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SUPPLEMENTARY MATERIAL TO

Synthesis and *in vitro* study of redox properties of pyrrole and halogenated pyrrole derivatives

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Synthetic procedures

5H-pyrrolo[2,1-a]isoindol-5-one (2) The mixture of (2-iodophenyl)(1H-pyrrol-1-yl)methanone **1** (1 mmol, 1 eq), K_3PO_4 (1.5 mmol, 1.5 eq), $Pd(OAc)_2$ (0,1 mmol, 0,1 eq) and PPh_3 (0,2 mmol, 0,2 eq) in acetonitrile (5 ml) was heated in a nitrogen atmosphere at reflux for 16 h. After completion of the reaction, the mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography to afford the product. Flash chromatography (SiO2, 9:1 v/v petroleum ether–diethyl ether) afforded the product (281.2 mg, 81%) as a yellow solid, mp 62–63 °C.

^{1}H NMR (400 MHz, CDCl3) δ 7.55 (d, J = 7.2 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.19 (d, J = 7.2 Hz, 1H), 7.09 (t, J = 7.0 Hz, 1H), 6.93 (s, 1H), 6.10 (d, J = 12.7 Hz, 2H);

^{13}C NMR (101 MHz, CDCl3) δ 163.0, 136.4, 135.6, 134.4, 132.1, 127.1, 125.8, 119.5, 117.1, 116.6, 107.3;

The spectral data are consistent with those reported in the literature.[24]

1,2,3-tribromo-5H-pyrrolo[2,1-a]isoindol-5-one (3) 5H-pyrrolo[2,1-a]isoindol-5-one (2) (0.5 mmol, 1 eq) was dissolved in CCl_4 (10 mL) and bromine (4 mmol, 8 eq) was added dropwise. After 16 hours at room temperature, the reaction mixture was diluted with CH_2Cl_2 (15 mL) and the organic solvent was washed with 10% $Na_2S_2O_3$ (20 mL) and brine (20 mL). After drying with anhydrous Na_2SO_4, the organic solvent was evaporated to obtain the product (195.3 mg, 97%) as an orange solid, mp 207-208 °C.

^{1}H NMR (400 MHz, CDCl3) δ 7.70 (d, J = 7.4 Hz, 1H), 7.57-7.51 (m, 2H), 7.31-7.26 (m, 1H).

^{13}C NMR (101 MHz, CDCl3) δ 160.7, 135.3, 134.1, 133.6, 129.5, 128.4, 126.7, 119.6, 111.3, 102.1, 100.2.

*General procedure for the synthesis of the amides **M1-M6** and **M10-M15***

Compound **2** or **3** (0.1 mmol, 1 eq) was dissolved in amine (0.5 mL) and heated at 100° C for 5 minutes. After cooling, the excess amine was removed under reduced pressure. The crude mixture was dissolved in CH_2Cl_2 (15 mL), washed with 2M HCl (10 mL) and brine (10 mL). After drying with anhydrous Na_2SO_4, the organic solvent was evaporated under reduced pressure to obtain the product.

*General procedure for the synthesis of the amides **M7-M8***

Compound **2** or **3** (0.1 mmol, 1 eq) was dissolved in ethylendiamine (0.5 mL) and heated at 100° C for 5 minutes. After cooling, the excess amine was removed under reduced pressure. To a solution of the crude mixture in THF (10 mL), vanillin (0.1 mmol, 1 eq) and $MgSO_4$ (0.5 mmol, 5 eq) were added and the mixture was stirred overnight. After filtration, the solvent was evaporated and the crude mixture was dissolved in MeOH (5 mL) and $NaBH_4$ (0.2 mmol, 2 eq) was added. The mixture was stirred for 2 hours at room temperature and, after evaporation of the solvent under reduced pressure, subjected directly to flash chromatography to obtain the product.

4-((benzylamino)methyl)-2-methoxyphenol (9) To a solution of benzylamine (0.1 mmol, 1 eq) in THF (10 mL), vanillin (0.1 mmol, 1 eq) and $MgSO_4$ (0.5 mmol, 5 eq) were added and the mixture was stirred overnight. After filtration, the solvent was evaporated and the crude mixture was dissolved in MeOH (5 mL) and $NaBH_4$ (0.2 mmol, 2 eq) was added. The mixture was stirred for 2 hours at room temperature and, after evaporation of the solvent under reduced pressure, subjected directly to flash chromatography. Flash chromatography (SiO2, EtOAc) afforded the product (133.7 mg, 55%) as a white, amorphous solid.

^{1}H NMR (400 MHz, CDCl3) δ 7.33 (d, J = 4.4 Hz, 4H), 7.25 (t, J = 4.2 Hz, 1H), 6.88 (s, 1H), 6.83 (d, J = 8.0 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 3.84 (s, 3H), 3.80 (s, 2H), 3.73 (s, 2H).

^{13}C NMR (101 MHz, CDCl3) δ 146.7, 144.8, 140.2, 132.0, 128.4, 128.2, 126.9, 121.0, 114.3, 110.9, 55.8, 53.1, 53.0.

The spectral data are consistent with those reported in the literature.[25]

Morpholin-4-yl -[2-(1H-pyrrol-2-yl)-phenyl]-methanone (M1)

Compound **M1** (17.9 mg, 70%) was synthesized following the general procedure, as a beige solid, mp: 162-163°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.44 – 7.36 (m, 1H), 7.30 – 7.21 (m, 2H), 6.85 (d, *J* = 1.4 Hz, 1H), 6.41 (s, 1H), 6.27 (dd, *J* = 5.9, 2.7 Hz, 1H), 4.05 (dd, *J* = 12.9, 2.3 Hz, 1H), 3.76 – 3.69 (m, 1H), 3.50 – 3.36 (m, 3H), 3.14 – 3.06 (m, 1H), 2.99 – 2.91 (m, 1H), 2.81-2-76 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 132.6, 130.4, 130.4, 129.5, 128.2, 126.6, 126.5, 119.4, 109.6, 108.4, 66.6, 66.6, 47.6, 42.4.

The spectral data are consistent with those reported in the literature.[23]

N-Allyl-2-(1H-pyrrol-2-yl)-benzamide (M2)

Compound M2 (16.0 mg, 71%) was synthesized following the general procedure, as a brown, amorphous solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.14 (s, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.29 – 7.21 (m, 1H), 6.85 (d, *J* = 1.5 Hz, 1H), 6.48 (s, 1H), 6.26 (d, *J* = 2.6 Hz, 1H), 5.91 (s, 1H), 5.87 – 5.75 (m, 1H), 5.21 – 5.08 (m, 2H), 4.00 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 133.4, 133.3, 131.3, 130.7, 130.4, 129.0, 127.9, 126.0, 119.4, 117.0, 109.2, 108.6, 42.6.

The spectral data are consistent with those reported in the literature.[23]

Pyrrolidin-1-yl-[2-(1H-pyrrol-2-yl)-phenyl]-methanone (M3)

Compound **M3** (19.7 mg, 82%) was synthesized following the general procedure as a light-brown solid, mp: 146-147°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.42 – 7.34 (m, 1H), 7.29 – 7.20 (m, 2H), 6.82 (d, *J* = 1.5 Hz, 1H), 6.46 (s, 1H), 6.24 (d, *J* = 3.2 Hz, 1H), 3.59 (t, *J* = 6.6 Hz, 2H), 3.02 (bs, 2H), 1.85 (dd, *J* = 13.7, 6.8 Hz, 2H), 1.71 (bs, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 133.8, 130.8, 130.0, 129.4, 128.4, 126.7, 126.1, 119.4, 109.1, 107.8, 48.6, 45.8, 25.8, 24.5.

The spectral data are consistent with those reported in the literature.[23]

Morpholino(2-(3,4,5-tribromo-1H-pyrrol-2-yl)phenyl)methanone (M4)

Compound **M4** (40.2 mg, 82%) was synthesized following the general procedure as a beige solid, mp: 221-222°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 7.3 Hz, 1H), 3.96 (d, *J* = 13.2 Hz, 1H), 3.75 (dd, *J* = 9.5, 5.9 Hz, 1H), 3.57 – 3.49 (m, 1H), 3.48 – 3.40 (m, 1H), 3.38 – 3.29 (m, 1H), 3.16 – 3.08 (m, 1H), 3.01 – 2.90 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 134.6, 130.5, 129.3, 129.1, 128.6, 127.2, 126.6, 102.8, 100.9, 98.9, 66.7, 66.7, 47.5, 42.3.

HRMS (ESI) m/z calcd. for $[C_{15}H_{13}Br_3N_2O_2\text{-}H]^-$ 488.84544; found, 488.84533.

N-allyl-2-(3,4,5-tribromo-1H-pyrrol-2-yl)benzamide (M5)

Compound **M5** (38.2 mg, 83%) was synthesized following the general procedure as a light-brown solid, mp: 171-172°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.00 (bs, 1H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 8.0 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 1H), 5.83 – 5.65 (m, 2H), 5.11 (dd, *J* = 18.3, 13.7 Hz, 2H), 3.87 (t, *J* = 5.8 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 135.2, 132.9, 131.3, 130.3, 129.1, 128.4, 128.3, 128.1, 117.4, 102.5, 101.1, 98.8, 42.6.

HRMS (ESI) m/z calcd. for $[C_{14}H_{11}Br_3N_2O$ -H]$^-$ 458.83487; found, 458.83470.

Pyrrolidin-1-yl(2-(3,4,5-tribromo-1H-pyrrol-2-yl)phenyl)methanone (M6)

Compound **M6** (45.5mg, 96%) was synthesized following the general procedure as a light-brown solid, mp: 161-162°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.41 (s, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.3 Hz, 1H), 7.30 (d, *J* = 7.1 Hz, 1H), 3.54 (t, *J* = 7.0 Hz, 2H), 3.07 (s, 2H), 1.88 (dd, *J* = 13.8, 6.9 Hz, 2H), 1.80 – 1.73 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 136.0, 130.6, 129.2, 129.1, 128.1, 127.1, 126.6, 102.6, 100.7, 98.3, 48.9, 45.9, 25.8, 24.4.

HRMS (ESI) m/z calcd. for $[C_{15}H_{13}Br_3N_2O$ -H]$^-$ 472.85052; found, 472.85027.

N-(2-((4-hydroxy-3-methoxybenzyl)amino)ethyl)-2-(1H-pyrrol-2-yl)benzamide (M7)

Compound **M7** was synthesized following the general procedure. Flash chromatography (SiO2, 1:1 v/v petroleum ether–EtOAc) afforded the product (19.0 mg, 52%) as an orange amorphous solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.37 (s, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.38 (d, *J* = 7.3 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 3H), 6.71 (d, *J* = 8.1 Hz, 1H), 6.51 (s, 1H), 6.45 (s, 1H), 6.23 (s, 1H), 3.75 (s, 3H), 3.67 (s, 2H), 3.45 (d, *J* = 4.8 Hz, 2H), 2.75 (t, *J* = 5.5 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 146.7, 145.0, 133.2, 131.2, 130.6, 130.3, 129.0, 128.1, 126.1, 121.3, 119.4, 114.4, 110.9, 109.2, 108.6, 55.8, 53.2, 47.7, 39.3.

HRMS (ESI) m/z calcd. for $[C_{21}H_{23}N_3O_3$-H]$^-$ 364.16667; found, 364.16636.

N-(2-((4-hydroxy-3-methoxybenzyl)amino)ethyl)-2-(3,4,5-tribromo-1H-pyrrol-2-yl)benzamide (M8)

Compound **M8** was synthesized following the general procedure. Flash chromatography (SiO2, 1:2 v/v petroleum ether–EtOAc) afforded the product (36.5 mg, 61%) as a light-brown solid, mp: 85-86°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.40 (s, 1H), 7.74 (d, J = 7.7 Hz, 0.23H, rotamer a), 7.69 (d, J = 7.7 Hz, 0.77H, rotamer b), 7.47 (dd, *J* = 15.5, 7.6 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 1H), 6.88 – 6.79 (m, 1H), 6.77 (s, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.47 (bs, 0.6H, rotamer b), 6.37 (bs, 0.4H, rotamer a), 3.81 (s, 3H), 3.66 (d, *J* = 5.8 Hz, 2H), 3.42 – 3.32 (m, 2H), 2.74-2.68 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 170.2, 146.6, 146.6, 145.2, 135.4, 131.5, 130.3, 129.7, 129.1, 128.6, 128.4, 128.2, 128.1, 121.6, 118.4, 114.3, 111.3, 100.7, 62.8, 55.9, 53.1, 50.8, 47.5, 47.3, 39.0, 29.7.

HRMS (ESI) m/z calcd. for $[C_{21}H_{20}Br_3N_3O_3$-H]$^-$ 597.89820; found, 597.89785.

N-(prop-2-yn-1-yl)-2-(1H-pyrrol-2-yl)benzamide (M10)

Compound **M10** (16.8 mg, 75%) was synthesized following the general procedure as a brown solid, mp: 91-92°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.05 (s, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.42 (dd, *J* = 9.7, 7.9 Hz, 2H), 7.23 (dd, *J* = 13.9, 6.4 Hz, 1H), 6.85 (s, 1H), 6.47 (s, 1H), 6.26 (d, *J* = 2.8 Hz, 1H), 6.07 (s, 1H), 4.13 (dd, *J* = 5.2, 2.5 Hz, 2H), 2.23 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 132.3, 131.4, 130.7, 130.4, 129.1, 128.1, 126.1, 119.6, 109.3, 108.8, 78.8, 72.1, 29.9.

HRMS (ESI) m/z calcd. for $[C_{14}H_{12}N_2O$ -H]$^-$ 223.08769; found, 223.08765.

N-Benzyl-2-(1H-pyrrol-2-yl)-benzamide (M11)

Compound **M11** (21.0 mg, 76%) was synthesized following the general procedure as a beige solid, mp: 109-110°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.49 – 7.36 (m, 2H), 7.34 – 7.24 (m, 3H), 7.20 (t, *J* = 7.9 Hz, 3H), 6.81 (s, 1H), 6.47 (s, 1H), 6.26 (d, *J* = 2.6 Hz, 1H), 6.13 (s, 1H), 4.54 (d, *J* = 5.7 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 137.4, 133.2, 131.3, 130.6, 130.4, 129.0, 128.8, 127.8, 127.7, 127.7, 126.0, 119.5, 109.2, 108.6, 44.3.

The spectral data are consistent with those reported in the literature.[23]

N-propyl-2-(1H-pyrrol-2-yl)benzamide (M12)

Compound **M12** (16.9 mg, 74%) was synthesized following the general procedure as a beige solid, mp: 109-110°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.21 (s, 1H), 7.61 (d, *J* = 8.3 Hz, 1H), 7.40 (dd, *J* = 7.2, 5.0 Hz, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 1.3 Hz, 1H), 6.47 (s, 1H), 6.26 (dd, *J* = 5.5, 2.7 Hz, 1H), 5.87 (s, 1H), 3.33 (dd, *J* = 13.5, 6.7 Hz, 2H), 1.53 (dd, *J* = 14.6, 7.3 Hz, 2H), 0.90 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 133.6, 131.2, 130.8, 130.2, 128.9, 127.8, 125.8, 119.4, 109.1, 108.4, 41.9, 22.6, 11.3.

HRMS (ESI) m/z calcd. for $[C_{14}H_{16}N_2O$ -H]$^-$ 227.11899; found, 227.11897.

N-(prop-2-yn-1-yl)-2-(3,4,5-tribromo-1H-pyrrol-2-yl)benzamide (M13)

Compound **M13** (40.3 mg, 88%) was synthesized following the general procedure as a beige solid, mp: 179-180°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.79 (s, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 5.93 (s, 1H), 4.06 (dd, *J* = 5.1, 2.4 Hz, 2H), 2.25 (d, *J* = 2.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 134.5, 131.5, 130.6, 128.9, 128.5, 128.4, 128.2, 102.7, 101.2, 99.1, 78.4, 72.3, 30.0.

HRMS (ESI) m/z calcd. for $[C_{14}H_9Br_3N_2O$ H]$^-$ 456.81922; found, 456.81911.

N-benzyl-2-(3,4,5-tribromo-1H-pyrrol-2-yl)benzamide (M14)

Compound **M14** (37.2 mg, 73%) was synthesized following the general procedure as a light-brown solid, mp: 160-161°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.89 (s, 1H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.52 – 7.44 (m, 2H), 7.36 – 7.27 (m, 4H), 7.12 (d, *J* = 7.0 Hz, 2H), 6.04 (s, 1H), 4.44 (d, *J* = 5.6 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 136.9, 135.4, 131.3, 130.2, 129.1, 128.9, 128.4, 128.3, 127.9, 127.8, 127.6, 102.6, 101.0, 98.9, 44.4.

HRMS (ESI) m/z calcd. for $[C_{18}H_{13}Br_3N_2O$ -H]$^-$ 508.85052; found, 508.85041.

N-propyl-2-(3,4,5-tribromo-1H-pyrrol-2-yl)benzamide (M15)

Compound **M15** (40.2 mg, 87%) was synthesized following the general procedure as a brown solid, mp: 147-148°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.28 (s, 1H), 7.65 (d, J = 7.7 Hz, 1H), 7.50 – 7.41 (m, 2H), 7.31 (t, J = 7.6 Hz, 1H), 5.71 (s, 1H), 3.19 (dd, J = 13.4, 6.7 Hz, 2H), 1.40 (dd, J = 14.5, 7.3 Hz, 2H), 0.83 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 135.5, 131.2, 130.1, 129.3, 128.4, 128.2, 128.2, 102.3, 101.0, 98.7, 41.9, 22.6, 11.2.

HRMS (ESI) m/z calcd. for $[C_{14}H_{13}Br_3N_2O - H]^-$ 460.85052; found, 460.85051.

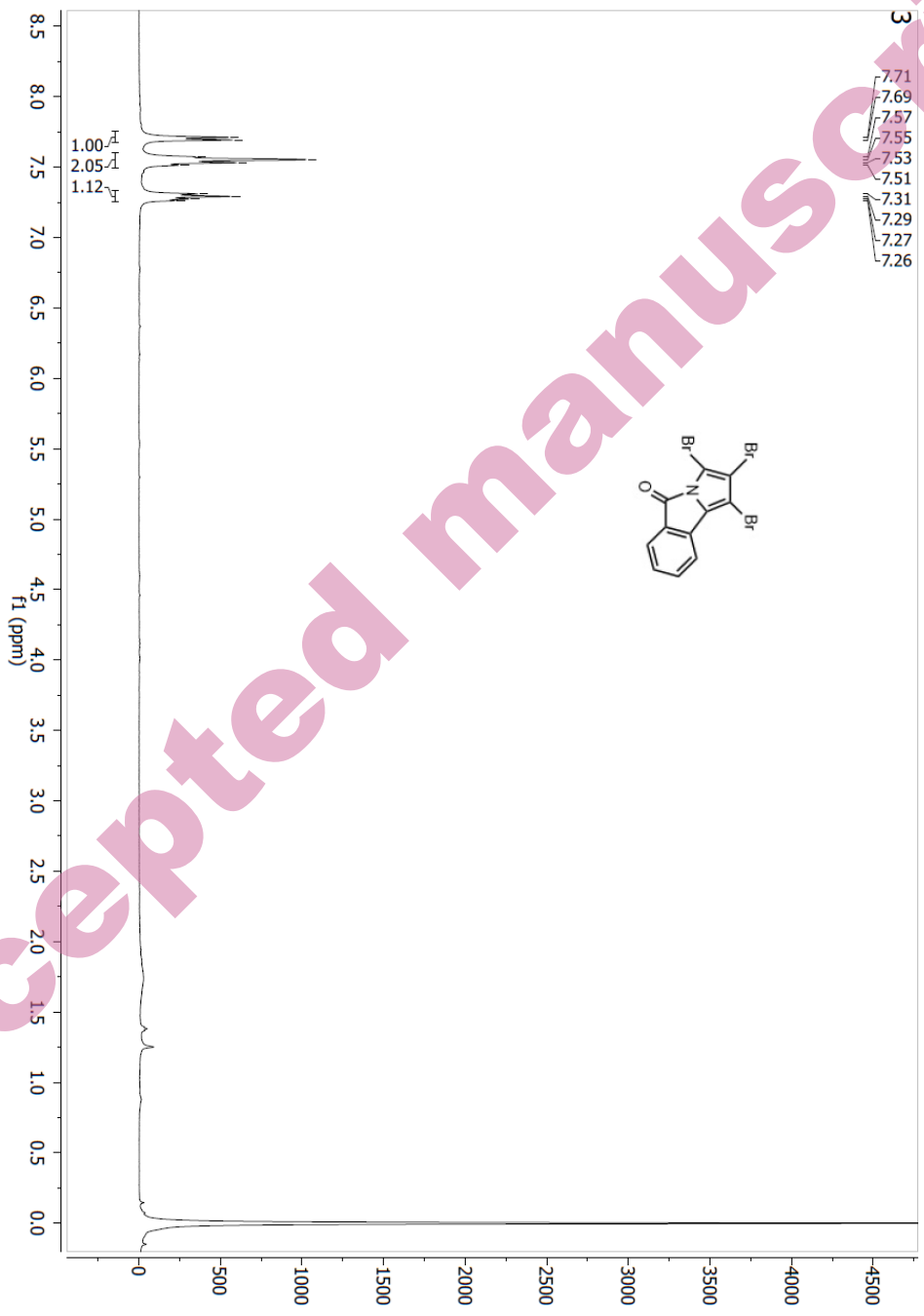

Fig S1. Compound **3** - ^{1}H NMR spectrum (400 MHz, $CDCl_3$)

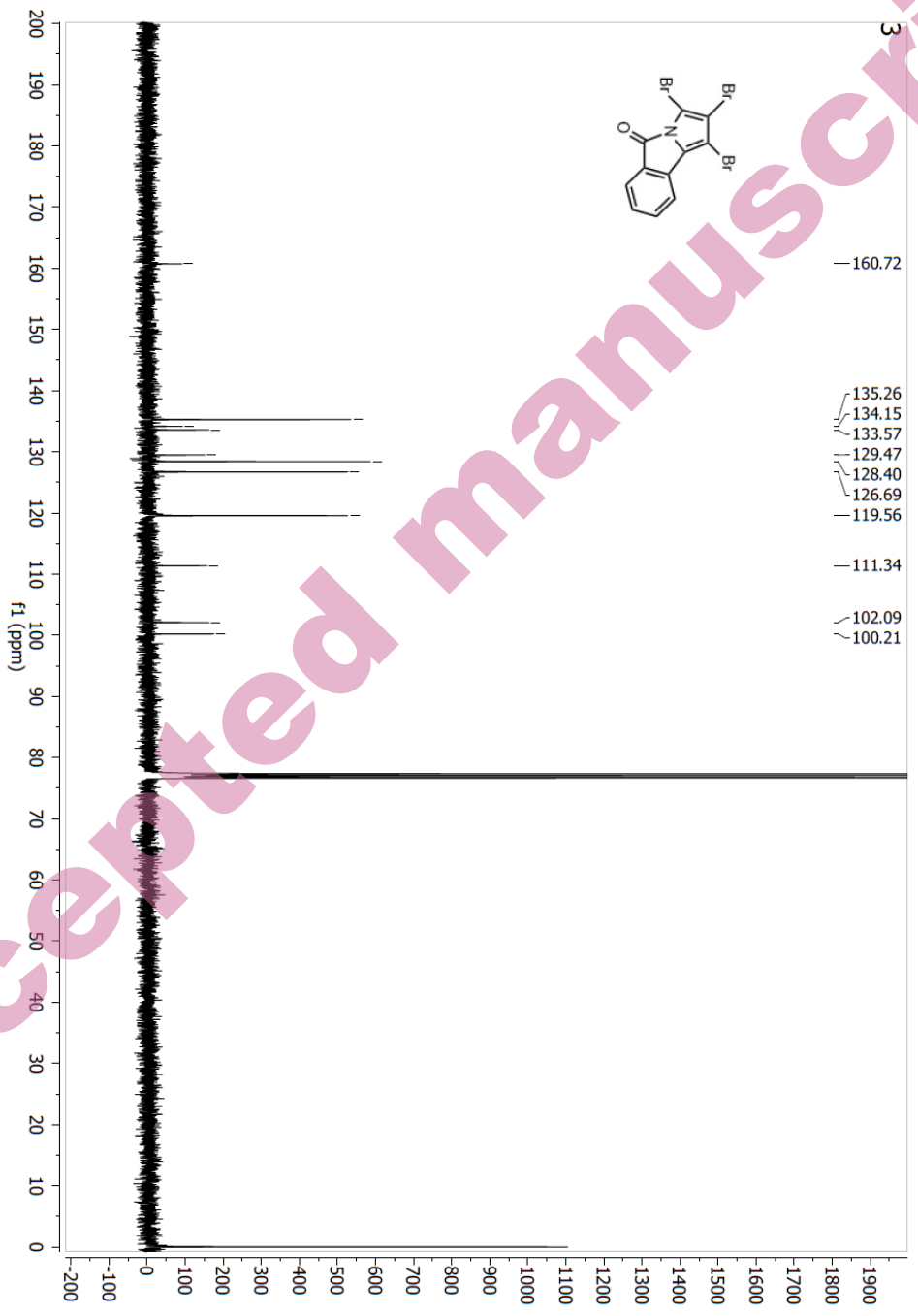

Fig S2. Compound **3** - ^{13}C NMR spectrum (101 MHz, $CDCl_3$)

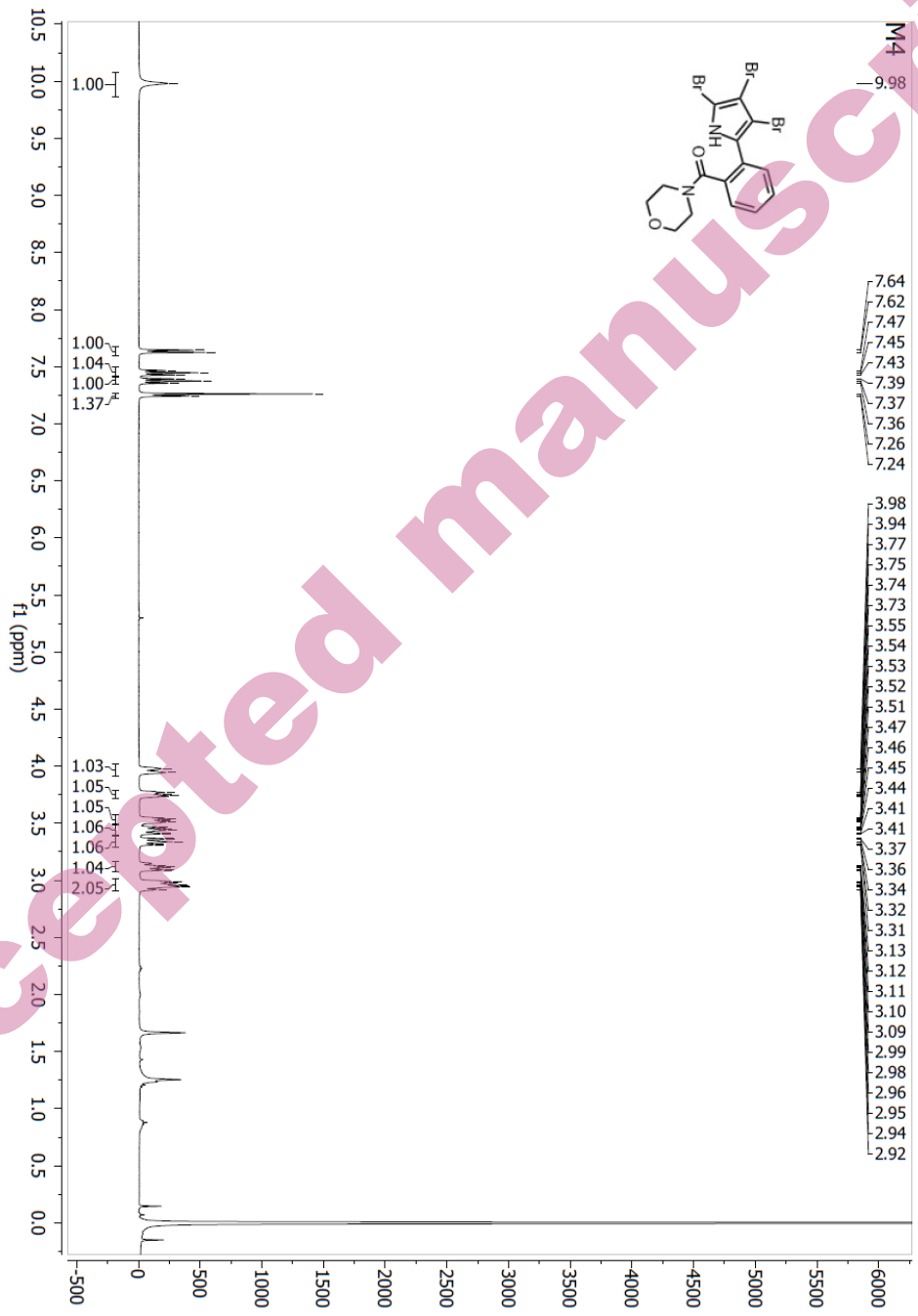

Fig S3. Compound **M4** - ^{1}H NMR spectrum (400 MHz, $CDCl_3$)

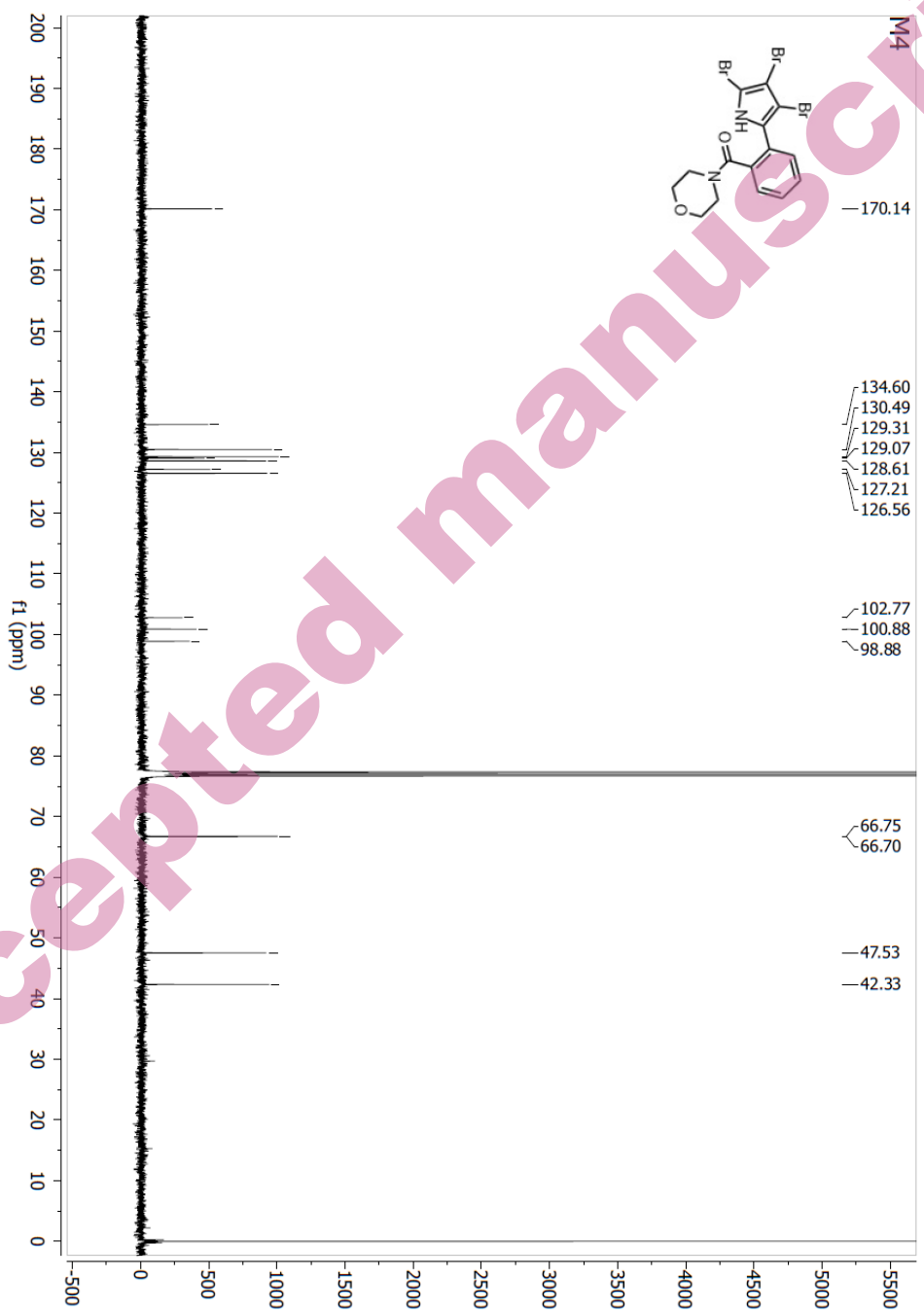

Fig S4. Compound **M4** - ^{13}C NMR spectrum (101 MHz, $CDCl_3$)

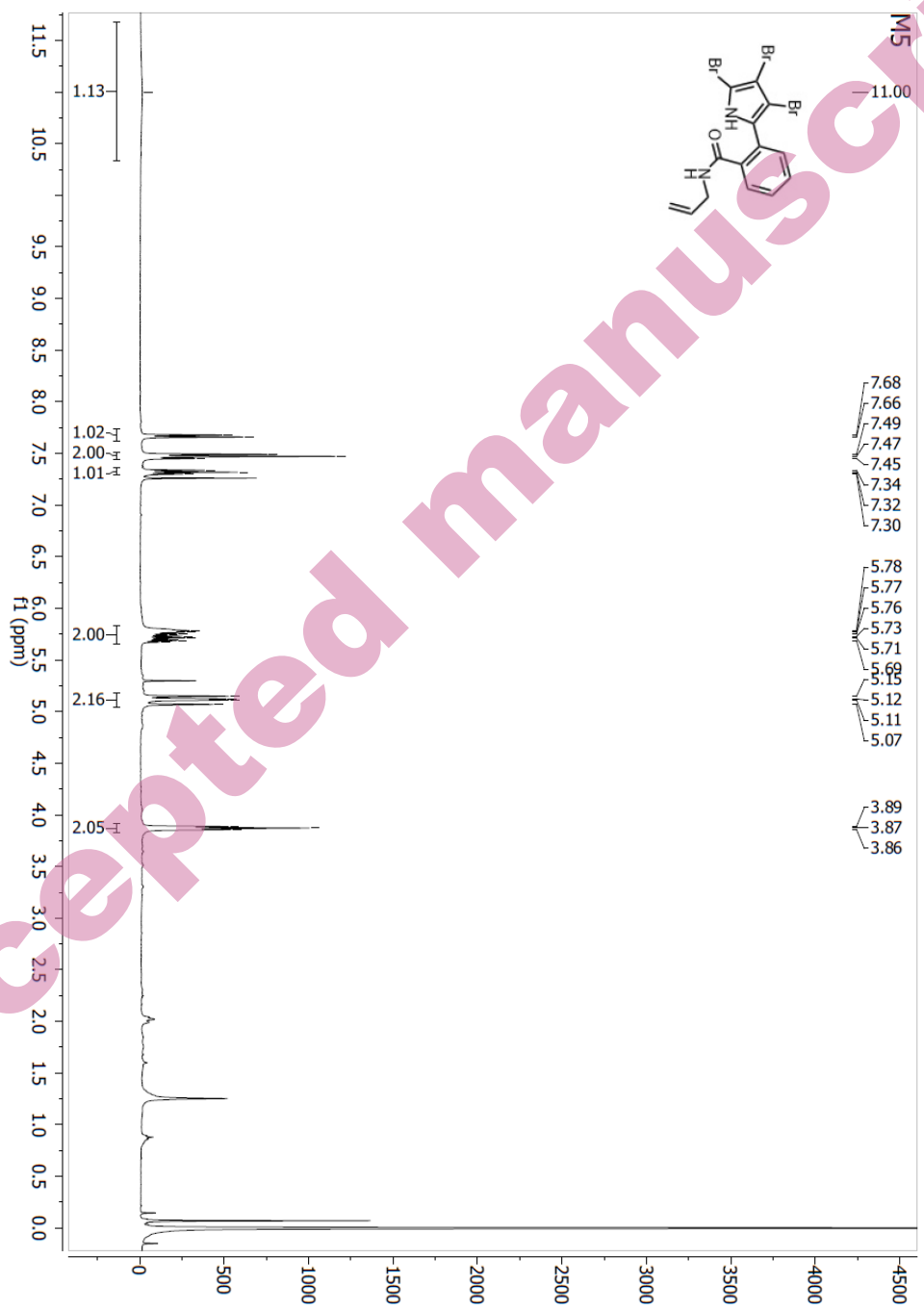

Fig S5. Compound **M5** - ^{1}H NMR spectrum (400 MHz, $CDCl_3$)

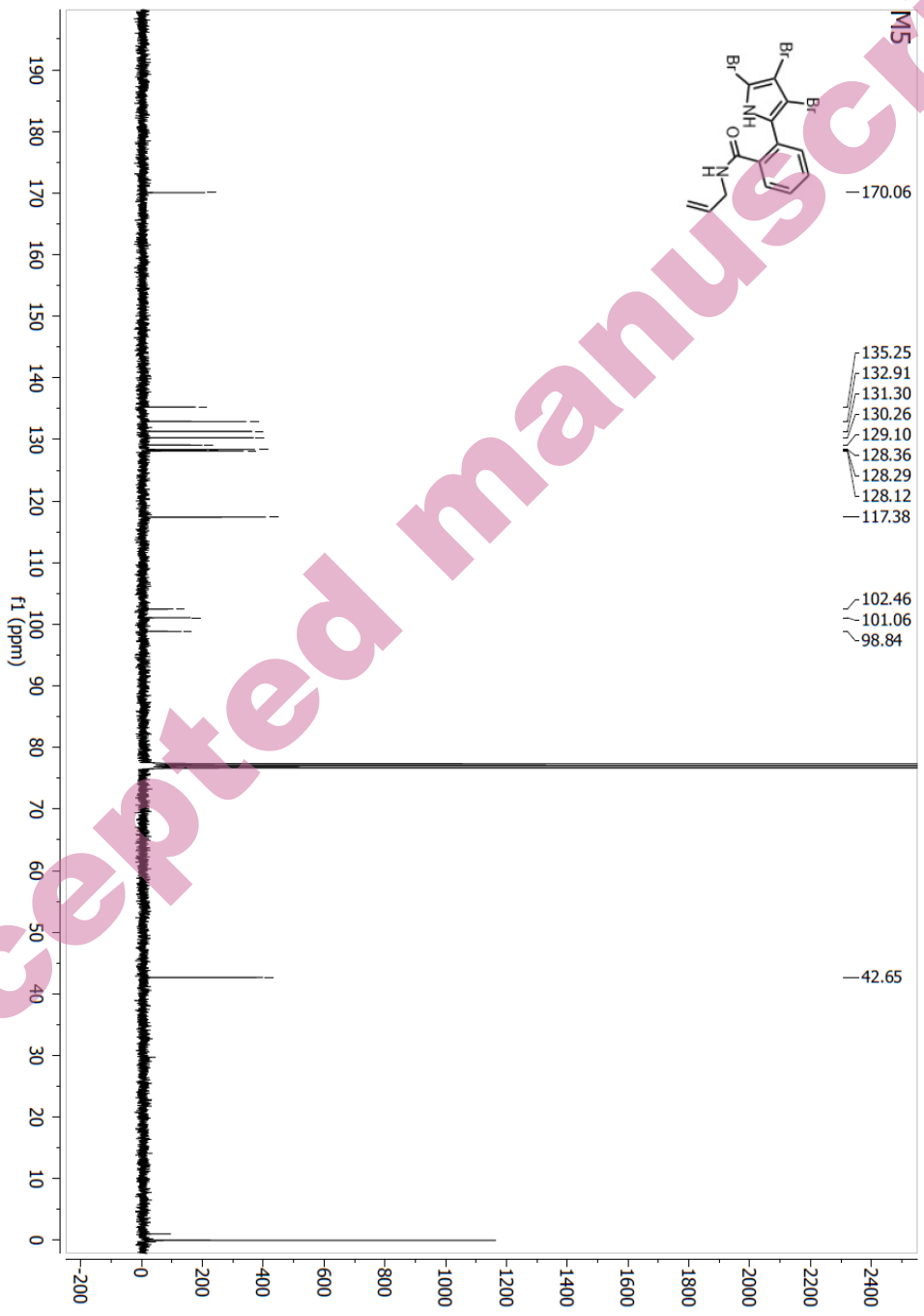

Fig S6. Compound **M5** - ^{13}C NMR spectrum (101 MHz, $CDCl_3$)

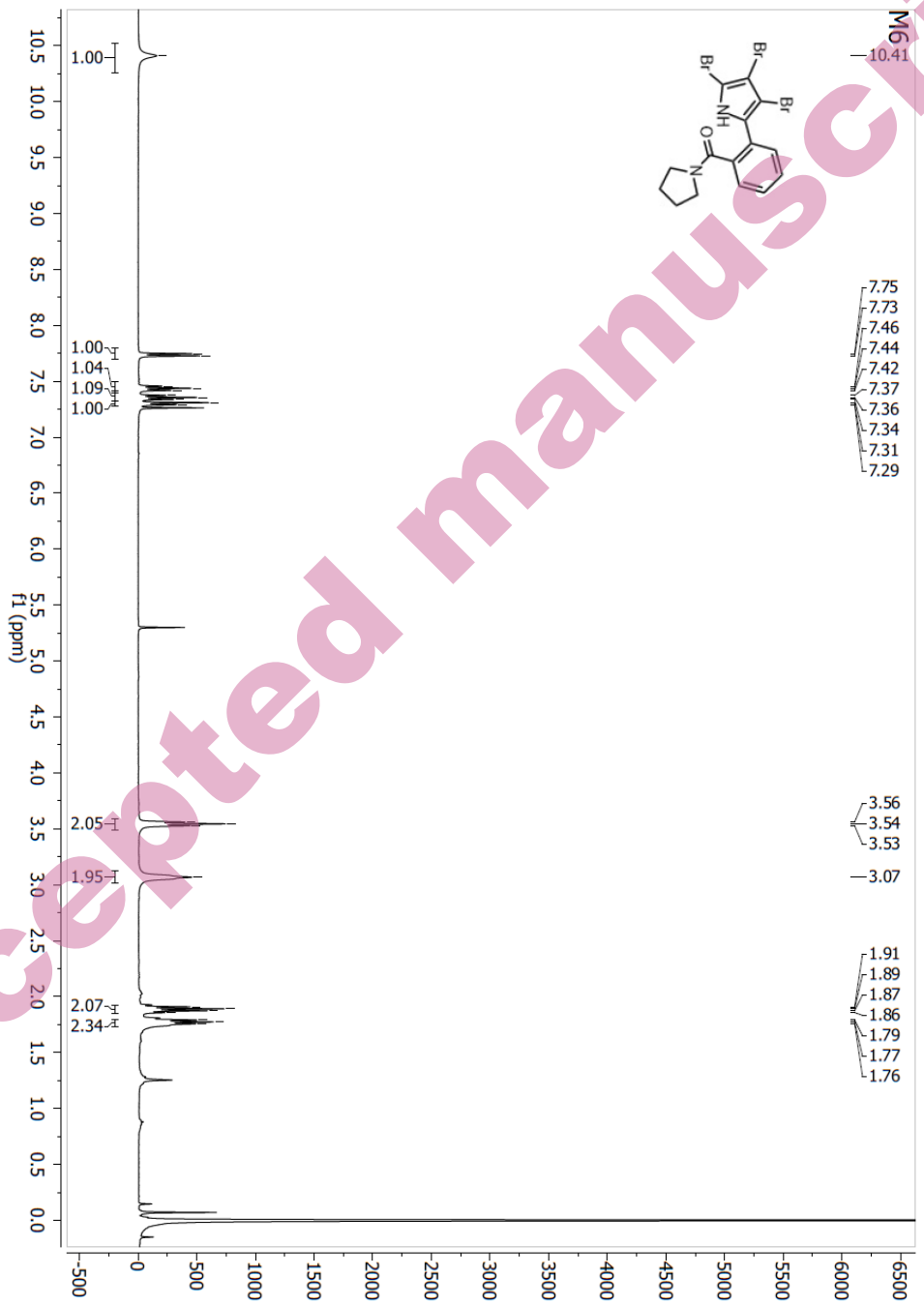

Fig S7. Compound **M6** - ^{1}H NMR spectrum (400 MHz, $CDCl_3$)

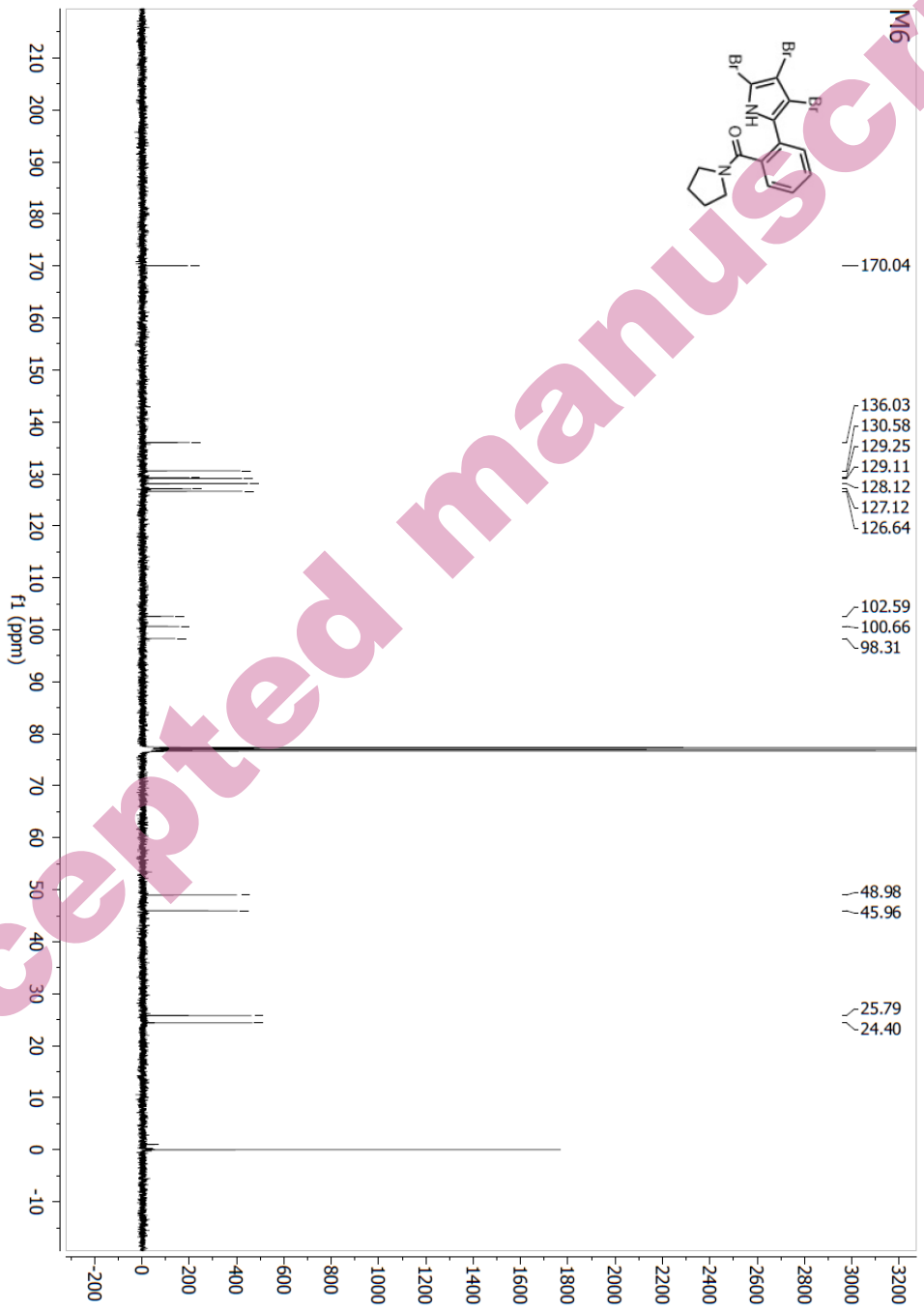

Fig S8. Compound **M6** - ^{13}C NMR spectrum (101 MHz, $CDCl_3$)

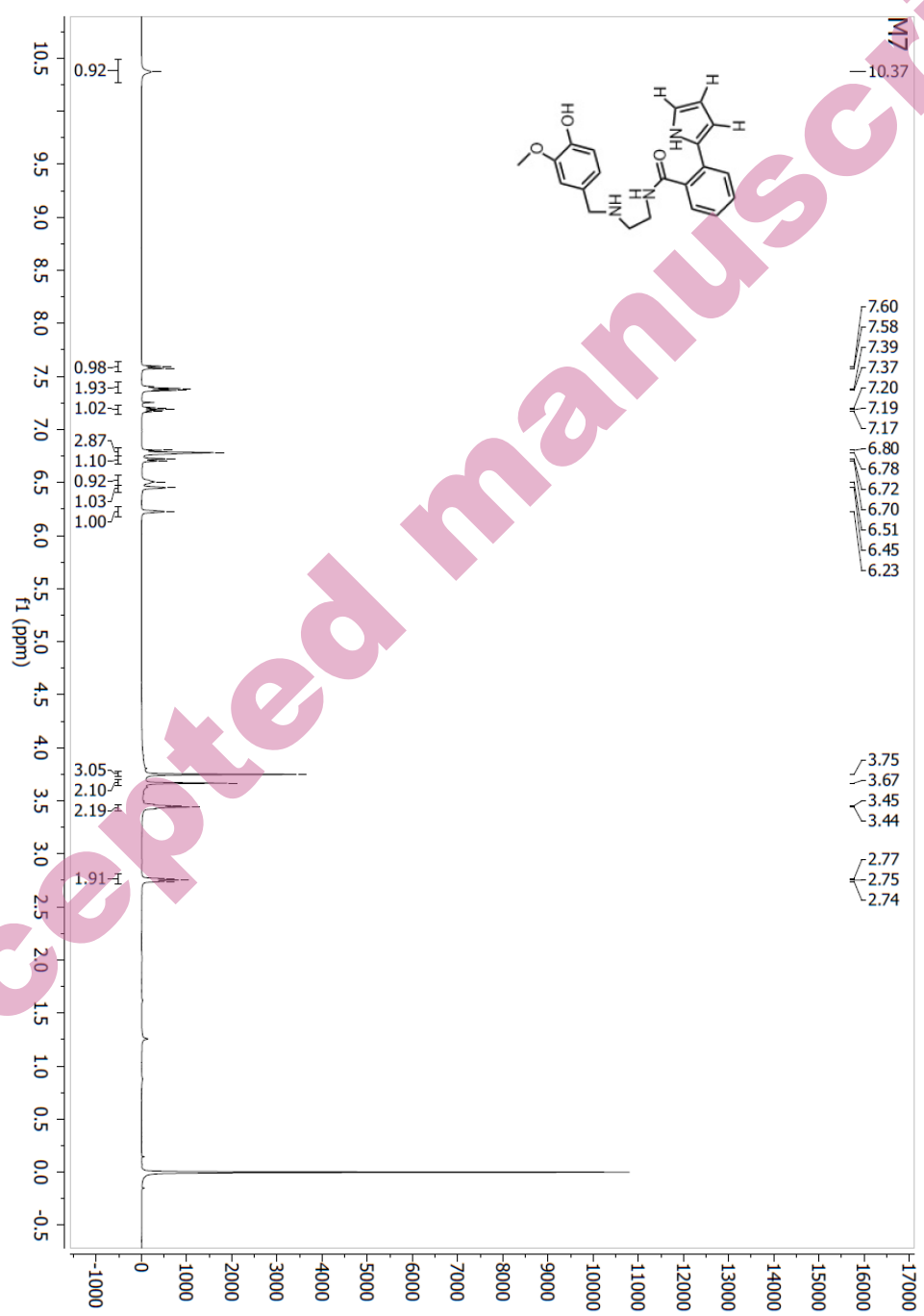

Fig S9. Compound M**7** - ^{1}H NMR spectrum (400 MHz, $CDCl_3$)

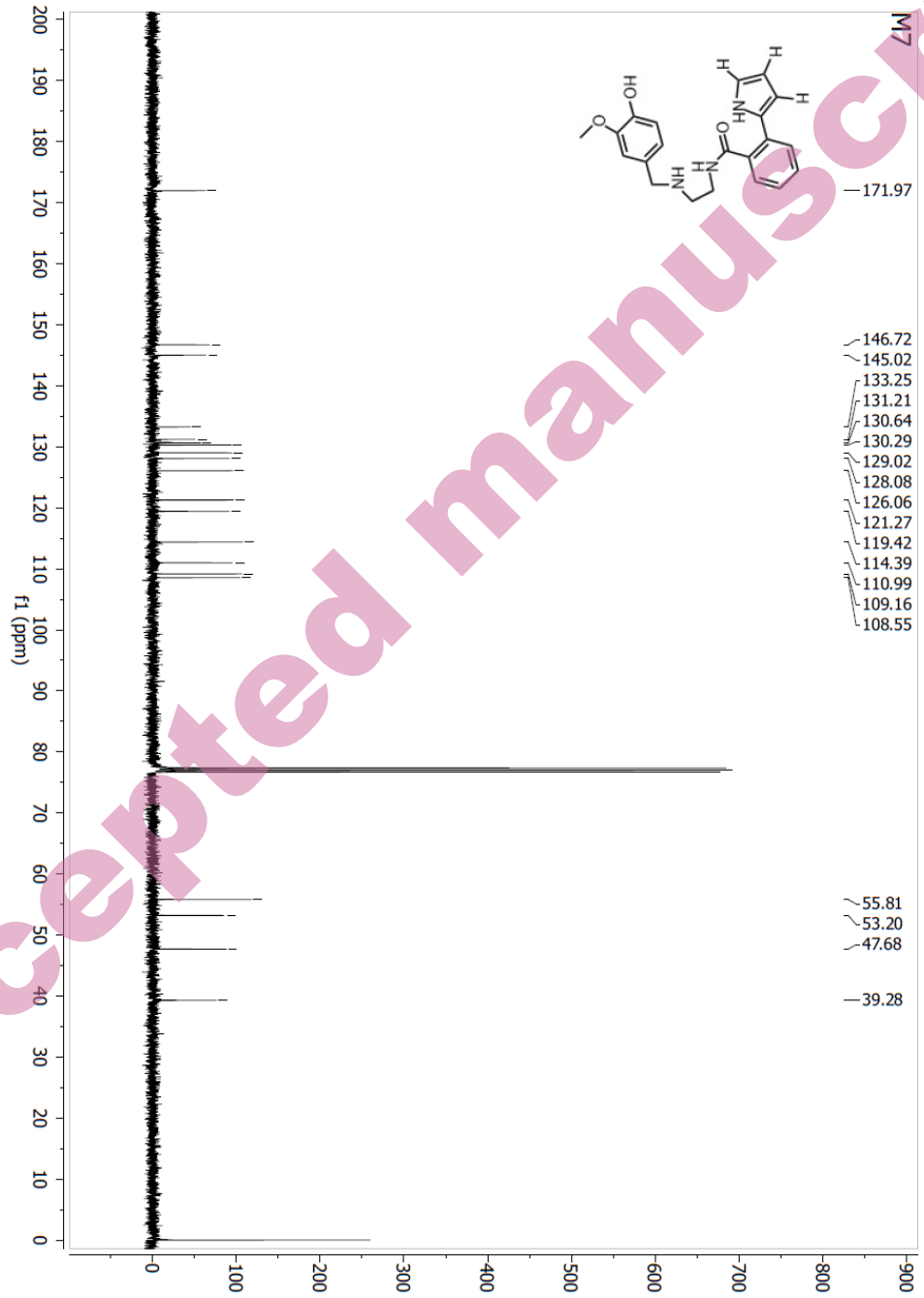

Fig S10. Compound M**7** - ^{13}C NMR spectrum (101 MHz, $CDCl_3$)

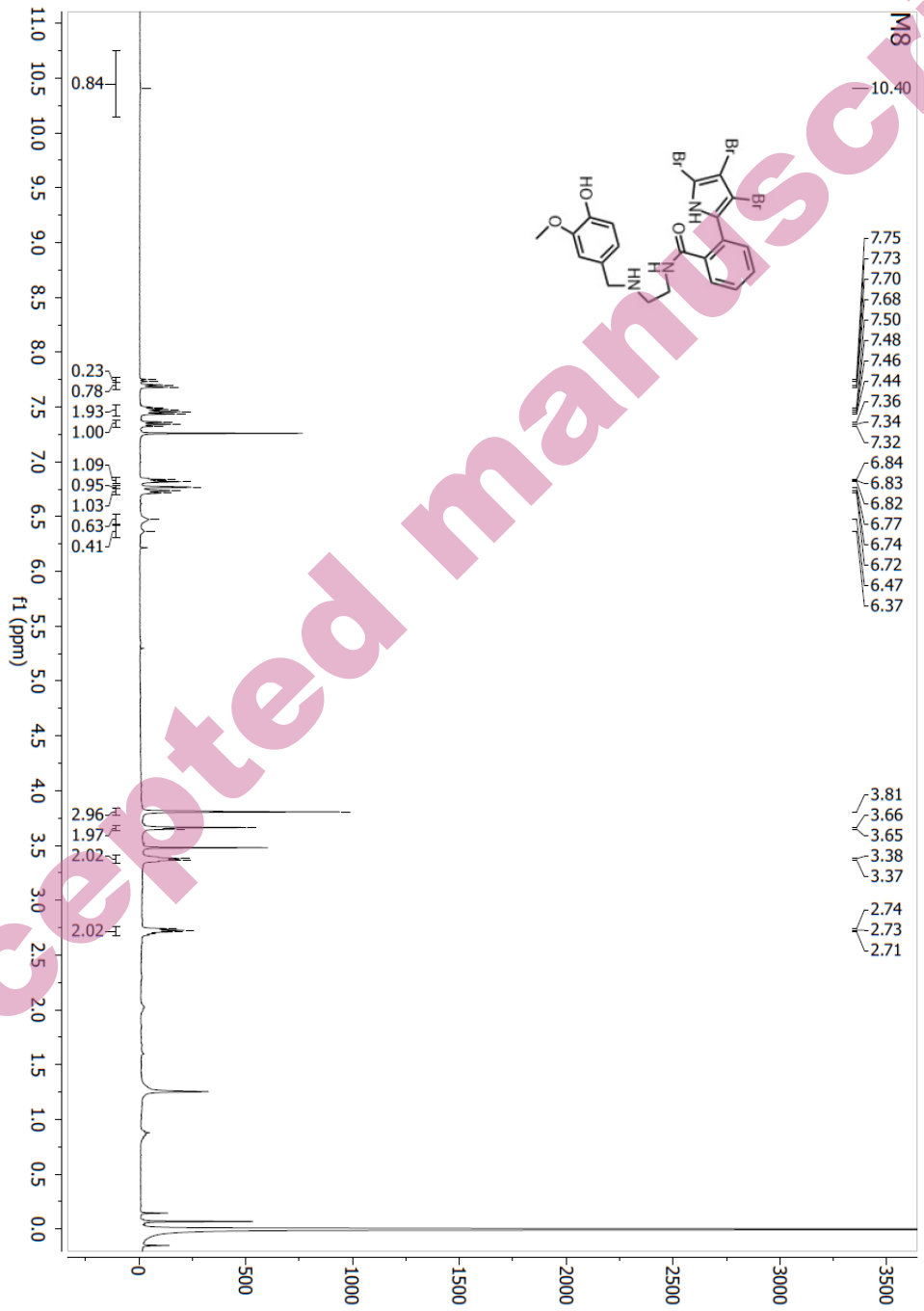

Fig S11. Compound **M8** - ^{1}H NMR spectrum (400 MHz, $CDCl_3$)

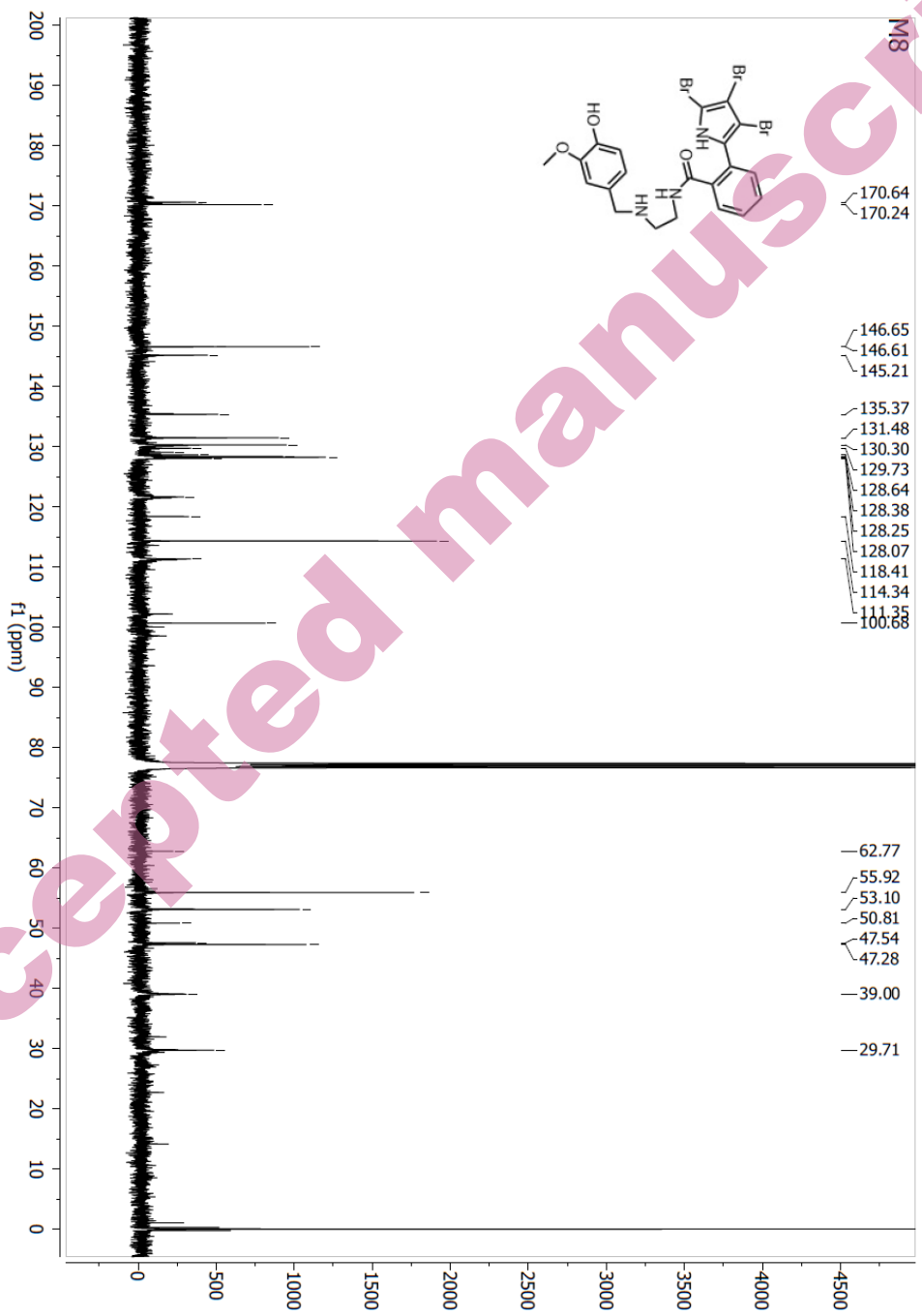

Fig S12. Compound **M8** - ^{13}C NMR spectrum (101 MHz, $CDCl_3$)

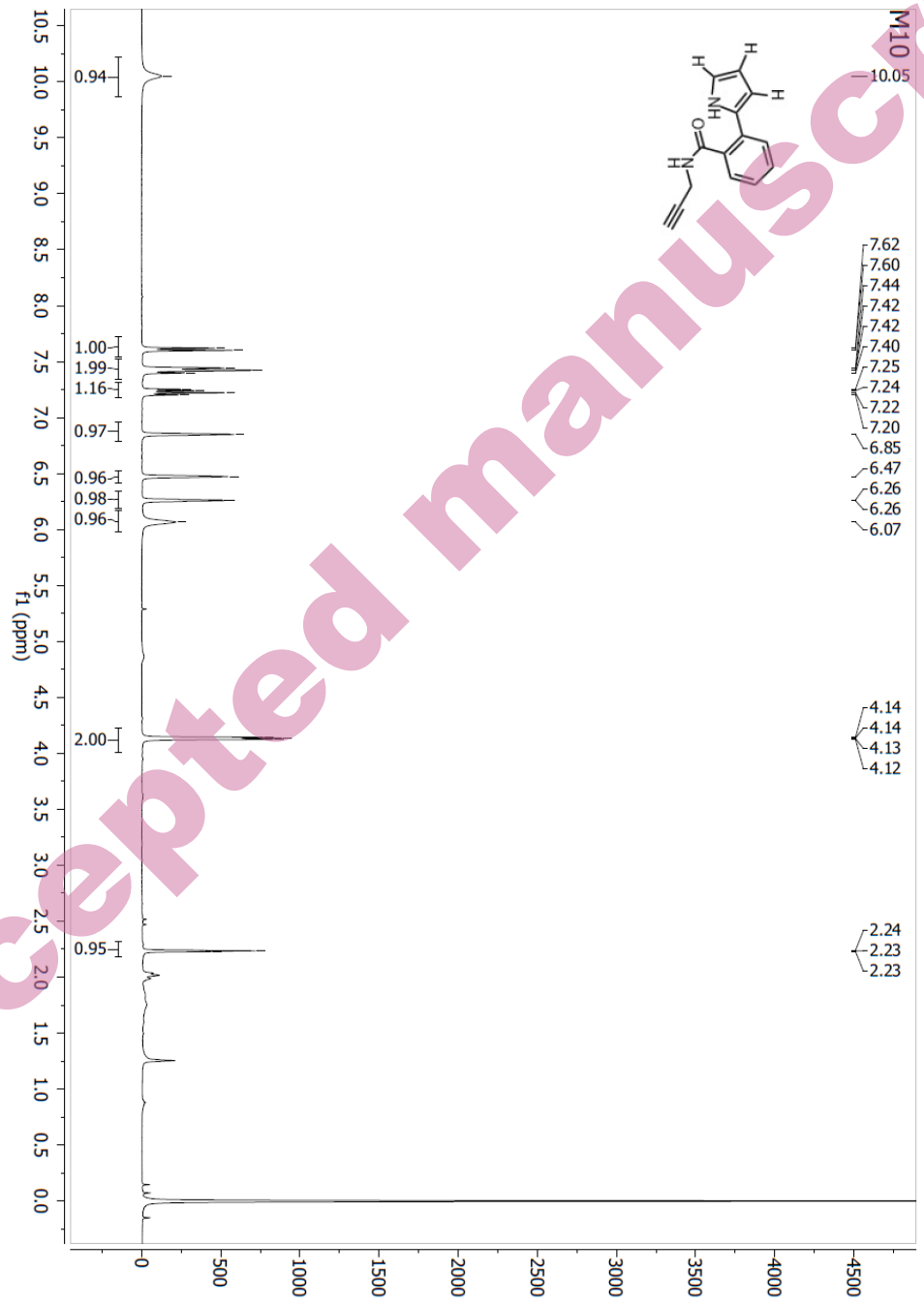

Fig S13. Compound **M10** - ^{1}H NMR spectrum (400 MHz, $CDCl_3$)

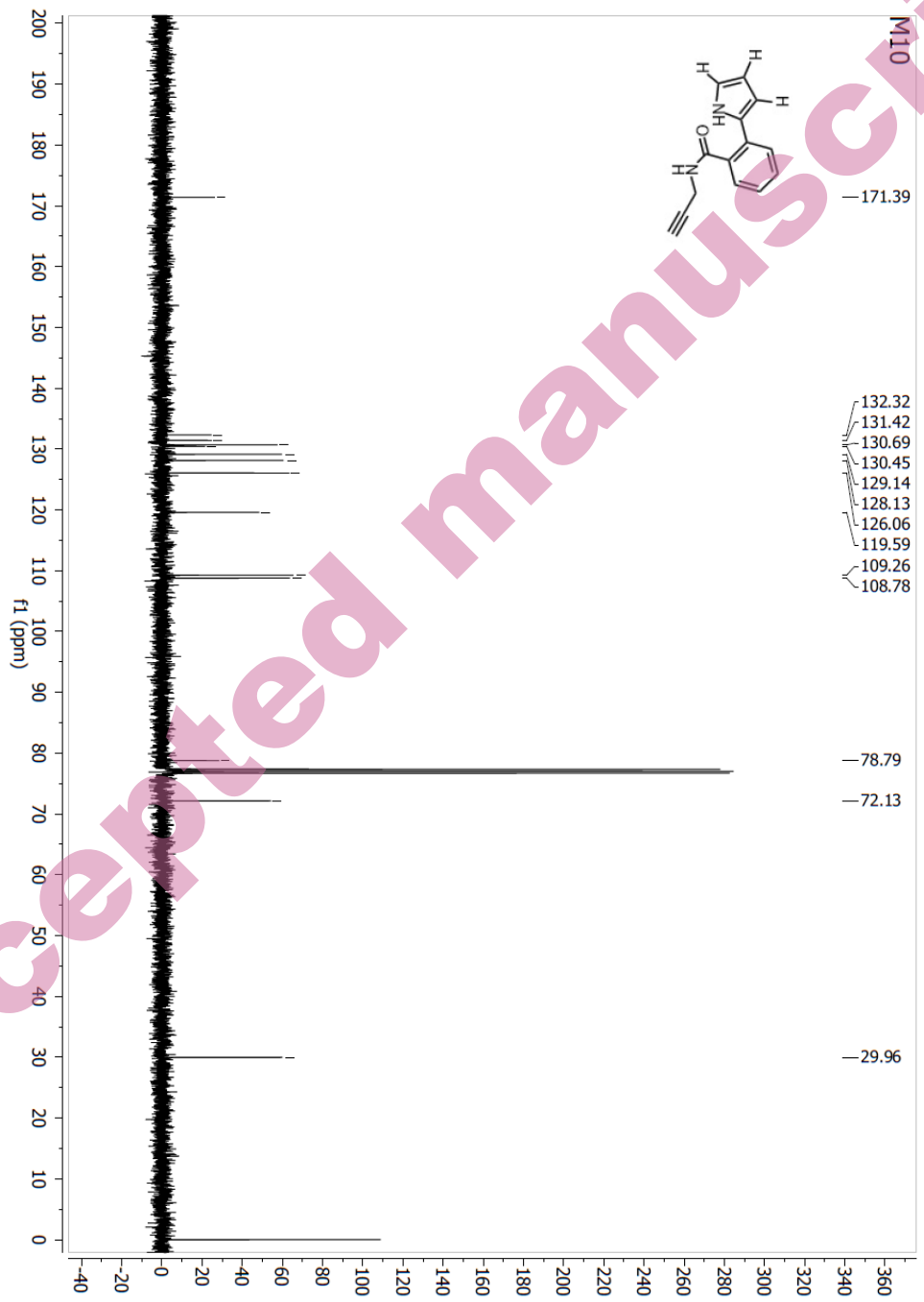

Fig S14. Compound **M10** - ^{13}C NMR spectrum (101 MHz, $CDCl_3$)

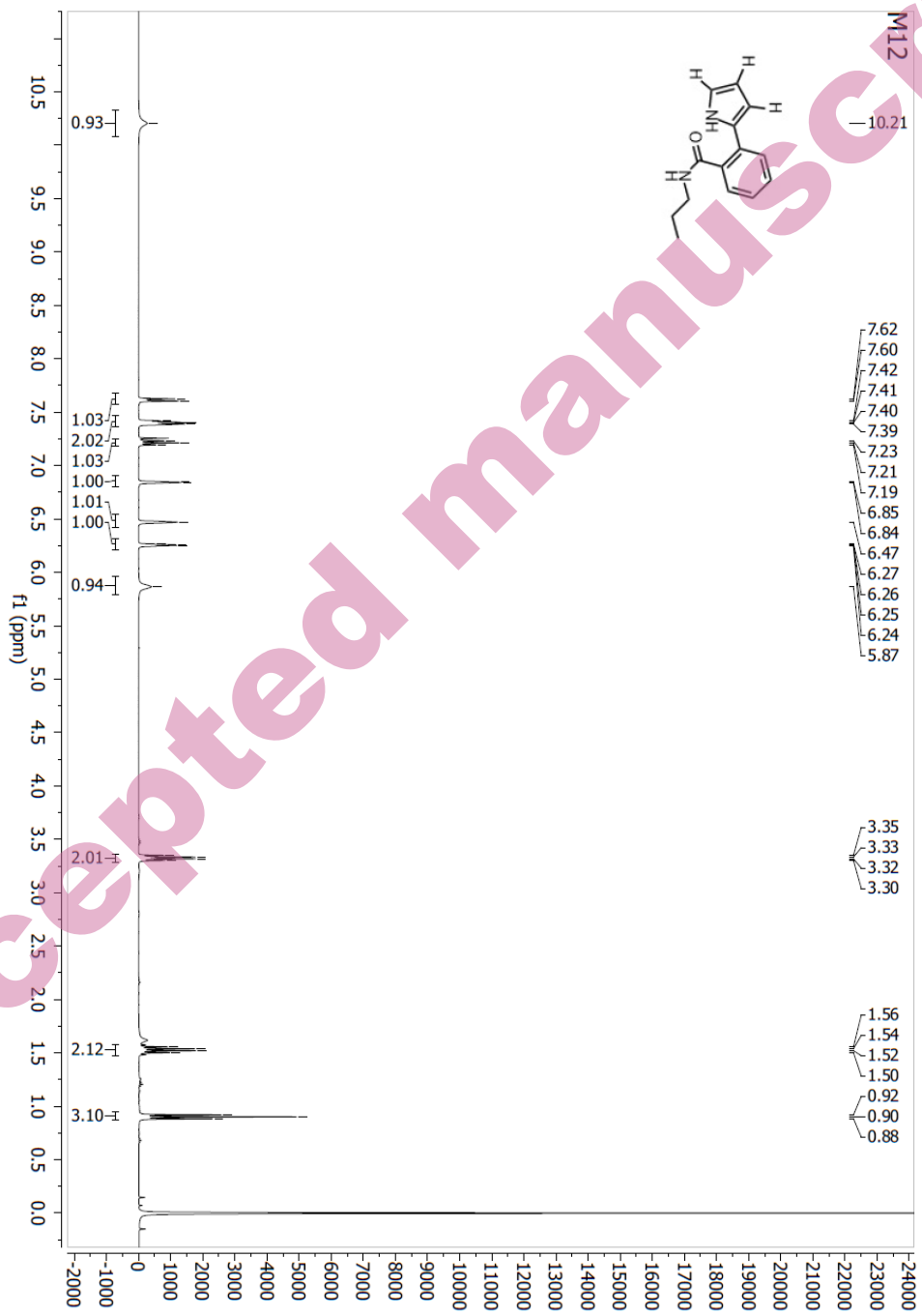

Fig S15. Compound **M12** - ^{1}H NMR spectrum (400 MHz, $CDCl_3$)

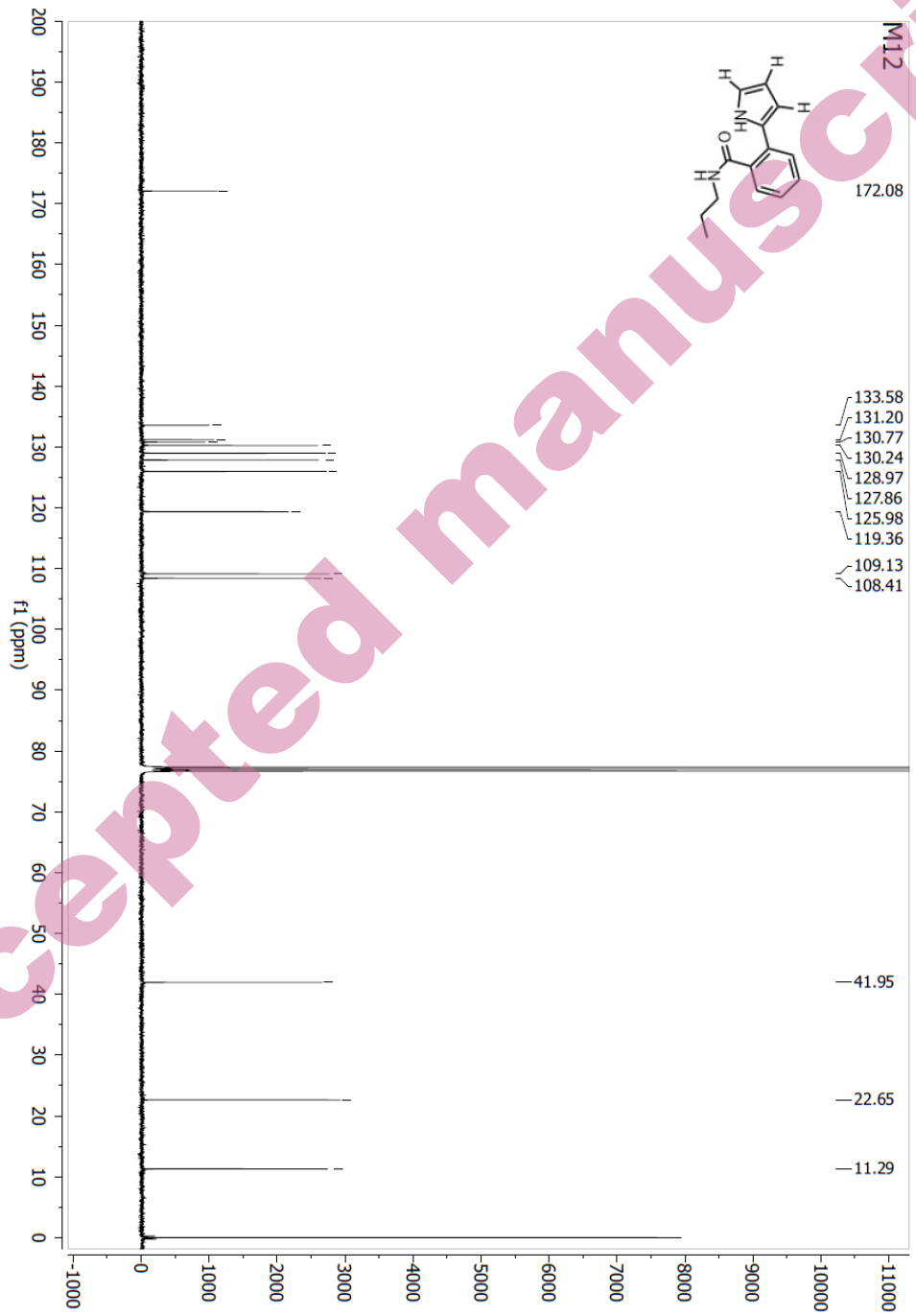

Fig S16. Compound **M12** - ^{13}C NMR spectrum (101 MHz, $CDCl_3$)

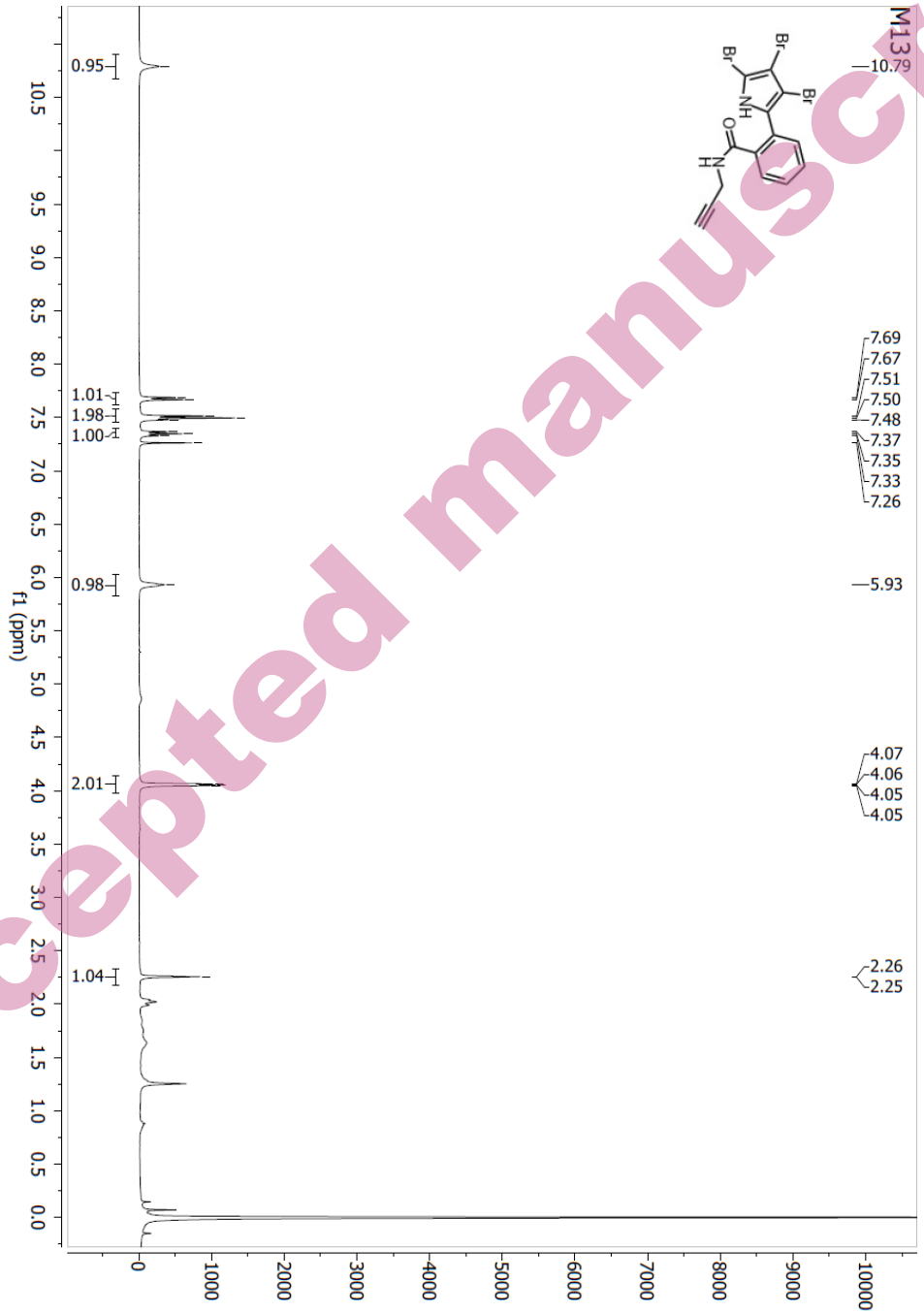

Fig S17. Compound **M13** - ^{1}H NMR spectrum (400 MHz, $CDCl_3$)

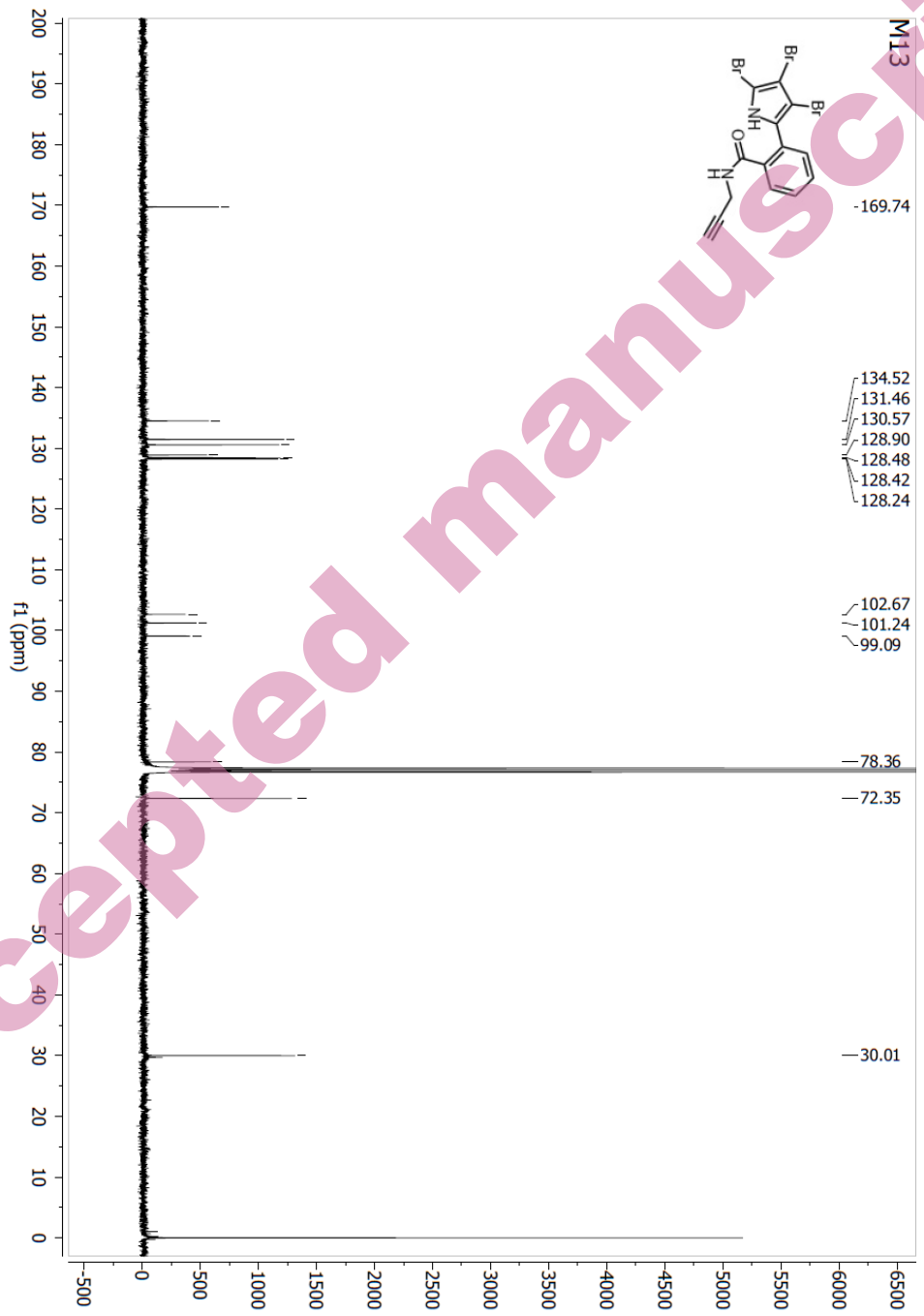

Fig S18. Compound **M13** - ^{13}C NMR spectrum (101 MHz, $CDCl_3$)

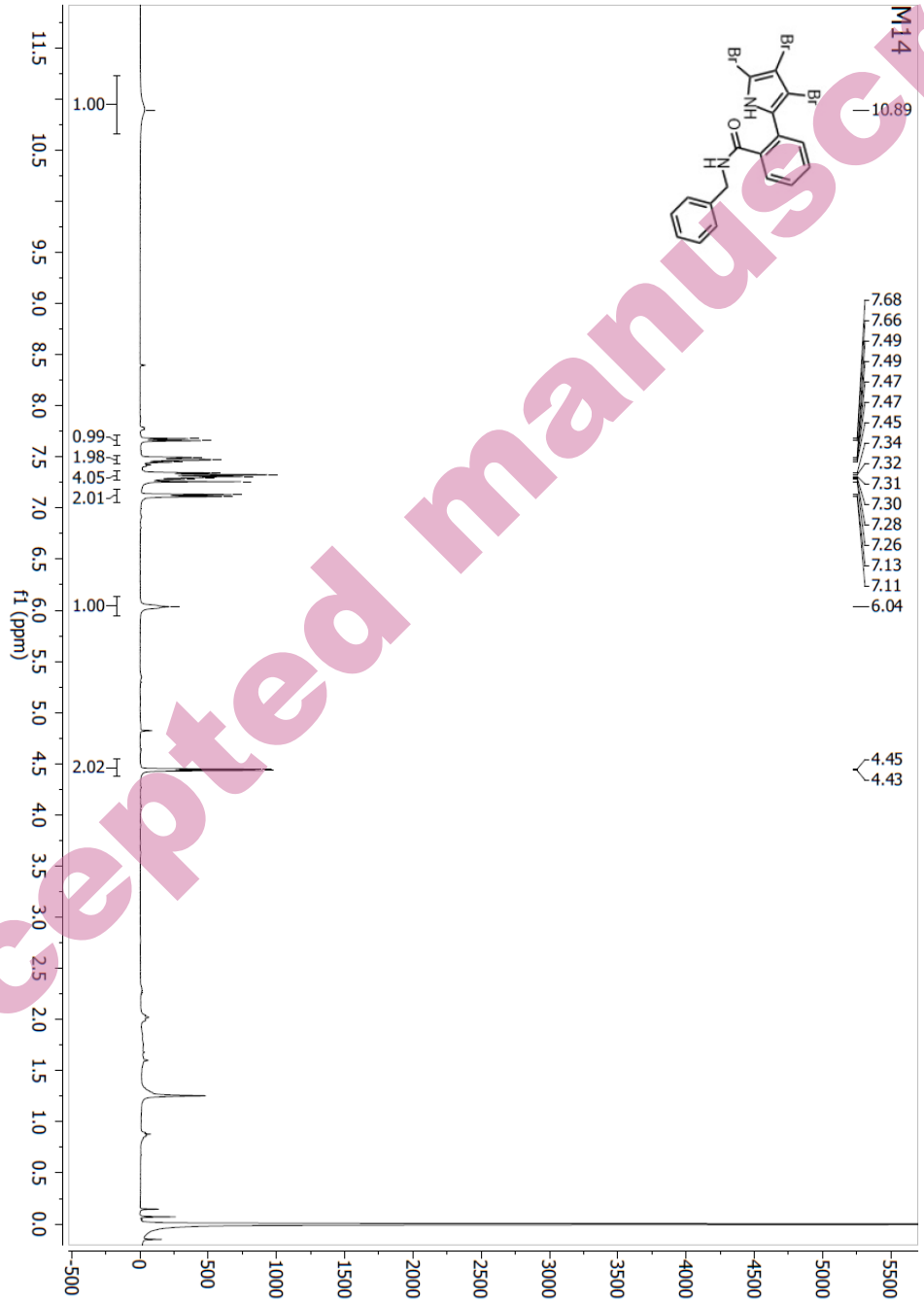

Fig S19. Compound **M14** - ^{1}H NMR spectrum (400 MHz, $CDCl_3$)

Fig S20. Compound **M14** - ^{13}C NMR spectrum (101 MHz, $CDCl_3$)

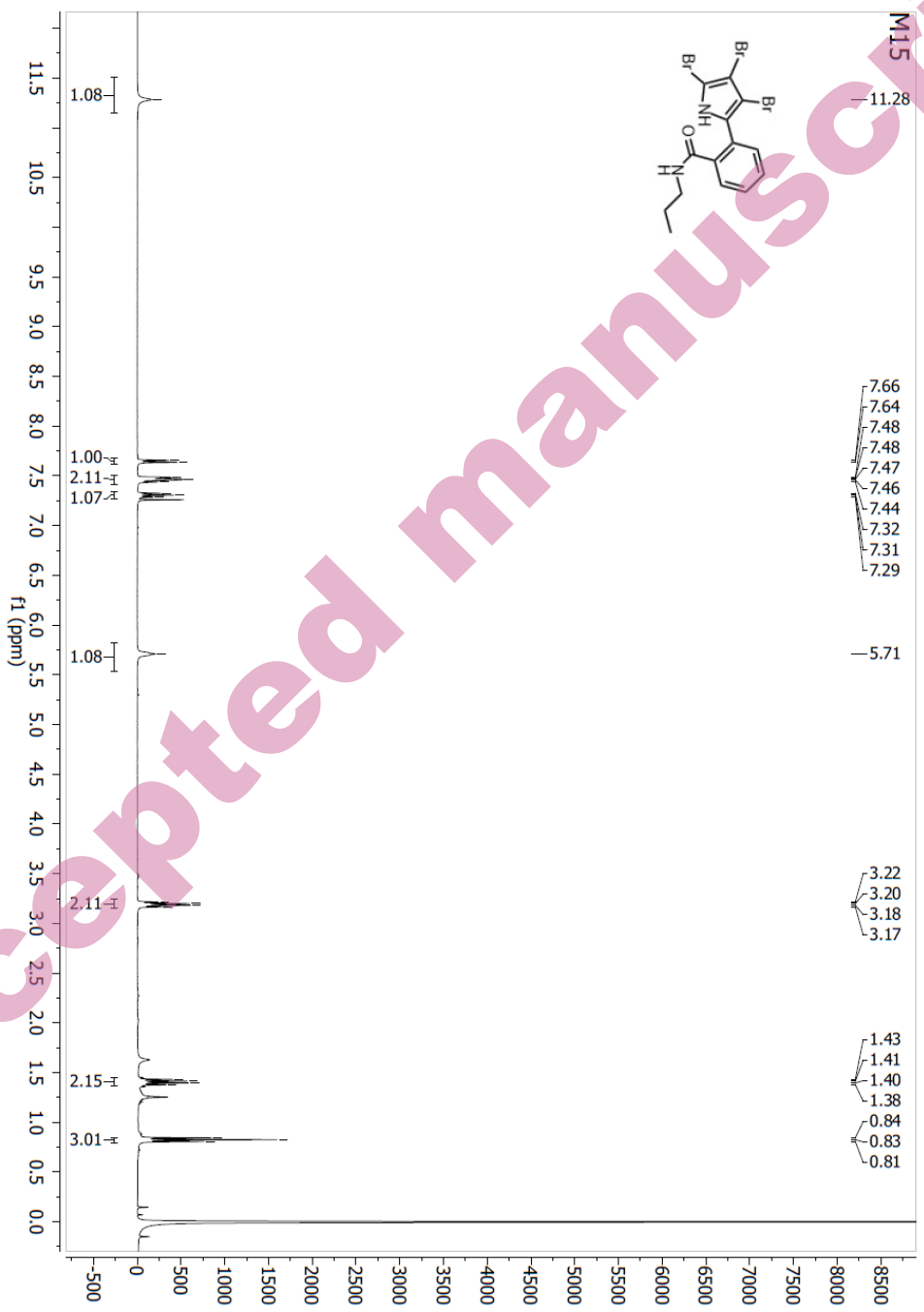

Fig S21. Compound **M15** - ^{1}H NMR spectrum (400 MHz, $CDCl_3$)

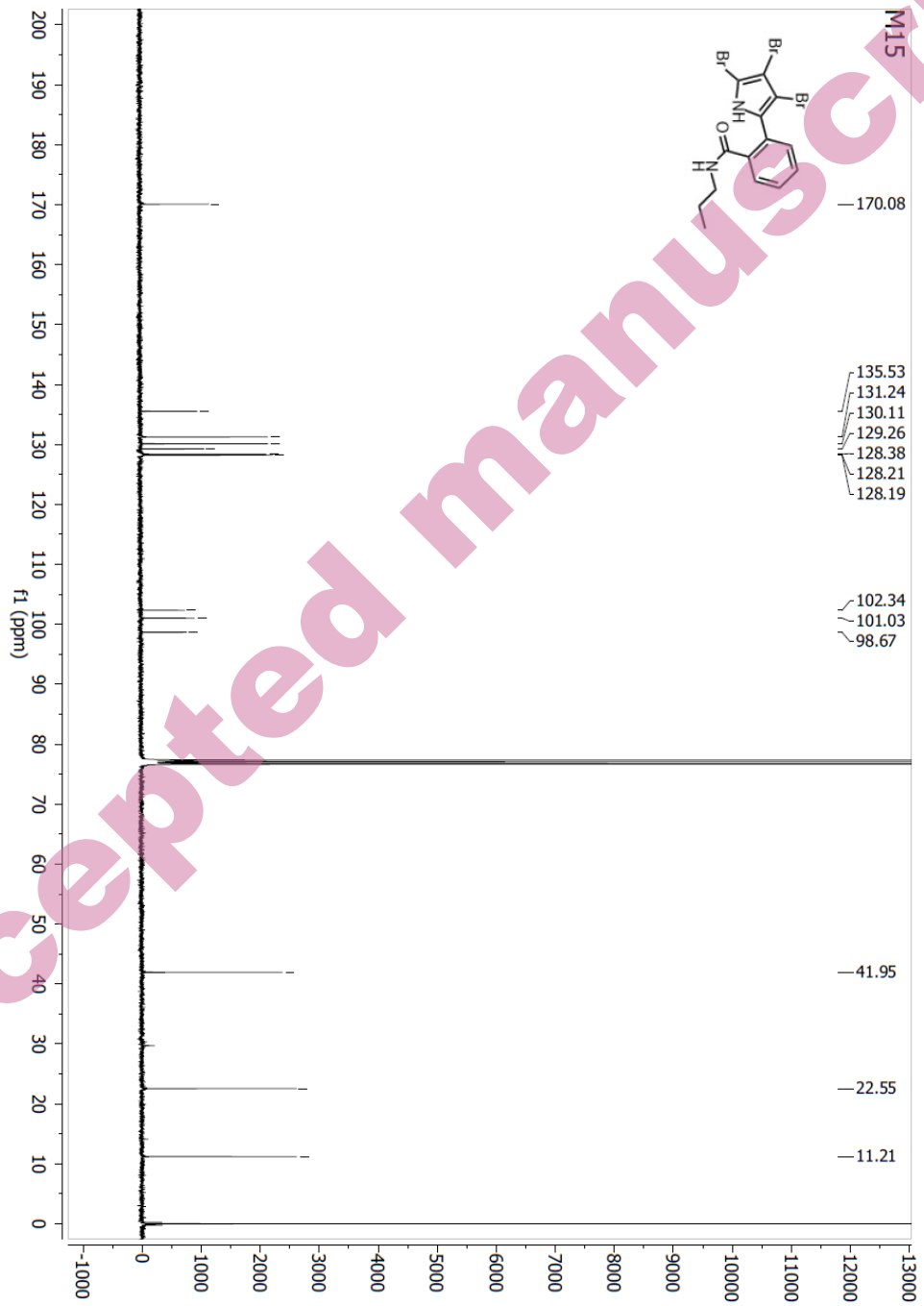

Fig S22. Compound **M15** - ^{13}C NMR spectrum (101 MHz, $CDCl_3$)

Table S1. Redox status parameters in serum pool after incubation with 15 new substances with or without TBH

Sample	PAB (U/L)	TOS (umol/L)	TAS (μmol/L)	SHG (mmol/L)
Blank (serum + H_2O)	100.7 ± 10.7	36.2±19.8	633±80	0.179±0.035
M1	66.8 ± 1.0*	23.5±3.1	923±29	0.280±0.012
M2	27.2 ± 1.5* M1	22.5±5.5	1030±23*	0.273±0.022
M3	63.0 ± 0.7* M2	18.7±0.7	896±8	0.260±0.006
M4	77.2 ± 1.2* M2, M4	18.4±1.8	852±23	0.334±0.117 *
M5	97.2 ± 1.2 M1,M2,M3	23.8±3.5	755±33	0.252±0.021
M6	96.1 ± 1.8 M1,M2,M3	25.0±1.8	734±35	0.312±0.028
M7	44.6 ± 4.2* M5,M6	21.2±0.4	1262±28* M3,M4,M5,M6	0.251±0.053
M8	95.1 ± 0.1 M1,M2,M3,M7	21.8±2.6	1070±18*	0.224±0.013
M9	96.9 ± 1.9 M1,M2,M3,M7	19.4±3.3	1051±19*	0.252±0.004
M10	43.0 ± 3.7* M4,M5,M6,M8, M9	82.5±14.6* M1,M2,M3, M4,M5,M6, M7,M8,M9	646±67 M2,M7,M8 M9	0.330±0.121 *
M11	40.9 ± 3.5* M4,M5,M6,M8, M9	65.3±8.3	492±93 M1,M2,M3, M4,M7,M8 M9	0.282±0.053
M12	41.0 ± 5.2* M4,M5,M6,M8, M9	45.8±1.2	405±12 M1,M2,M3 M4,M5,M7 M8,M9	0.268±0.046
M13	79.7 ± 4.0 M2,M7,M10,M11 M12	51.0±1.0	280±37* M1,M2,M3 M4,M5,M6, M7,M8,M9 M10	0.241±0.004
M14	82.3 ± 3.3 M2,M7,M10,M11 M12	48.5±12.1	727±69 M7,M8	0.270±0.057
M15	85.1 ± 1.1 M2,M7,M10, M11,M12	111.9±7.8* M1,M2,M3, M4,M5,M6,	533±28 M2,M3,M7 M8,M9	0.388±0.107 *

		M7,M8,M9, M12,M13, M15		
M1+TBH	91.0 ± 1.0	51.5±1.0	858±28	0.153±0.001
M2+TBH	54.4 ± 0.7*,# M1TBH	51.5±0.3	919±30	0.141±0.003
M3+TBH	88.4 ± 0.1 M2TBH	62.3±0.9	822±56	0.127±0.042
M4+TBH	88.6 ± 0.3 M2TBH	55.1±0.1	776±25	0.160±0.001 #
M5+TBH	106.9 ± 0.2 M2TBH	50.6±4.4	757±1	0.152±0.018
M6+TBH	108.1 ± 1.1 M2TBH	59.3±0.4	703±7	0.117±0.018 #
M7+TBH	72.3 ± 0.8*,# M5TBH,M6TBH	51.9±2.8	1142±39 M4TBH,M5TBH M6TBH	0.131±0.009
M8+TBH	105.9 ± 0.2 M2TBH, M7TBH	53.7±3.4	931±14	0.132±0.037
M9+TBH	106.1 ± 1.0 M2TBH, M7TBH	53.3±7.6	842±82	0.123±0.021
M10+TBH	47.7 ± 1.0* M1TBH,M3TBH, M4TBH, M5TBH, M6TBH, M7TBH, M8TBH, M9TBH	56.6±3.3	546±25 M2TBH,M7TBH M8TBH	0.155±0.022 #
M11+TBH	62.6 ± 10.7* M1TBH, M4TBH, M5TBH, M6TBH, M8TBH, M9TBH	53.6±8.7	470±97 M1TBH,M2TBH M3TBH,M7TBH M8TBH,M9TBH	0.152±0.018
M12+TBH	65.9 ± 8.0* M5TBH, M6TBH, M8TBH, M9TBH	65.9±9.0	770±165# M7TBH	0.181±0.037
M13+TBH	100.3 ± 1.6 M2TBH,M7TBH, M10TBH, M11TBH, M12TBH	63.3±8.2	570±47 M2TBH,M7TBH M8TBH	0.150±0.016

M14+TBH	101.2 ± 2.7 M2TBH, M7TBH, M10TBH,M11TBH, M12TBH	67.9±21.4	361±39# M13,M1TBH M2TBH,M3TBH M4TBH,M5TBH M7TBH,M8TBH M9TBH,M12TBH	0.147±0.002
M15+TBH	96.6 ± 2.6 M2TBH, M10TBH, M11TBH, M12TBH	69.8±8.8	355±19 M1TBH,M2TBH M3TBH,M4TBH M5TBH,M6TBH M7TBH,M8TBH M9TBH,M12TBH	0.174±0.028# #
Trolox+serum	71.9 ± 5.5* M2,M7,M10,M11, M12,M5TBH, M6TBH, M8TBH, M9TBH, M12TBH	74.6±40.2 M1,M2,M3, M4,M5,M6, M7,M8,M9	960±5* M11,M12,M13, M15,M10TBH M13TBH,M14TBH M15TBH	0.227±0.012
DMSO+serum	96.6 ± 13.0 M1,M2,M3, M10,M11,M12 M2TBH, M7TBH, M10TBH, M11TBH, M13TBH, M14TBH,TROLOX	35.7±15.5 M10,M15	615±167 M1,M2,M7 M8,M9,M13 M2TBH,M7TBH M8TBH,M11TBH, TROLOX	0.241±0.046 M15
TBH+serum	104.6 ± 12.2 M1,M2,M3,M4, M7,M10,M11, M12,M13,M14 M2TBH, M7TBH, M10TBH, M11TBH M11TBH, M12TBH,TROLOX	74.1±11.9* M1,M2,M3, M4,M6,M7, M8,M9,DMSO	579±186 M1,M2,M3 M7,M8,M9 M13,M2TBH, M7TBH,M8TBH TROLOX	0.121±0.011 M1,M2,M4, M10,M11 M12,M14,M15
P	<0.001	<0.001	<0.001	<0.001

P from ANOVA; post hoc Tukey test with letters indicate significant differences with distinct substances

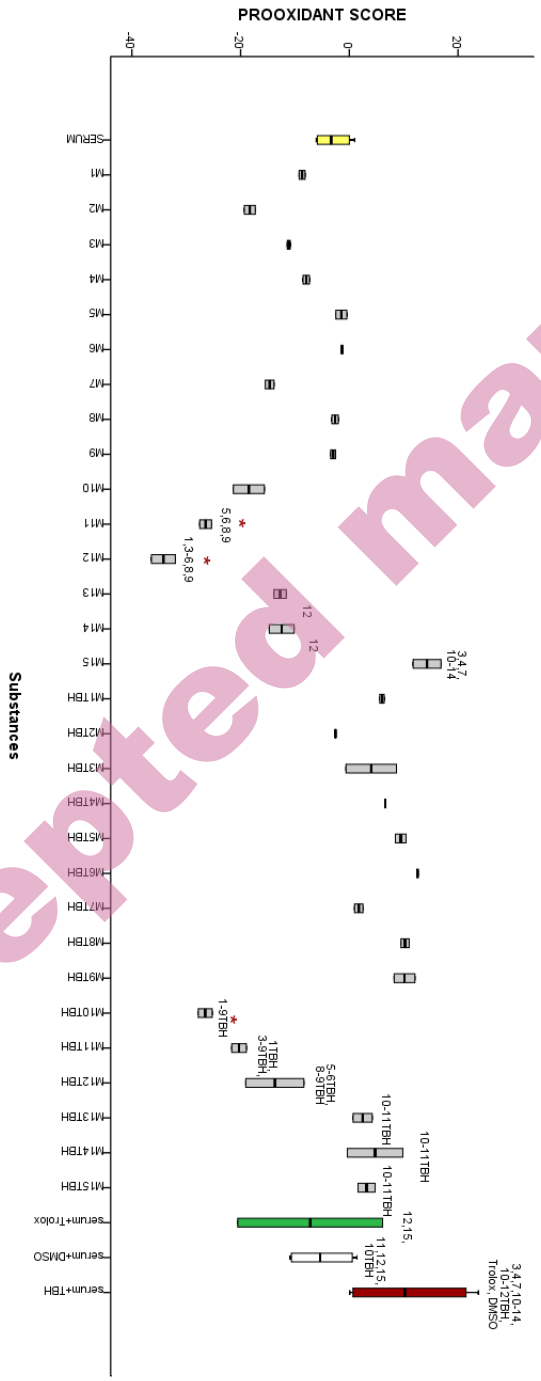

Fig S23. Prooxidant score (PS) in tested substances with and without TBH, along with native serum, serum with Trolox (2000 μmol/L) and serum with TBH (0,25 mM)

*P<0,05, *vs.* native SERUM; # P<0,05, *vs.* the same substance sample without TBH; numbers: statistically significant difference vs. distinct substance without or with TBH.

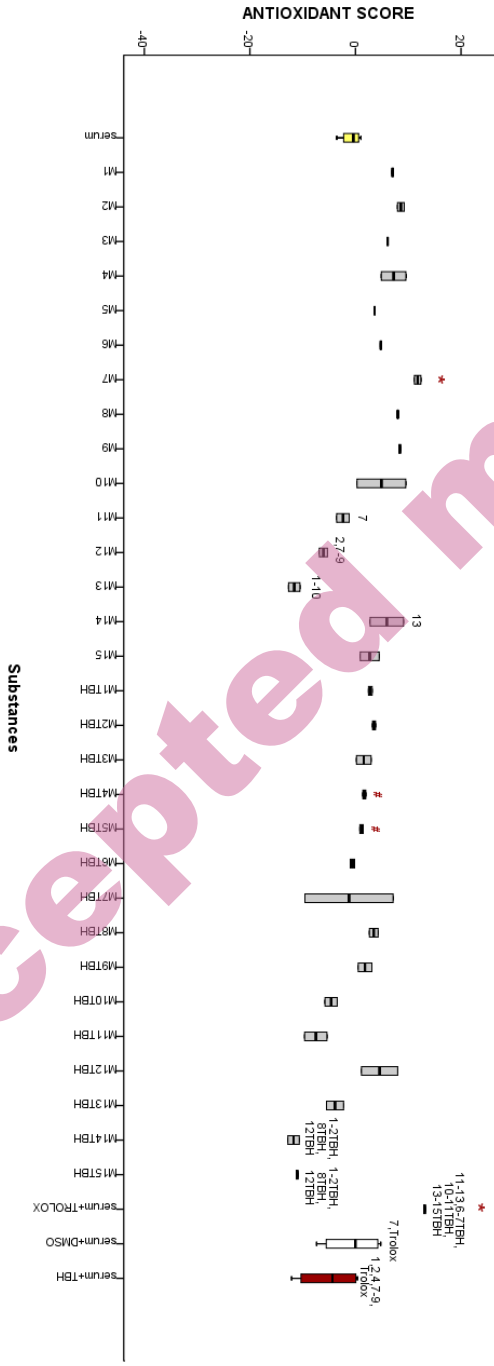

Fig S24. Antioxidant score (AS) in tested substances with and without TBH, along with native serum, serum with Trolox (2000 µmol/L) and serum with TBH (0,25 mM)

*P<0,05, *vs.* native SERUM; # P<0,05, *vs.* the same substance sample without TBH; numbers: statistically significant difference vs. distinct substance without or with TBH.

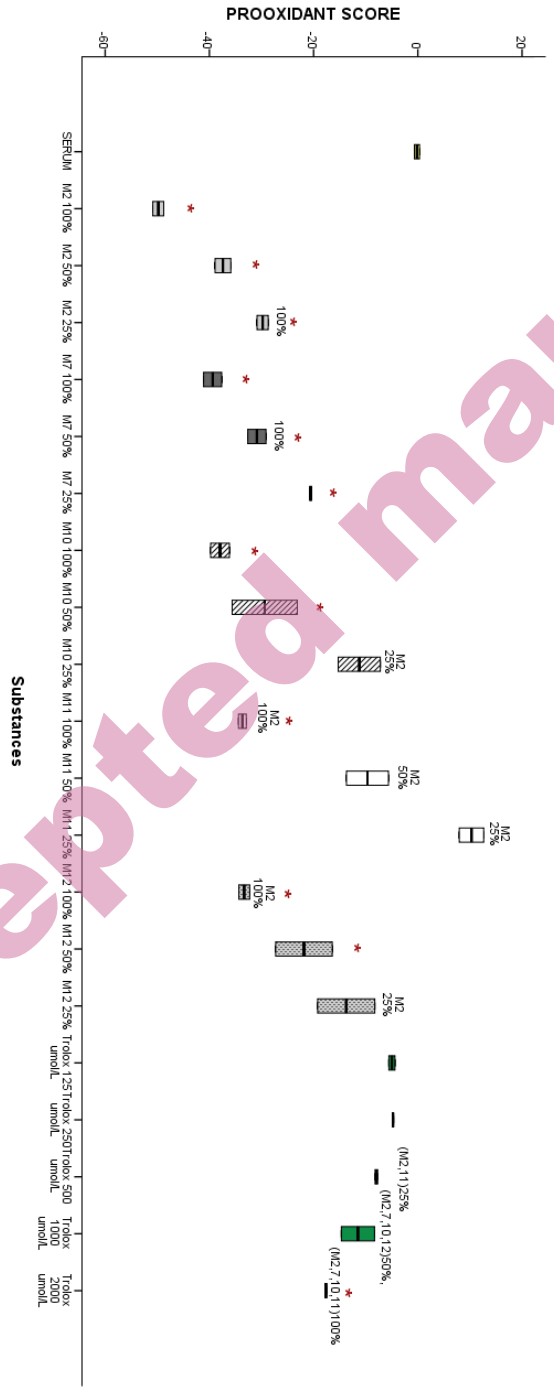

Fig S25. Prooxidant score in three different concetrations of M2, M7, M10, M11 i M12 samples, so as in samples with Trolox (125-2000 μmol/L)

*P<0.05 *vs.* native serum (blank);

100%, 50%: P<0.05 *vs.* sample of the same substance with different concentration;

Mx, My…Mi %: P<0.05 *vs.* indicated sample of a specific dilution;

#P<0.05 *vs.* Trolox (125 μmol/L).

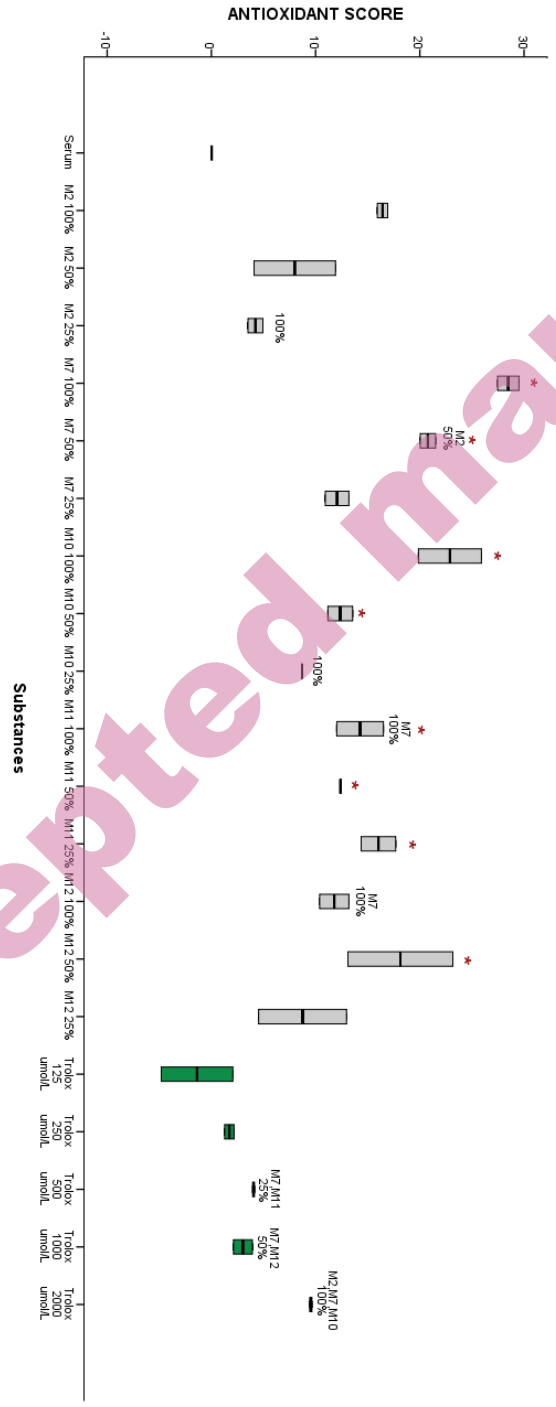

Figure S26. Antioxidant score in three different concentrations of M2, M7, M10, M11 i M12 samples, so as in samples with Trolox (125-2000 µmol/L)

*P<0.05 *vs.* native serum (blank);

100%, 50%: P<0.05 *vs.* sample of the same substance with different concentration;

Mx, My…Mi %: P<0.05 *vs.* indicated sample of a specific dilution;

#P<0.05 *vs.* Trolox (125 µmol/L).

Table S2. Calculated values of prooxy, antioxy and oxy score of tested compounds in three different concentrations

Samples	Prooxi score	Antioxi score	Oxy score
Serum	-0.2 (-0.7 - 0.3)	0.0 (0.0 - 0.0)	-0.2 (-0.7 - 0.3)
M2-100%	-49.8 (-50.9 - -48.8)	16.4 (15.9- 16.9)	-66.2 (-66.8 - -65.7)
M2-50%	-37.4 (-38.9 - -35.9)	8.0 (4.1- 11.9)	-45.4 (-47.8 - -43.0)
M2-25%	-29.8 (-30.9 - -28.7)	4.2 (3.5- 4.9)	-34.0 (-34.4 - -33.6)
M7-100%	-39.4 (-41.1 - -37.6)	28.5 (27.5 - 29.5)	-67.8 (-70.6 - -65.1)
M7-50%	-30.9 (-32.6 - -29.1)	20.8 (20.0 - 21.5)	-51.7 (-52.7 - -50.6)
M7-25%	-20.6 (-20.7 - -20.4)	12.1 (10.9 - 13.2)	-32.6 (-33.9 - -31.4)
M10 100%	-38.0 (-39.8 - -36.2)	22.9 (19.9 - 25.9)	-60.8 (-65.7 - -56.0)
M10 50%	-29.4 (-35.6 - -23.1)	12.4 (11.2 - 13.6	-41.7 (-49.2 - -34.3)
M10 25%	-11.2 (-15.3 - -7.2)	8.7 (8.6-8.8)	-19.9 (-24.0 - -15.8)
M11 100%	-33.7 (-34.4 - -32.9)	14.3 (12.0 - 16.5	-47.9 (-49.4 - -46.4)
M11 50%	-9.7 (-13.7 - -5.6)	12.4 (12.3-12.5)	-22.0 (-26.0 - -18.0)
M11 25%	10.3 (8.0 - 12.7)	16.0 (14.4 - 17.7)	-5.7 (-9.7 - -1.7)
M12 100%	-33.3 (-34.4 - -32.3)	11.8 (10.4 - 13.2)	-45.1 (-45.5 - -44.7)
M12 50%	-21.8 (-27.3 - -16.4)	18.1 (13.1 - 23.2)	-40.0 (-50.4 - -29.5)
M12 25%	-13.8 (-19.2 - -8.3)	8.8 (4.5 - 13.0)	-22.5 (-23.8 - -21.2)
E 2.0	-17.6 (-17.8 - -17.5)	9.5 (9.4 - 9.6)	-27.2 (-27.2 - -27.1)
E 1.0	-11.5 (-14.7 - -8.3)	3.0 (2.1 - 3.9)	-14.5 (-18.6 - -10.4)
E 0.500	-8.0 (-8.2 - -7.7)	4.0 (3.9 - 4.1)	-12.0 (-12.3 - -11.7)
E 0.250	-4.8 (-4.9 - -4.7)	1.7 (1.3 - 2.2)	-6.5 (-7.0 - -5.9)
Serum+Trolox 0.125	-5.0 (-5.6 - -4.4)	-1.4 (-4.8 - 2.1)	-3.6 (-7.6 - 0.4)