Supporting Information

Synthesis of disulfides tethered pyrroles from β-ketothioamides via bicyclization/ring-opening/oxidative coupling reaction

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Contents

General procedure

Synthesis of 4

The mixture of thioamides **1** (0.6 mmol), ethyl 2-cyanoacetate **2** (0.6 mmol), arylglyoxals **3** (0.6 mmol) and EtOH (2 mL) was stirred at 50 ^{o}C in a 25 mL flask for the indicated time until complete consumption of starting materials as monitored by TLC(petroleum ether/EtOAc, 1:2, v/v). After completion of the reaction, the solid product was filtered, washed with EtOH, and subsequently dried and recrystallized with EtOH to give the pure product **4**.

Synthesis of 5

Under O_2, a 20 mL of Schlenk tube equipped with a stir bar was charged with disulfides (0.2 mmol), AIBN (0.3 mmol), CuI (0.04 mmol), $KHCO_3$ (0.2 mmol) and CH_3CN (2 mL). The tube was sealed with a Teflon lined cap. The reaction mixture was stirred at 100 ℃ for 12 h. After the completion of the reaction (monitored by TLC), the solvent was concentrated under vacuum and the residue was purified by flash column chromatography on silica gel with petroleum ether-ethyl acetate as the eluent to give the desired product **5**.

Synthesis of 6

To a stirred solution of **1a** (0.6 mmol), **2a** (0.6 mmol) and **3** (0.6 mmol) in EtOH (2 mL) was added DIPEA (0.3 mmol) and then the reaction mixture was stirred at room temperature for 1.5 h. After completion of the reaction as monitored by TLC (petroleum ether/EtOAc, 4:1, v/v), amounts of solid were precipitated. The reaction mixture was filtered, washed with EtOH, and subsequently dried to give the pure product **6**.

Diethyl 2,2'-(disulfanediylbis(4-benzoyl-1,2-diphenyl-1*H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4a) (CCDC 950534)

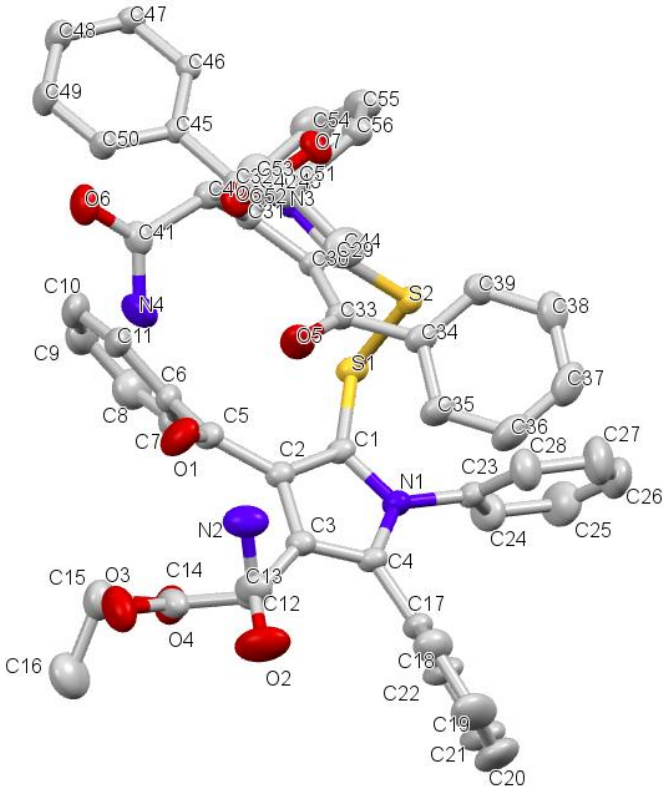


Figure S1. X-Ray crystal structure of **4a** with 25% probability displacement ellipsoids**.**

Table S1. Crystal Data and Structure Refinement for **4a**

Chemical formula	$C_{31}H_{26}ClNO_3S$
Color / shape	Yellow / Plate
Formula weight	967.09
Temperature, K	296(2)
Wavelength, Å	0.71073
Crystal system,	Triclinic,
space group	*P* 2 (1)/c
Unit cell dimensions	a = 11.660(3) Å α = 75.148(11) ° b = 12.790(2) Å β= 83.740(12) ° c = 20.164(5) Å γ = 72.575(13) °
Volume, $Å^3$	2771.6(10)
Z	2
Density (calculated), mg/m^3	1.159
Absorption coefficient, mm^{-1}	0.150
θ range for data collection, deg	1.05-25.00

Limiting indices	-13<=h<=13, -15<=k<=15, -23<=l<=23
Reflections collected / unique	29909 / 9737 [R(int) = 0.0563]
Completeness to theta = 25.00	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.000, 0.7413
Data / restraints / parameters	9737 / 126 / 674
Goodness-of-fit on F^2	1.081
Final R indices [I>2σ(I)]	R_1 = 0.0710, wR_2 = 0.1810
R indices (all data)	R_1 = 0.0873, wR_2 = 0.1936
Largest diff. peak and hole, e. Å^{-3}	0.268, -0.314
F (000)	1012.0

Ethyl 2-(4-benzoyl-2-(4-fluorophenyl)-1-phenyl-5-thiocyanato-1*H*-pyrrol-3-yl)-2-oxacetate (5) (CCDC 1430509**)**

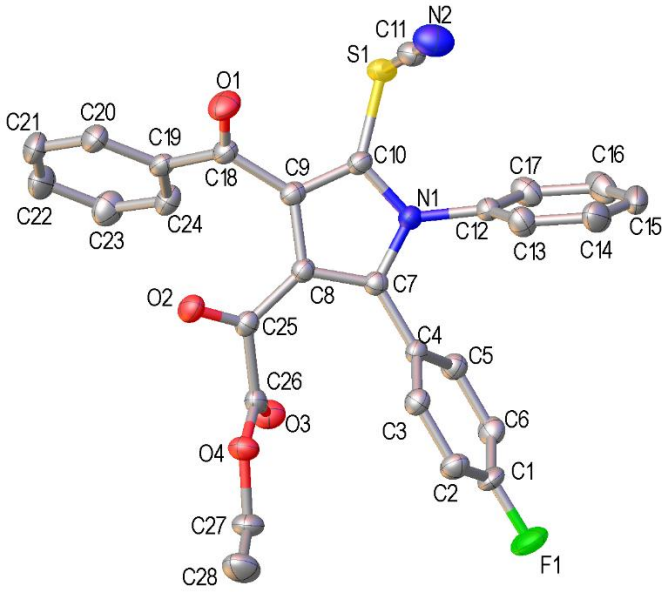


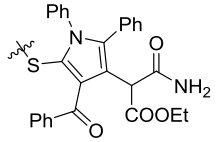
Figure S2. X-Ray crystal structure of **5** with 50% probability displacement ellipsoids.

Table S2. Crystal Data and Structure Refinement for **5**

Empirical formula	C28 H19 F N2 O4 S
Formula weight	498.51
Temperature	173.1500 K
Wavelength	0.71073 Å
Crystal system	Monoclinic

Space group	*P* 1 21/c 1
Unit cell dimensions	a = 18.382 (3) Å = 90 °. b = 12.608 (15) Å = 97.036(3) ° c = 10.333(3) Å = 90 °.
Volume	2376.8(10) $Å^3$
Z	4
Density (calculated)	1.393Mg/m^3
Absorption coefficient	0.183 mm^{-1}
F(000)	1032
Crystal size	0.52 x 0.4 x 0.11 mm^3
Theta range for data collection	2.756 to 27.492 °.
Index ranges	-22<=h<=23, -15<=k<=16, -12<=l<=13
Reflections collected	16112
Independent reflections	5404 [R(int) = 0.0306]
Completeness to theta = 26.000 °	99.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.7754
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5404 / 0 / 326
Goodness-of-fit on F^2	1.168
Final R indices [I>2sigma(I)]	R1 = 0.0485, wR2 = 0.0899
R indices (all data)	R1 = 0.0555, wR2 = 0.0939
Extinction coefficient	n/a
Largest diff. peak and hole	0.433 and -0.250 $e.Å^{-3}$

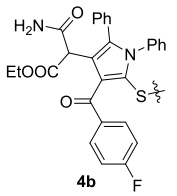
Diethyl 2,2'-(disulfanediylbis(4-benzoyl-1,2-diphenyl-*1H* -pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4a)



4a

yellow solid, mp:172–174 ℃. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.06 (t, J = 7.1 Hz, 3H, CH_3), 3.87–4.07 (m, 2H, CH_2), 4.45 (s, 1H, CH), 5.56 (d, J =7.3 Hz, 1H, ArH), 6.04 (s, 1H, NH_2), 6.76 (m, 1H, ArH), 7.11 (t, J = 7.4 Hz, 1H, ArH), 7.19–7.25 (m, 4H, ArH), 7.27–7.31 (m, 3H, ArH), 7.38 (t, J = 7.7 Hz, 2H, ArH), 7.55 (t, J = 7.40 Hz, 1H, ArH), 7.71 (d, J = 7.5 Hz, 2H, ArH), 9.06 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 194.6, 171.0, 168.7, 141.3, 140.3, 136.1, 132.4, 130.9, 130.1, 129.7, 129.3, 128.9, 128.7, 128.3, 128.2, 126.6, 117.7, 61.9, 53.6, 14.0; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{56}H_{47}N_4O_8S_2$, 967.2835; found, 967.2846.

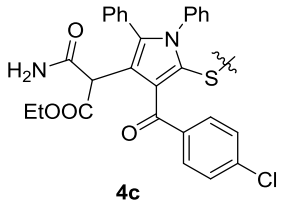
Diethyl 2,2'-(disulfanediylbis(4-(4-fluorobenzoyl)-1,2-diphenyl-*1H*-pyrrole-5,3-diyl)) bis(3-amino-3-oxopropanoate) (4b)



4b

yellow solid, mp:160–162 ℃. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.08 (t, J = 7.0 Hz, 3H, CH_3), 3.87–4.09 (m, 2H, CH_2), 4.44 (s, 1H, CH), 5.66 (s, 1H, ArH), 6.00 (s, 1H, NH_2), 6.86 (s, 1H, ArH), 7.06 (t, J = 7.9 Hz, 2H, ArH), 7.10–7.22 (m, 5H, ArH), 7.26–7.30 (m, 3H, ArH), 7.72-7.75 (m, 2H, ArH), 9.00 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.9, 53.3, 61.9, 115.3 (d, $^2J_{C\text{-}F}$ = 21.4 Hz) 117.8, 126.3, 128.3, 1287 (d, $^3J_{C\text{-}F}$ = 54.8 Hz), 129.6, 130.8, 132.6, 136.3 (d, $^3J_{C\text{-}F}$ = 63.7 Hz), 141.4, 165.6 (d, $^1J_{C\text{-}F}$ = 255.0 Hz), 169.8 (d, $^1J_{C\text{-}F}$ = 262.3 Hz), 193.1; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{56}H_{45}F_2N_4O_8S_2$, 1003.2647; found, 1003.2661.

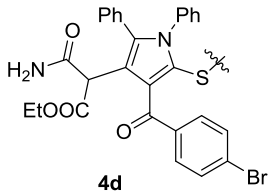
Diethyl 2,2'-(disulfanediylbis(4-(4-chlorobenzoyl)-1,2-diphenyl-*1H*-pyrrole-5,3-diyl)) bis(3-amino-3-oxopropanoate) (4c)



4c

yellow solid, mp: 195–198 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.09 (t, J = 6.9 Hz, 3H, CH_3), 3.88–4.13 (m, 2H, CH_2), 4.45 (s, 1H, CH), 5.65 (d, J = 8.1Hz, 1H, ArH), 6.00 (s, 1H, NH_2), 6.92 (s, 1H, ArH), 7.11-7.18 (m, 4H, ArH), 7.27-7.33 (m, 4H, ArH), 7.34–7.36 (m, 2H, ArH), 7.64–7.66 (m, 2H, ArH), 8.98 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.0, 53.4, 62.0, 117.8, 126.5, 128.3, 128.5, 128.8, 129.0, 129.1, 129.6, 130.8, 131.4, 136.0, 138.6, 139.2, 141.5, 168.7, 170.8, 193.4; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{56}H_{45}Cl_2N_4O_8S_2$, 1035.2056; found, 1035.2062.

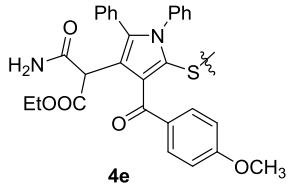
Diethyl 2,2'-(disulfanediylbis(4-(4-bromobenzoyl)-1,2-diphenyl-*1H*-pyrrole-5,3-diyl)) bis(3-amino-3-oxopropanoate) (4d)



4d

yellow solid, mp: 197–199 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.09 (t, J = 6.9 Hz, 3H, CH_3), 3.88–4.09 (m, 2H, CH_2), 4.44 (s, 1H, CH), 5.68 (d, J = 5.5 Hz, 1H, ArH), 5.98 (s, 1H, NH_2), 6.96 (s, 1H, ArH), 7.15-7.18 (m, 4H, ArH), 7.30–7.31 (m, 4H, ArH), 7.51–7.58 (m, 4H, ArH), 8.94 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.0, 53.3, 61.9, 115.2, 117.9, 126.5, 127.7, 128.2, 128.6, 128.8, 128.9, 129.1, 129.5, 130.8, 131.5, 136.1, 139.1, 141.5, 168.4, 170.7, 193.6; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{56}H_{45}Br_2N_4O_8S_2$, 1123.1046; found, 1123.1072.

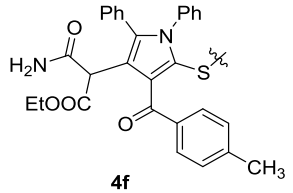
Diethyl 2,2'-(disulfanediylbis(4-(4-methoxybenzoyl)-1,2-diphenyl-*1H*-pyrrole-5,3-diyl)) bis(3-amino-3-oxopropanoate) (4e)



4e

yellow solid, mp: 213–215 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.06 (t, J = 6.9 Hz, 3H, CH_3), 3.84–4.14 (m, 2H, CH_2), 4.41 (s, 1H, CH), 5.59 (d, J = 7.2 Hz, 1H, ArH), 6.04 (s, 1H, NH_2), 6.75-6.78 (m, 1H, ArH), 6.86-6.88 (m, 2H, ArH), 6.98–7.02 (m, 1H, ArH), 7.11–7.18 (m, 3H, ArH), 7.21-7.24 (m, 2H, ArH), 7.28-7.31 (m, 2H, ArH), 7.69-7.71 (m, 2H, ArH), 9.06 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.0, 21.0, 53.6, 55.4, 59.2, 60.4, 61.4, 61.8, 73.5, 113.4, 117.1, 126.0, 128.0, 128.1, 128.3, 128.7, 129.1, 129.7, 130.9, 131.7, 132.5, 132.8, 136.3, 138.8, 141.1, 163.5, 168.8, 171.2, 192.8; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{58}H_{51}N_4O_{10}S_2$, 1027.3047; found, 1027.3052.

Diethyl 2,2'-(disulfanediylbis(4-(4-methylbenzoyl)-1,2-diphenyl-1*H*-pyrrole-5,3-diyl)) bis(3-amino-3-oxopropanoate) (4f)

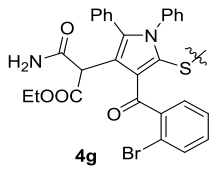


4f

yellow solid, mp: 164–166 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.05 (t, J = 7.1 Hz, 3H, CH_3), 2.40 (s, 3H, CH_3), 3.81–4.09 (m, 2H, CH_2), 4.41 (s, 1H, CH), 5.58(d, J = 6.3 Hz, 1H, ArH), 6.02 (s, 1H, NH_2), 6.73 (m, 1H, ArH), 7.10-7.13 (m, 1H, ArH), 7.16–7.19 (m, 6H, ArH), 7.26–7.30 (m, 3H, ArH), 7.60 (d, J = 7.6 Hz, 2H, ArH), 9.05 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.0, 14.0, 21.7, 53.6, 61.8, 117.7, 126.3, 128.1, 128.3, 128.7, 128.9, 129.1, 129.5, 129.8, 130.0, 130.3, 130.6, 130.9, 136.3, 137.7, 141.1, 143.4, 168.8, 171.1, 194.1;

HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{58}H_{51}N_4O_8S_2$, 995.3148; found, 995.3165.

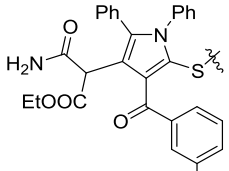
Diethyl 2,2'-(disulfanediylbis(4-(2-bromobenzoyl)-1,2-diphenyl-1*H*-pyrrole-5,3-diyl)) bis(3-amino-3-oxopropanoate) (4g)



4g

yellow solid, mp: 155–157 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.20 (s, 3H, CH_3), 4.15 (s, 2H, CH_2), 4.58 (s, 1H, CH), 5.60 (s, 1H, NH_2), 5.60- 6.96 (m, 3H, ArH), 7.17-7.26 (m, 8H, ArH), 7.26–7.56 (m, 3H, ArH, NH_2), 8.57 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.4, 62.0，127.5, 128.1, 128.2, 129.1, 130.2, 131.2, 133.3, 136.5, 141.1, 142.4, 169.2, 170.3, 193.6,; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{56}H_{45}Br_2N_4O_8S_2$, 1123.10401; found, 1123.10388.

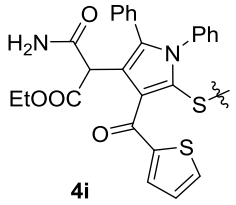
Diethyl 2,2'-(disulfanediylbis(4-(3-chlorobenzoyl)-1,2-diphenyl-1*H*-pyrrole-5,3-diyl)) bis(3-amino-3-oxopropanoate) (4h)



4h

yellow solid, mp: 161–162 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.09 (t, J = 7.0 Hz, 1H, CH_3), 3.86–4.08 (m, 2H, CH_2), 4.45 (s, 1H, CH), 5.68 (s, 1H, ArH), 6.01 (s, 1H, NH_2), 6.84(s, 1H, ArH), 7.14-7.26 (m, 5H, ArH), 7.26–7.33 (m, 4H, ArH), 7.51–7.55 (m, 1H, ArH), 7.59-7.60 (m, 1H, ArH), 7.66 (s, 1H, ArH), 8.80 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.0, 14.0, 53.3, 62.0, 117.8, 126.4, 127.7, 128.2, 128.3, 128.5, 128.7, 128.7, 128.9, 129.0, 129.7, 130.2, 131.1, 132.0, 132.4, 134.6, 136.0, 136.2, 141.6, 141.8, 141.9, 168.7, 170.7, 193.4; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{56}H_{45}Cl_2N_4O_8S_2$, 1035.2056; found, 1035.2075.

Diethyl 2,2'-(disulfanediylbis(1,2-diphenyl-4-(thiophene-2-carbonyl)-1*H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4i)

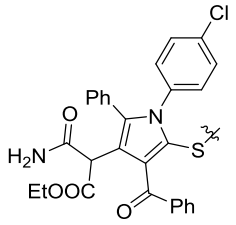


4i

yellow solid, mp: 167–169 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.06 (t, J = 7.1 Hz, 3H, CH_3), 3.83–4.11 (m, 2H, CH_2), 4.39 (s, 1H, CH), 5.79 (s, 1H, ArH), 5.95 (s, 1H, NH_2), 6.88 (s, 1H, ArH), 7.09-7.19 (m, 5H, ArH, CH), 7.19-7.26 (m, 4H, ArH), 7.44 (d, J = 3.05 Hz,1H, ArH), 7.66 (d, J = 4.96 Hz, 1H, CH), 8.68 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ : 13.9, 14.0, 53.3, 61.8, 117.5, 125.7, 127.5, 127.9, 128.1, 128.3, 128.7, 129.1, 129.2, 129.6, 130.9, 133.8, 135.5, 135.7, 136.4, 141.2, 145.5, 168.7, 170.7, 185.5; HRMS (ESI–TOF, $[M + H]^+$): calcd

for $C_{52}H_{43}N_4O_8S_4$, 979.1964; found, 979.1982.

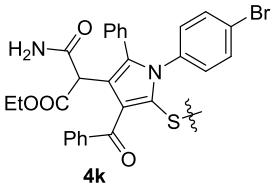
Diethyl 2,2'-(disulfanediylbis(4-benzoyl-1-(4-chlorophenyl)-2-phenyl-*1H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4j)



4j

yellow solid, mp: 175–178 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.07 (t, J = 7.1 Hz, 3H, CH_3), 3.84–4.10 (m, 2H, CH_2), 4.44 (s, 1H, CH), 5.46 (d, J = 2.93 Hz, 1H, ArH), 6.09 (s, 1H, NH_2), 6.74-6.76 (m, 1H, ArH), 7.16-7.26 (m, 4H, ArH), 7.28–7.35 (m, 3H, ArH), 7.40 (t, J = 7.7 Hz, 2H, ArH), 7.57 (t, J = 7.3 Hz, 1H, ArH), 7.71 (d, J = 7.3 Hz, 2H, ArH), 9.03 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.0, 46.8, 53.4, 61.9, 118.0, 126.3, 128.4, 128.5, 129.0, 129.2, 130.1, 130.5, 130.8, 132.5, 134.4, 134.6, 140.1, 141.3, 168.6, 170.8, 194.4; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{56}H_{45}Cl_2N_4O_8S_2$, 1035.2056; found, 1035.2052.

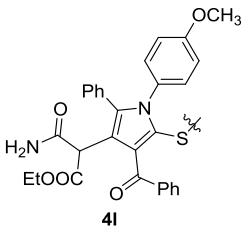
Diethyl 2,2'-(disulfanediylbis(4-benzoyl-1-(4-bromophenyl)-2-phenyl-*1H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4k)



4k

yellow solid, mp: 170–172 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.05 (t, J = 6.9 Hz, 3H, CH_3), 3.84–4.07 (m, 2H, CH_2), 4.43 (s, 1H, CH), 5.38(d, J = 6.9 Hz, 1H, ArH), 6.06 (s, 1H, NH_2), 6.89(d, J = 7.30 Hz, 1H, ArH), 7.09 (d, J = 7.00 Hz , 1H, ArH), 7.20 (s, 2H, ArH), 7.28–7.36 (m, 3H, ArH), 7.36-7.44 (m, 3H, ArH), 7.55 (t, J = 7.18 Hz, 1H, ArH), 7.69 (d, J = 6.95 Hz , 2H, ArH), 9.02 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.0, 53.4, 61.9, 118.1, 122.6, 126.2, 128.3, 128.7, 129.0, 129.3, 130.1, 130.9, 131.2, 131.5, 132.5, 135.2, 140.2, 141.3, 168.6, 170.7, 194.3; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{56}H_{45}Br_2N_4O_8S_2$, 1123.10401; found, 1123.10425.

Diethyl 2,2'-(disulfanediylbis(4-benzoyl-1-(4-methoxyphenyl)-2-phenyl-*1H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4l)

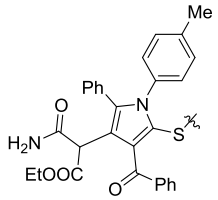


4l

yellow solid, mp: 168–170 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.07 (t, J = 7.1 Hz, 3H, CH_3),

3.70 (s, 3H, OCH_3), 3.85–4.09 (m, 2H, CH_2), 4.45 (s, 1H, CH), 5.46 (d, *J* = 7.65 Hz, 1H, ArH), 6.10 (s, 1H, NH_2), 6.26 (t, *J* = 4.24 Hz, 1H, ArH), 6.75 (q, *J* = 3.78 Hz, 1H, ArH), 7.11 (d, *J* = 7.15 Hz, 1H, ArH), 7.21 (d, *J* = 7.35 Hz, 2H, ArH), 7.29-7.34 (m, 3H, ArH), 7.39 (t, *J* = 7.70 Hz, 2H, ArH), 7.55 (t, *J* = 7.4 Hz, 1H, ArH), 7.71 (d, *J* = 7.4 Hz, 2H, ArH), 9.08 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) *δ*: 14.0, 53.6, 55.2, 61.8, 113.1, 113.3, 117.5, 127.0, 128.2, 128.2, 128.7, 128.8, 129.1, 130.0, 130.3, 130.6, 130.9, 132.3, 140.3, 141.4, 159.0, 168.8, 171.1, 194.7; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{58}H_{51}N_4O_{10}S_2$, 1027.3047; found, 1027.3030.

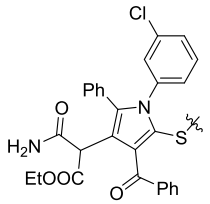
Diethyl 2,2'-(disulfanediylbis(4-benzoyl-2-phenyl-1-(p-tolyl)-*1H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4m)



4m

yellow solid, mp: 161–163 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) *δ*: 1.06 (t, *J* = 7.0 Hz, 3H, CH_3), 2.19 (s, 3H, CH_3), 3.84–4.08 (m, 2H, CH_2), 4.45 (s, 1H, CH), 5.44 (d, *J* = 6.7 Hz, 1H, ArH), 6.04 (s, 1H, NH_2), 6.56 (d, *J* = 8.5 Hz, 1H, ArH), 7.02-7.04 (m, 2H, ArH), 7.20–7.21 (m, 2H, ArH), 7.29–7.30 (m, 3H, ArH), 7.38 (t, *J* = 7.5 Hz, 2H, ArH), 7.54 (d, *J* = 7.2 Hz, 1H, ArH), 7.70 (d, *J* = 7.3 Hz, 2H, ArH), 9.05 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) *δ*: 13.9, 13.9, 21.0, 53.5, 61.7, 117.6, 126.7, 128.1, 128.2, 128.6, 128.8, 129.0, 129.1, 129.3, 130.0, 130.9, 132.3, 133.6, 133.8, 138.1, 138.2, 140.4, 141.3, 168.7, 170.9, 194.6; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{58}H_{51}Br_2N_4O_8S_2$, 995.3148; found, 995.3172.

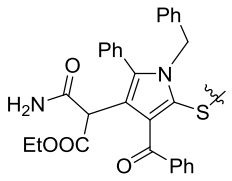
Diethyl 2,2'-(disulfanediylbis(4-benzoyl-1-(3-chlorophenyl)-2-phenyl-1*H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4n)



4n

yellow solid, mp: 165–167 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) *δ*: 1.06 (m, 3H, CH_3), 3.86-4.06 (m, 2H, CH_2), 4.44 (s, 1H, CH), 6.06 (s, 1H, NH_2), 6.70 (m, 1H, ArH), 7.12-7.13 (m, 2H, ArH), 7.20 (s, 2H, ArH), 7.33–7.41 (m, 6H, ArH), 7.54-7.61 (m, 1H, ArH), 7.69-7.70 (m, 2H, ArH), 9.00-9.06 (m, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.9, 53.5, 61.9, 117.9, 126.3, 127.6, 129.1, 129.9, 130.9, 132.5, 133.8, 134.0, 137.2, 140.1, 141.3, 168.6, 170.7, 194.4, 194.6; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{56}H_{45}Cl_2N_4O_8S_2$, 1035.2056; found, 1035.2083.

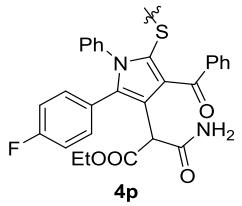
Diethyl 2,2'-(disulfanediylbis(4-benzoyl-1-benzyl-2-phenyl-1*H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4o)



4o

yellow solid, mp: 168–170 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.11 (s, 3H, CH_3), 4.00–4.10 (m, 2H, CH_2), 4.41 (s, 1H, CH), 4.75-4.89 (m, 2H, CH_2), 5.24 (s, 1H, NH_2), 6.60 (s, 2H, ArH), 7.04-7.10 (m, 4H, ArH), 7.26–7.40 (m, 5H, ArH), 7.50 (m, 4H, ArH), 8.47 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.9, 48.5, 50.6, 52.3, 61.7, 125.5, 127.1, 128.2, 128.5, 129.4, 129.8, 132.3, 137.5, 140.0, 140.6, 169.9, 195.4; HRMS (ESI–TOF, $[M+H]^+$): calcd for $C_{58}H_{51}N_4O_8S_2$, 995.3148; found, 995.3175.

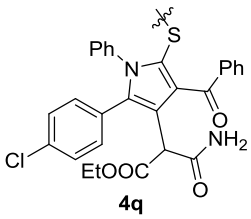
Diethyl 2,2'-(disulfanediylbis(4-benzoyl-2-(4-fluorophenyl)-1-phenyl-1*H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4p)



4p

yellow solid, mp: 173–175 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.07 (t, J = 7.1 Hz, 3H, CH_3), 3.84–4.10 (m, 2H, CH_2), 4.41 (s, 1H, CH), 5.52 (d, J = 6.8 Hz, 1H, ArH), 6.06 (s, 1H, NH_2), 6.77-6.80 (m, 1H, ArH), 7.00 (t, J = 8.3 Hz, 2H, ArH), 7.12–7.18 (m, 4H, ArH), 7.23–7.24 (m, 1H, ArH), 7.38 (t, J = 7.6 Hz, 2H, ArH), 7.57 (t, J = 7.4 Hz, 1H, ArH), 7.70 (d, J = 7.5 Hz, 2H, ArH), 9.07 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ : 14.0, 53.5, 61.9, 115.4 (d, $^{2}J_{C\text{-}F}$ = 21.6 Hz), 117.9, 125.0, 126.7, 128.3, 128.5, 128.8, 129.3, 129.7, 130.1, 132.5, 132.8, 132.9, 136.0, 141.2, 162.8 (d, $^{1}J_{C\text{-}F}$ = 249.8 Hz), 169.8 (d, $^{1}J_{C\text{-}F}$ = 290.5 Hz), 194.5; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{56}H_{45}F_2N_4O_8S_2$, 1003.2647; found, 1003.2657.

Diethyl 2,2'-(disulfanediylbis(4-benzoyl-2-(4-chlorophenyl)-1-phenyl-1*H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4q)

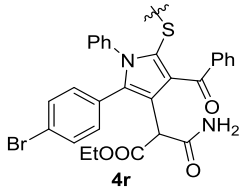


4q

yellow solid, mp: 198–200 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.06 (t, J = 7.0 Hz, 3H, CH_3), 3.85–4.10 (m, 2H, CH_2), 4.40 (s, 1H, CH), 5.51 (d, J = 6.9 Hz, 1H, ArH), 6.04 (s, 1H, NH_2), 6.78-6.81 (m, 1H, ArH), 7.13-7.17 (m, 4H, ArH), 7.24–7.25 (m, 2H, ArH), 7.26–7.28 (m, 1H, ArH), 7.38 (t, J = 7.6 Hz, 2H, ArH), 7.68-7.69 (m, 3H, ArH), 9.08 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.9, 14.0, 14.1, 14.1,14.2, 21.0, 53.5, 61.8, 61.9, 118.1, 127.0, 127.4,

128.3, 128.4, 128.5, 128.9, 129.3, 129.6, 129.9, 130.0, 132.2, 132.3, 132.5, 135.1, 135.9, 139.9, 140.2, 168.5, 170.8, 171.1, 194.4; HRMS (ESI–TOF, $[M+H]^+$): calcd for $C_{56}H_{45}Cl_2N_4O_8S_2$, 1035.20504; found, 1035.20508.

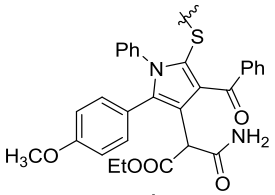
Diethyl 2,2'-(disulfanediylbis(4-benzoyl-2-(4-bromophenyl)-1-phenyl-1*H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4r)



4r

yellow solid, mp: 195–197 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.06 (t, J = 7.1 Hz, 3H, CH_3), 3.84–4.09 (m, 2H, CH_2), 4.39 (s, 1H, CH), 5.51 (d, J = 7.1 Hz, 1H, ArH), 6.04 (s, 1H, NH_2), 6.78-6.81 (m, 1H, ArH), 7.07 (d, J = 7.6 Hz, 2H, ArH), 7.14–7.16 (m, 2H, ArH), 7.24–7.25 (m, 1H, ArH), 7.36-7.44 (m, 4H, ArH), 7.57 (t, J = 7.4 Hz, 1H, ArH), 7.68 (d, J = 7.5 Hz, 2H, ArH), 9.08 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.0, 53.5, 58.4，61.9，62.0, 118.0, 115.8, 123.4, 127.1, 127.9，128.3, 128.5, 128.6, 128.9, 129.3, 129.6, 129.9, 130.0, 131.5, 132.4, 132.6, 135.9, 140.0, 140.2, 168.5, 170.8, 194.4; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{56}H_{45}Br_2N_4O_8S_2$, 1123.10401; found, 1123.10400.

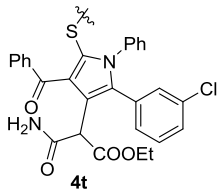
Diethyl 2,2'-(disulfanediylbis(4-benzoyl-2-(4-methoxyphenyl)-1-phenyl-1*H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4s)



4s

yellow solid, mp: 163–165 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.06 (t, J = 7.1 Hz, 3H, CH_3), 3.77 (s, 1H, OCH_3), 3.83–4.09 (m, 2H, CH_2), 4.44 (s, 1H, CH), 5.55 (d, J = 7.0 Hz, 1H, ArH), 6.04 (s, 1H, NH_2), 6.80-6.85 (m, 3H, ArH), 7.11-7.24 (m, 5H, ArH), 7.37 (t, J = 7.5 Hz, 2H, ArH), 7.54 (t, J = 7.3 Hz, 1H, ArH), 7.69 (d, J = 7.5 Hz, 2H, ArH), 9.09 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.9, 53.7, 55.1, 61.8, 113.7, 117.6, 121.2, 126.4, 128.2, 128.9, 129.4, 129.7, 130.1, 132.3, 136.3, 140.4, 141.3, 159.8, 168.8, 171.1, 194.7; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{58}H_{51}O_{10}N_4S_2$, 1027.30411; found, 1027.30408.

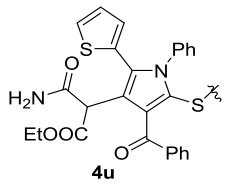
Diethyl 2,2'-(disulfanediylbis(4-benzoyl-2-(3-chlorophenyl)-1-phenyl-1*H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4t)



4t

yellow solid, mp: 154–156 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.07 (t, J = 6.7 Hz, 3H, CH_3), 3.86–4.09 (m, 2H, CH_2), 4.43 (s, 1H, CH), 5.53 (d, J = 7.0 Hz, 1H, ArH), 6.05 (s, 1H, NH_2), 6.79-6.82 (m, 1H, ArH), 7.14-7.17 (m, 5H, ArH), 7.25–7.26 (m, 2H, ArH), 7.39–7.42 (m, 2H, ArH), 7.57-7.60 (m, 1H, ArH), 7.70-7.71 (m, 2H, ArH), 9.01 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.9, 14.0, 53.4, 62.0, 118.1, 118.2, 127.0, 128.4, 128.4, 128.5, 128.7, 128.8, 128.9, 129.0, 129.0, 129.2, 129.6, 130.0, 130.1, 130.7, 130.8, 130.9, 132.6, 134.0, 135.8, 139.6, 140.1, 168.6, 170.7, 194.4;HRMS (ESI–TOF, $[M+H]^+$): calcd for $C_{56}H_{45}Cl_2N_4O_8S_2$, 1035.20504; found, 1035.20508.

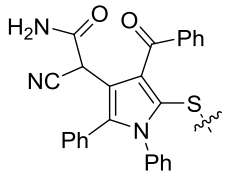
Diethyl 2,2'-(disulfanediylbis(4-benzoyl-1-phenyl-2-(thiophen-2-yl)-1*H*-pyrrole-5,3-diyl))bis(3-amino-3-oxopropanoate) (4u)



4u

yellow solid, mp: 164-166 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.08 (t, J = 7.1 Hz, 3H, CH_3), 3.85–4.12 (m, 2H, CH_2), 4.48 (s, 1H, CH), 5.65 (d, J = 7.1 Hz, 1H, ArH), 6.02 (s, 1H, NH_2), 6.86-6.87 (m, 1H, CH), 7.02-7.04 (m, 1H, ArH), 7.19–7.22 (m, 2H, ArH), 7.26–7.30 (m, 3H, ArH), 7.38 (t, J = 7.6 Hz, 2H, ArH), 7.56 (t, J = 7.4 Hz, 1H, ArH), 7.65 (d, J = 7.5 Hz, 2H, CH), 9.02 (s, 1H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.9, 53.4, 61.9, 119.0, 127.0, 127.4, 128.0, 128.2, 128.4, 128.9, 129.3, 129.4, 129.9, 131.2, 132.4, 134.6, 135.9, 140.2, 168.5, 170.7, 194.5; HRMS (ESI–TOF, $[M+H]^+$): calcd for $C_{52}H_{43}N_4O_8S_2$, 979.1964; found, 979.1985.

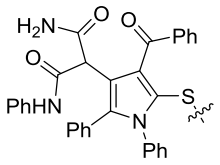
2,2'-(disulfanediylbis(4-benzoyl-1,2-diphenyl-1*H*-pyrrole-5,3-diyl))bis(2-cyanoacetamide) (4v)



4v

yellow solid, mp: 272-274 ℃. ^{1}H NMR (DMSO, 500 MHz) δ: 4.75 (br s, 1H, NH_2), 5.09 (br s, 1H, NH_2), 5.36 (br s, 1H, CH), 6.10-8.11 (m, 15H, ArH); ^{13}C NMR (DMSO, 125 MHz) δ: 192.2, 165.9, 140.2, 140.0, 136.3, 132.7, 130.9, 130.0, 129.4, 129.3, 128.6, 128.5, 126.1, 117.5, 114.2, 36.3; HRMS (ESI–TOF): calcd for $C_{52}H_{36}N_6O_4S_2Na$ $[M+Na]^+$ 895.2132, found 895.2132; calcd for $C_{52}H_{40}N_7O_4S_2$ $[M+NH_4]^+$ 890.2578, found 890.2593.

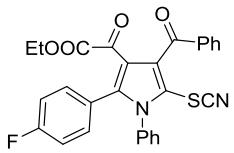
2,2'-(disulfanediylbis(4-benzoyl-1,2-diphenyl-1*H*-pyrrole-5,3-diyl))bis(*N*-1-phenylmalon amide) (4w)



4w

yellow solid, mp: 260-262 ℃. ^{1}H NMR (DMSO, 500 MHz) δ: 4.36 (br s, 1H, CH), 5.46-8.00 (m, 22H, ArH, NH_2), 9.35-11.41 (m, 1H, NH); ^{13}C NMR (DMSO, 125 MHz) δ: 40.8, 120.1, 123.7, 128.4, 128.9, 130.2, 131.2, 132.6, 136.8, 139.2, 140.3, 140.7, 167.0, 171.3, 193.5; HRMS (ESI–TOF, $[M+H]^+$): calcd for $C_{64}H_{49}N_6O_6S_2$, 1061.31495; found 1061.31506.

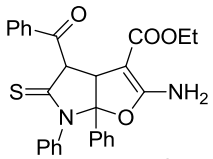
Ethyl 2-(4-benzoyl-2-(4-fluorophenyl)-1-phenyl-5-thiocyanato-1*H*-pyrrol-3-yl)-2-oxacetate (5)



5

white solid; m.p.: 121-123 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.08 (t, J = 7.2 Hz, 3H, CH_3), 3.80-3.85 (m, 2H, CH_2), 6.96 (t, J = 8.5 Hz, 2H, NH_2), 7.23-7.26 (m, 4H, ArH), 7.44-7.45 (m, 3H, ArH), 7.54 (t, J = 7.6 Hz, 2H, ArH), 7.63-7.66 (m, 1H, ArH), 7.99 (d, J = 7.5 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.5, 29.7, 62.5, 108.4, 112.4, 115.3 (d, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 120.8, 124.3, 128.9 (d, $^{1}J_{C\text{-}F}$ = 14.3 Hz), 129.6, 130.1, 133.0, 133.9, 134.3, 134.9, 137.5, 144.4, 162.3, 164.4, 180.4, 190.9; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{28}H_{20}FN_2O_4S$, 499.1122; found, 499.1119.

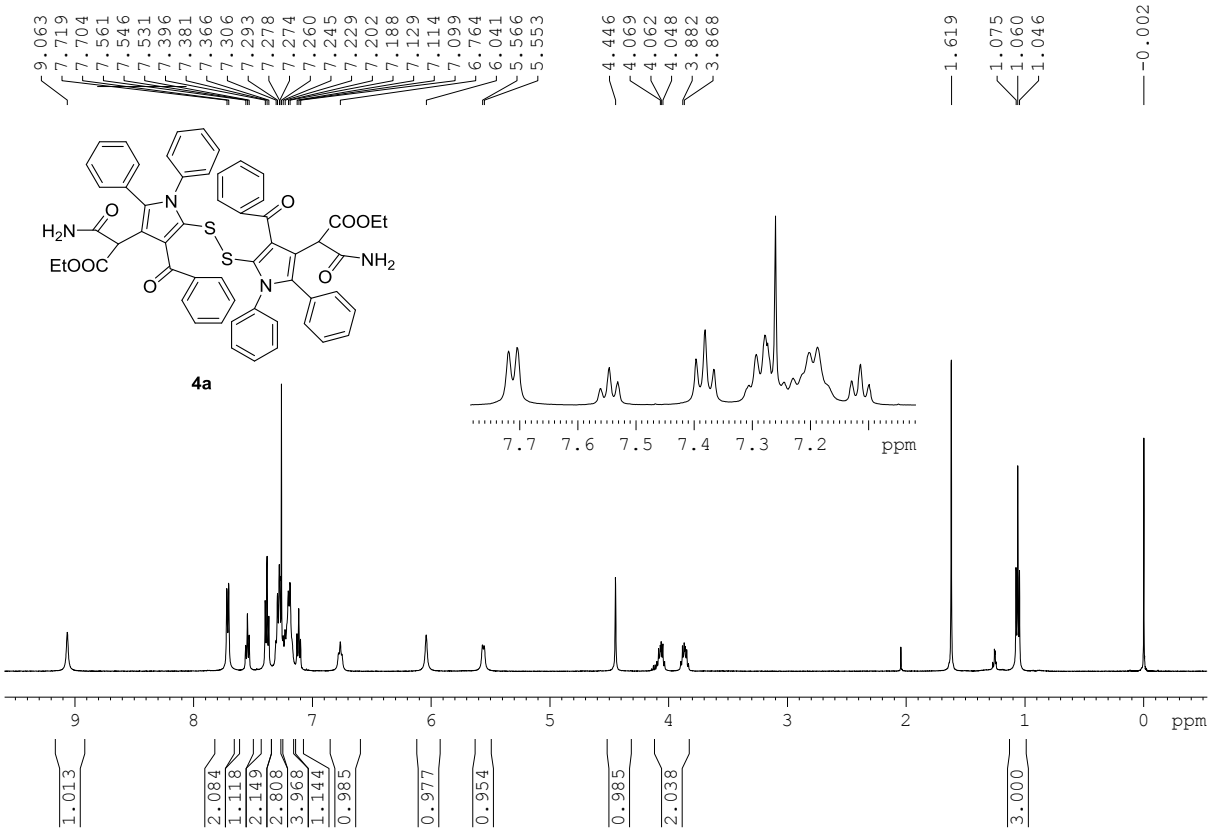
Ethyl 2-amino-4-benzoyl-6,6a-diphenyl-5-thioxo-3a,5,6,6a-tetrahydro-4*H*-furo[2,3-*b*] pyrrole-3-carboxylate (6)



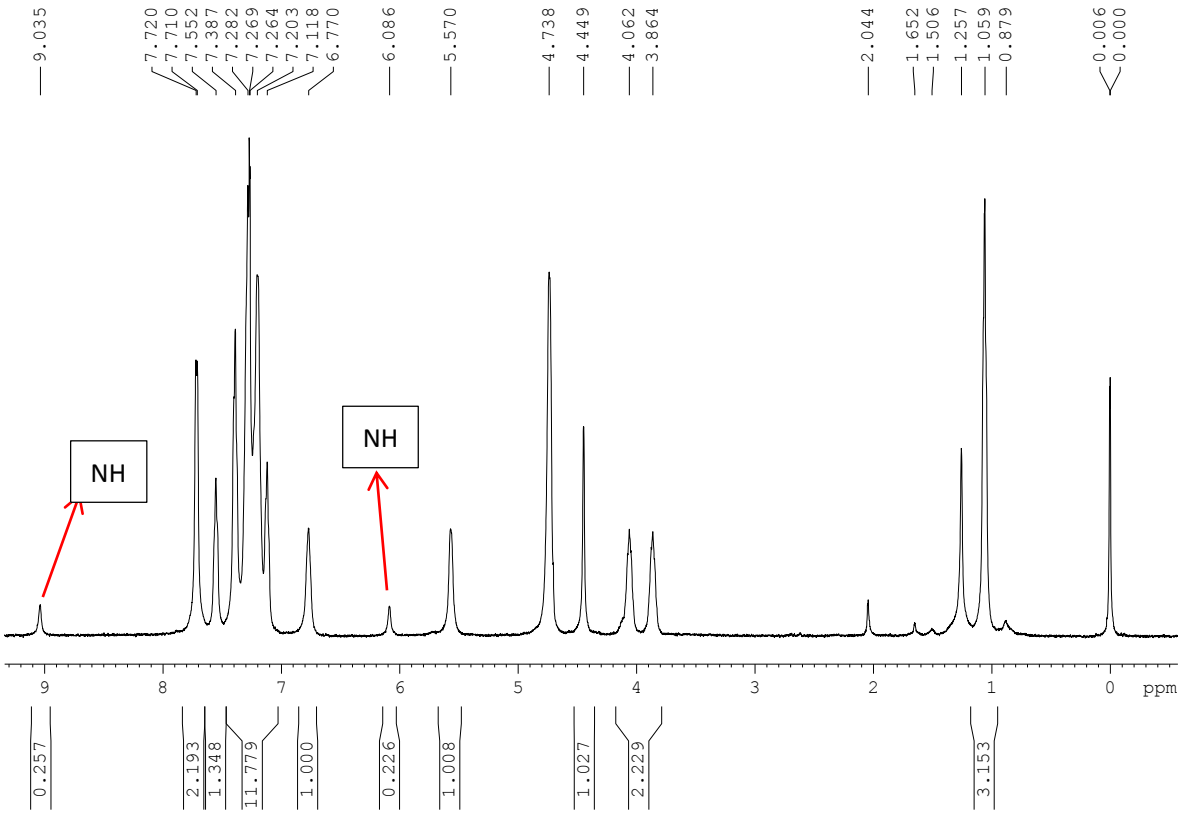
6

white solid; mp 192–194 ℃; ^{1}H NMR ($CDCl_3$, 500 MHz): δ: 0.71 (brs, 3H), 3.90 (brs, 2H), 4.43 (d, J = 3.35 Hz, 1H), 5.40 (d, J = 2.90 Hz, 1H), 5.86 (s, 2H), 7.11–7.13 (m, 2H), 7.23–7.25 (m, 1H), 7.27–7.32 (m, 3H), 7.35 (t, J = 7.50 Hz, 2H), 7.54 (t, J = 7.68 Hz, 2H), 7.63 (t, J = 7.32 Hz, 1H), 7.75 (d, J = 7.45 Hz, 2H), 8.22 (d, J = 7.60 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.8, 54.0, 59.1, 68.4, 77.9, 111.0, 126.4, 128.4, 128.6, 128.7, 128.9, 129.2, 130.1, 133.6, 136.8, 137.1, 137.5, 164.1, 166.5, 197.4, 202.9; HRMS (ESI–TOF, $[M + H]^+$): calcd for $C_{28}H_{25}N_2O_4S$, 485.1530; found, 485.1545.

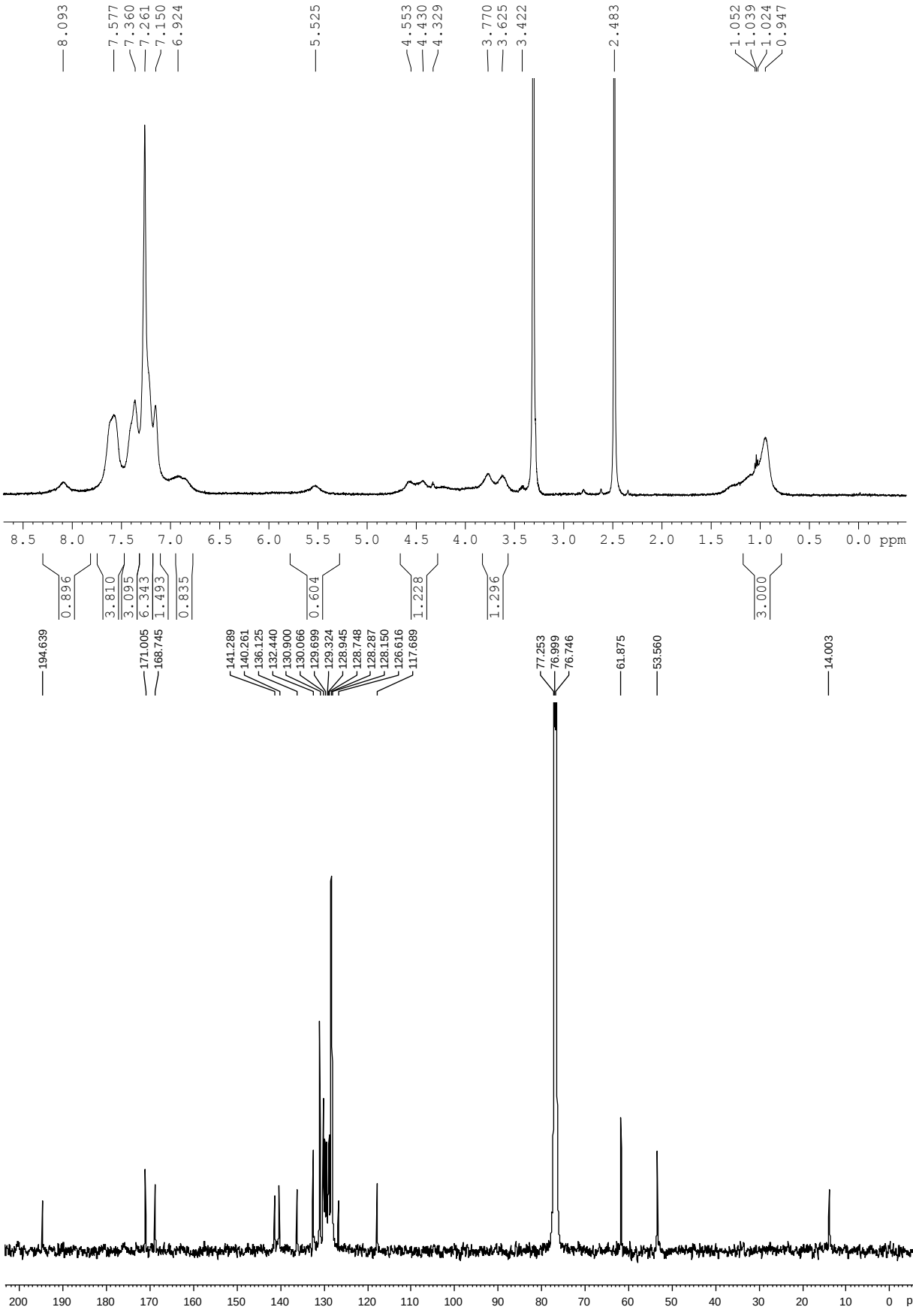
NMR spectra copies



4a (exchanged with D_2O)



4a (in DMSO)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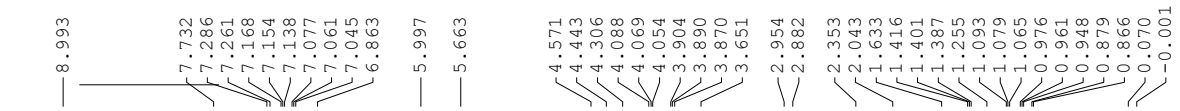
7.577
7.360
7.261
7.150
6.924
5.525
4.553
4.430
4.329
3.770
3.625
3.422
2.483
1.052
1.039
1.024
0.947
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.896
3.810
3.095
6.343
1.493
0.835
0.604
1.228
1.296
3.000
194.639
171.005
168.745
141.289
140.261
136.125
132.440
130.900
130.066
129.699
129.324
128.945
128.748
128.287
128.150
126.616
117.689
77.253
76.999
76.746
61.875
53.560
14.003
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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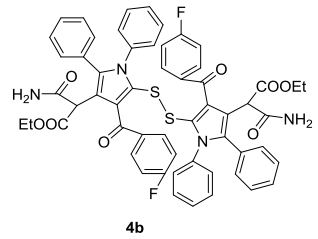
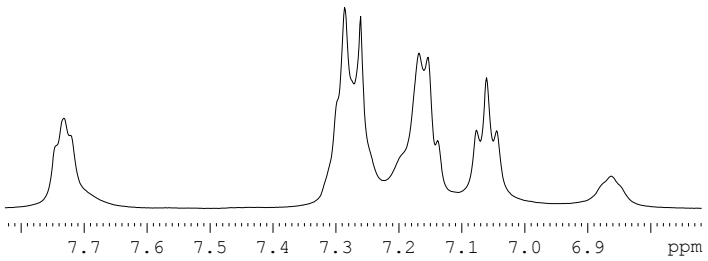
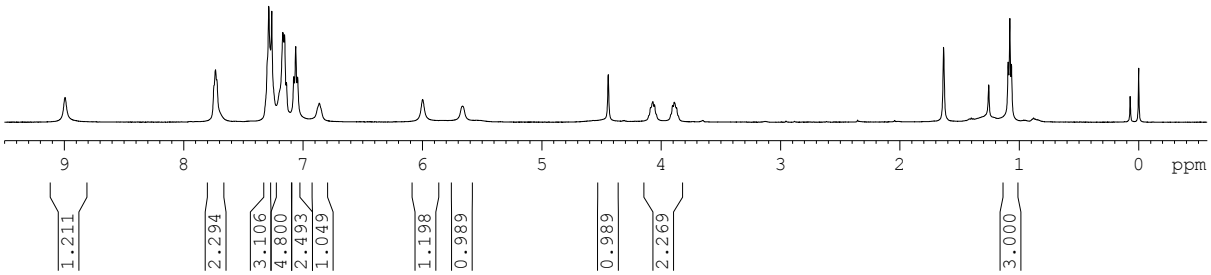
7.732
7.286
7.261
7.168
7.154
7.138
7.077
7.061
7.045
6.863
5.997
5.663
4.571
4.443
4.306
4.088
4.069
4.054
3.904
3.890
3.870
3.651
2.954
2.882
2.353
2.043
1.633
1.416
1.401
1.387
1.255
1.093
1.079
1.065
0.976
0.961
0.948
0.879
0.866
0.070
-0.001

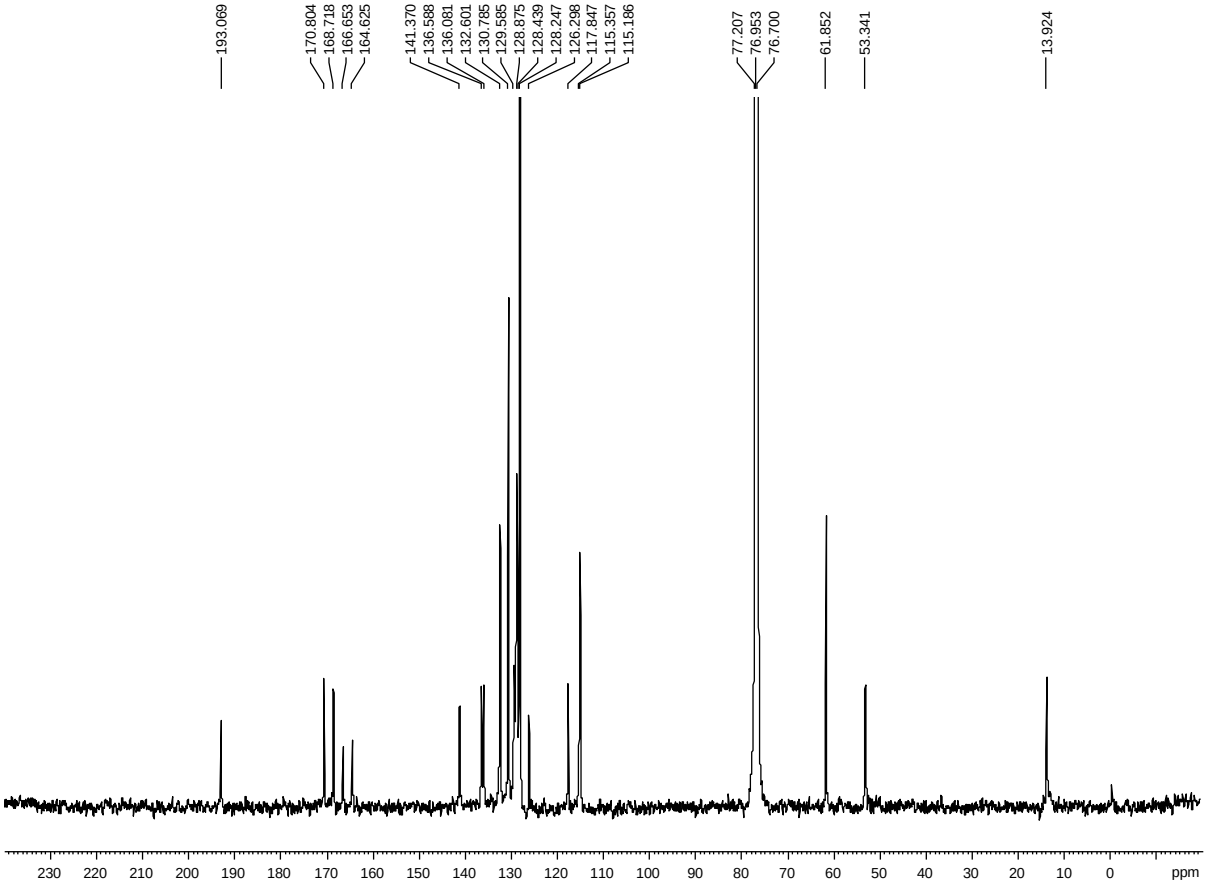

F
O
COOEt
H_2N
O
S
S
EtOOC
O
O
NH_2
N
N
F

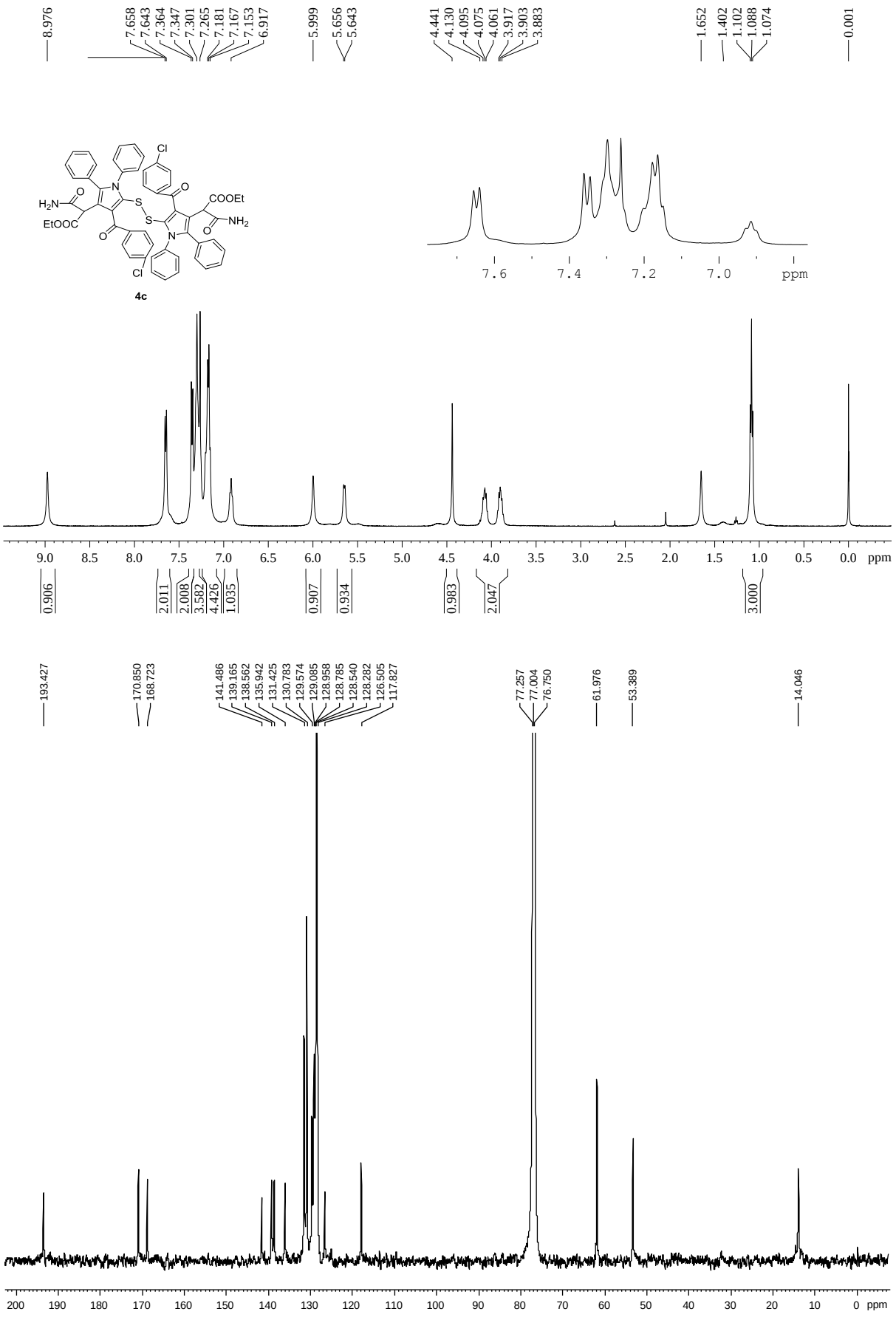
4b


7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
ppm


9
8
7
6
5
4
3
2
1
0
ppm

1.211
2.294
3.106
4.800
2.493
1.049
1.198
0.989
0.989
2.269
3.000


193.069
170.804
168.718
166.653
164.625
141.370
136.588
136.081
132.601
130.785
129.585
128.875
128.439
128.247
126.298
117.847
115.357
115.186
77.207
76.953
76.700
61.852
53.341
13.924
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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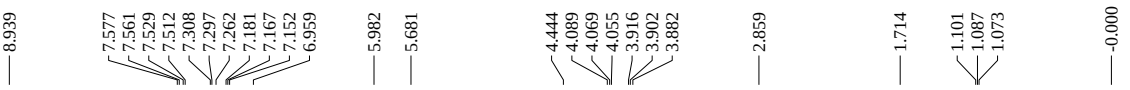
7.658
7.643
7.364
7.347
7.301
7.265
7.181
7.167
7.153
6.917
5.999
5.656
5.643
4.441
4.130
4.095
4.075
4.061
3.917
3.903
3.883
1.652
1.402
1.102
1.088
1.074
0.001
4c
7.6
7.4
7.2
7.0
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.906
2.011
2.008
3.582
4.426
1.035
0.907
0.934
0.983
2.047
3.000
193.427
170.850
168.723
141.486
139.165
138.562
135.942
131.425
130.783
129.574
129.085
128.958
128.785
128.540
128.282
126.505
117.827
77.257
77.004
76.750
61.976
53.389
14.046
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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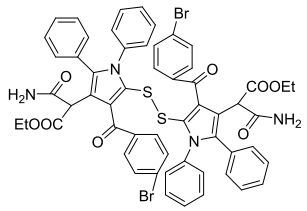
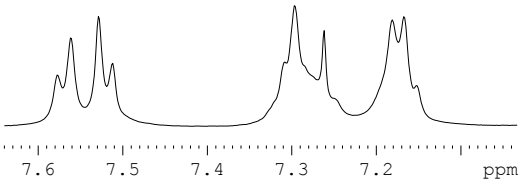
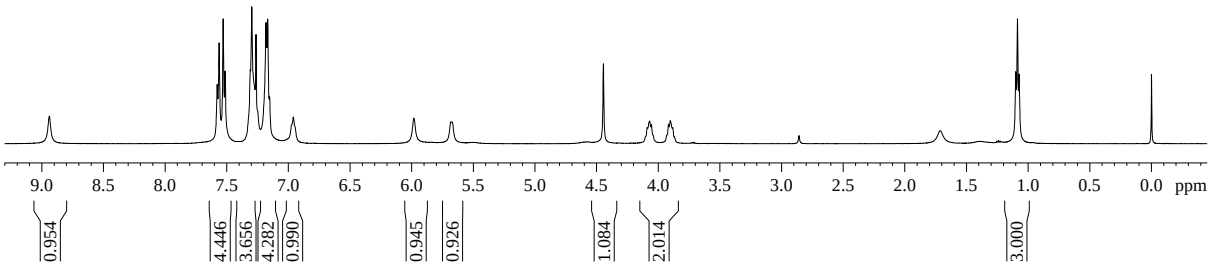
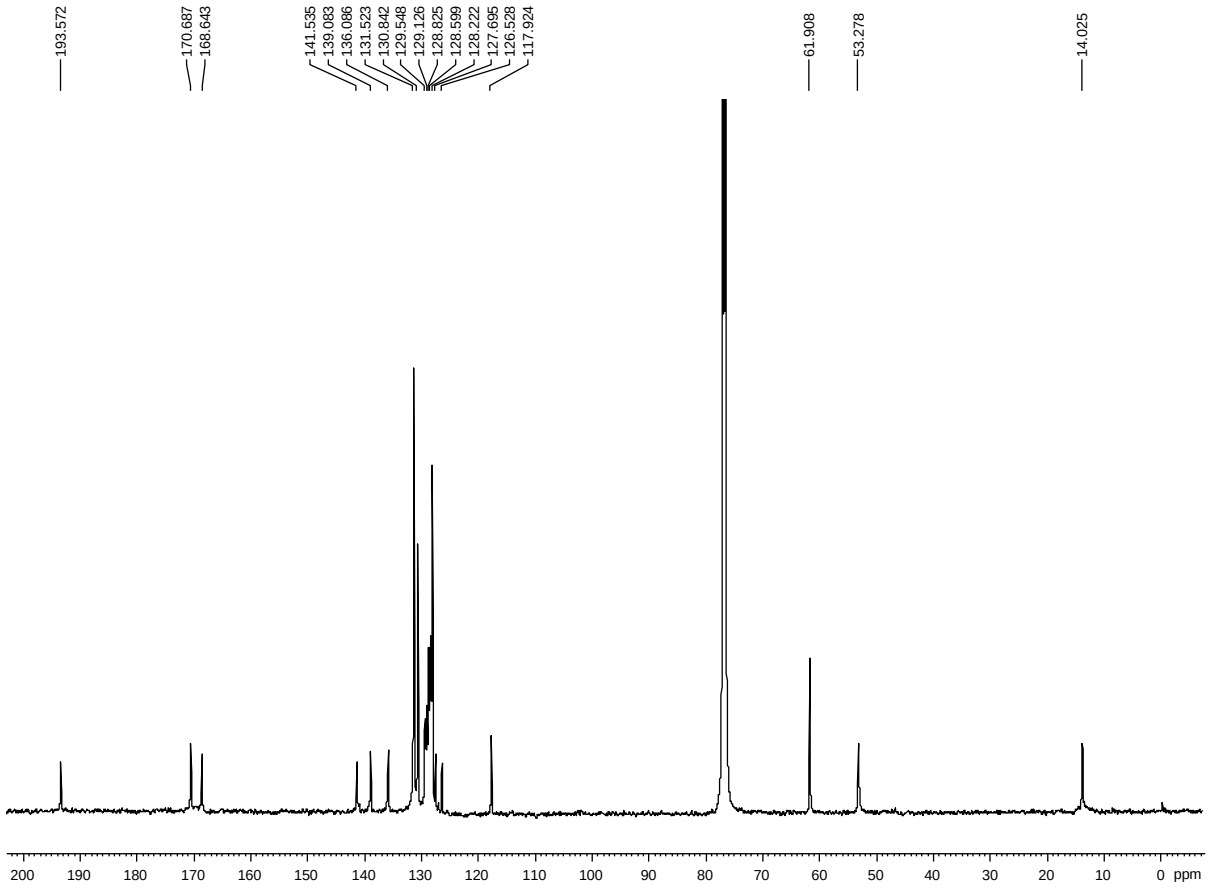
7.561
7.529
7.512
7.308
7.297
7.262
7.181
7.167
7.152
6.959
5.982
5.681
4.444
4.089
4.069
4.055
3.916
3.902
3.882
2.859
1.714
1.101
1.087
1.073
-0.000

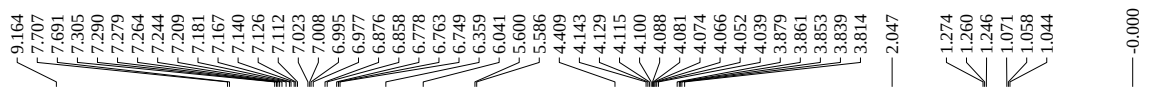

Br
O
N
S
S
O
COOEt
H_2N
O
EtOOC
O
N
O
NH_2
Br

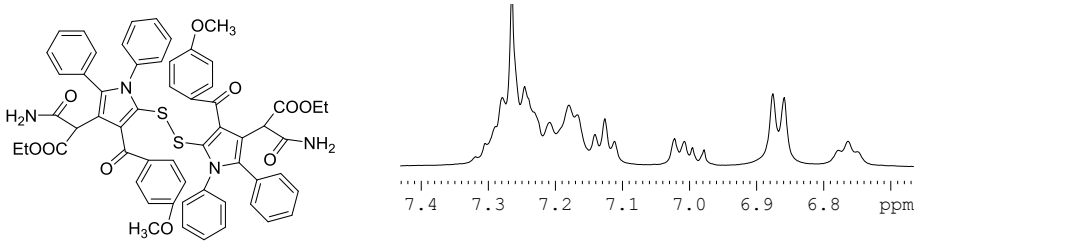
4d


7.6
7.5
7.4
7.3
7.2
ppm

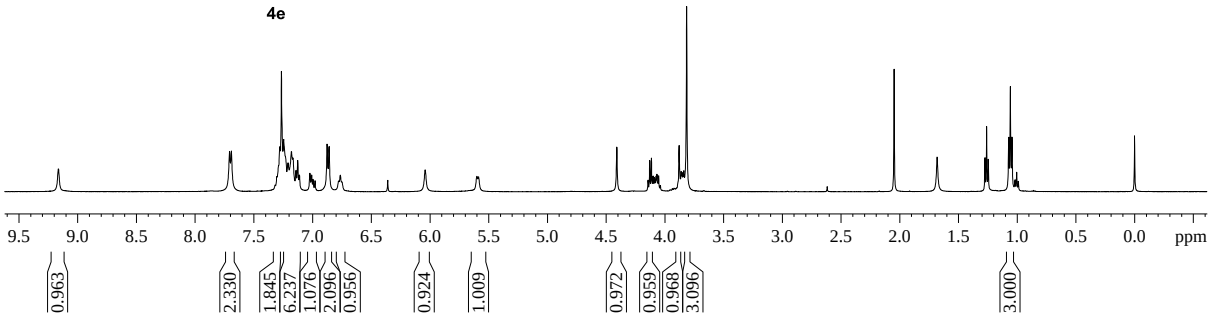

9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0 ppm
0.954
4.446
3.656
4.282
0.990
0.945
0.926
1.084
2.014
3.000

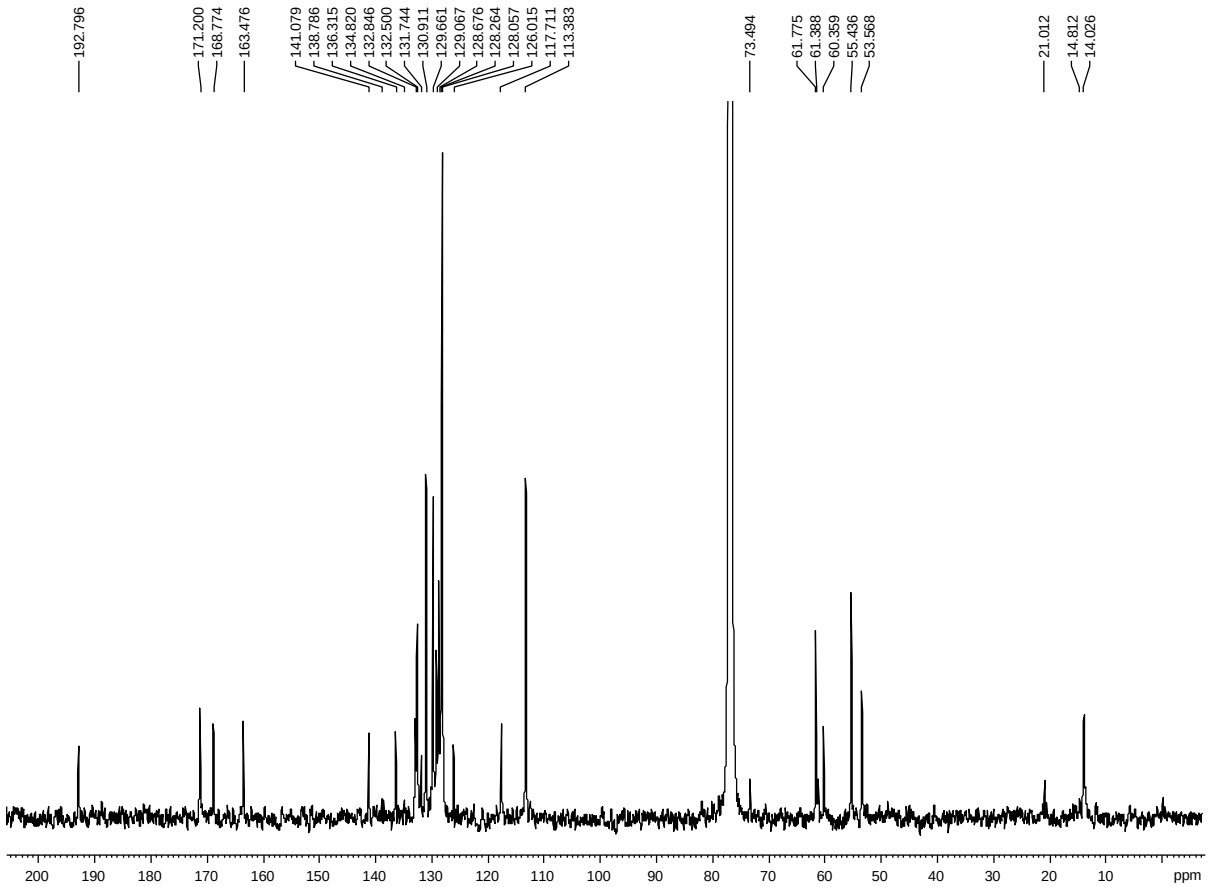

193.572
170.687
168.643
141.535
139.083
136.086
131.523
130.842
129.548
129.126
128.825
128.599
128.222
127.695
126.528
117.924
61.908
53.278
14.025
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

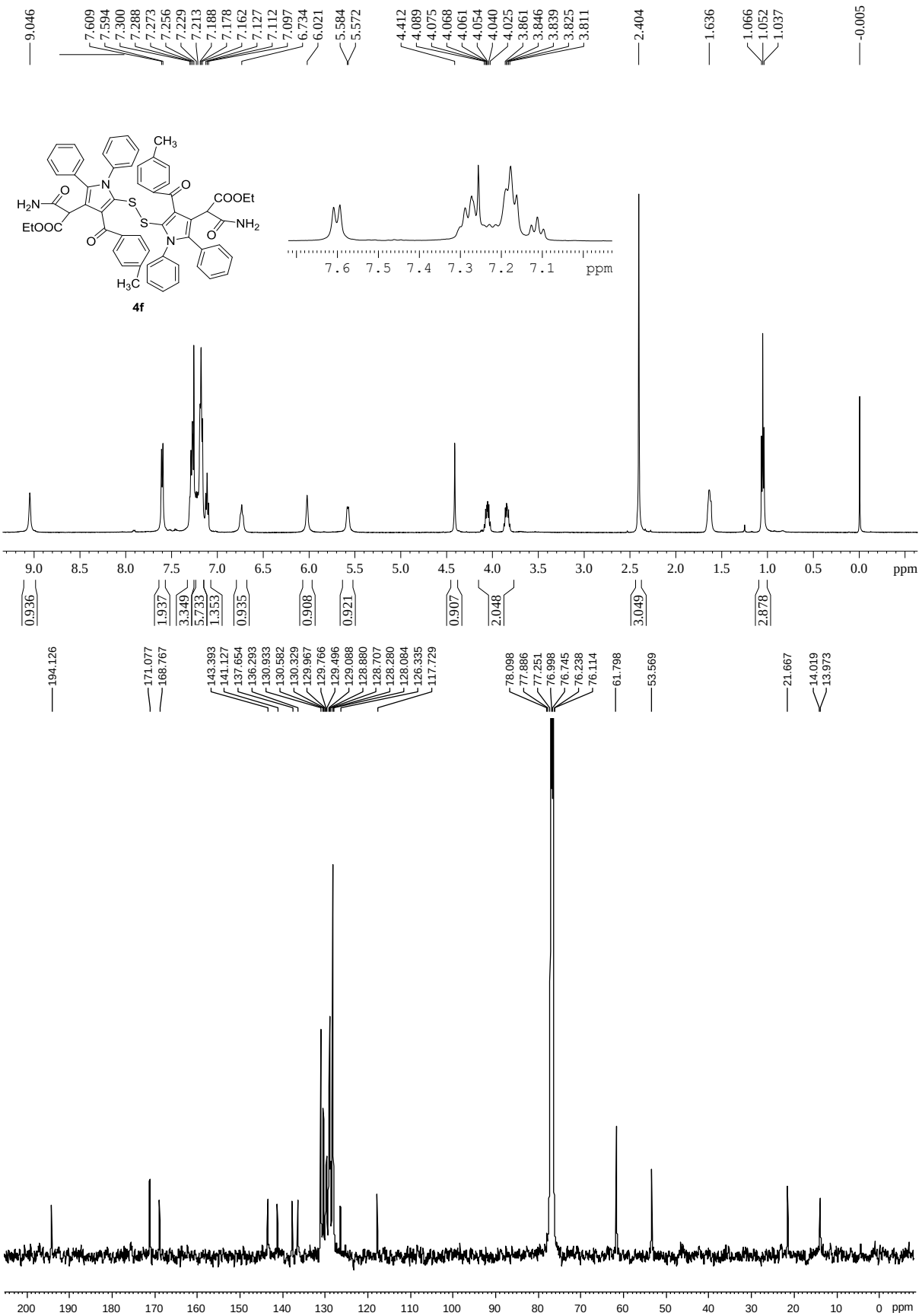

9.164
7.707
7.691
7.305
7.290
7.279
7.264
7.244
7.209
7.181
7.167
7.140
7.126
7.112
7.023
7.008
6.995
6.977
6.876
6.858
6.778
6.763
6.749
6.359
6.041
5.600
5.586
4.409
4.143
4.129
4.115
4.100
4.088
4.081
4.074
4.066
4.052
4.039
3.879
3.861
3.853
3.839
3.814
2.047
1.274
1.260
1.246
1.071
1.058
1.044
-0.000


OCH3
O
N
S
S
N
O
COOEt
H2N
O
NH2
EtOOC
O
H3CO
7.4
7.3
7.2
7.1
7.0
6.9
6.8
ppm

4e


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.963
2.330
1.845
6.237
1.076
2.096
0.956
0.924
1.009
0.972
0.959
0.968
3.096
3.000


192.796
171.200
168.774
163.476
141.079
138.786
136.315
134.820
132.846
132.500
131.744
130.911
129.661
129.067
128.676
128.264
128.057
126.015
117.711
113.383
73.494
61.775
61.388
60.359
55.436
53.568
21.012
14.812
14.026
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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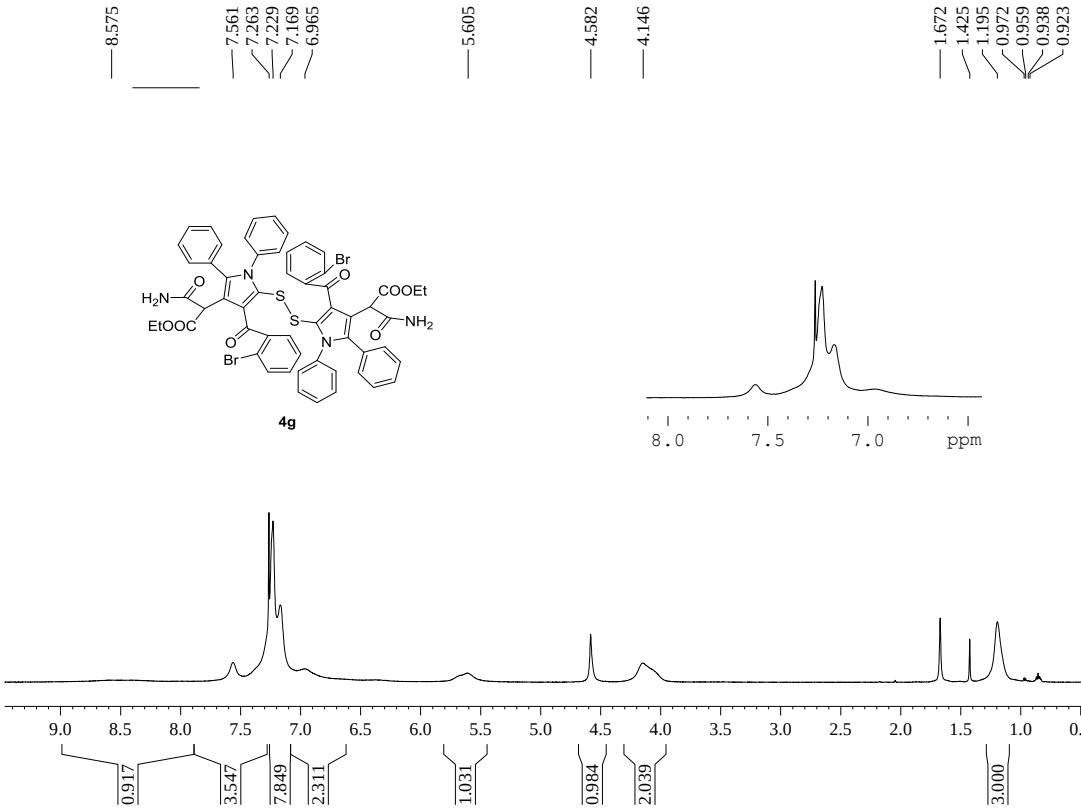
7.288
7.273
7.256
7.229
7.213
7.188
7.178
7.162
7.127
7.112
7.097
6.734
6.021
5.584
5.572
4.412
4.089
4.075
4.068
4.061
4.054
4.040
4.025
3.861
3.846
3.839
3.825
3.811
2.404
1.636
1.066
1.052
1.037
-0.005
CH3
H2N
EtOOC
COOEt
NH2
H3C
4f
7.6 7.5 7.4 7.3 7.2 7.1 ppm
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.936
1.937
3.349
5.733
1.353
0.935
0.908
0.921
0.907
2.048
3.049
2.878
194.126
171.077
168.767
143.393
141.127
137.654
136.293
130.933
130.582
130.329
129.967
129.766
129.496
129.088
128.880
128.707
128.280
128.084
126.335
117.729
78.098
77.886
77.251
76.998
76.745
76.238
76.114
61.798
53.569
21.667
14.019
13.973
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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7.229
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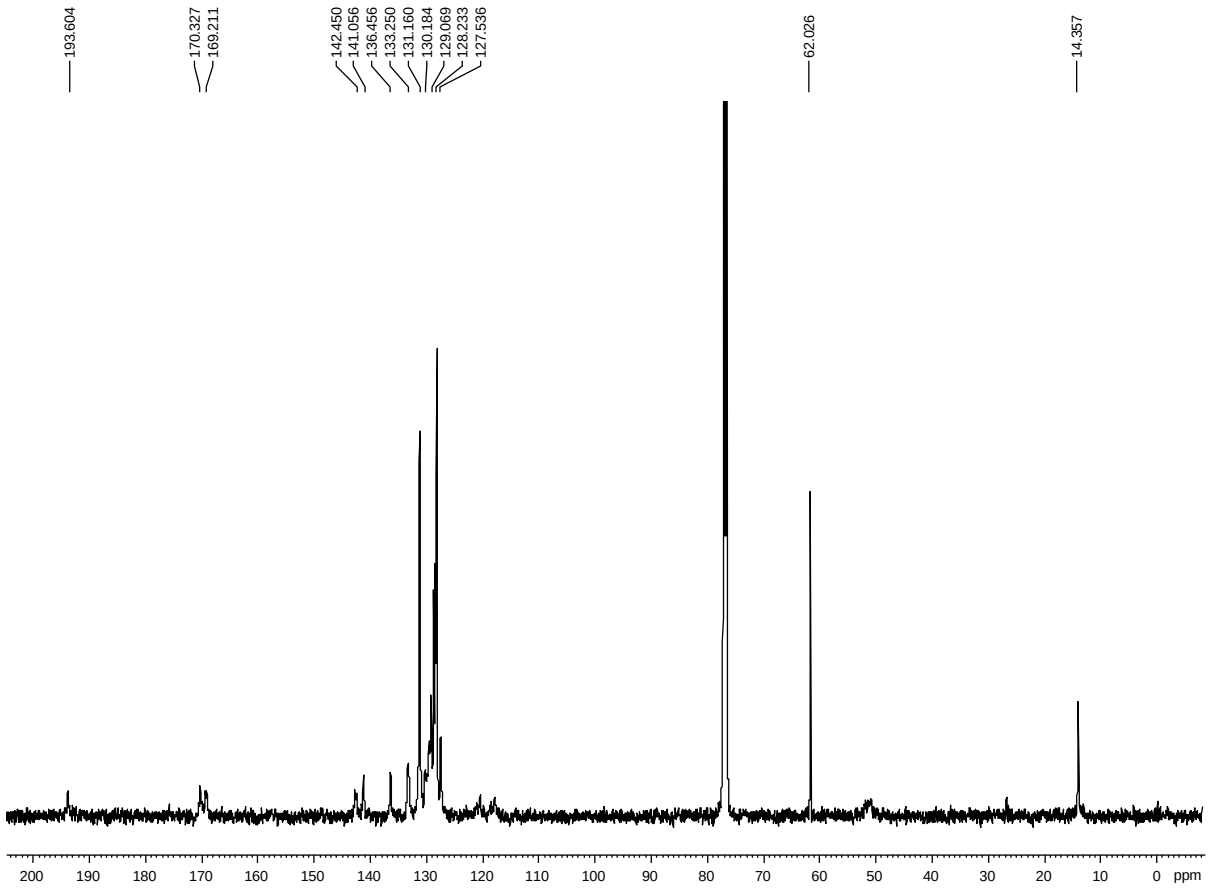
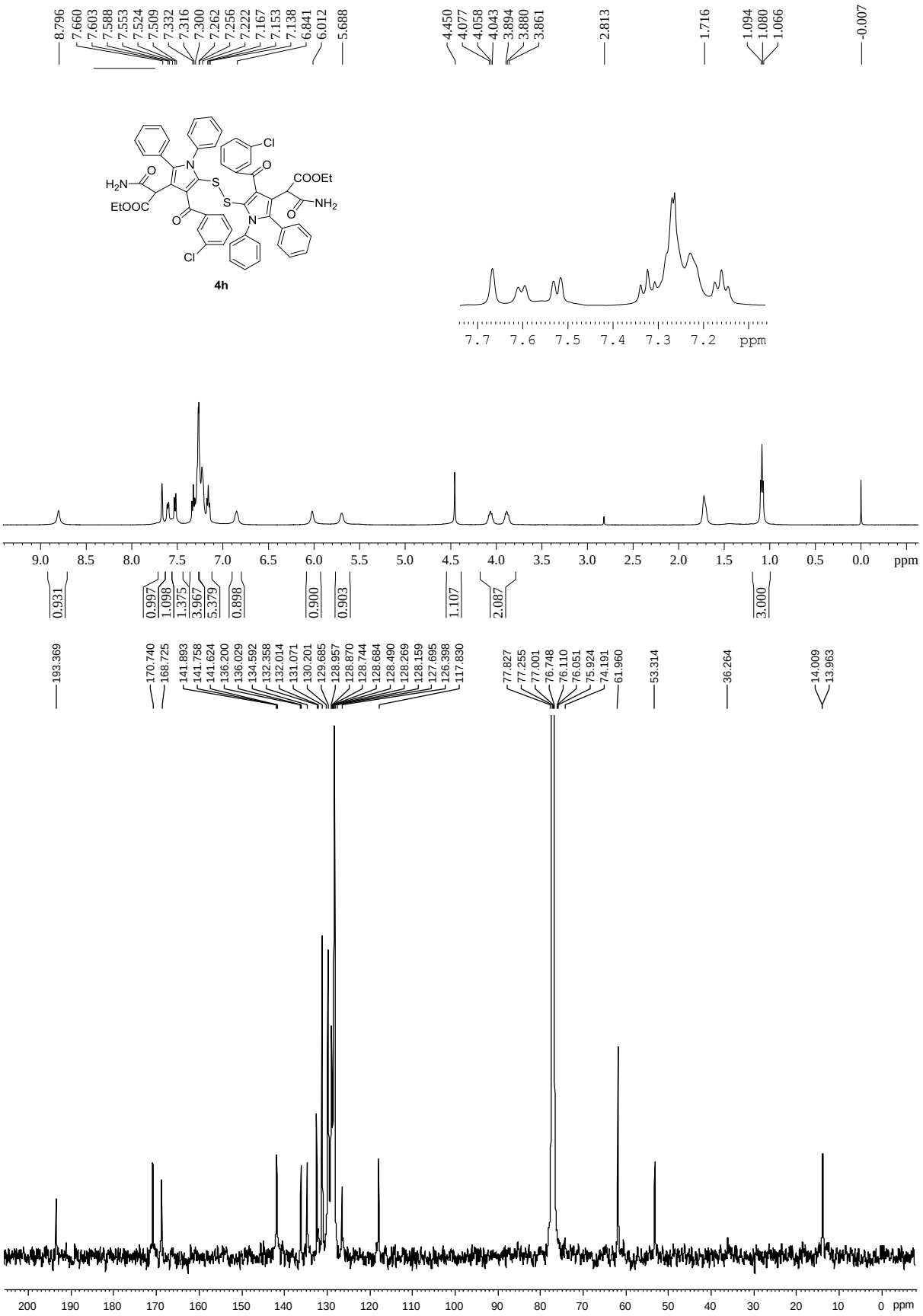
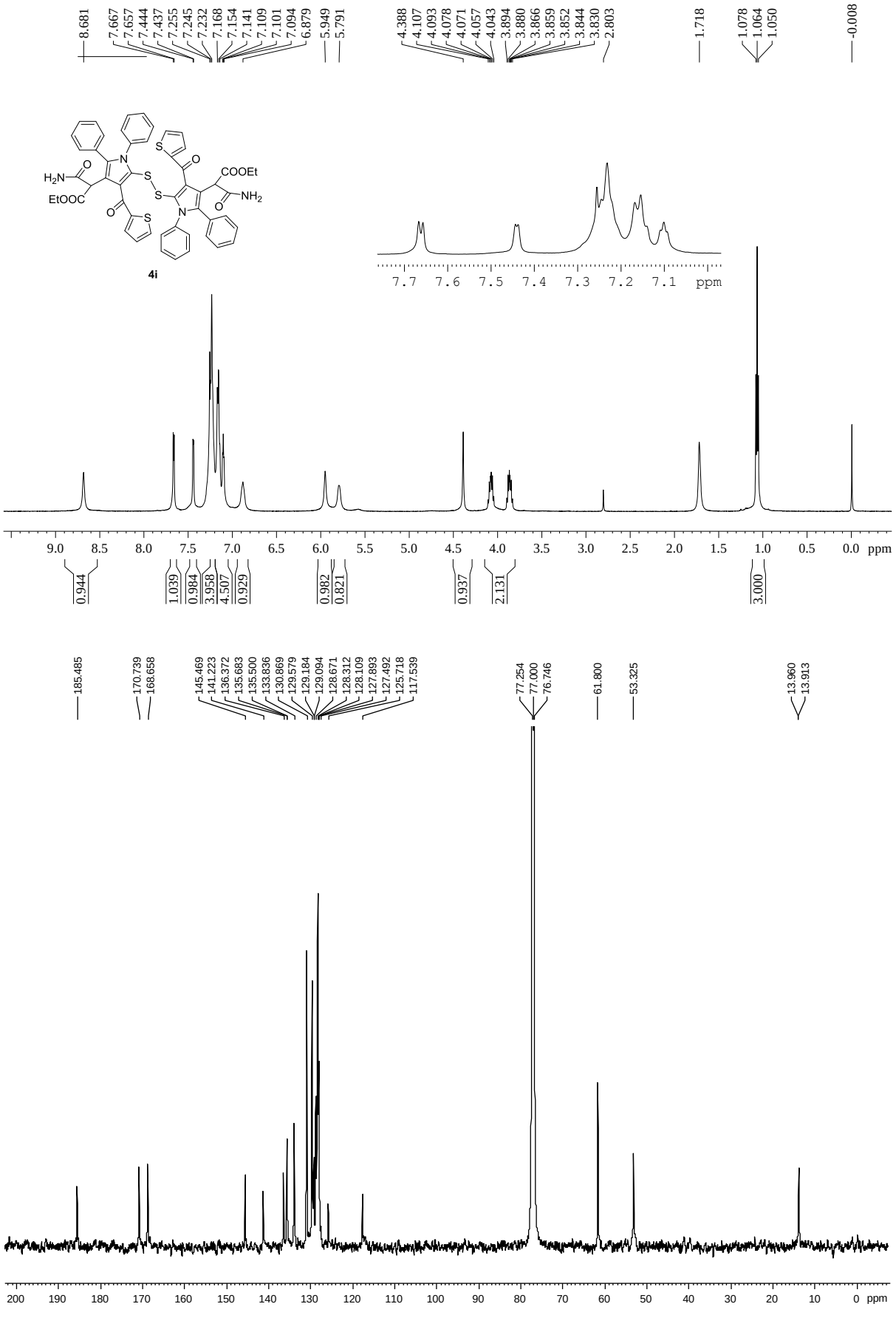
4.582
4.146
1.672
1.425
1.195
0.972
0.959
0.938
0.923
4g
8.0
7.5
7.0
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.917
3.547
7.849
2.311
1.031
0.984
2.039
3.000


193.604
170.327
169.211
142.450
141.056
136.456
133.250
131.160
130.184
129.069
128.233
127.536
62.026
14.357
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


8.796
7.660
7.603
7.588
7.553
7.524
7.509
7.332
7.316
7.300
7.262
7.256
7.222
7.167
7.153
7.138
6.841
6.012
5.688
4.450
4.077
4.058
4.043
3.894
3.880
3.861
2.813
1.716
1.094
1.080
1.066
-0.007
Cl
O
N
S
S
O
COOEt
H_2N
O
EtOOC
O
N
NH_2
O
Cl
4h
7.7 7.6 7.5 7.4 7.3 7.2 ppm
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.931
0.997
1.098
1.375
3.967
5.379
0.898
0.900
0.903
1.107
2.087
3.000
193.369
170.740
168.725
141.893
141.758
141.624
136.200
136.029
134.592
132.358
132.014
131.071
130.201
129.685
128.957
128.870
128.744
128.684
128.490
128.269
128.159
127.695
126.398
117.830
77.827
77.255
77.001
76.748
76.110
76.051
75.924
74.191
61.960
53.314
36.264
14.009
13.963
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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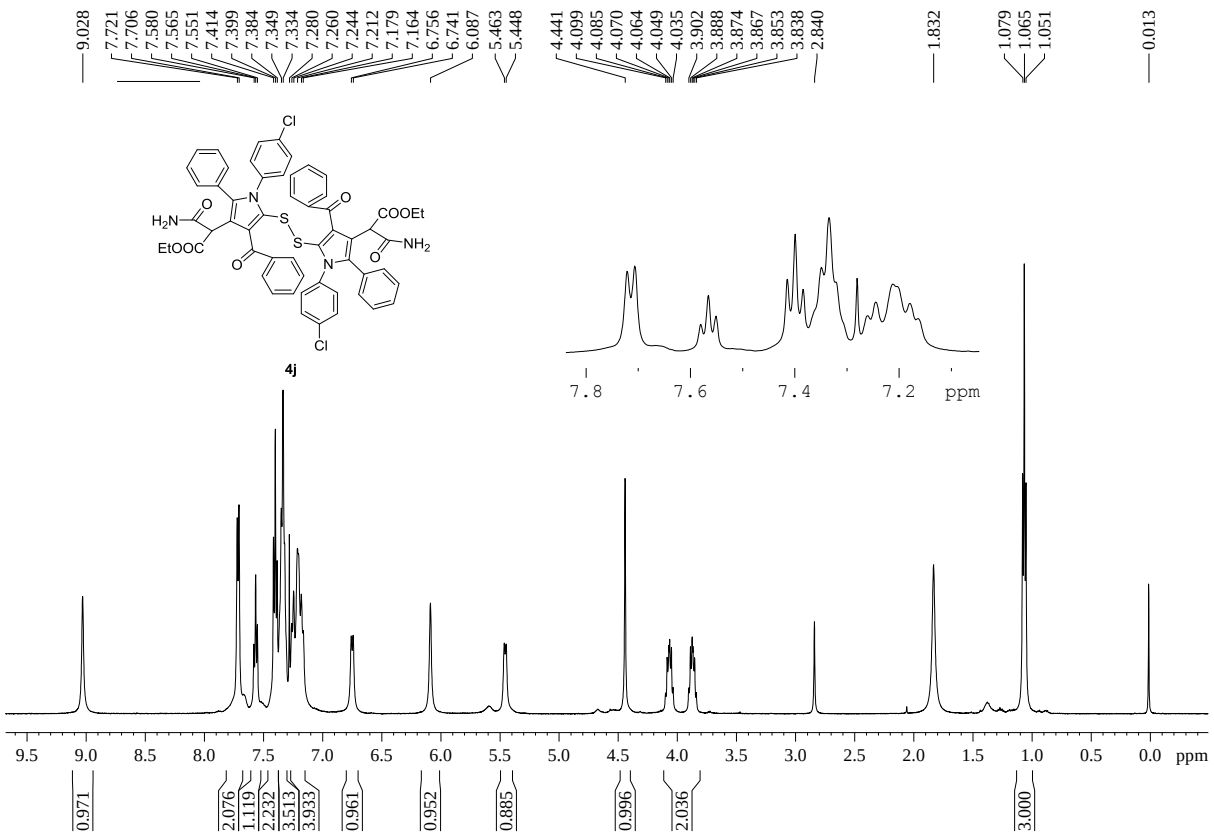
7.657
7.444
7.437
7.255
7.245
7.232
7.168
7.154
7.141
7.109
7.101
7.094
6.879
5.949
5.791
4.388
4.107
4.093
4.078
4.071
4.057
4.043
3.894
3.880
3.866
3.859
3.852
3.844
3.830
2.803
1.718
1.078
1.064
1.050
-0.008
4i
7.7 7.6 7.5 7.4 7.3 7.2 7.1 ppm
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.944
1.039
0.984
3.958
4.507
0.929
0.982
0.821
0.937
2.131
3.000
185.485
170.739
168.658
145.469
141.223
136.372
135.683
135.500
133.836
130.869
129.579
129.184
129.094
128.671
128.312
128.109
127.893
127.492
125.718
117.539
77.254
77.000
76.746
61.800
53.325
13.960
13.913
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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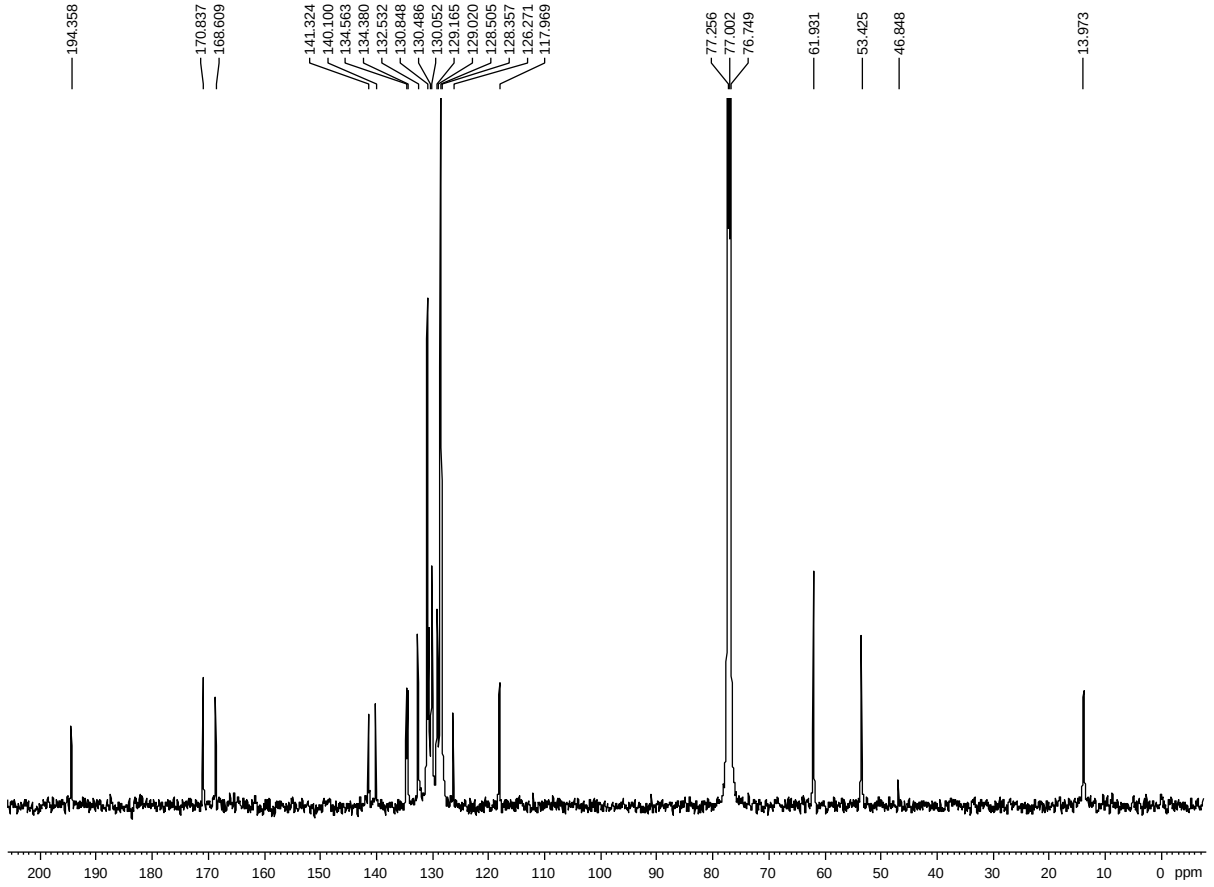
7.721
7.706
7.580
7.565
7.551
7.414
7.399
7.384
7.349
7.334
7.280
7.260
7.244
7.212
7.179
7.164
6.756
6.741
6.087
5.463
5.448
4.441
4.099
4.085
4.070
4.064
4.049
4.035
3.902
3.888
3.874
3.867
3.853
3.838
2.840
1.832
1.079
1.065
1.051
0.013
Cl
H2N
O
EtOOC
N
S
S
O
COOEt
NH2
O
O
N
Cl
4j
7.8
7.6
7.4
7.2
ppm
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.971
2.076
1.119
2.232
3.513
3.933
0.961
0.952
0.885
0.996
2.036
3.000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170.837
168.609
141.324
140.100
134.563
134.380
132.532
130.848
130.486
130.052
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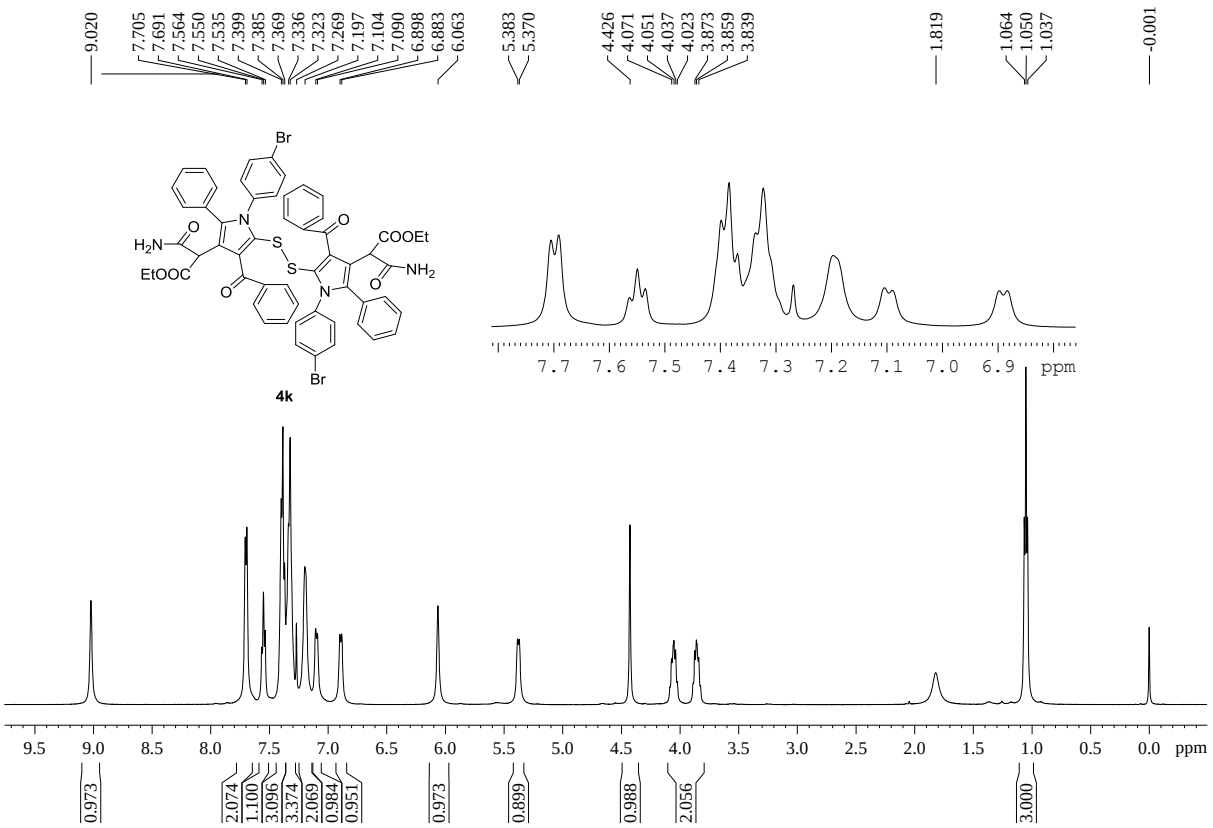
129.020
128.505
128.357
126.271
117.969
77.256
77.002
76.749
61.931
53.425
46.848
13.973
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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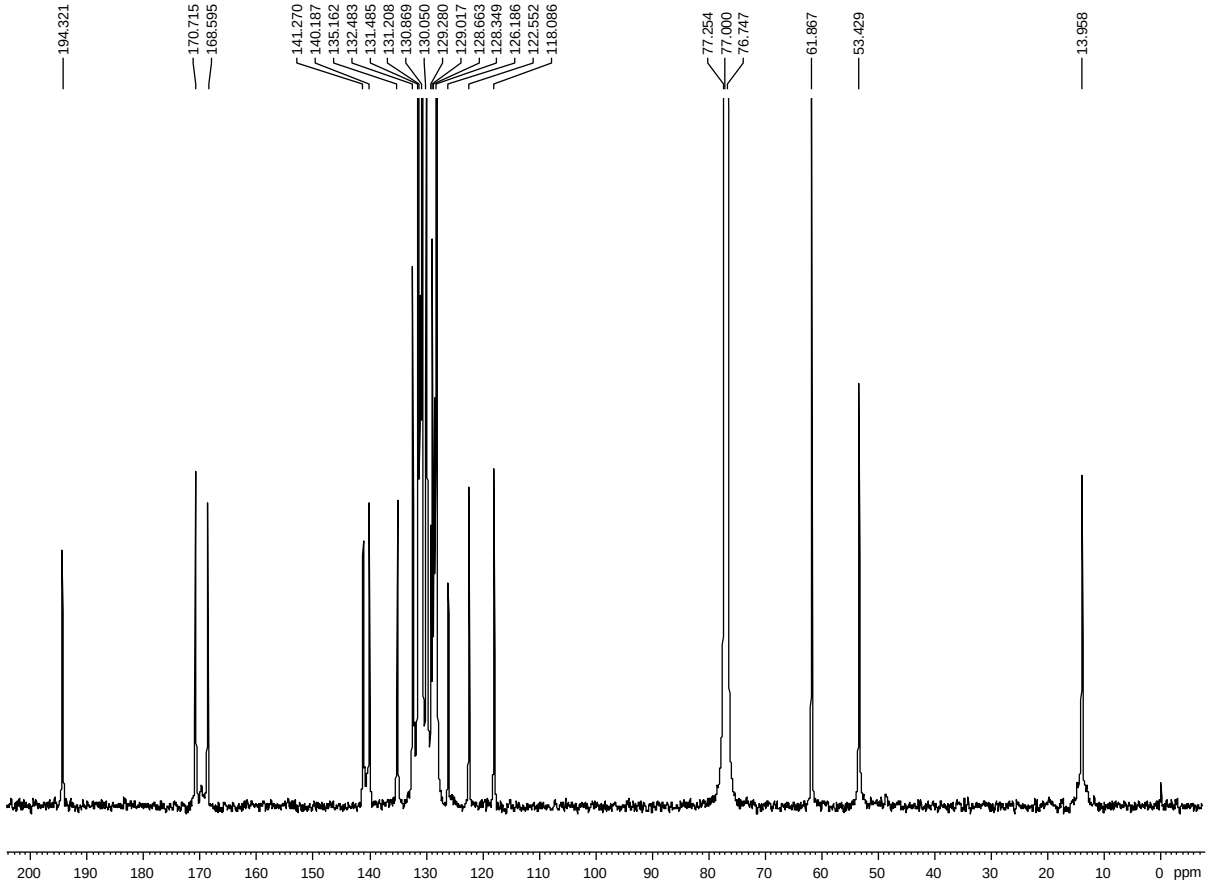
7.705
7.691
7.564
7.550
7.535
7.399
7.385
7.369
7.336
7.323
7.269
7.197
7.104
7.090
6.898
6.883
6.063
5.383
5.370
4.426
4.071
4.051
4.037
4.023
3.873
3.859
3.839
1.819
1.064
1.050
1.037
-0.001
Br
H_2N
O
EtOOC
O
S
S
N
O
COOEt
NH_2
O
N
Br
4k
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.973
2.074
1.100
3.096
3.374
2.069
0.984
0.951
0.973
0.899
0.988
2.056
3.000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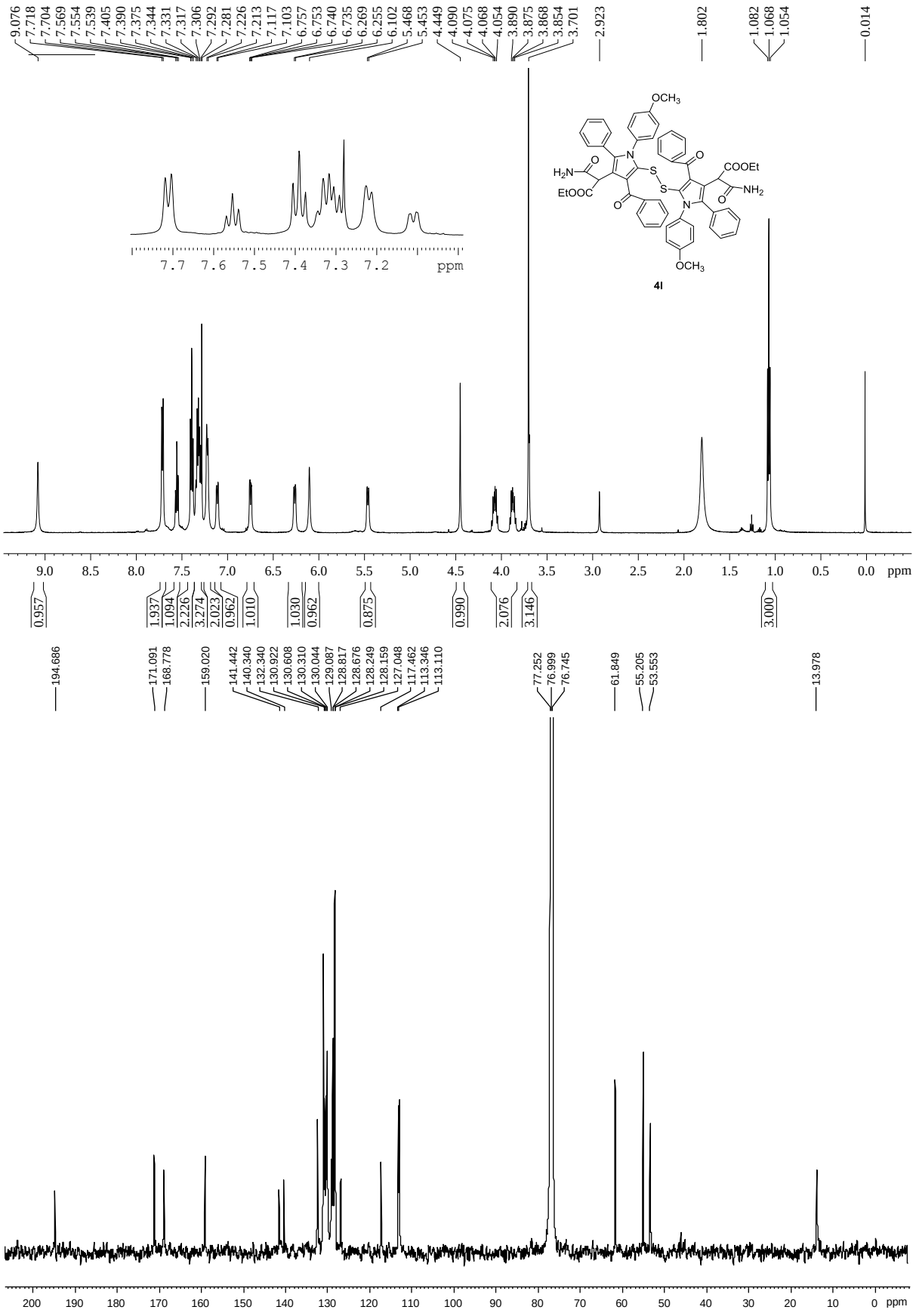
170.715
168.595
141.270
140.187
135.162
132.483
131.485
131.208
130.869
130.050
129.280
129.017
128.663
128.349
126.186
122.552
118.086
77.254
77.000
76.747
61.867
53.429
13.958
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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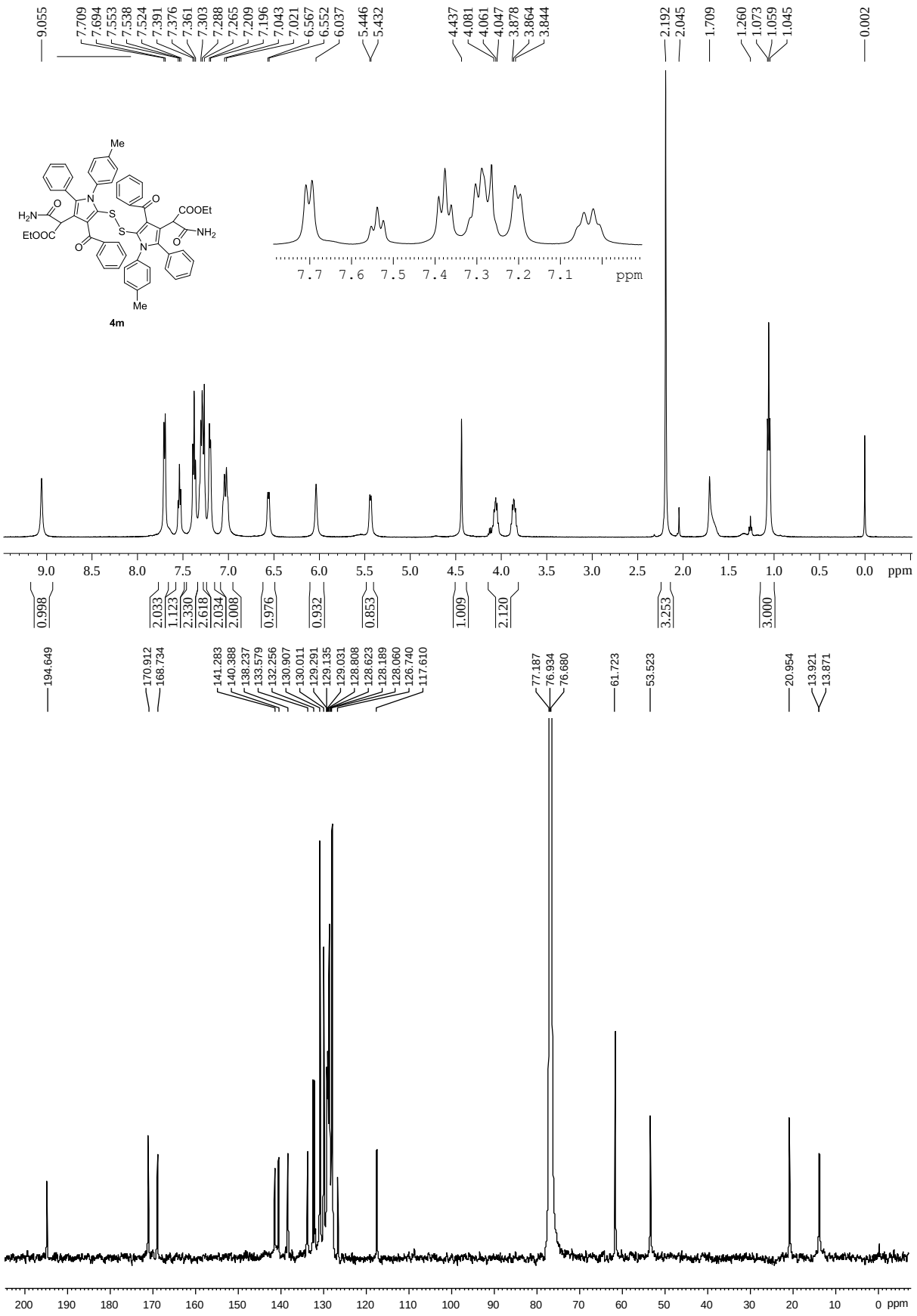
7.704
7.569
7.554
7.539
7.405
7.390
7.375
7.344
7.331
7.317
7.306
7.292
7.281
7.226
7.213
7.117
7.103
6.757
6.753
6.740
6.735
6.269
6.255
6.102
5.468
5.453
4.449
4.090
4.075
4.068
4.054
3.890
3.875
3.868
3.854
3.701
2.923
1.802
1.082
1.068
1.054
0.014
7.7 7.6 7.5 7.4 7.3 7.2 ppm
OCH3
H2N
EtOOC
COOEt
NH2
4l
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.957
1.937
1.094
2.226
3.274
2.023
0.962
1.010
1.030
0.962
0.875
0.990
2.076
3.146
3.000
194.686
171.091
168.778
159.020
141.442
140.340
132.340
130.922
130.608
130.310
130.044
129.087
128.817
128.676
128.249
128.159
127.048
117.462
113.346
113.110
77.252
76.999
76.745
61.849
55.205
53.553
13.978
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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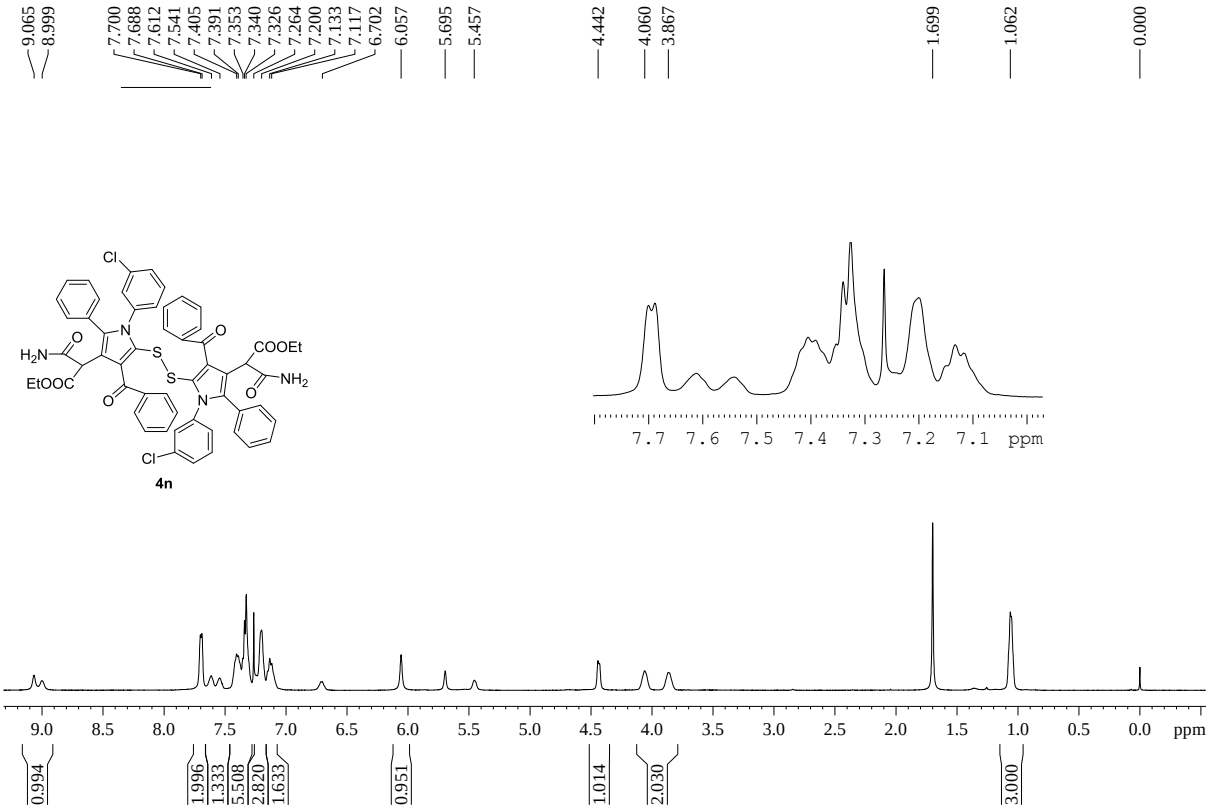
7.709
7.694
7.553
7.538
7.524
7.391
7.376
7.361
7.303
7.288
7.265
7.209
7.196
7.043
7.021
6.567
6.552
6.037
5.446
5.432
4.437
4.081
4.061
4.047
3.878
3.864
3.844
2.192
2.045
1.709
1.260
1.073
1.059
1.045
0.002
Me
COOEt
H_2N
EtOOC
NH_2
Me
4m
7.7 7.6 7.5 7.4 7.3 7.2 7.1 ppm
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.998
2.033
1.123
2.330
2.618
2.034
2.008
0.976
0.932
0.853
1.009
2.120
3.253
3.000
194.649
170.912
168.734
141.283
140.388
138.237
133.579
132.256
130.907
130.011
129.291
129.135
129.031
128.808
128.623
128.189
128.060
126.740
117.610
77.187
76.934
76.680
61.723
53.523
20.954
13.921
13.871
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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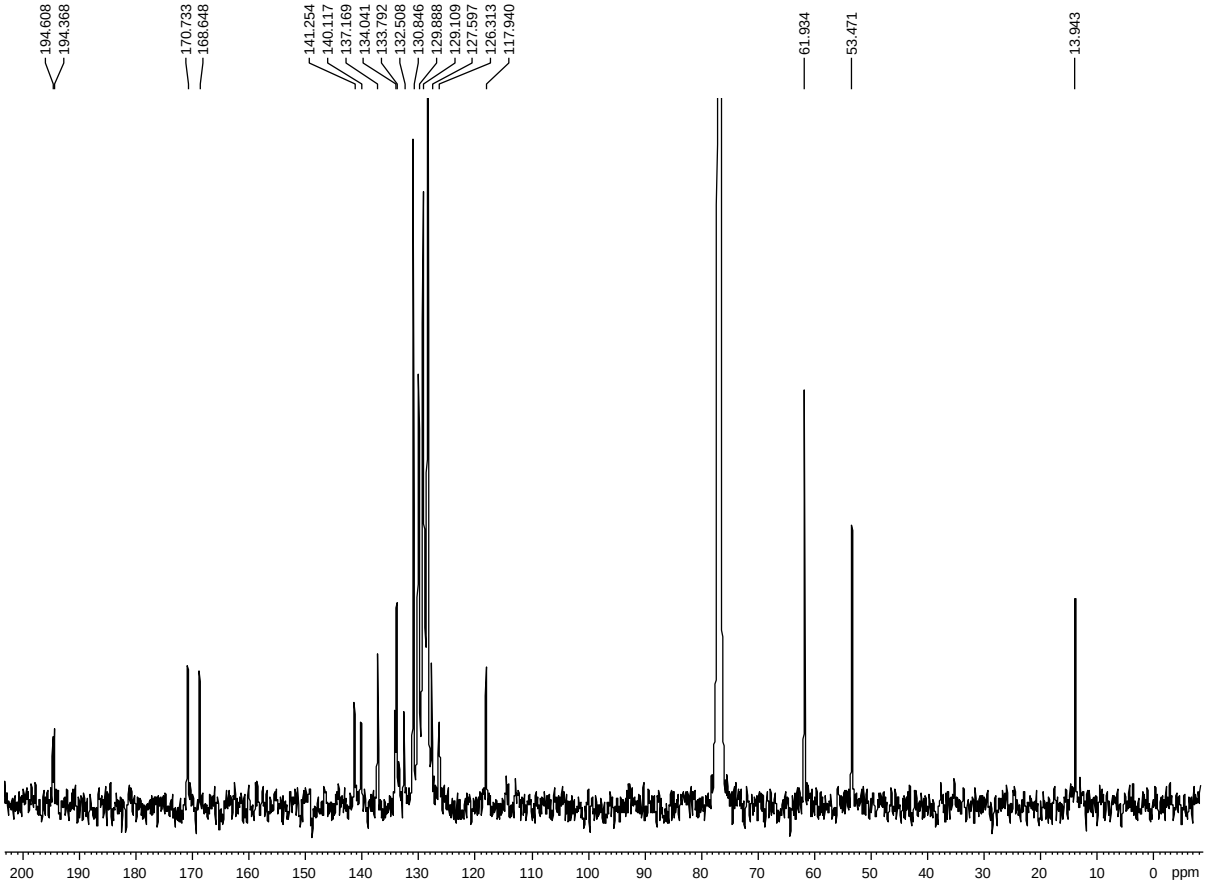
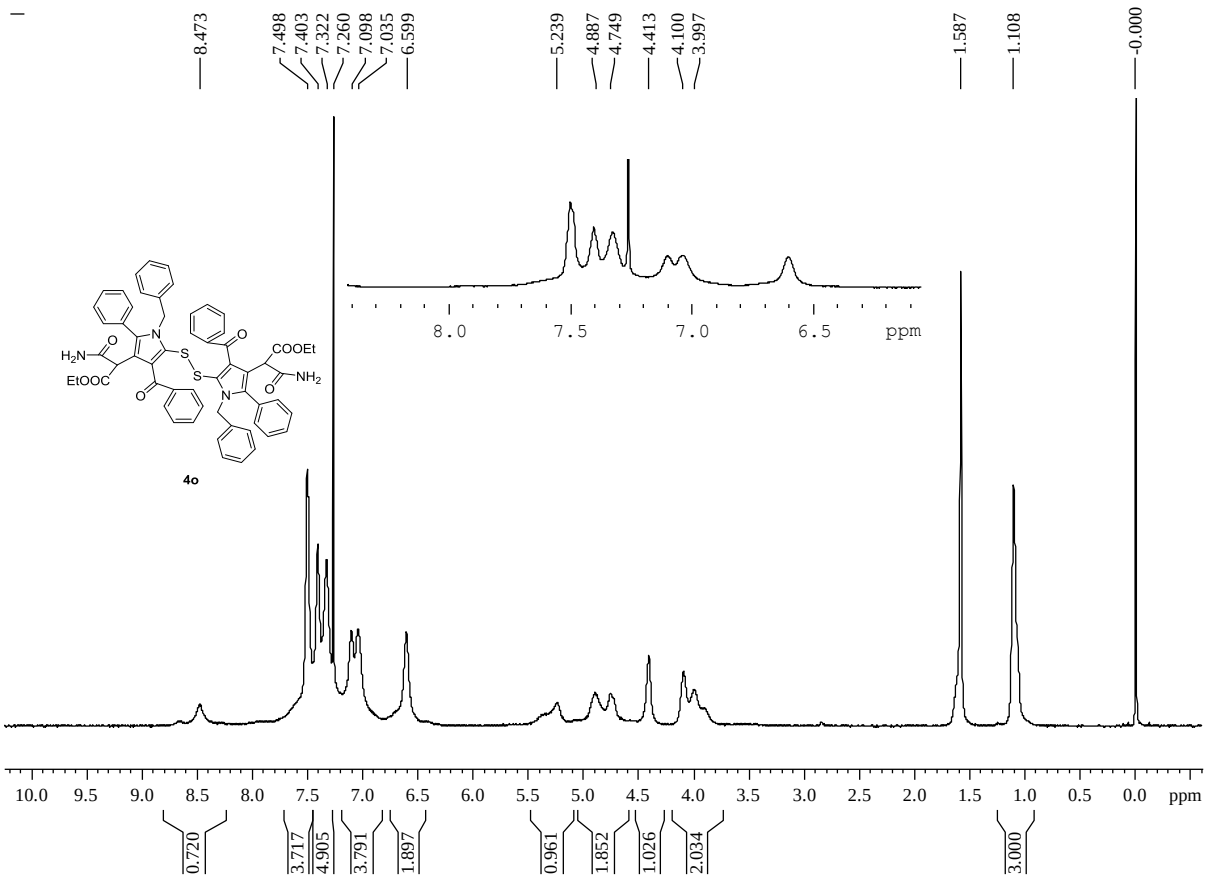
8.999
7.700
7.688
7.612
7.541
7.405
7.391
7.353
7.340
7.326
7.264
7.200
7.133
7.117
6.702
6.057
5.695
5.457
4.442
4.060
3.867
1.699
1.062
0.000
Cl
N
S
S
N
O
O
O
O
O
H_2N
EtOOC
COOEt
NH_2
Cl
4n
7.7 7.6 7.5 7.4 7.3 7.2 7.1 ppm
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.994
1.996
1.333
5.508
2.820
1.633
0.951
1.014
2.030
3.000


194.608
194.368
170.733
168.648
141.254
140.117
137.169
134.041
133.792
132.508
130.846
129.888
129.109
127.597
126.313
117.940
61.934
53.471
13.943
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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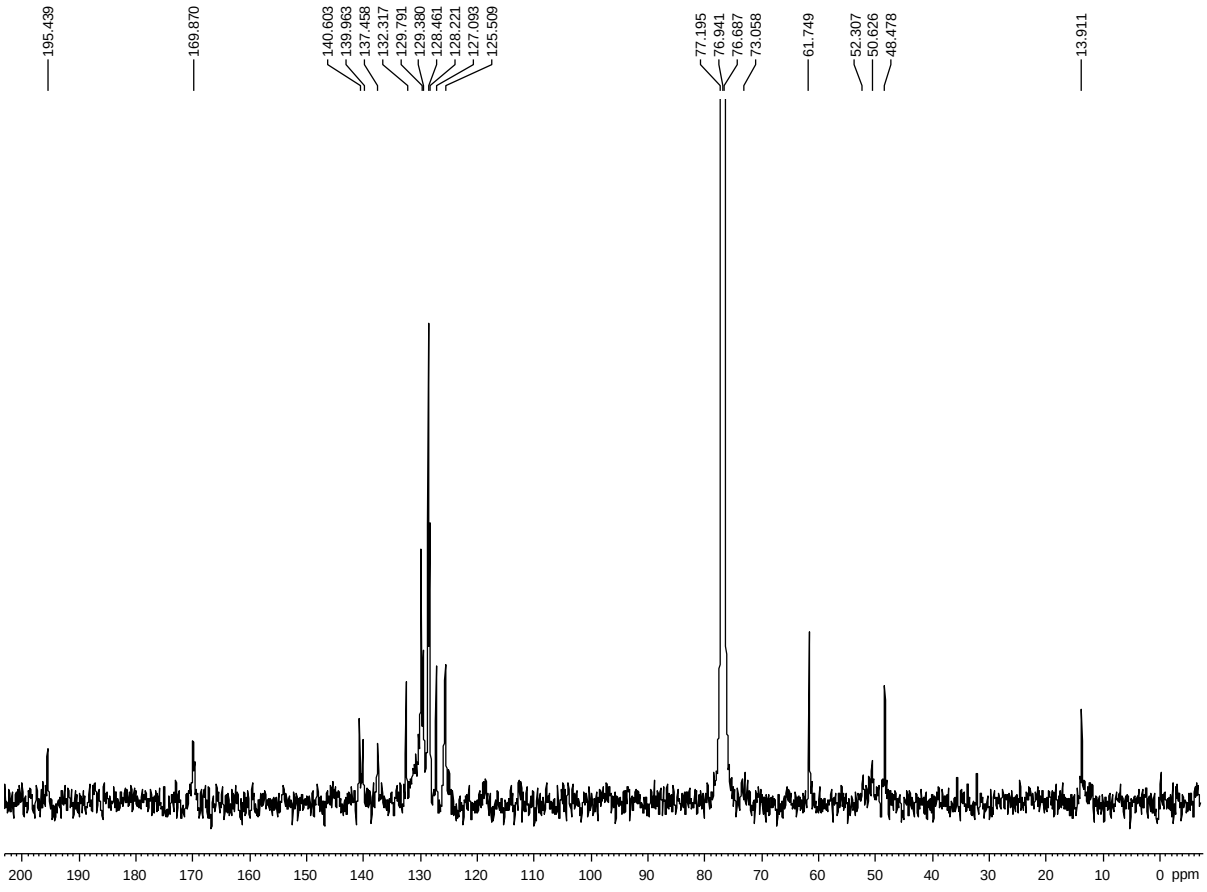
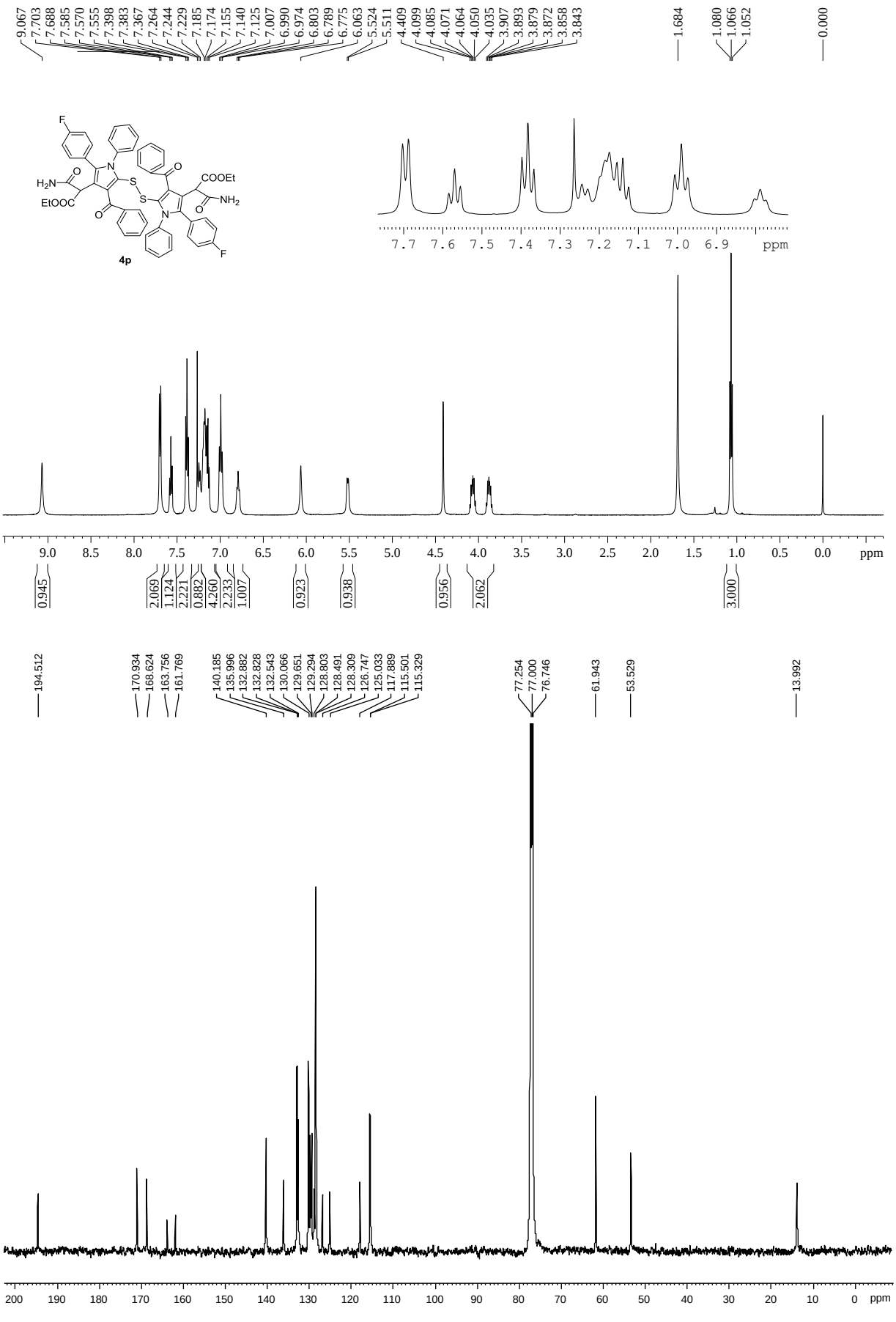
7.498
7.403
7.322
7.260
7.098
7.035
6.599
5.239
4.887
4.749
4.413
4.100
3.997
1.587
1.108
-0.000
8.0
7.5
7.0
6.5
ppm
4o
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.720
3.717
4.905
3.791
1.897
0.961
1.852
1.026
2.034
3.000


195.439
169.870
140.603
139.963
137.458
132.317
129.791
129.380
128.461
128.221
127.093
125.509
77.195
76.941
76.687
73.058
61.749
52.307
50.626
48.478
13.911
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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7.703
7.688
7.585
7.570
7.555
7.398
7.383
7.367
7.264
7.244
7.229
7.185
7.174
7.155
7.140
7.125
7.007
6.990
6.974
6.803
6.789
6.775
6.063
5.524
5.511
4.409
4.099
4.085
4.071
4.064
4.050
4.035
3.907
3.893
3.879
3.872
3.858
3.843
1.684
1.080
1.066
1.052
0.000
4p
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 ppm
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.945
2.069
1.124
2.221
0.882
4.260
2.233
1.007
0.923
0.938
0.956
2.062
3.000
194.512
170.934
168.624
163.756
161.769
140.185
135.996
132.882
132.828
132.543
130.066
129.651
129.294
128.803
128.491
128.309
126.747
125.033
117.889
115.501
115.329
77.254
77.000
76.746
61.943
53.529
13.992
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


9.082
7.692
7.677
7.583
7.569
7.554
7.391
7.376
7.361
7.280
7.264
7.251
7.236
7.174
7.162
7.148
7.133
6.808
6.794
6.780
6.043
5.612
5.519
5.506
4.399
4.097
4.083
4.068
4.062
4.048
4.033
3.908
3.894
3.880
3.874
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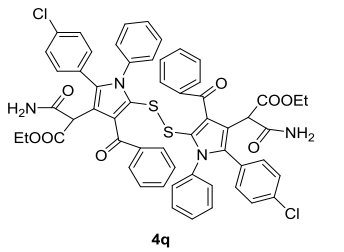
3.449
2.882
2.858
1.731
1.079
1.064
1.050
0.071
-0.001


Cl
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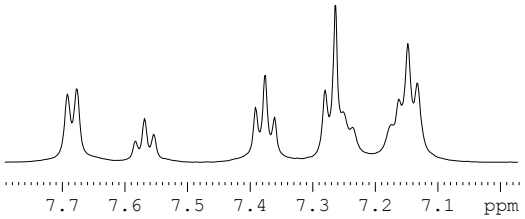
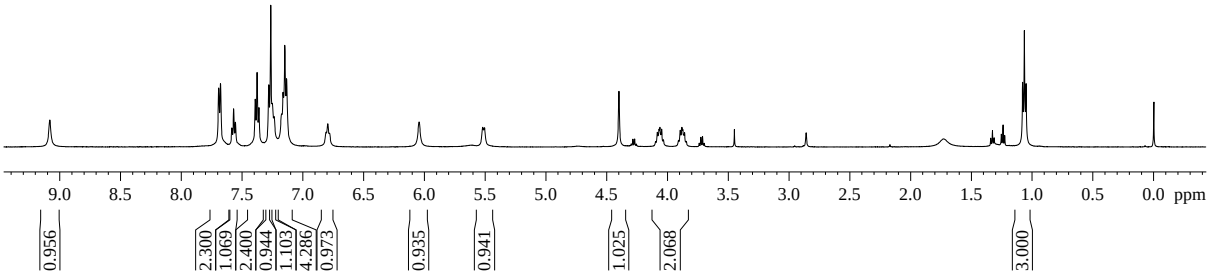
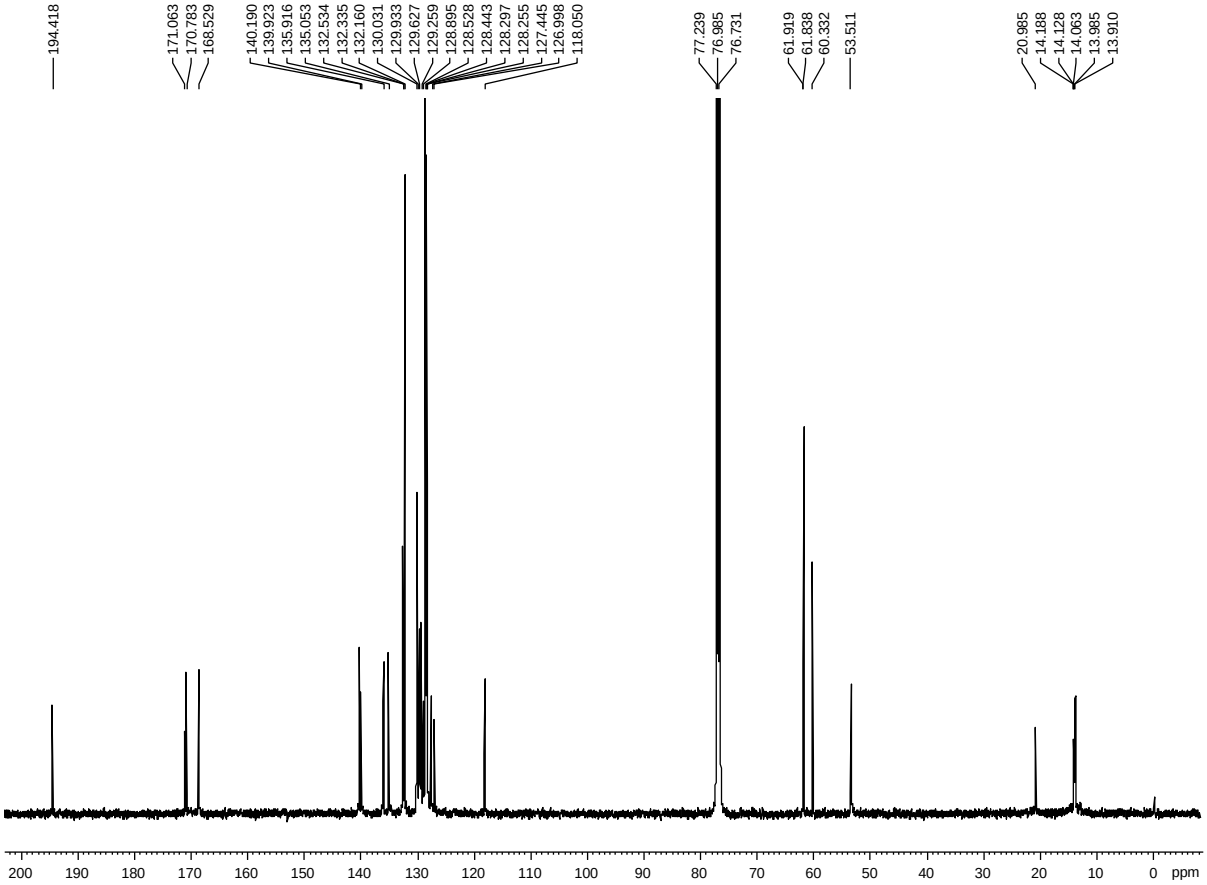
O
H2N
O
EtOOC
S
S
O
COOEt
NH2
O
N
O
Cl

4q


7.7
7.6
7.5
7.4
7.3
7.2
7.1
ppm


9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.956
2.300
1.069
2.400
0.944
1.103
4.286
0.973
0.935
0.941
1.025
2.068
3.000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171.063
170.783
168.529
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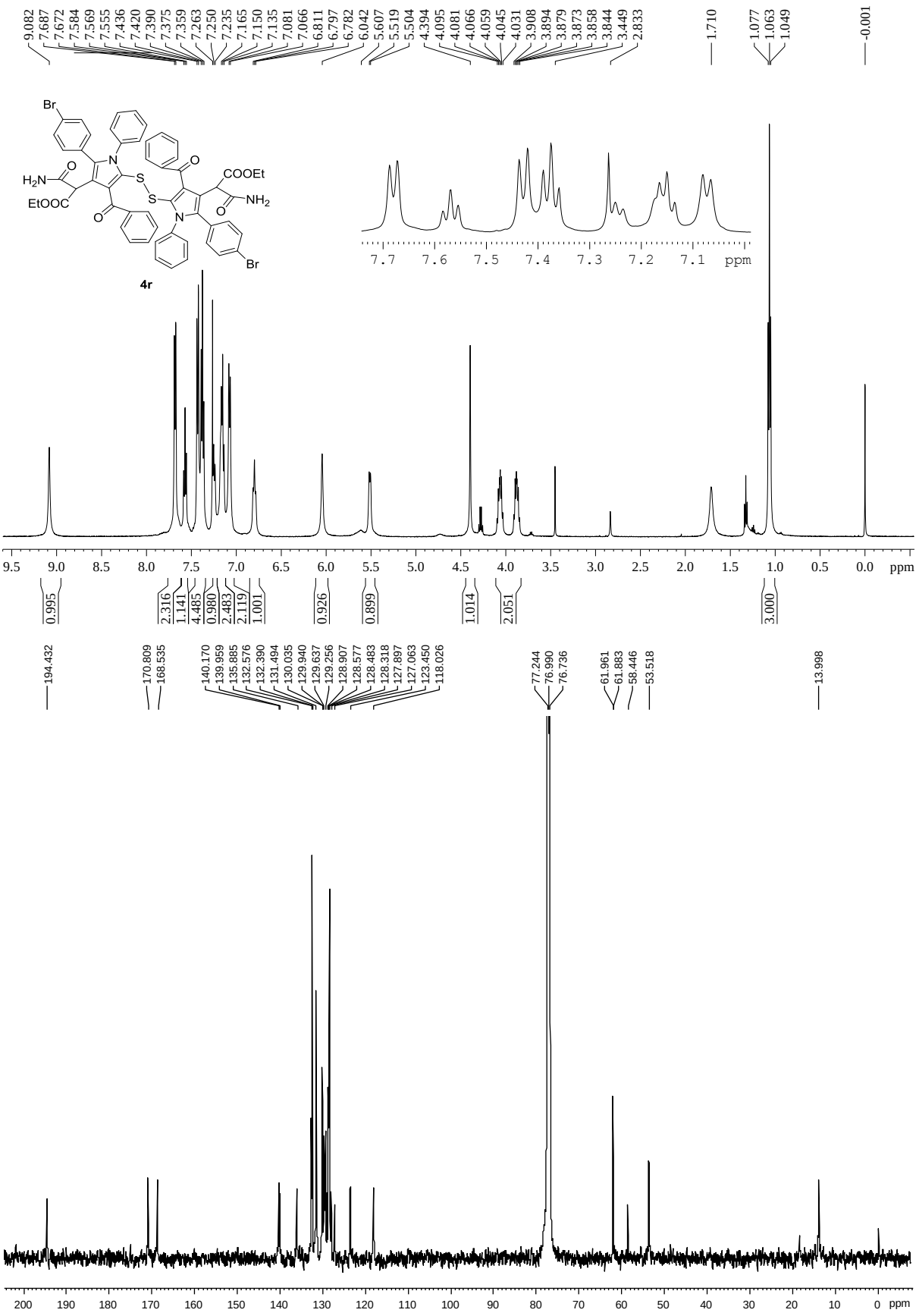
139.923
135.916
135.053
132.534
132.335
132.160
130.031
129.933
129.627
129.259
128.895
128.528
128.443
128.297
128.255
127.445
126.998
118.050
77.239
76.985
76.731
61.919
61.838
60.332
53.511
20.985
14.188
14.128
14.063
13.985
13.910
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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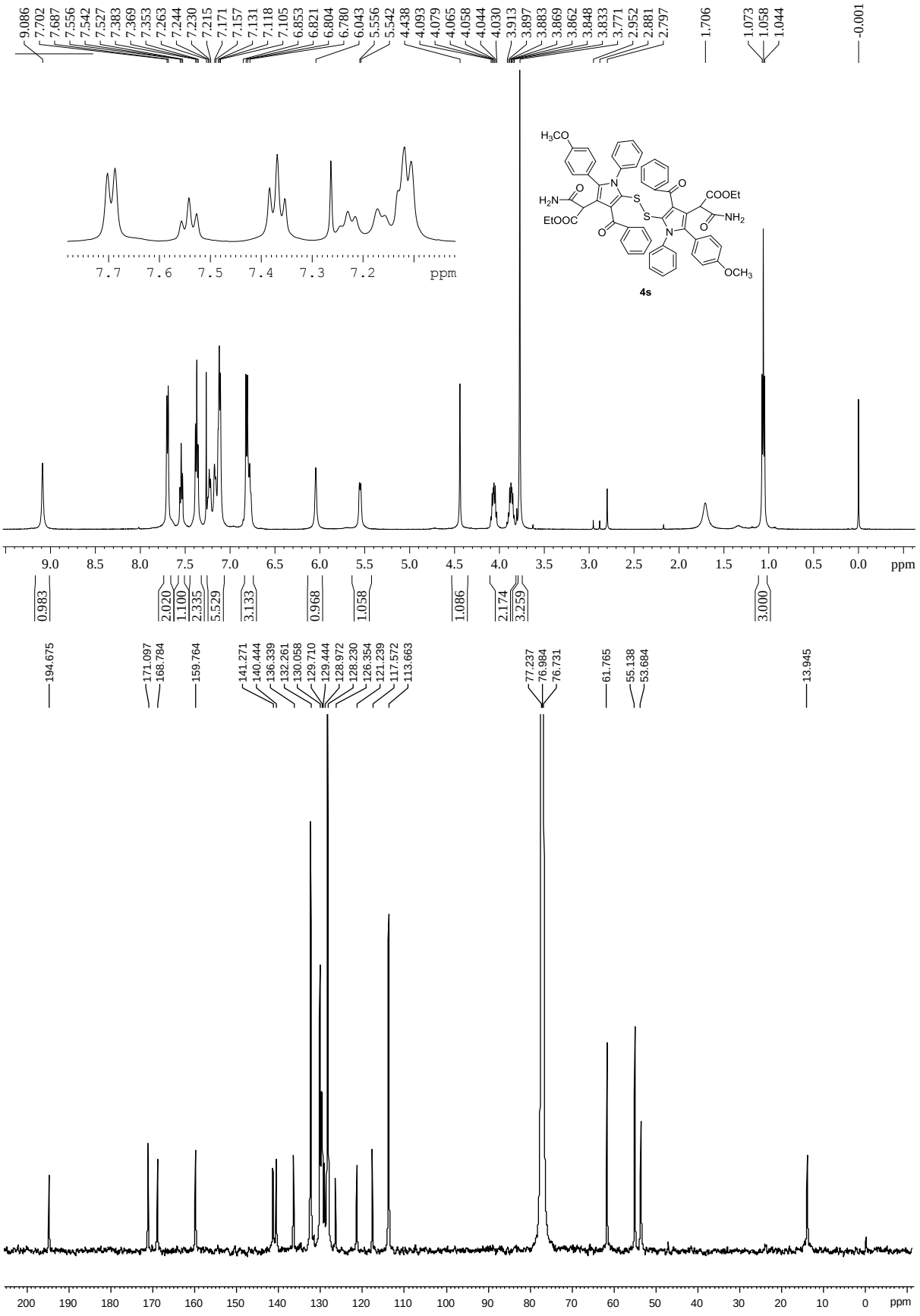
7.672
7.584
7.569
7.555
7.436
7.420
7.390
7.375
7.359
7.263
7.250
7.235
7.165
7.150
7.135
7.081
7.066
6.811
6.797
6.782
6.042
5.607
5.519
5.504
4.394
4.095
4.081
4.066
4.059
4.045
4.031
3.908
3.894
3.879
3.873
3.858
3.844
3.449
2.833
1.710
1.077
1.063
1.049
-0.001
Br
H2N
O
EtOOC
N
S
S
COOEt
NH2
O
O
O
N
Br
4r
7.7 7.6 7.5 7.4 7.3 7.2 7.1 ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.995
2.316
1.141
4.485
0.980
2.483
2.119
1.001
0.926
0.899
1.014
2.051
3.000
194.432
170.809
168.535
140.170
139.959
135.885
132.576
132.390
131.494
130.035
129.940
129.637
129.256
128.907
128.577
128.483
128.318
127.897
127.063
123.450
118.026
77.244
76.990
76.736
61.961
61.883
58.446
53.518
13.998
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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7.687
7.556
7.542
7.527
7.383
7.369
7.353
7.263
7.244
7.230
7.215
7.171
7.157
7.131
7.118
7.105
6.853
6.821
6.804
6.780
6.043
5.556
5.542
4.438
4.093
4.079
4.065
4.058
4.044
4.030
3.913
3.897
3.883
3.869
3.862
3.848
3.833
3.771
2.952
2.881
2.797
1.706
1.073
1.058
1.044
-0.001
7.7 7.6 7.5 7.4 7.3 7.2 ppm
H3CO
H2N
EtOOC
COOEt
NH2
OCH3
4s
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.983
2.020
1.100
2.335
5.529
3.133
0.968
1.058
1.086
2.174
3.259
3.000
194.675
171.097
168.784
159.764
141.271
140.444
136.339
132.261
130.058
129.710
129.444
128.972
128.230
126.354
121.239
117.572
113.663
77.237
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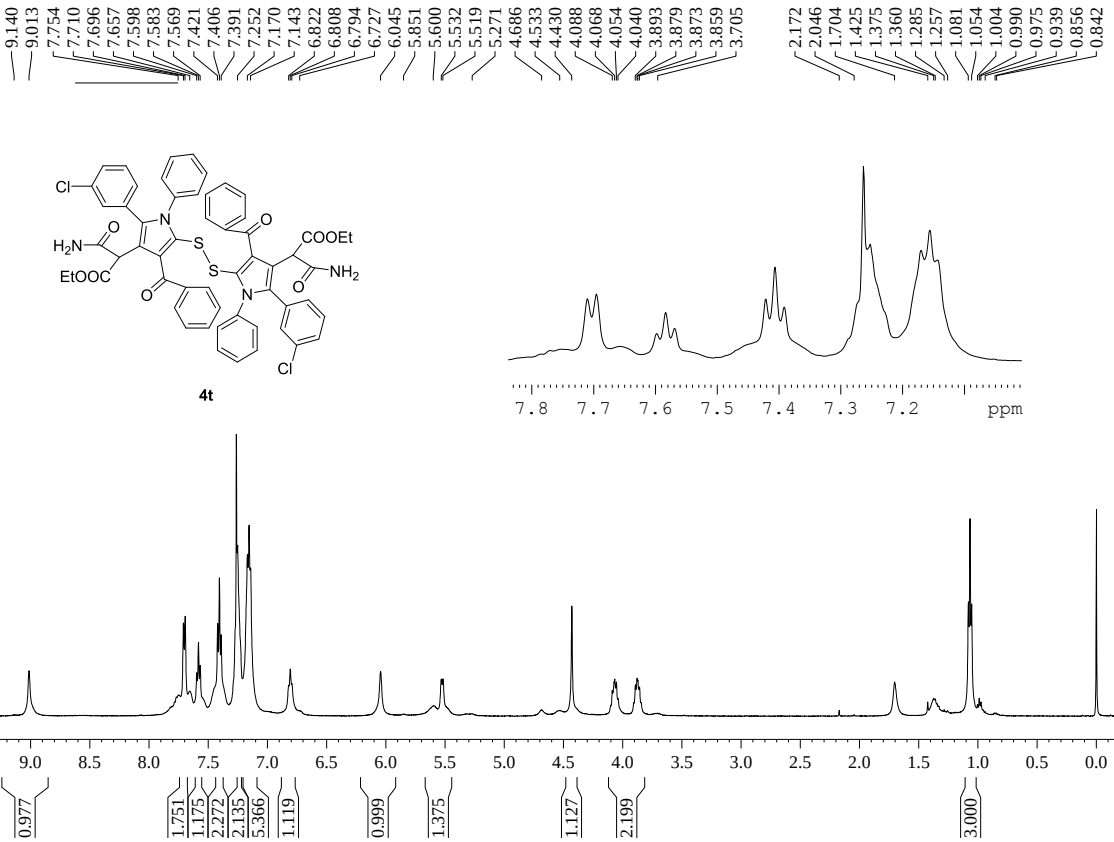
61.765
55.138
53.684
13.945
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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9.013
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7.696
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7.598
7.583
7.569
7.421
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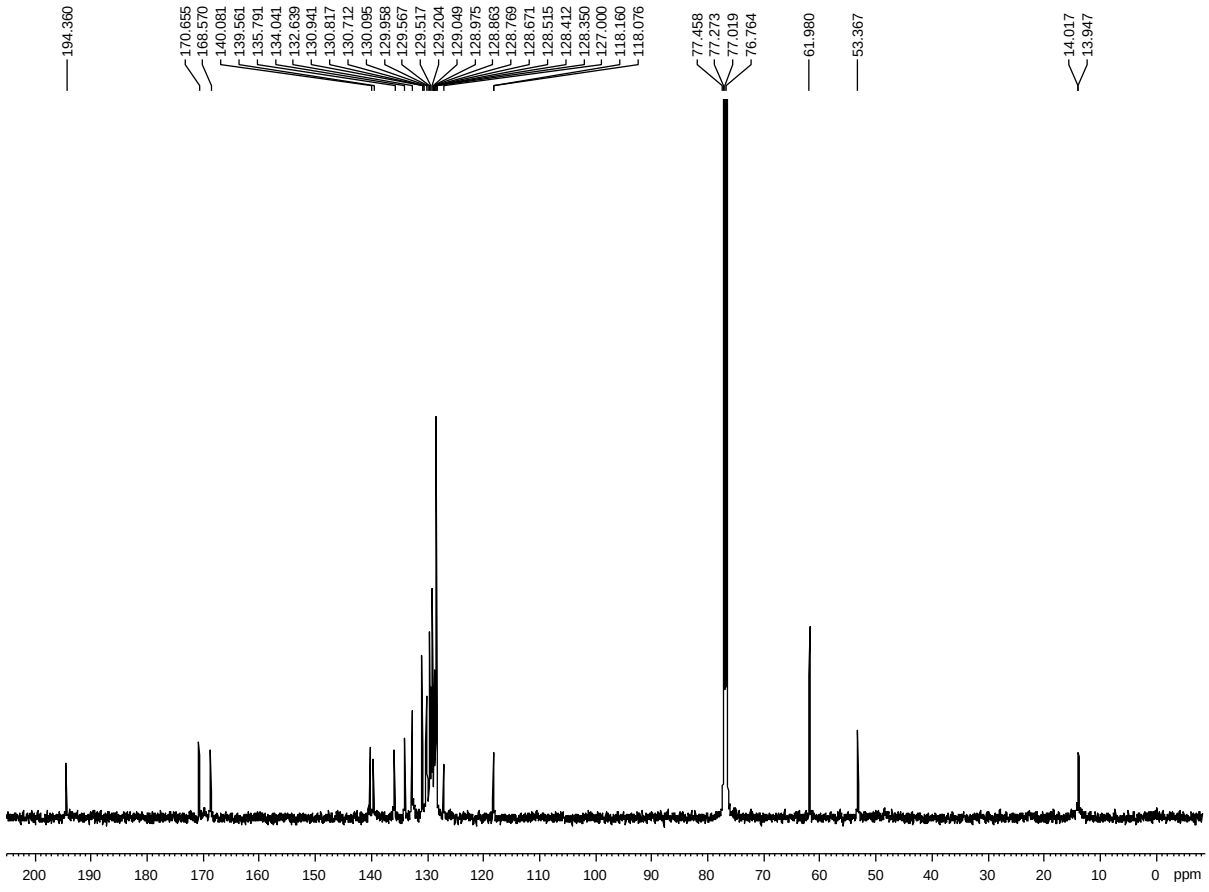
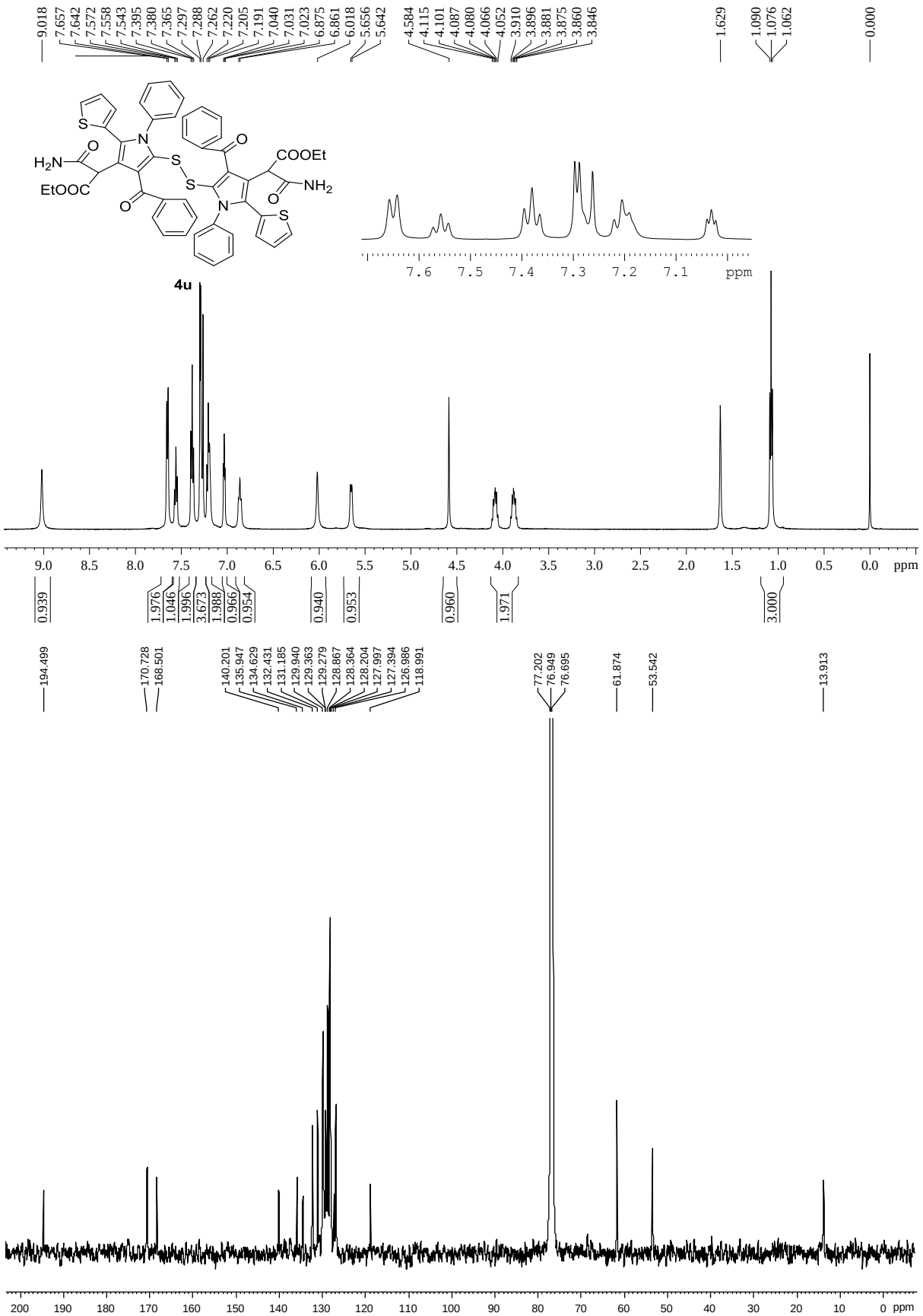
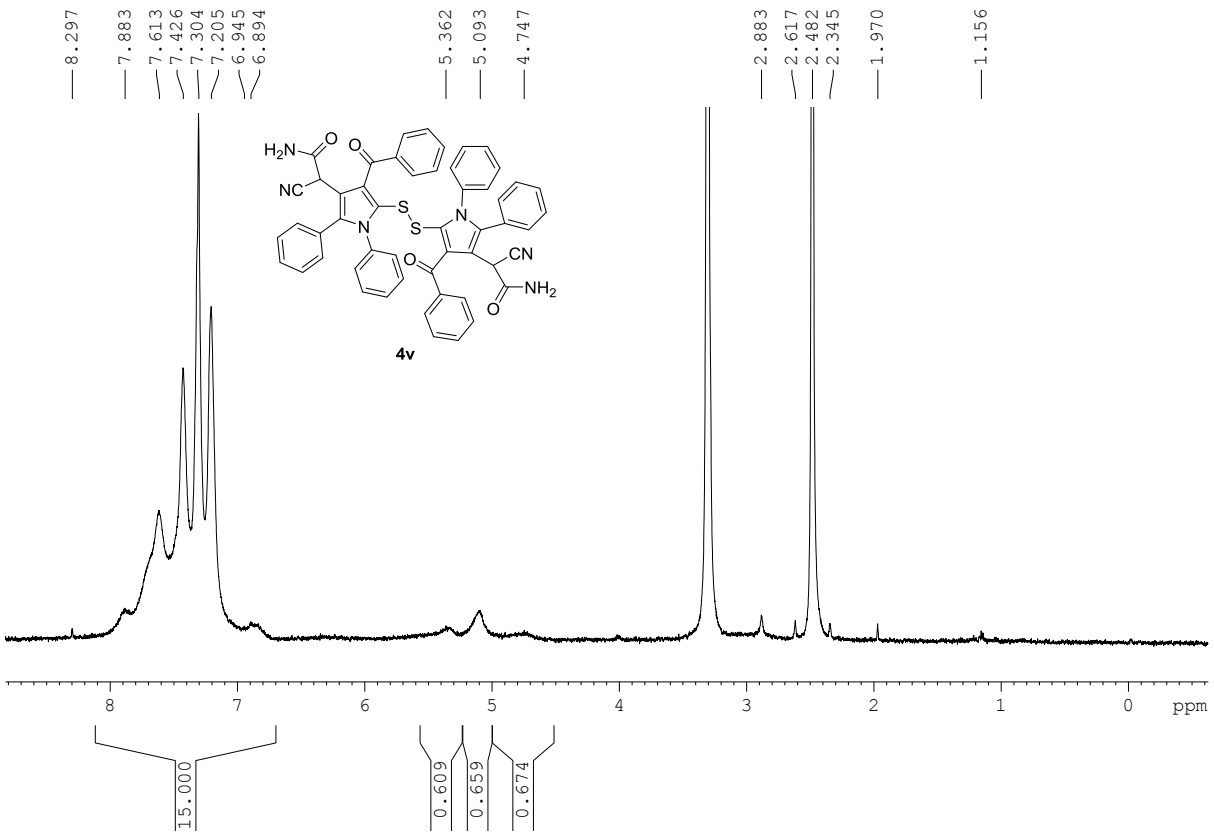
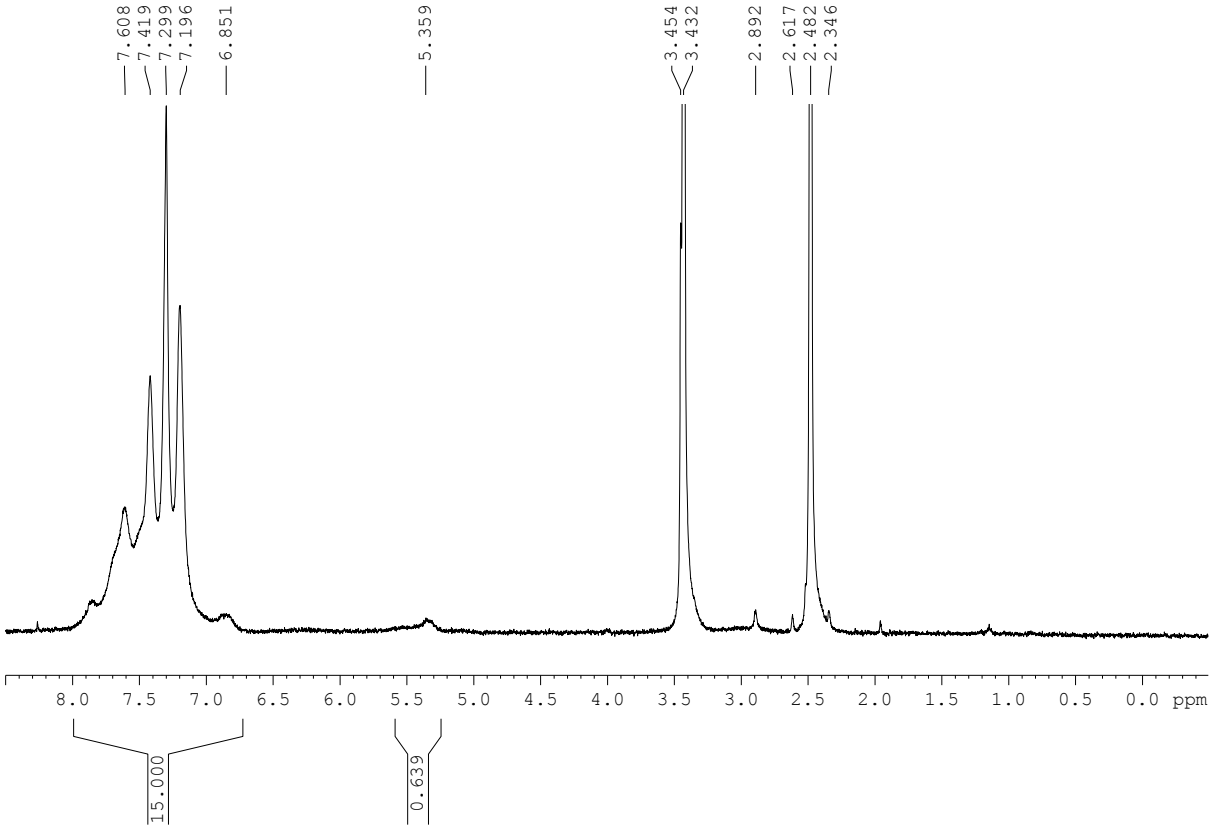
7.391
7.252
7.170
7.143
6.822
6.808
6.794
6.727
6.045
5.851
5.600
5.532
5.519
5.271
4.686
4.533
4.430
4.088
4.068
4.054
4.040
3.893
3.879
3.873
3.859
3.705
2.172
2.046
1.704
1.425
1.375
1.360
1.285
1.257
1.081
1.054
1.004
0.990
0.975
0.939
0.856
0.842
Cl
N
O
S
S
O
COOEt
H_2N
EtOOC
O
N
O
NH_2
Cl
4t
7.8 7.7 7.6 7.5 7.4 7.3 7.2 ppm
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.977
1.751
1.175
2.272
2.135
5.366
1.119
0.999
1.375
1.127
2.199
3.000

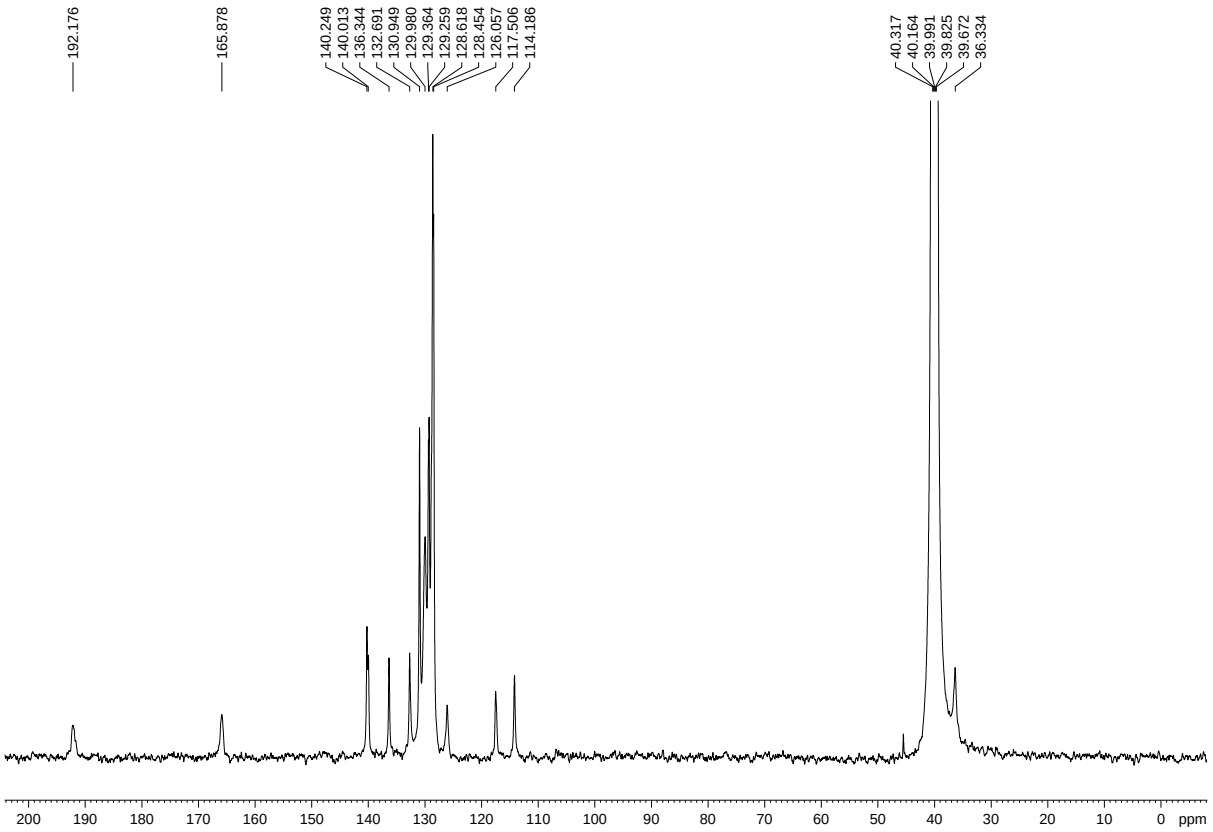

194.360
170.655
168.570
140.081
139.561
135.791
134.041
132.639
130.941
130.817
130.712
130.095
129.958
129.567
129.517
129.204
129.049
128.975
128.863
128.769
128.671
128.515
128.412
128.350
127.000
118.160
118.076
77.458
77.273
77.019
76.764
61.980
53.367
14.017
13.947
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

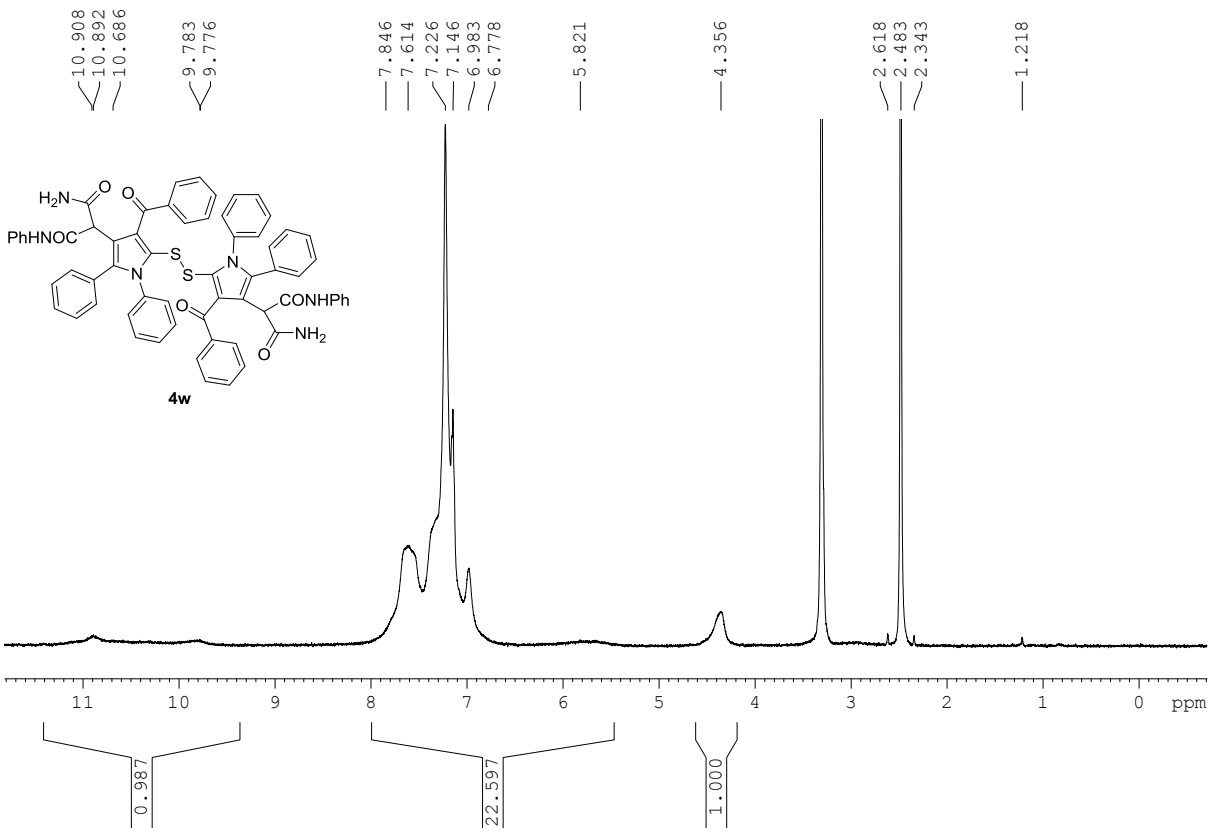

9.018
7.657
7.642
7.572
7.558
7.543
7.395
7.380
7.365
7.297
7.288
7.262
7.220
7.205
7.191
7.040
7.031
7.023
6.875
6.861
6.018
5.656
5.642
4.584
4.115
4.101
4.087
4.080
4.066
4.052
3.910
3.896
3.881
3.875
3.860
3.846
1.629
1.090
1.076
1.062
0.000
4u
7.6 7.5 7.4 7.3 7.2 7.1 ppm
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.939
1.976
1.046
1.996
3.673
1.988
0.966
0.954
0.940
0.953
0.960
1.971
3.000
194.499
170.728
168.501
140.201
135.947
134.629
132.431
131.185
129.940
129.363
129.279
128.867
128.364
128.204
127.997
127.394
126.986
118.991
77.202
76.949
76.695
61.874
53.542
13.913
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



4v (exchanged with D_2O)



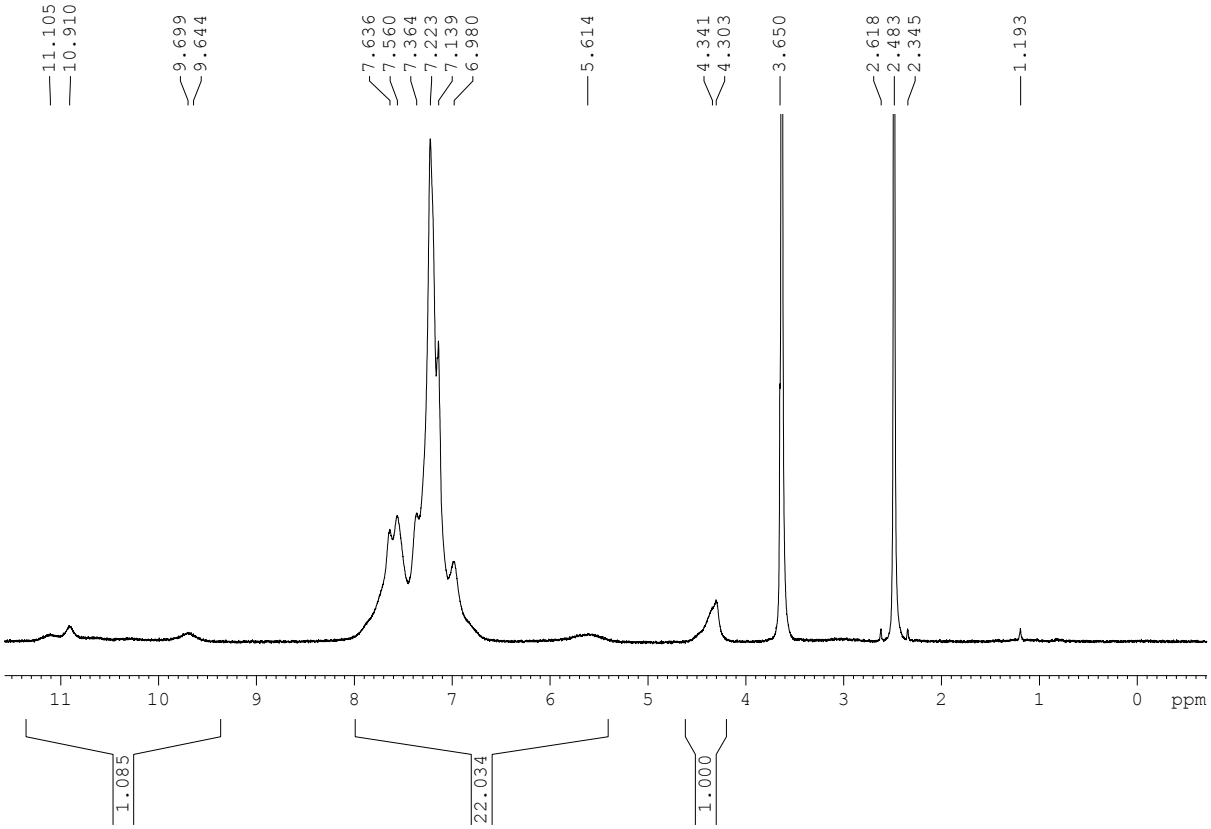

192.176
165.878
140.249
140.013
136.344
132.691
130.949
129.980
129.364
129.259
128.618
128.454
126.057
117.506
114.186
40.317
40.164
39.991
39.825
39.672
36.334
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

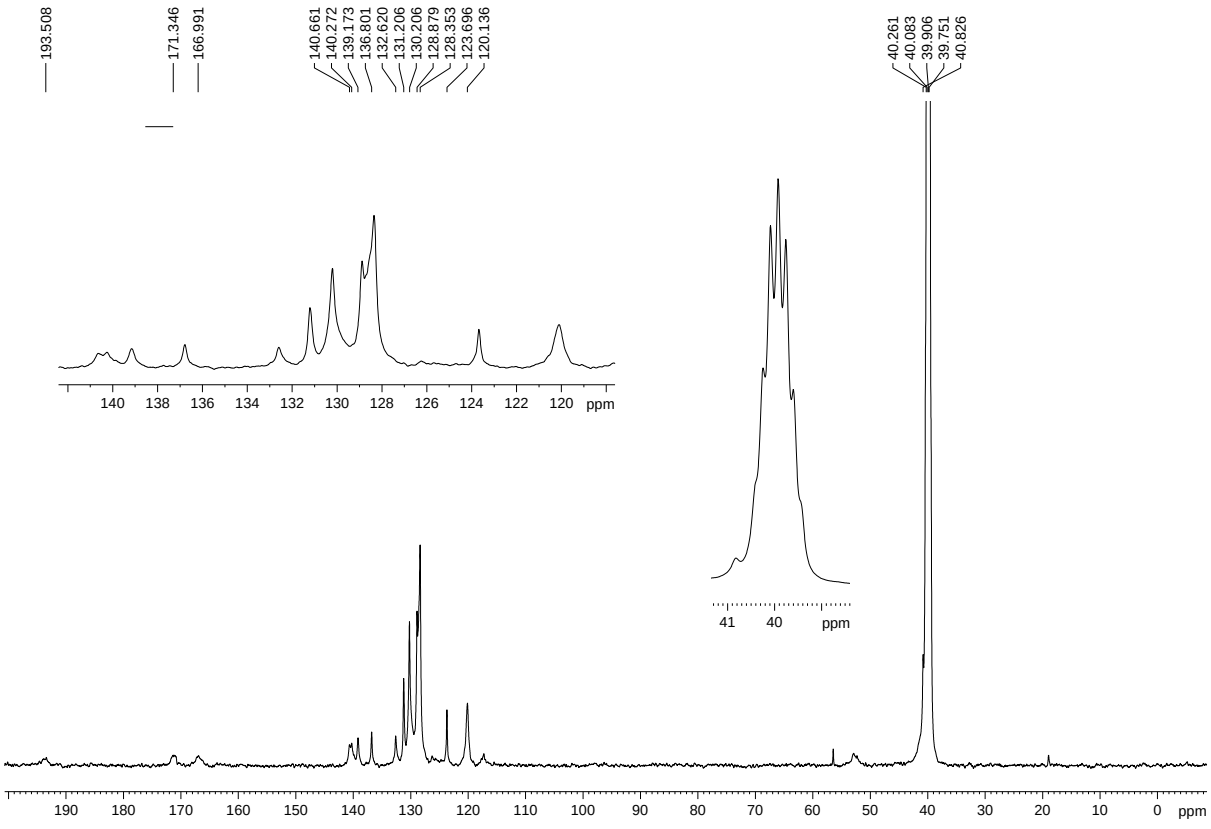

10.908
10.892
10.686
9.783
9.776
7.846
7.614
7.226
7.146
6.983
6.778
5.821
4.356
2.618
2.483
2.343
1.218
11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.987
22.597
1.000

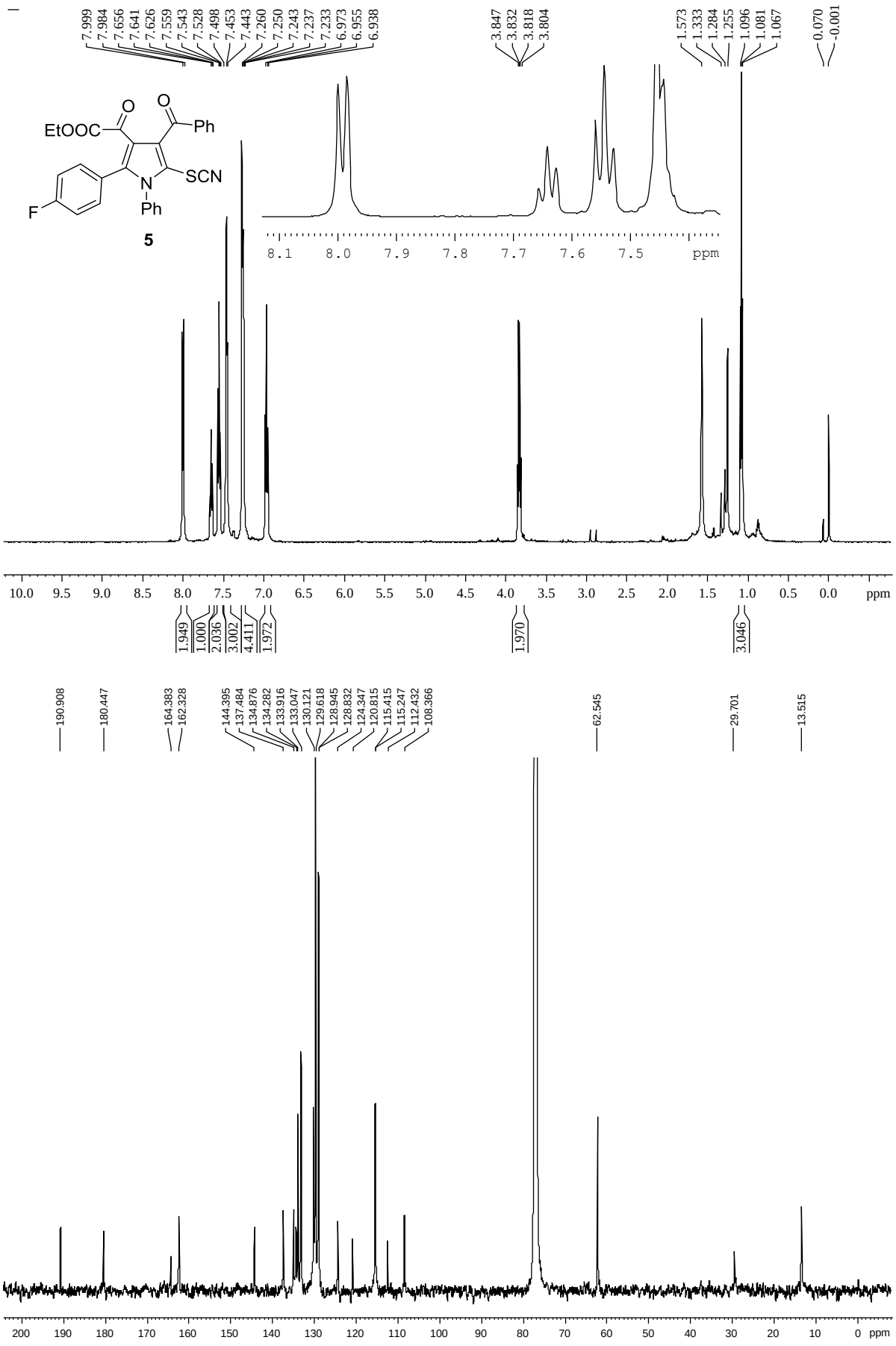
H2N
O
O
PhHNOC
S
S
N
N
CONHPh
O
NH2
O

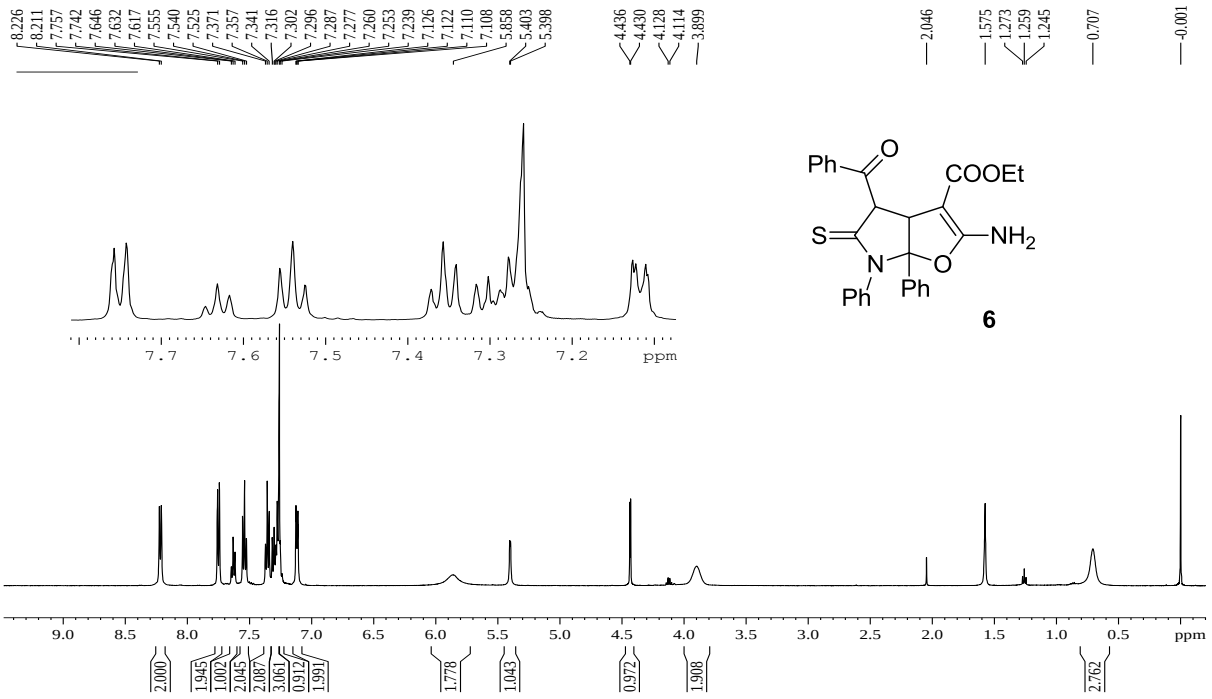
4w

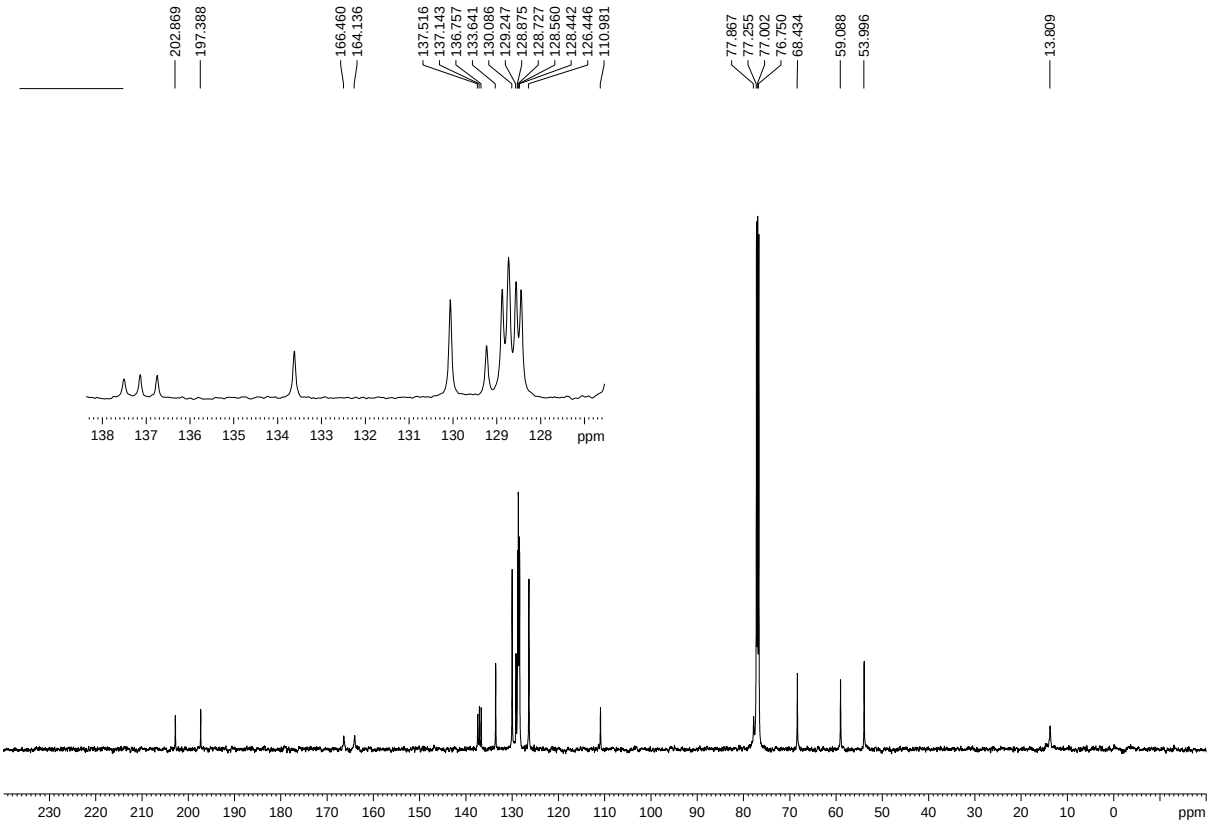
4w (exchanged with D_2O)






7.999
7.984
7.656
7.641
7.626
7.559
7.543
7.528
7.498
7.453
7.443
7.260
7.250
7.243
7.237
7.233
6.973
6.955
6.938
3.847
3.832
3.818
3.804
1.573
1.333
1.284
1.255
1.096
1.081
1.067
0.070
-0.001
EtOOC
O
O
Ph
SCN
N
Ph
F
5
8.1
8.0
7.9
7.8
7.7
7.6
7.5
ppm
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.949
1.000
2.036
3.002
4.411
1.972
1.970
3.046
190.908
180.447
164.383
162.328
144.395
137.484
134.876
134.282
133.916
133.047
130.121
129.618
128.945
128.832
124.347
120.815
115.415
115.247
112.432
108.366
62.545
29.701
13.515
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


8.226
8.211
7.757
7.742
7.646
7.632
7.617
7.555
7.540
7.525
7.371
7.357
7.341
7.316
7.302
7.296
7.287
7.277
7.260
7.253
7.239
7.126
7.122
7.110
7.108
5.858
5.403
5.398
4.436
4.430
4.128
4.114
3.899
2.046
1.575
1.273
1.259
1.245
0.707
-0.001
Ph
O
COOEt
S
NH2
N
O
Ph
Ph
6
7.7
7.6
7.5
7.4
7.3
7.2
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.000
1.945
1.002
2.045
2.087
3.061
0.912
1.991
1.778
1.043
0.972
1.908
2.762


202.869
197.388
166.460
164.136
137.516
137.143
136.757
133.641
130.086
129.247
128.875
128.727
128.560
128.442
126.446
110.981
77.867
77.255
77.002
76.750
68.434
59.088
53.996
13.809
138
137
136
135
134
133
132
131
130
129
128
ppm
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm