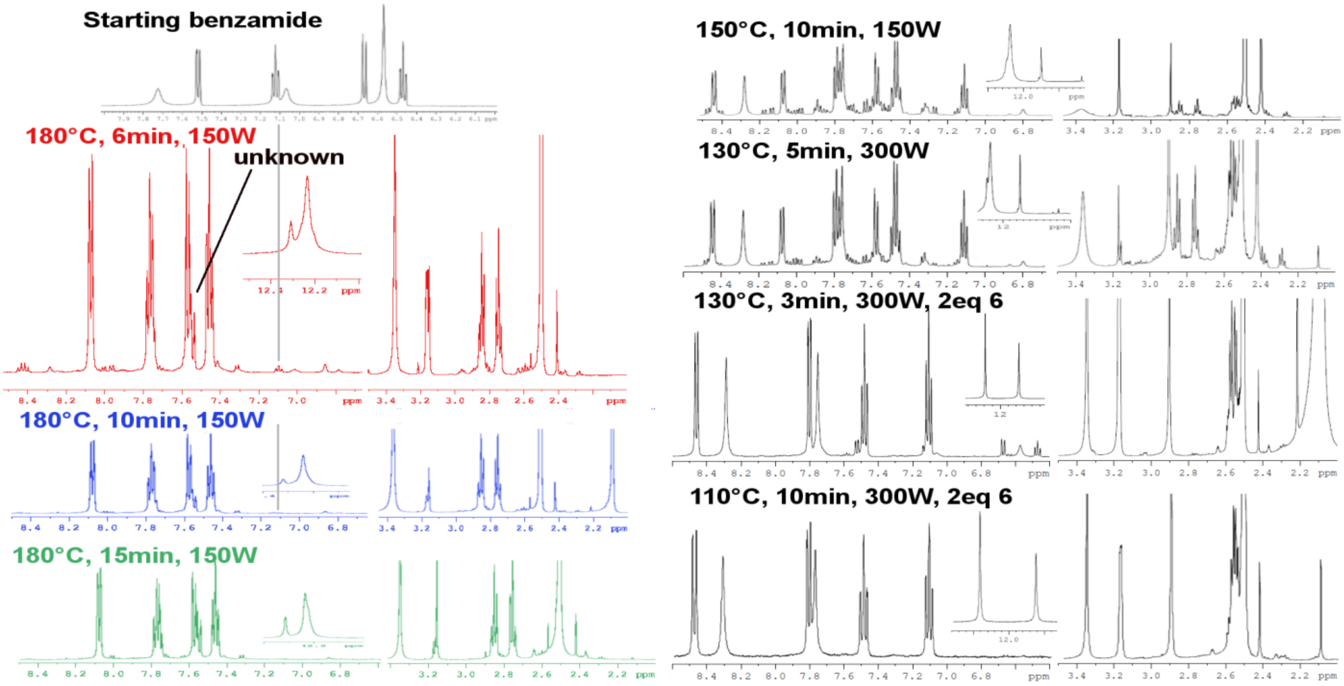


Figure S1. ^{1}H NMR spectra of the crude reactions during optimizations studies in the 2.0-3.5, 6.4-8.5 and 11.5-12.5 ppm ranges.

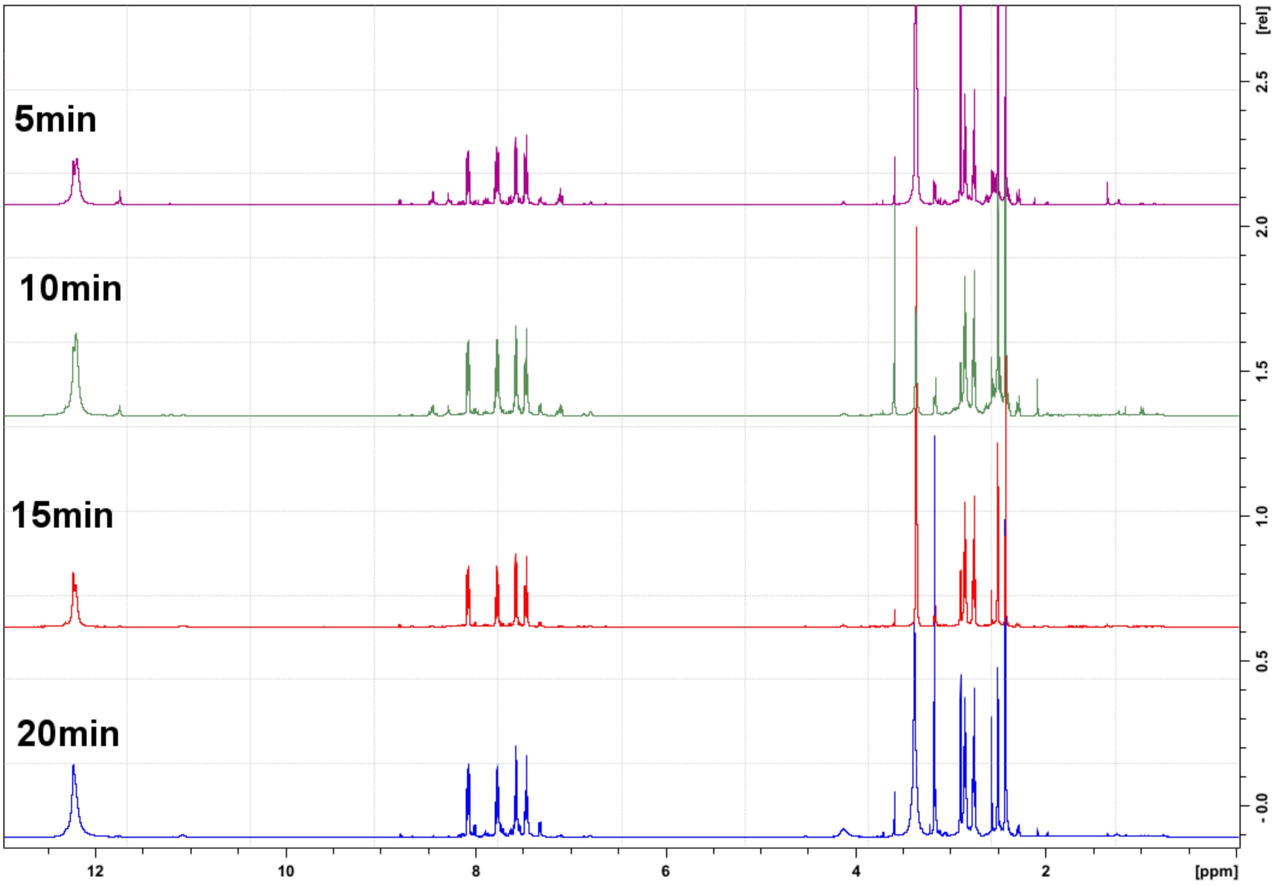


Figure S2. ^{1}H NMR spectra of the crude reactions at 180°C and 300W, leading to quinazolinone **8a**.