SUPPLEMENTARY MARERIALS

Synthesis of new 1,3-thiazol derivatives of maleopimaric acid as anticancer, antibacterial and antifungal agents

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Abstract
A series of new 1,3-thiazol derivatives of maleopimaric acid 6a-f, 7a-f were synthesized and evaluated for anticancer, antibacterial and antifungal activities. Evaluation of cytotoxic activity against human embryonic kidney 293 cells (HEK293), human neuroblastoma cell line (SH-SY5Y), hepatocellular carcinoma cell line (HepG2) and human T-cell lymphoblast-like line (Jurkat), showed that introduction of the aminothiazole fragment at position 6 of the diterpenoid molecule leads to decrease of cell viability. Substance 3 was found to be the most active against all tested cell lines, inhibiting cell viability with IC_{50} values in the range of 2 - 24 μM. The structure–activity relationship of these compounds was studied and the results show that the compounds 6c and 7e exhibited *in vitro* antifungal activity against *Candida albicans* and also possessed antibacterial profile against *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli* and *Proteus vulgaris*.

Keywords: maleopimaric acid; α-bromoketones; α-diazoketone; thiourea; Hantzsch reaction; thiazoles; cytotoxic activity; antimicrobial activity

Data S1: Data Analysis of 3, 4, **6a-f, 7a-f**

6-(Bromoacetyl)-12-isopropyl-6,9a-dimethyldodecahydro-1H-3b,11-ethenophenanthro[1,2-c]furan-1,3(3aH)-dione (**3**). Yield 0.535 g, 99%, as white solid, m.p.: 162°C, Elemental analysis (Found: C, 62.87; H, 6.65; Br, 16.78. $C_{25}H_{33}BrO_4$ Requires: C, 62.89; H, 6.97; Br, 16.74%). IR (KBr/cm^{-1}) 1841 (C=O), 1778 and 1715(C=O anhydride), 1465 (C=C). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.61 (3H, s, CH_3-17), 0.98 (3H, d, *J* = 6.9 Hz, CH_3-15), 0.97 (3H, d, *J* = 6.9 Hz, CH_3-16), 1.23 (3H, s, CH_3-18), 1.23−1.74 (13H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10, CH-5a), 2.26 (1H, quint, *J* = 6.7 Hz, CH-14), 2.54 (1H, d.d, *J* = 3.0, 13.8 Hz, CH-9b), 2.75 (1H, d, *J* = 8.5 Hz, CH-3a), 3.10-3.12 (1H, m, CH-11), 3.13 (1H, d, *J* = 9 Hz, CH-11a), 4.15 (2H, q, CH_2-20), 5.51 (1H, s, CH-13). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.66 (C17), 16.3 (C18), 16.83 (C8), 19.95 (C16), 20.56 (C15), 21.75 (C5), 27.22 (C10), 32.13 (C20), 32.75 (C14), 34.65 (C4), 35.61 (C11), 36.38 (C7), 37.71 (C9a), 40.37 (C3b), 45.59 (C11a), 48.58 (C5a), 52.40 (C6), 53.00 (C3a), 53.30 (C9b), 125.09 (C13), 148.21 (C12), 170.91 (C1), 172.68 (C3), 206.76 (C19).

6-(bromoacetyl)-12-isopropyl-6,9a-dimethyl-2-phenyldodecahydro-3b,11-ethenonaphtho[2,1-e]isoindole-1,3(3aH)-dione(**4**). Yield 0.546 g, 99%, as white solid, m.p.: 265°C, Elemental analysis (Found: C, 67.41; H, 6.90; Br, 14.49; N, 2.58. $C_{31}H_{38}BrNO_3$ Requires: C, 67.39; H, 6.93; Br, 14.46; N, 2.53. IR (KBr/cm^{-1}) 1856 (C=O), 1779 and 1709(C=O imide), 1456 (C=C). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.65 (3H, s, CH_3-17), 1.00 (3H, d, *J* = 6.9, Hz CH_3-15), 0.96 (3H, d, *J* = 6.4 Hz, CH_3-16), 1.17 (3H, s, CH_3-18), 1.20−1.80 (m, 12H, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 2.28 (1H, quint, *J* = 6.7 Hz, CH-5a), 2.6 (1H, d.t, *J* = 3.0, 13.8 Hz, CH-9b), 2.73 (1H, d, *J* = 8.7, Hz, CH-3a), 2.95 (1H, d d., J = 8.6, 3.0 Hz, CH-11), 3.21 (1H, d, *J* = 9 Hz, CH-11a), 4.18 (2H, s, CH_2-20), 5.51 (1H, s, CH-13). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.86 (C17), 16.58 (C18), 16.94 (C8), 20.11 (C16), 20.83 (C15), 21.98 (C5), 27.66 (C10), 32.11 (C20), 32.83 (C14), 35.22 (C7), 36.11 (C11), 36.15 (C4), 36.44 (C9), 37.86 (C9a), 41.04 (C3b), 45.04 (C11a), 48.88 (C5a), 52.39 (C3a), 52.57 (C6), 54.29 (C9b), 124.48 (C13), 126.43 (C C2',6'), 128.44 (4'), 129.06 (C C3',5'), 147.50 (C12), 176.26 (C1), 177.50 (C3), 206.77 (C19).

6-(2-Amino-1,3-thiazol-4-yl)-12-isopropyl-6,9a-dimethyldodecahydro-1H-3b,11-ethenophenanthro[1,2-c]furan-1,3(3aH)-dione **(6a).** Yield 0.295 g, 66%, as yellowish solid, m.p.: 146°C, Elemental analysis (Found: C, 68.70; H, 7.53; N, 6.14; S, 7.02. $C_{26}H_{34}N_2O_3S$ Requires: C, 68.69; H, 7.54; N, 6.16; S, 7.05%). IR (KBr/cm^{-1}) 3400 (N–H), 1776 (C=O anhydride), 1617 (C=N), 1196 (C–N), 730 (C–S). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.64 (3H, s, CH_3-17), 0.98 (3H, d, *J* = 6.2 Hz, CH_3-16), 0.99 (3H, d, *J* = 6.2 Hz, CH_3-15), 1.25 (3H, s, CH_3-18), 1.10−1.83 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 2.1-2.25 (1H, m, CH-14), 1.87 (1H, quint, *J* = 6.7 Hz, CH-5a), 1.65 (1H, d.d, *J* = 3.8, 11.0 Hz, CH-9b), 2.97 (1H, d, *J* = 8.5 Hz, CH-3a), 3.14 (1H, d, *J* = 9 Hz, CH-11), 3.29 (1H, d d., *J* = 8.5, 2.5 Hz, CH-11a), 5.50 (1H, s, CH-13), 6.19 (1H, s, CH-5'), 8.68 (2H, br d NH_2). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.72 (CH_3, C-17), 17.40 (CH_2, C-8), 18.19 (CH_3, C-18), 20.00 (CH_3, C-16), 20.25 (CH_2, C-5), 20.60 (CH_3, C-15), 27.24 (CH_2, C-10), 32.74 (CH, C-14), 34.32 (CH_2, C-4), 35.72 (CH, C-11), 37.45 (CH_2, C-9), 38.39 (C-9a), 39.02 (CH_2, C-7), 40.45 (C-3b), 41.24 (C-6), 45.79 (CH, C-11a), 50.42 (CH, C-5a), 52.66 (CH, C-9b), 52.99 (CH, C-3a), 101.40 (CH, C-5'), 124.98 (CH, C-13), 148.45 (C-12), 149.71(C-4'), 170.32 (C-2'), 171.71 (C-1), 173.16 (C-3). Mass spectrum (CI), *m/z*: 455 $[M + H]^+$, (calcd for $C_{26}H_{34}N_2O_3S$ *m/z*: 454).

N-[4-(12-Isopropyl-6,9a-dimethyl-1,3-dioxotetradecahydro-1H-3b,11-ethenophenanthro[1,2-c]furan-6-yl)-1,3-thiazol-2-yl]acetamide **(6b).** Yield 0.286 g, 54% as yellowish solid, m.p.: 108°C, Elemental analysis (Found: C, 67.73; H, 7.35; N, 5.61; S, 6.44. $C_{28}H_{36}N_2O_4S$ Requires: C, 67.71; H, 7.31; N, 5.64; S, 6.46%). IR (KBr/cm^{-1}) 3133 (N–H), 1778 (C=O anhydride), 1617 (C=N), 1577 (C=O amid), 1194 (C–N), 756 (C–S). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.64 (3H, s, CH_3-17), 0.98 (3H, d, *J* = 6.2 Hz, CH_3-16), 1.01 (3H, d, *J* = 6.2 Hz, CH_3-15), 1.31 (3H, s, CH_3-18), 1.41−1.93 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 2.1-2.23 (1H, m, CH-14), 2.35 (3H, s, $CH_3C(O)$), 1.87 (1H, quint, *J* = 6.7 Hz, CH-5a), 1.71 (1H, d.t, *J* = 3.0, 13.8 Hz, CH-9b), 2.89 (1H, d, *J* = 8.7 Hz, CH-3a), 3.10-3.12 (1H, m, CH-11),3.15 (1H, d d., *J* = 8.6, 2.5

Hz, CH-11a), 5.47 (1H, s, CH-13), 6.62 (1H, s, CH-5'), 12.59 (1H, br s NH). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.72 (CH_3, C-17), 17.34 (CH_2, C-8), 18.31(CH_3, C-18), 19.96 (CH_3, C-15), 20.27 (CH_2, C-5), 20.59 (CH_3, C-16), 23.34 (CH_3, Ac), 27.28 (CH_2, C-10), 32.73 (CH, C-14), 34.24 (CH_2, C-4), 35.71 (CH, C-11), 37.30 (CH_2, C-9), 38.42(C-9a), 39.54 (CH_2, C-7), 40.42 (C-3b), 41.45(C-6), 45.5 (CH, C-11a), 50.69 (CH, C-5a), 52.66 (CH, C-9b), 52.80(CH, C-3a), 107.27 (CH, C-5'), 124.97 (CH, C-13), 148.33 (C-12), 150.41 (C-4'), 161.66 (C-2'), 168.38 (CO), 171.25 (C-1), 172.95 (C-3). Mass spectrum (CI), *m/z*: 497 $[M + H]^+$, (calcd for $C_{28}H_{36}N_2O_4S$ *m/z*: 496).

6-[2-(Allylamino)-1,3-thiazol-4-yl]-12-isopropyl-6,9a-dimethyldodecahydro-1H-3b,11-ethenophenanthro[1,2-c]furan-1,3(3aH)-dione **(6c).** Yield 0.469 g, 95%, as yellowish solid, m.p.: 114°C, Elemental analysis (Found C, 70.44; H, 7.78; N, 5.61; S, 6.42. $C_{29}H_{38}N_2O_3S$ Requires: C, 70.41; H, 7.74; N, 5.66; S, 6.48%). IR (KBr/cm^{-1}) 3214 (N-H), 1778 (C=O anhydride), 1608 (C=N), 1195 (C–N), 728 (C–S). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.64 (3H, s, CH_3-17), 0.96 (3H, d, *J* = 6.9 Hz, CH_3-16), 0.98 (3H, d, *J* = 6.9 Hz, CH_3-15), 1.18 (3H, s, CH_3-18), 1.34−1.93 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 1.95-2.06 (1H, m, CH-14), 2.26 (1H, quint, *J* = 6.7, Hz CH-5a), 2.44 (1H, d.d, *J* = 3.0, 13.8 Hz, CH-9b), 2.93 (1H, d, *J* = 8.7, CH-3a), 3.11 (1H, d d., *J* = 8.6, 3.0 Hz, CH-11a), 3.12-3.14 (1H, m, CH-11), 3.86−3.95 (2H, m, CH_2-All), 5.46 (1H, s, CH-13), 5.37 (2H, d d., *J* = 10, 1.3 Hz, CH_2-All), 5.78-5.82 (1H, m, CH-All), 6.15 (1H, s, CH-5'), 9.23 (H, br s NH). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.66 (CH_3, C-17), 17.32 (CH_2, C-8), 18.12 (CH_3, C-18), 19.98 (CH_3, C-16), 20.28 (CH_2, C-5), 20.60 (CH_3, C-15), 27.27 (CH_2, C-10), 32.74 (CH, C-14), 34.19 (CH_2, C-4), 35.77 (CH, C-11), 37.25 (CH_2, C-9), 38.35 (CH_2, C-7), 39.00 (C-9a), 40.40 (C-3b), 41.54(C-6), 45.50 (CH, C-11a), 49.44(CH, C-5a), 50.24 (CH_2, All), 52.40 (CH, C-9b), 52.78 (CH, C-3a), 99.39 (CH, C-5'), 120.57 (CH_2, All), 125.16 (CH, C-13), 129.38 (CH, All), 148.31 (C-12), 152.08 (C-4'), 170.47 (C-2'), 171.20 (C-1), 172.94 (C-3). Mass spectrum (CI), *m/z*: 495 $[M + H]^+$, (calcd for $C_{29}H_{38}N_2O_3S$ *m/z*: 494).

6-(2-Anilino-1,3-thiazol-4-yl)-12-isopropyl-6,9a-dimethyldodecahydro-1H-3b,11-ethenophenanthro[1,2-c]furan-1,3(3aH)-dione **(6 d).** Yield 0.270 g, 51%, as yellowish solid, m.p.: 158°C, Elemental analysis (Found: C, 72.44; H, 7.26; N, 5.23; S, 6.00. $C_{32}H_{38}N_2O_3S$ Requires: C, 72.42; H, 7.22; N, 5.28; S, 6.04%). IR (KBr/cm^{-1}) 3400 (N-H), 1778 (C=O anhydride), 1608 (C=N), 1530 (Ar–C), 1192 (C–N), 756 (C–S). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.64 (3H, s, CH_3-17), 0.98 (3H, d, *J* = 6.2 Hz, CH_3-16), 1.1 (3H, d, *J* = 6.2 Hz, CH_3-15), 1.25 (3H, s, CH_3-18), 1.22−1.75 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 1.8-1.9 (1H, m, CH-14), 2.22 (1H, quint, *J* = 6.7, Hz CH-5a), 2.45 (1H, d. t, *J* = 3.0, 13.8 Hz, CH-9b), 2.9 (1H, d, *J* = 8.7 Hz, CH-3a), 3.09 (1H, d.d, *J* = 8.6, 3.0, Hz CH-11), 3.11 (1H, d, *J* = 9 Hz, CH-11a), 5.50 (1H, s, CH-13), 6.17 (1H, s, CH-5'), 7.49-7.91 (5H, Ph), 11.19 (1H, br s NH). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.69 (CH_3, C-17), 17.34 (CH_3, C-18), 17.34 (CH_2, C-8), 19.98 (CH_3, C-16), 20.33 (CH_2, C-5), 20.60 (CH_3, C-15), 27.28 (CH_2, C-10), 32.74 (CH, C-14), 34.21 (CH_2, C-4), 35.76 (CH, C-11), 37.28 (CH_2, C-9), 38.39 (C-9a), 39.16 (CH_2, C-7), 40.40 (C-3b), 41.58 (C-6), 45.49 (CH, C-11a), 50.42 (CH, C-5a), 52.44 (CH, C-9b), 52.78 (CH, C-3a), 99.50 (CH, C-5'), 121.04 (2CH, Ph), 125.12 (CH, Ph), 127.44 (CH, C-13), 130.20 (2CH, Ph), 136.47 (C, Ph), 148.34 (C-12), 151.80 (C-4'), 167.83 (C-2'), 171.17 (C-1), 172.92 (C-3). Mass spectrum (CI), *m/z*: 531 $[M + H]^+$, (calcd for $C_{32}H_{38}N_2O_3S$ *m/z*: 530).

12-Isopropyl-6,9a-dimethyl-6-{2-[(2-methylphenyl)amino]-1,3-thiazol-4-yl}dodecahydro-1H-3b,11-ethenophenanthro[1,2-c]furan-1,3(3aH)-dione **(6e).** Yield 0.326 g, 60%, as yellowish solid, m.p.: 138°C, Elemental analysis (Found: C, 72.75; H, 7.43; N, 5.16; S, 5.84. $C_{33}H_{40}N_2O_3S$ Requires: C, 72.76; H, 7.40; N, 5.14; S, 5.89%). IR (KBr/cm^{-1}) 3400 (N-H), 1778 (C=O anhydride), 1615 (C=N), 1583 (Ar–C), 1192 (C–N), 759 (C–S). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.67 (3H, s, CH_3-17), 0.99 (3H, d, *J* = 6.9 Hz, CH_3-16), 1.04 (3H, d, *J* = 6.9 Hz, CH_3-15), 1.21 (3H, s, CH_3-18), 1.34−1.98 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 1.8-1.9 (1H, m, CH-14), 2.16 (1H, quint, *J* = 6.7 Hz, CH-5a), 2.21 (1H, d.t, *J* = 3.0, 13.8 Hz, CH-9b), 2.21-2.30 (1H, m, CH-3a), 2.47 (3H, s, CH_3-Tol), 2.95 (1H, m, CH-11), 3.11 (1H, d.d, *J* = 8.6,

3.0 Hz, CH-11a), 5.45 (1H, s, CH-13), 6.15 (1H, s, CH-5'), 7.1-7.38 (4H, Tol), 10.61 (1H, d, *J* = 11 Hz, NH). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.66 (CH_3, C-17), 17.34 (CH_2, C-8), 18.18 (CH_3, C-18), 18.39 (CH_3, C-16), 19.99 (CH_3, C-15), 20.34 (CH_2, C-5), 20.61 (CH_3, Tol), 27.29 (CH_2, C-10), 32.75 (CH, C-14), 34.23 (CH_2, C-4), 35.77 (CH, C-11), 37.27 (CH_2, C-9), 38.39 (C-9a), 39.11 (CH_2, C-7), 40.42 (C-3b), 41.61 (C-6), 45.49 (CH, C-11a), 50.36 (CH, C-5a), 52.43 (CH, C-9b), 52.77 (CH, C-3a), 99.40 (CH, C-5'), 122.14 (CH, Tol), 125.16 (CH, Tol), 127.48 (CH, C-13), 128.33 (2CH, Ph), 133.20 (CH, Tol), 135.49 (C, Tol)), 148.33 (C-12), 151.99 (C-4'), 169.46 (C-2'), 171.28 (C-1), 172.92 (C-3). Mass spectrum (CI), *m/z*: 545 $[M + H]^+$, (calcd for $C_{33}H_{40}N_2O_3S$ *m/z*: 544).

12-Isopropyl-6,9a-dimethyl-6-(2-methyl-1,3-thiazol-4-yl)dodecahydro-1H-3b,11-ethenophenanthro[1,2-c]furan-1,3(3aH)-dione **(6f).** Yield 0.208 g, 46%, as yellowish solid, m.p.: 264 °C, Elemental analysis (Found: C 71.70; H 7.73; N, 3.11; S, 7.02. $C_{27}H_{35}NO_3S$ Requires: C, 71.49; H, 7.78; N, 3.09; S, 7.07%). IR (KBr/cm^{-1}) 1781 (C=O anhydride), 1600 (C=N), 1196 (C–N), 840 (C–S). δ_H ^{1}H NMR (500 MHz, DMSO-d_6) 0.60 (3H, s, CH_3-17), 1.00 (3H, d, *J* = 6.9 Hz, CH_3-15), 0.96 (3H, d, *J* = 6.4 Hz, CH_3-16), 1.17 (3H, s, CH_3-18), 1.21−1.91 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 1.8-1.9 (1H, m, CH-14), 2.26 (1H, quint, *J* = 6.7 Hz, CH-5a), 2.54 (1H, d.t, *J* = 3.0, 13.8 Hz, CH-9b), 2.70 (3H, s, CH_3), 2.73 (1H, d, *J* = 8.7 Hz, CH-3a), 3.09-3.11 (1H, m, CH-11), 3.30(1H, d.d., *J* = 8.6, 3.0 Hz, CH-11a), 5.54 (1H, s, CH-13), 7.20 (1H, s, CH-5). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.82 (CH_3), 17.60 (CH_2, C-8), 18.19 (CH_3, C-17), 19.15 (CH_3, C-18), 19.95 (CH_2, C-5), 20.38 (CH_3, C-16), 20.84 (CH_3, C-15), 27.12 (CH_2, C-10), 32.63 (CH, C-14), 34.75 (CH_2, C-4), 35.60 (CH, C-11), 37.76 (CH_2, C-9), 38.35 (C-9a), 39.22 (CH_2, C-7), 41.60 (C-3b), 45.88 (CH, C-11a), 50.91 (CH, C-5a), 40.57 (C-6), 52.75 (CH, C-9b), 53.25 (CH, C-3a), 115.31 (CH, C-5'), 125.47 (CH, C-13), 147.83 (C-12), 162.11 (C-4'), 168.74 (C-2'), 172.38 (C-1), 174.07 (C-3). Mass spectrum (CI), *m/z*: 454 $[M + H]^+$, (calcd for $C_{27}H_{35}NO_3S$ *m/z*: 453).

6-(2-Amino-1,3-thiazol-4-yl)-12-isopropyl-6,9a-dimethyl-2-phenyldodecahydro-3b,11-ethenonaphtho[2,1-e]isoindole-1,3(3aH)-dione **(7a).** Yield 0.349 g, 66%, as yellowish solid, m.p.: 246°C, Elemental analysis (Found: C, 72.57; H, 7.46; N, 7.95; S, 6.02. $C_{32}H_{39}N_3O_2S$ Requires: C, 72.55; H, 7.42; N, 7.93; S, 6.05%).3400 (N–H), 1776 (C=O imide), 1617 (C=N), 1196 (C–N), 730 (C–S). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.65 (3H, s, CH_3-17), 0.95 (3H, d, *J* = 6.2 Hz, CH_3-16), 1.01 (3H, d, *J* = 6.2 Hz, CH_3-15), 1.25 (3H, s, CH_3-18), 1.40−1.83 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 1.83 (1H, m, CH-5a), 2.2-2.23 (1H, m, CH-14), 2.45 (1H, d.t, *J* = 3.0, 13.8 Hz, CH-9b), 2.79 (1H, d, *J* = 8.7 Hz,CH-3a), 3.09-3.11 (1H, m,CH-11), 3.20 (1H, d.d, *J* = 8.6, 3.0 Hz, CH-11a), 5.33 (1H, s, CH-13), 6.14 (1H, s, CH-5'), 7.1-7.55 (5H, m, Ph), 8.61 (2H, br s NH_2). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.85 (CH_3, C-17), 17.41 (CH_2, C-8), 20.37 (CH_2, C-5), 18.20 (CH_3, C-16), 20.14 (CH_3, C-15), 20.84 (CH_3, C-18), 27.57 (CH_2, C-10), 32.79 (CH, C-14), 34.85 (CH_2, C-4), 37.55 (CH_2, C-9), 36.13 (CH, C-11), 38.45 (C-9a), 39.04 (CH_2, C-7), 41.08 (C-3b), 41.24 (C-6), 45.09 (CH, C-11a), 50.55 (CH, C-5a), 52.24 (CH, C-9b), 53.55 (CH, C-3a), 100.96 (CH, C-5'), 124.30 (CH, C-13), 126.47 (2CH, Ph), 128.32 (CH, Ph), 129.11 (2CH, Ph), 131.99 (C, Ph), 147.68 (C-12), 149.94 (C-4'), 170.34 (C-2'), 177.16 (C-1), 177.86 (C-3). Mass spectrum (CI), *m/z*: 530 $[M + H]^+$, (calcd for $C_{32}H_{39}N_3O_2S$ *m/z*: 529).

N-[4-(12-Isopropyl-6,9a-dimethyl-1,3-dioxo-2-phenylhexadecahydro-3b,11-ethenonaphtho[2,1-e]isoindol-6-yl)-1,3-thiazol-2-yl]acetamide **(7b).** Yield 0.319 g, 56%, as yellowish solid, m.p.: 102°C, Elemental analysis (Found: C, 71.44; H, 7.26; N, 7.31; S, 5.61. $C_{34}H_{41}N_3O_3S$ Requires: C, 71.42; H, 7.23; N, 7.35; S, 5.61%). IR (KBr/cm^{-1}) 3133 (N–H), 1703 (C=O imide), 1600 (C=N), 1495 (C=O amid), 1189 (C–N), 780 (C–S). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.64 (3H, s, CH_3-17), 0.98 (3H, d, *J* = 6.2 Hz, CH_3-16), 1.01 (3H, d, *J* = 6.2 Hz, CH_3-15), 1.31 (3H, s, CH_3-18), 1.41−1.93 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 2.1-2.23 (1H, m, CH-14), 2.35 (3H, s, $CH_3C(O)$), 2.55 (1H, quint, *J* = 6.7 Hz, CH-5a), 2.58 (1H, d.t, *J* = 3.0, 13.8 Hz, CH-9b), 2.89 (1H, d, *J* = 8.7 Hz, CH-3a), 3.11-3.13 (1H, m, CH-11), 3.15 (1H, d.d, *J* = 8.6, 3.0 Hz, CH-11a), 5.47 (1H, s, CH-13), 6.62 (1H, s, CH-5'), 7.1-7.55 (5H, m, Ph), 12.8 (1H, br s

NH). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.72 (CH_3, C-17), 17.34 (CH_2, C-8), 18.31 (CH_3, C-18), 19.96 (CH_3, C-15), 20.27 (CH_2, C-5), 20.59 (CH_3, C-16), 23.34 (CH_3, Ac), 27.28 (CH_2, C-10), 32.73 (CH, C-14), 34.24 (CH_2, C-4), 35.71 (CH, C-11), 37.30 (CH_2, C-9), 38.42 (C-9a), 39.54 (CH_2, C-7), 40.42 (C-3b), 41.45 (C-6), 45.5 (CH, C-11a), 50.69 (CH, C-5a), 52.66 (CH, C-9b), 52.80 (CH, C-3a), 107.33 (CH, C-5'), 124.97 (CH, C-13), 126.65 (2CH, Ph), 128.34 (CH, Ph), 129.12 (2CH, Ph), 132.01 (C, Ph), 148.33 (C-12), 151.61 (C-4'), 161.90 (C-2'), 168.27 (CO), 176.51 (C-1), 177.71 (C-3). Mass spectrum (CI), *m/z*: 572 $[M + H]^+$, (calcd for $C_{34}H_{41}N_3O_3S$ *m/z*: 571).

6-[2-(Allylamino)-1,3-thiazol-4-yl]-12-isopropyl-6,9a-dimethyl-2-phenyldodecahydro-3b,11-ethenonaphtho[2,1-e]isoindole-1,3(3aH)-dione **(7c).** Yield 0.558 g, 98%, as yellowish solid, m.p.: 117°C, Elemental analysis (Found: C, 73.75; H, 7.64; N, 7.34; S, 5.61. $C_{35}H_{43}N_3O_2S$ Requires: C, 73.78; H, 7.61; N, 7.37; S, 5.63%). IR (KBr/cm^{-1}) 3220 (N-H), 1707 (C=O imide), 1607 (C=N), 1185 (C–N), 756 (C–S). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.62 (3H, s, CH_3-17), 0.96 (3H, d, *J* = 6.9 Hz, CH_3-16), 0.91 (3H, d, *J* = 6.9 Hz, CH_3-15), 1.28 (3H, s, CH_3-18), 1.34−1.93 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 1.95-2.06 (1H, m, CH-14), 2.27 (1H, quint, *J* = 6.7 Hz,CH-5a), 2.49 (1H, d.t, *J* = 3.0, 13.8 Hz, CH-9b), 2.77 (1H, d, *J* = 8.7 Hz, CH-3a), 3.00-3.02 (1H, m, CH-11a), 3.16 (1H, d.d, *J* = 8.6, 3.0 Hz, CH-11), 3.86−3.95 (2H, m, CH_2-All), 5.49 (1H, s, CH-13), 5.37 (2H, d.d, *J* = 10, 1.3 Hz, CH_2-All,), 5.78-5.82 (1H, m, CH-All), 6.15 (1H, s, CH-5'), 7.1-7.55 (5H, m, Ph), 9.29 (2H, br s NH). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.84 (CH_3, C-17), 17.34 (CH_2, C-8), 18.20 (CH_3, C-16), 20.13 (CH_3, C-16), 20.39 (CH_2, C-5), 20.85 (CH_3, C-15), 27.63 (CH_2, C-10), 32.79 (CH, C-14), 34.81 (CH_2, C-4), 36.19 (CH, C-11), 37.39 (CH_2, C-9), 38.44 (C-9a), 38.92 (CH_2, C-7), 40.99 (C-3b), 41.55 (C-6), 44.91 (CH, C-11a), 49.92 (CH_2, All), 50.66 (CH, C-5a), 51.16 (CH, C-9b), 53.41 (CH, C-3a), 99.24 (CH, C-5'), 120.50 (CH_2, All), 124.43 (CH, C-13), 126.45 (2CH, Ph), 128.40 (CH, Ph), 129.05 (2CH, Ph), 129.43 (CH, All), 132.00 (C, Ph), 147.56 (C-12), 152.13 (C-4'), 170.41 (C-2'), 176.63 (C-1), 177.79 (C-3). Mass spectrum (CI), *m/z*: 570 $[M + H]^+$, (calcd for $C_{35}H_{43}N_3O_2S$ *m/z*: 569).

6-(2-Anilino-1,3-thiazol-4-yl)-12-isopropyl-6,9a-dimethyl-2-phenyldodecahydro-3b,11-ethenonaphtho[2,1-e]isoindole-1,3(3aH)-dione **(7d).** Yield 0.363 g, 60%, as yellowish solid, m.p.: 64°C, Elemental analysis (Found: C, 75.35; H, 7.11; N, 6.94; S, 5.25. $C_{38}H_{43}N_3O_2S$ Requires: C, 75.34; H, 7.15; N, 6.94; S, 5.29%). IR (KBr/cm^{-1}) 3273 (N-H), 1709 (C=O imide), 1606 (C=N), 1581 (Ar–C), 1182 (C–N), 754 (C–S). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.69 (3H, s, CH_3-17), 0.98 (3H, d, *J* = 6.2 Hz, CH_3-16), 1.1 (3H, d, *J* = 6.2 Hz, CH_3-15), 1.28 (3H, s, CH_3-18), 1.22−1.91 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 1.95-1.98 (1H, m, CH-14), 2.27 (1H, quint, *J* = 6.7 Hz, CH-5a), 2.54 (1H, d.t, *J* = 3.0, 13.8 Hz, CH-9b,), 2.77 (1H, d, *J* = 8.7 Hz, CH-11a), 3.00 (1H, d, *J* = 9 Hz, CH-3a), 3.16 (1H, d.d, *J* = 8.6, 3.0 Hz, CH-11), 5.50 (1H, s, CH-13), 7.1-7.55 (5H, m, Ph), 6.17 (1H, s, CH-5'), 7.49-7.91 (5H, Ph), 11.25 (1H, br s NH). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.85 (CH_3, C-17), 17.36 (CH_2, C-8), 18.28 (CH_3, C-18), 20.13 (CH_3, C-16), 20.46 (CH_2, C-5), 20.86 (CH_3, C-15), 27.64 (CH_2, C-10), 32.79 (CH, C-14), 34.86 (CH_2, C-4), 36.19 (CH, C-11), 37.43 (CH_2, C-9), 38.48 (C-9a), 39.09 (CH_2, C-7), 40.99 (C-3b), 41.57 (C-6), 44.90 (CH, C-11a), 50.84 (CH, C-5a), 52.17 (CH, C-9b), 53.48 (CH, C-3a), 99.44 (CH, C-5'), 121.09 (2CH, Ph), 124.42 (CH, C-13), 126.45 (CH, Ph), 126.51 (2CH, Ph), 128.31 (CH, Ph), 129.04 (2CH, Ph), 130.16 (2CH, Ph), 131.99 (C, Ph), 136.52 (C, Ph), 147.59 (C-12), 151.84 (C-4'), 167.80 (C-2'), 176.59 (C-1), 177.75 (C-3). Mass spectrum (CI), *m/z*: 606 $[M + H]^+$, (calcd for $C_{38}H_{43}N_3O_2S$ *m/z*: 605).

12-Isopropyl-6,9a-dimethyl-6-{2-[(2-methylphenyl)amino]-1,3-thiazol-4-yl}-2-phenyldodecahydro-3b,11-ethenonaphtho[2,1-e]isoindole-1,3(3aH)-dione **(7e).** Yield 0.538 g, 87%, as yellowish solid, m.p.: 71°C, Elemental analysis (Found: C, 75.59; H, 7.36; N, 6.75; S, 5.18. $C_{39}H_{45}N_3O_2S$ Requires: C, 75.57; H, 7.32; N, 6.78; S, 5.17%). IR (KBr/cm^{-1}) 3400 (N-H), 1707 (C=O imide), 1610 (C=N), 1583 (Ar–C), 1181 (C–N), 721 (C–S). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.69 (3H, s, CH_3-17), 0.98 (3H, d, *J* = 6.9 Hz, CH_3-16), 0.99 (3H, d, *J* = 6.9 Hz, CH_3-15), 1.29 (3H, s, CH_3-18), 1.34−1.98 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10),

1.95-2.01 (1H, m, CH-14), 2.29 (1H, quint, *J* = 6.7 Hz, CH-5a), 2.47 (3H, s, CH_3-Tol), 2.54 (1H, d.t, *J* = 3.0, 13.8Hz, CH-9b), 2.81 (1H, d, *J* = 8.7 Hz, CH-3a), 3.09 (1H, m, CH-11), 3.11 (1H, d.d, *J* = 8.6, 3.0 Hz, CH-11a), 5.51 (1H, s, CH-13), 6.10 (1H, s, CH-5'), 7.1-7.48 (9H, Ar), 10.81 (1H, d, *J* = 11 Hz, NH,). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.66 (CH_3, C-17), 17.36 (CH_2, C-8), 18.29 (CH_3, C-18), 18.43 (CH_3, C-16), 20.15 (CH_3, C-15), 20.48 (CH_2, C-5), 20.86 (CH_3Tol), 27.68 (CH_2, C-10), 32.80 (CH, C-14), 34.87 (CH_2, C-4), 36.22 (CH, C-11), 37.42 (CH_2, C-9), 38.49 (C-9a), 39.08 (CH_2, C-7), 41.01 (C-3b), 41.61 (C-6), 44.90 (CH, C-11a), 50.78 (CH, C-5a), 52.18 (CH, C-9b), 53.47 (CH, C-3a), 99.23 (CH, C-5'), 122.11 (CH, Tol), 124.48 (CH, C-13), 126.45 (CH, Tol), 126.50 (2CH, Ph), 127.42 (CH, Ph), 128.39 (2CH, Ph), 129.04 (2CH, Ph), 131.98 (C, Ph), 132.02 (CH, Tol), 135.58 (C, Ph), 147.58 (C-12), 152.07 (C-4'), 169.38 (C-2'), 176.63 (C-1), 177.74 (C-3). Mass spectrum (CI), *m/z*: 620 $[M + H]^+$, (calcd for $C_{39}H_{45}N_3O_2S$ *m/z*: 619).

12-Isopropyl-6,9a-dimethyl-6-[2-(methylamino)-1,3-thiazol-4-yl]-2-phenyldodecahydro-3b,11-ethenonaphtho[2,1-e]isoindole-1,3(3aH)-dione **(7f).** Yield 0.496 g, 94%, as yellowish solid, m.p.: 187 °C, Elemental analysis (Found: C, 74.93; H, 7.67; N, 5.32; S, 6.06. $C_{33}H_{40}N_3O_2S$ Requires: C, 74.96; H, 7.63; N, 5.30; S, 6.06%). 1781 (C=O imide), 1959 (C=N), 1190 (C–N), 815 (C–S). δ_H ^{1}H NMR (500 MHz, $CDCl_3$) 0.60 (3H, s, CH_3-17), 1.00 (3H, d, *J* = 6.9 Hz, CH_3-15,), 0.96 (3H, d, *J* = 6.4 Hz, CH_3-16), 1.17 (3H, s, CH_3-18), 1.21−1.91 (12H, m, CH_2-4, CH_2-5, CH_2-7, CH_2-8, CH_2-9, CH_2-10), 1.8-1.9 (1H, m, CH-14), 2.26 (1H, quint, *J* = 6.7 Hz, CH-5a), 2.54 (1H, d.t, *J* = 3.0, 13.8 Hz, CH-9b), 2.70 (3H, s, $CH_3C(O)$), 2.73 (1H, d, *J* = 8.7 Hz, CH-3a), 3.09 (1H, m, CH-11), 3.30 (1H, d, *J* = 8.6, CH-11a), 5.20 (1H, s, CH-5'), 5.54 (1H, s, CH-13), 7.1-7.48 (5H, Ar). δ_C ^{13}C NMR (125 MHz, $CDCl_3$) 15.82 (CH_3, Ac), 17.60 (CH_2, C-8), 18.19 (CH_3, C-17), 19.15 (CH_3, C-18), 19.95 (CH_2, C-5), 20.38 (CH_3, C-16), 20.84 (CH_3, C-15), 27.12 (CH_2, C-10), 32.63 (CH, C-14), 34.75 (CH_2, C-4), 35.60 (CH, C-11), 37.76 CH_2, C-9), 38.34 (C-9a), 39.22 (CH_2, C-7), 41.60 (C-3b), 45.88 (CH, C-11a), 50.91 (CH, C-5a), 51.95 (C-6), 52.75 (CH, C-9b), 53.25 (CH, C-3a), 115.31 (CH, C-5'), 125.47 (CH, C-13), 126.65 (2CH, Ph), 128.34 (CH, Ph), 129.12 (2CH, Ph), 132.01 (C, Ph), 147.56 (C-12), 162.11 (C-4'), 172.38 (C-2'), 176.74 (C-1), 177.62 (C-3). Mass spectrum (CI), *m/z*: 529 $[M + H]^+$, (calcd for $C_{33}H_{40}N_3O_2S$ *m/z*: 528).

NMR Data

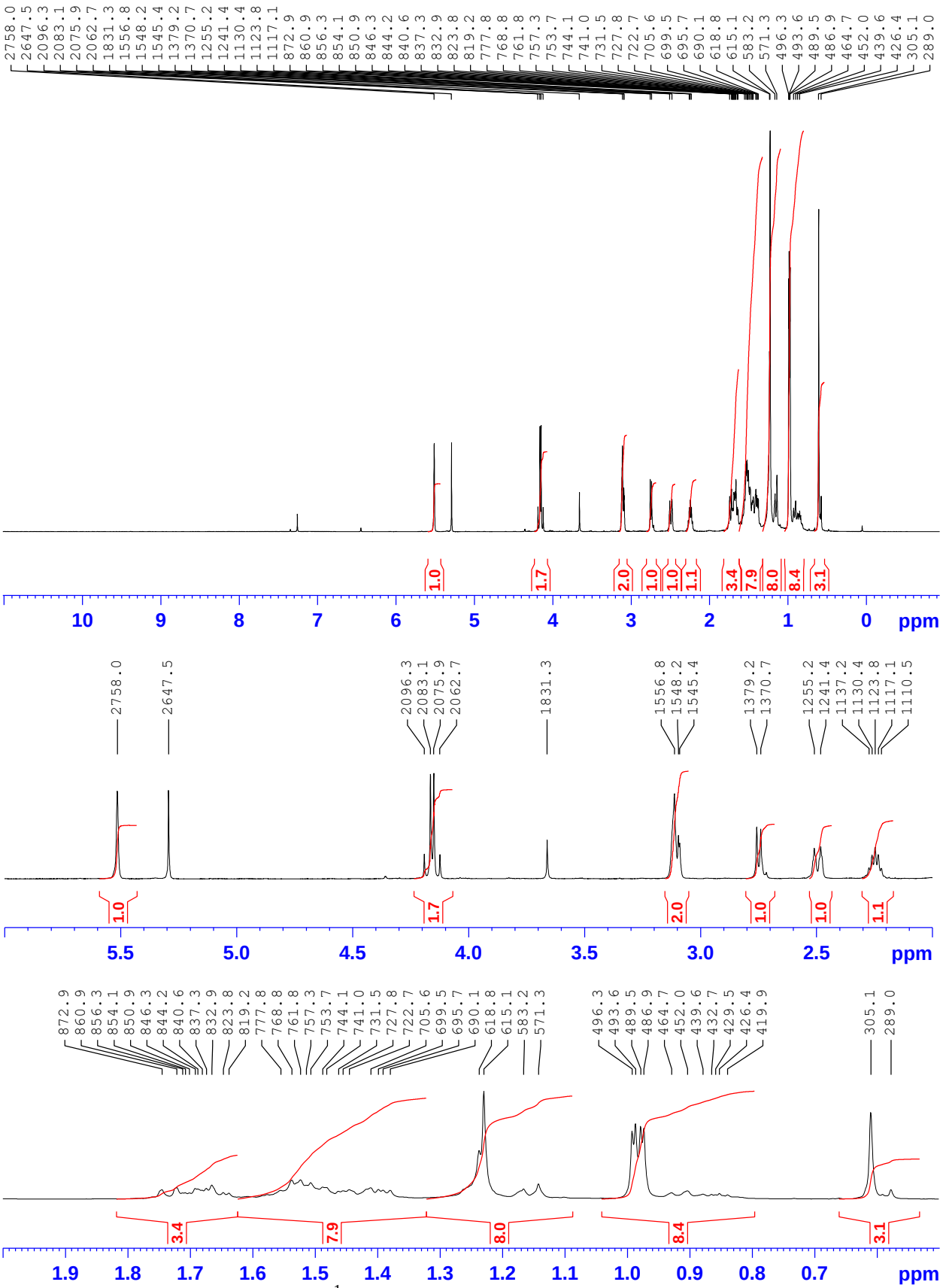

Figure S1. Complete and detailed ^{1}H NMR spectrum of compound **3** in $CDCl_3$ solution, 500 MHz.

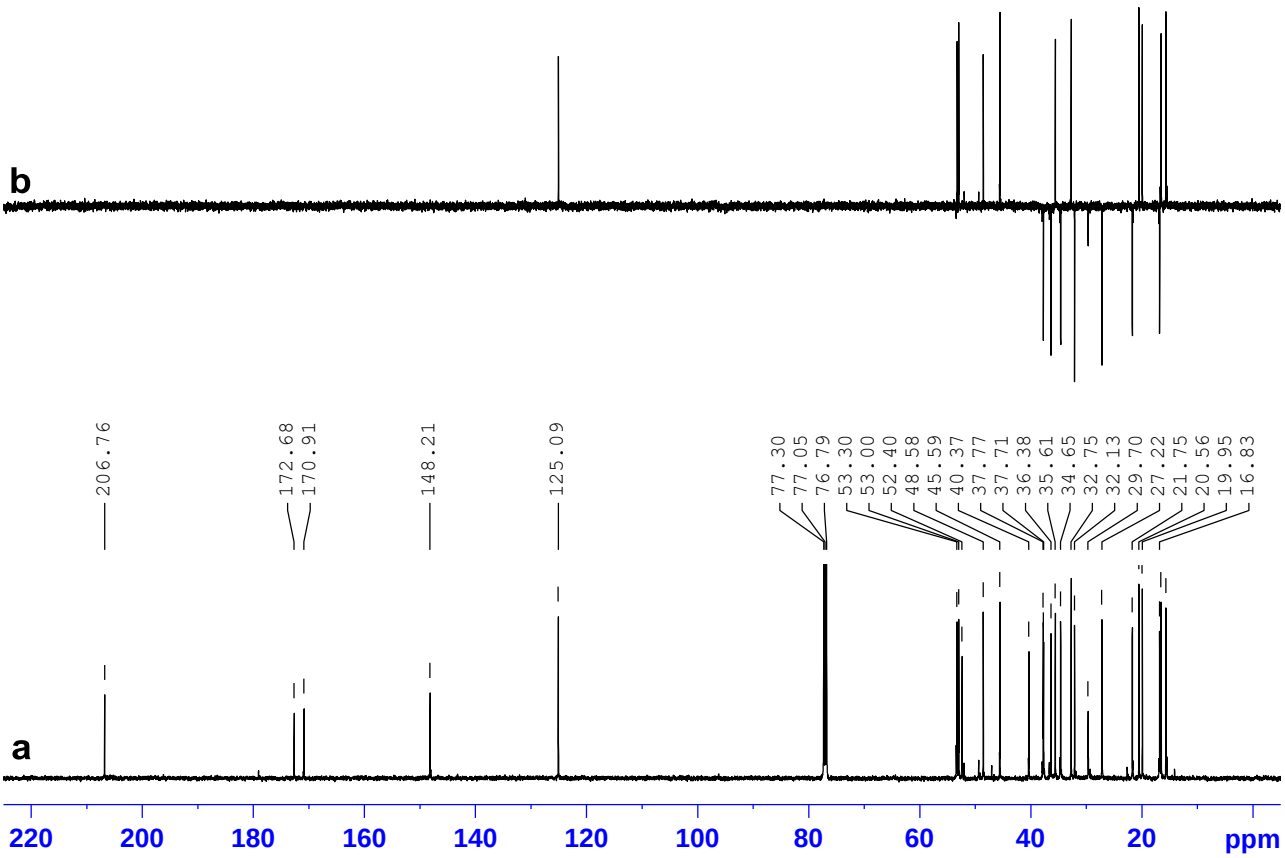

Figure S2. Complete $^{13}C\{^{1}H\}$(**a**) and DEPT-135(**b**) spectra of compound **3** in $CDCl_3$ solution, solution, 500 MHz.

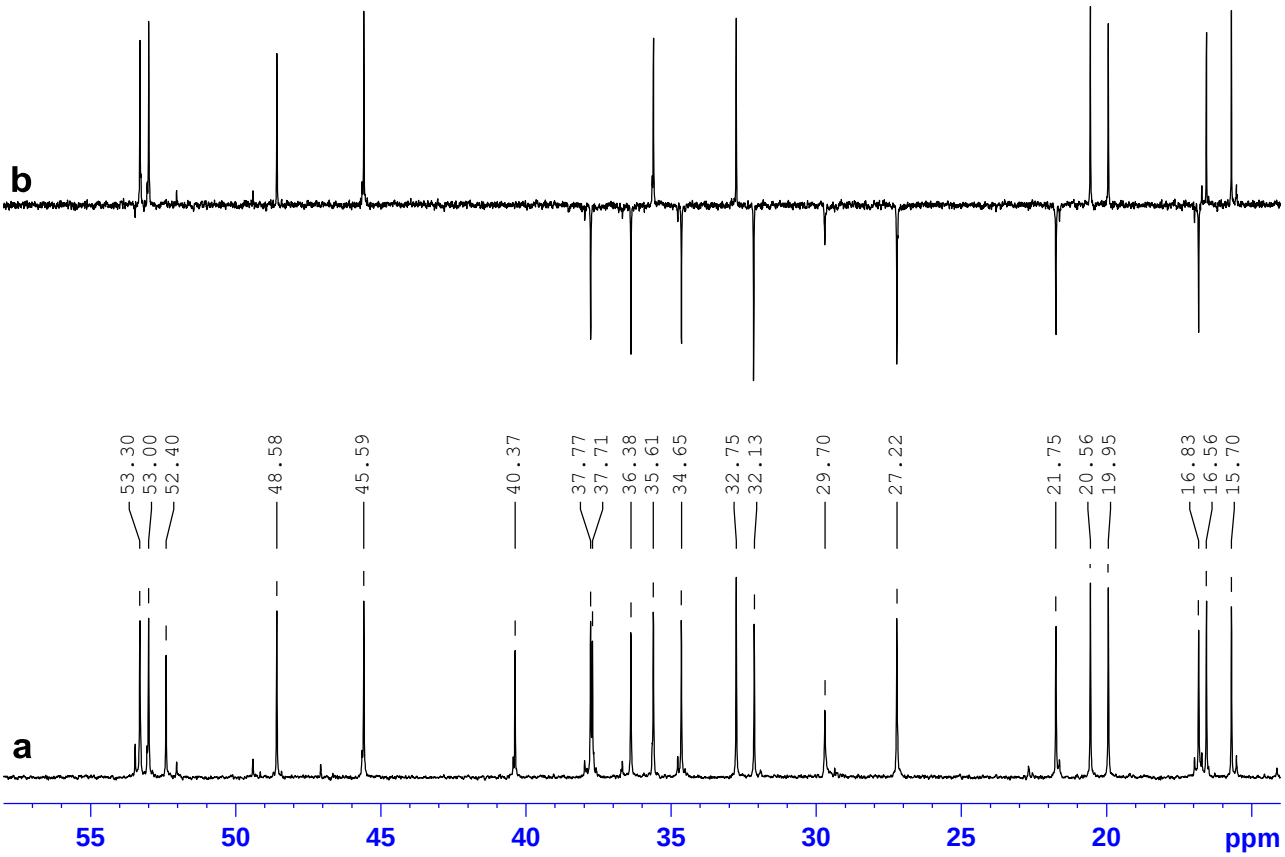

Figure S3. Expanded $^{13}C\{^{1}H\}$(**a**) and DEPT-135(**b**) spectra of compound **3** in $CDCl_3$ solution, solution, 500 MHz.

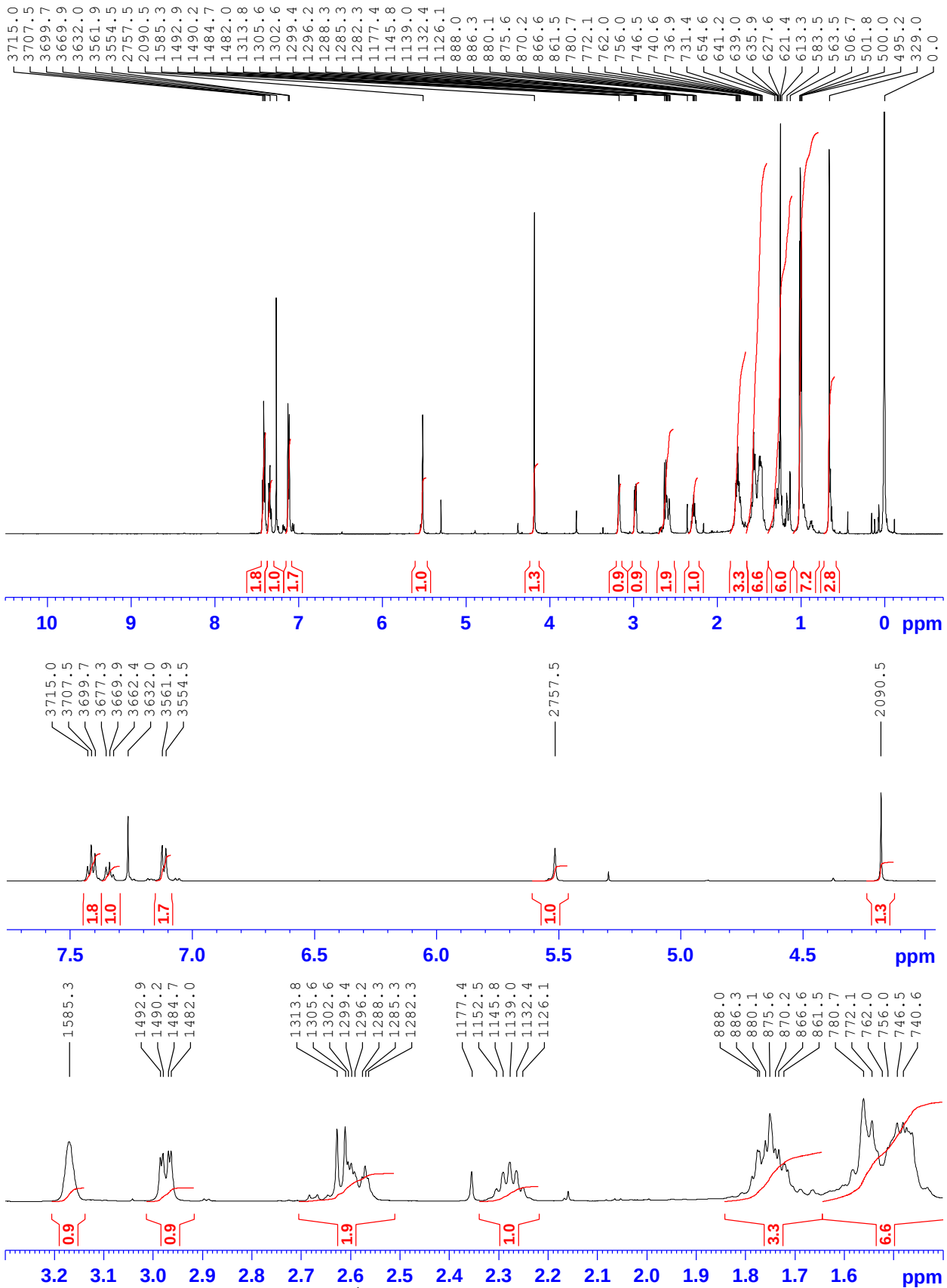

Figure S4. Complete and detailed ^{1}H NMR spectrum of compound **4** in $CDCl_3$ solution, 500 MHz.

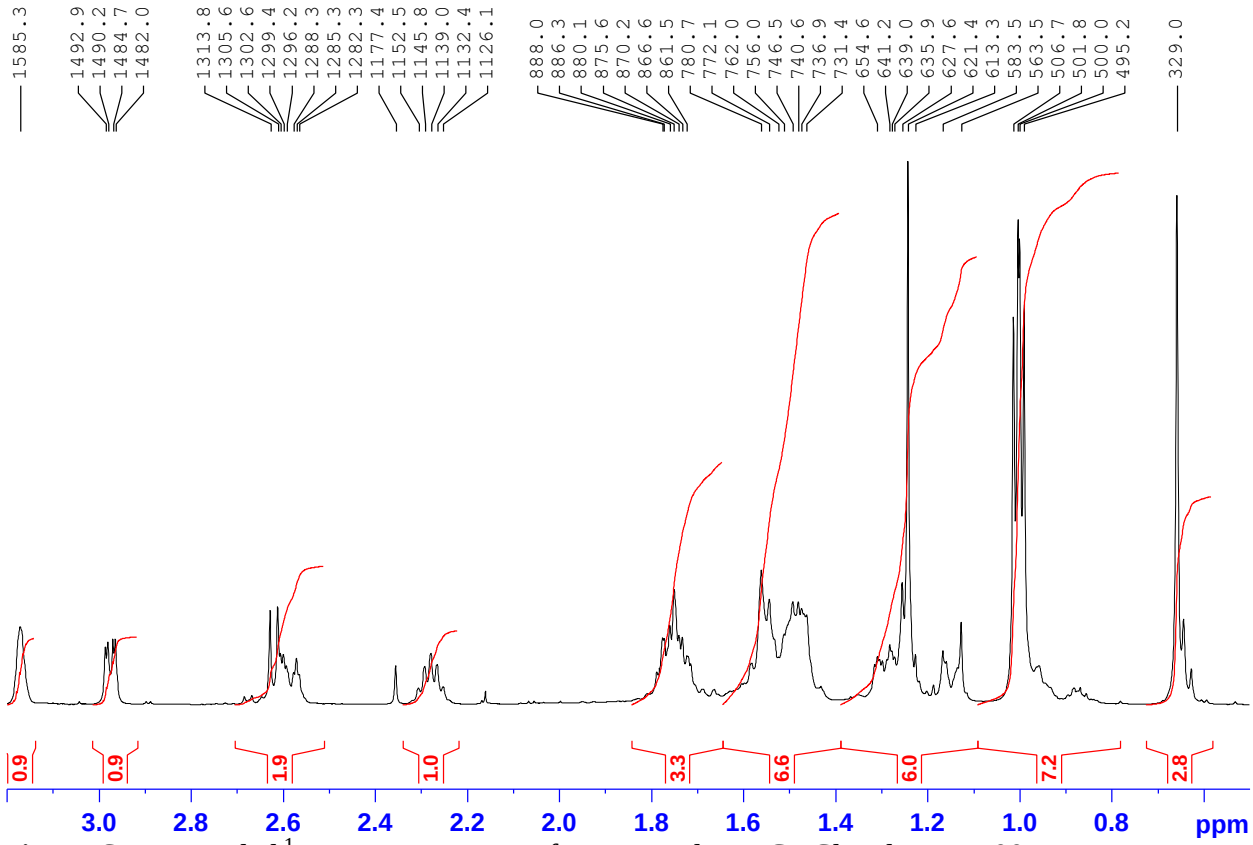

Figure S5. Expanded ^{1}H NMR spectrum of compound **4** in $CDCl_3$ solution, 500 MHz.

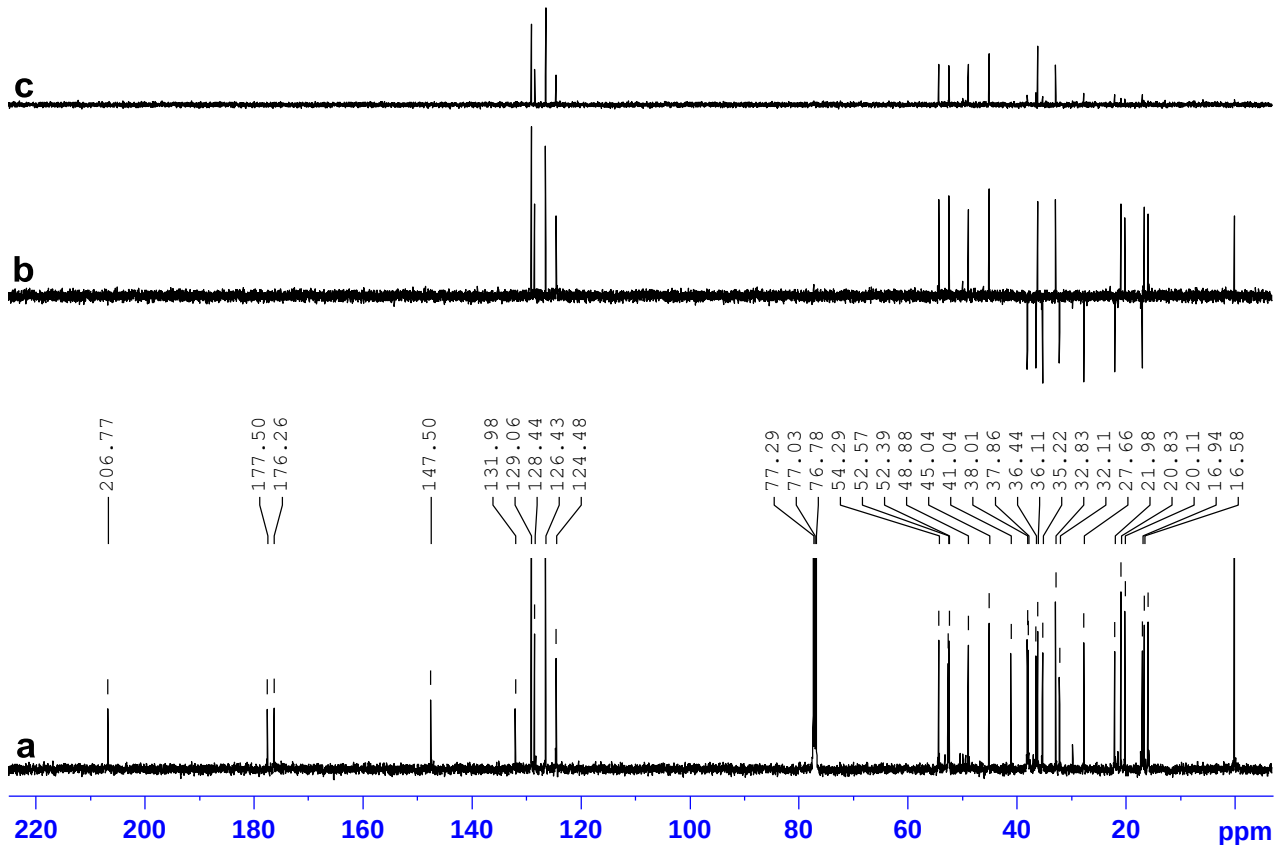

Figure S6. Complete ^{13}C{^{1}H}(**a**), DEPT-135 (**b**) and DEPT-90 (**c**) spectra of compound **4** in $CDCl_3$ solution, 500 MHz.

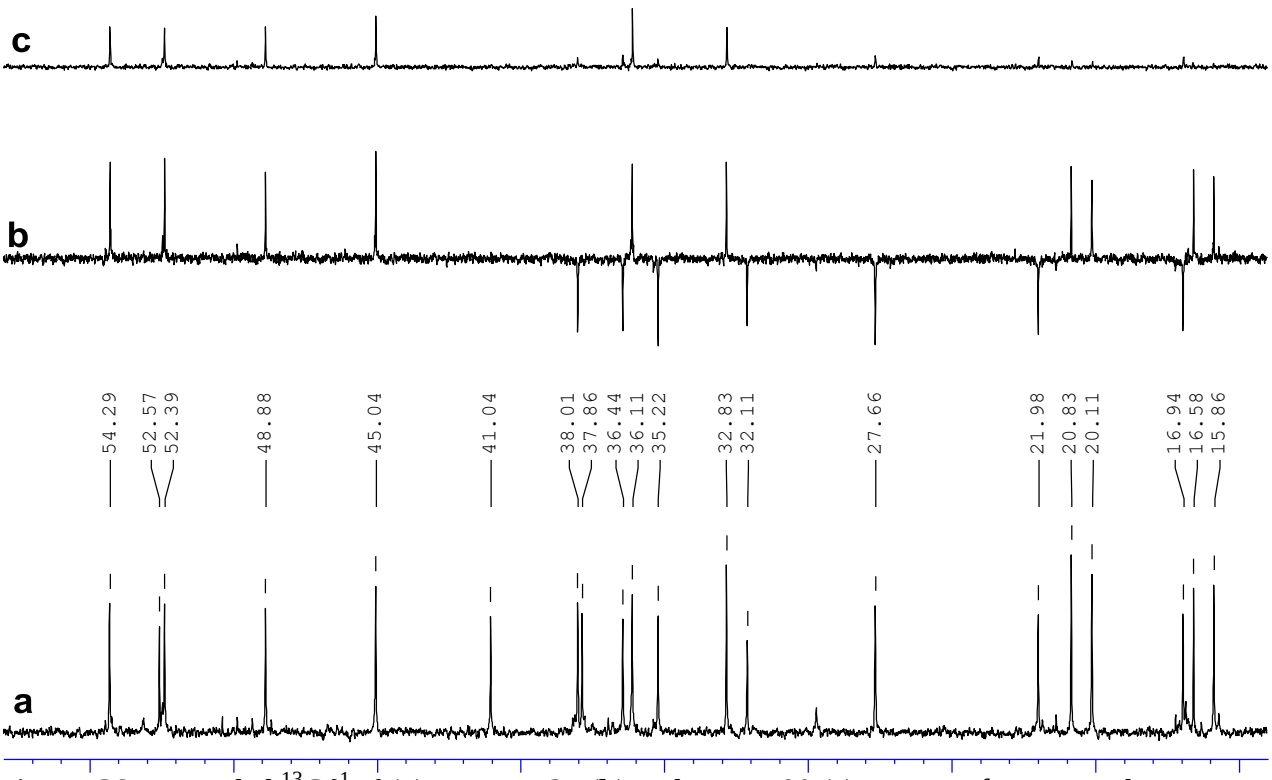

Figure S6. Expanded $^{13}C\{^{1}H\}$(**a**), DEPT-135 (**b**) and DEPT-90 (**c**) spectra of compound **4** in $CDCl_3$ solution, 500 MHz.

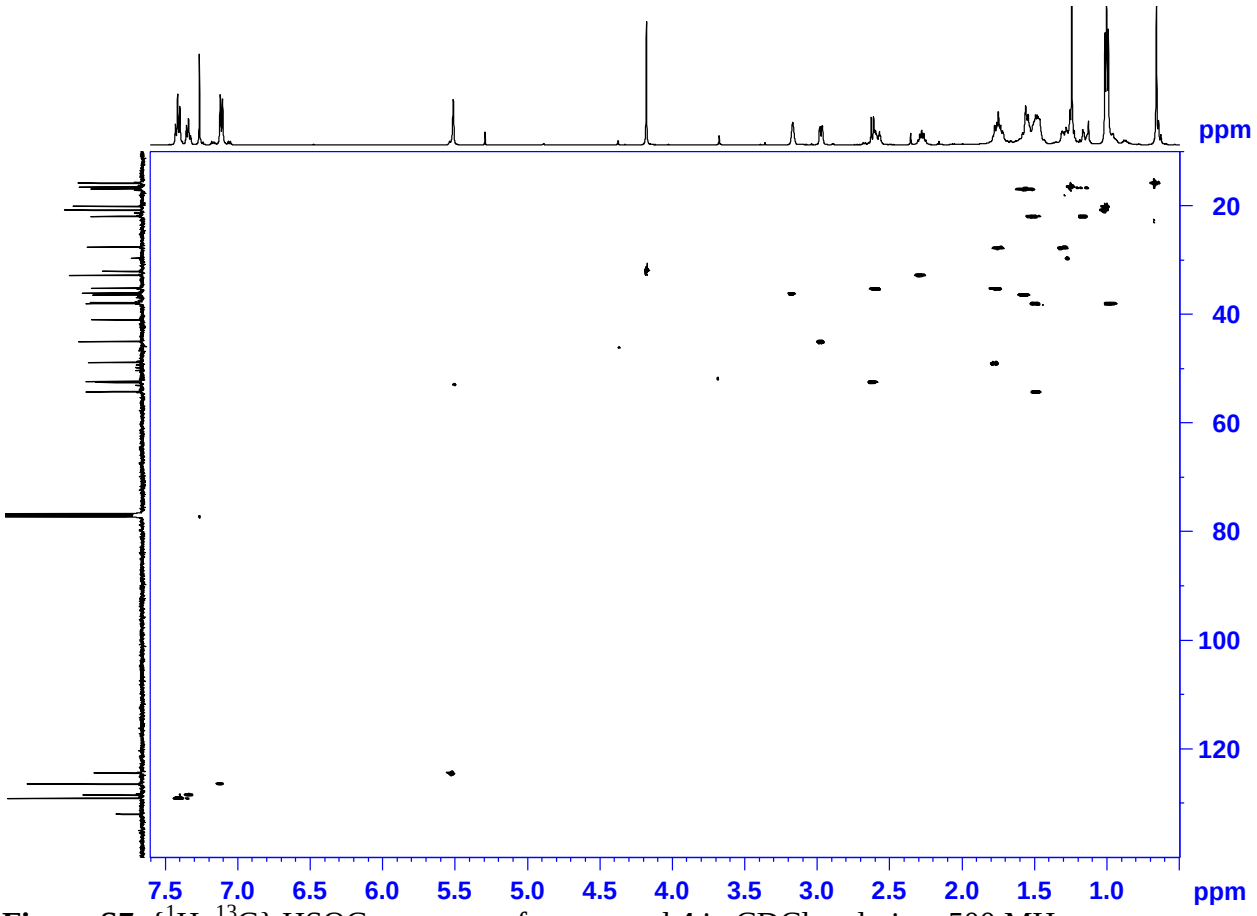

Figure S7. $\{^{1}H, ^{13}C\}$ HSQC spectrum of compound **4** in $CDCl_3$ solution, 500 MHz.

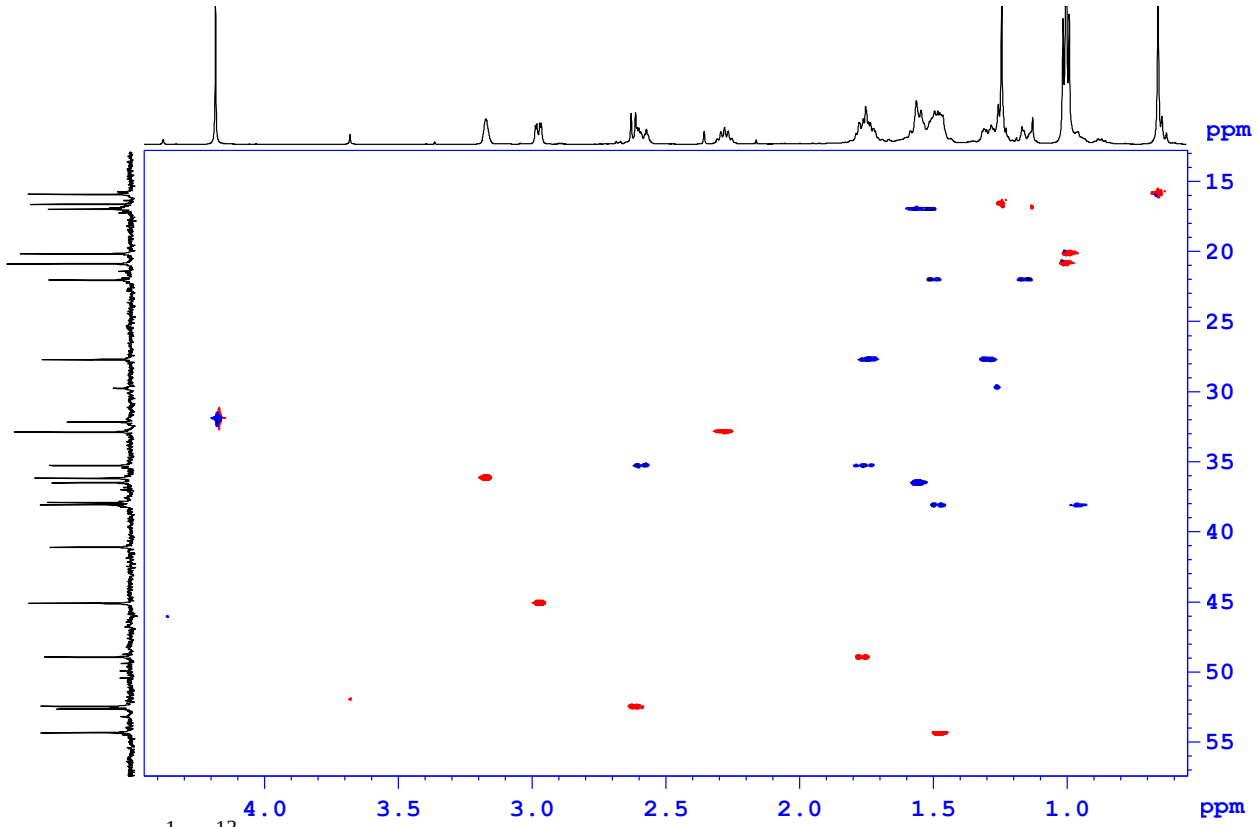

Figure S8. {^{1}H, ^{13}C} HSQCed spectrum of compound **4** in $CDCl_3$ solution, 500 MHz.

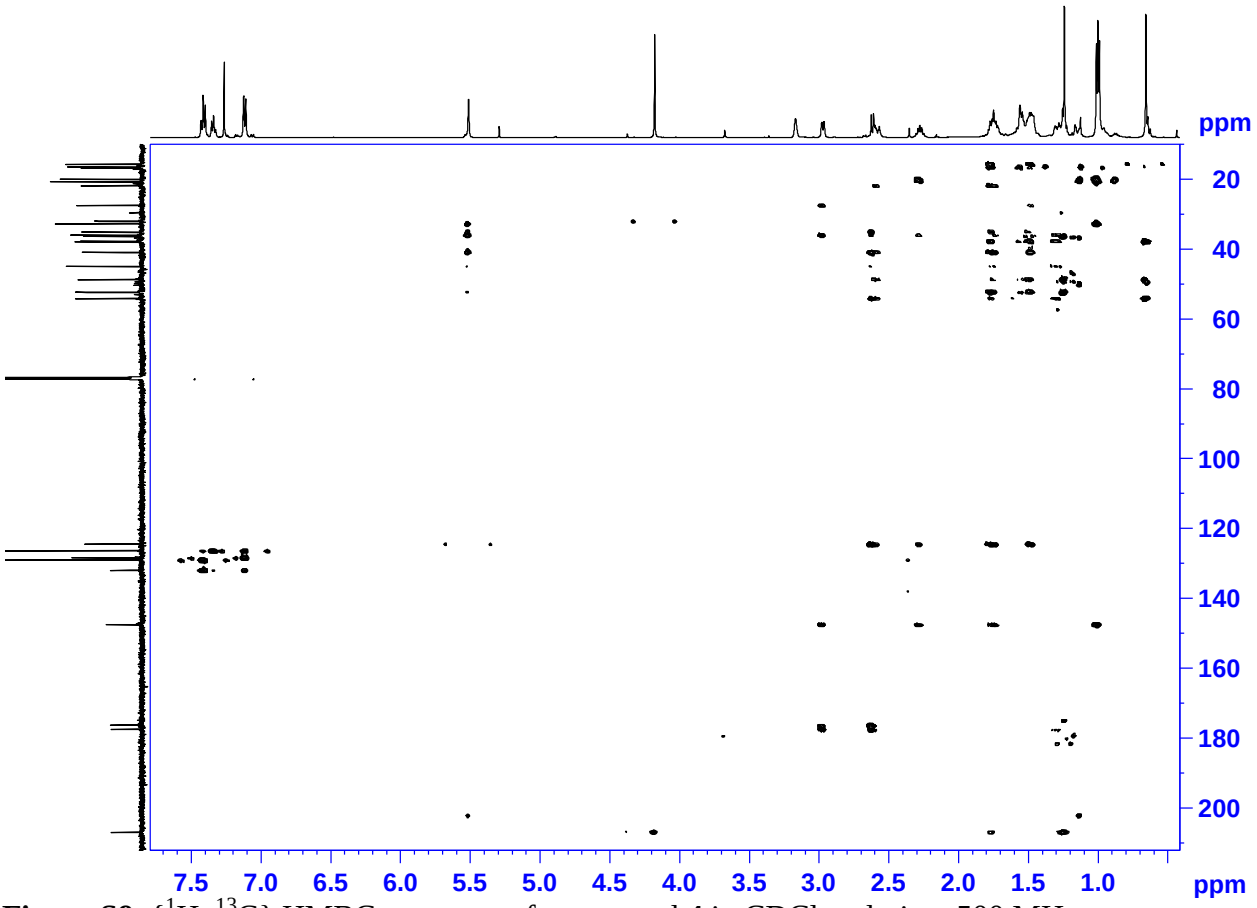

Figure S9. {^{1}H, ^{13}C} HMBC spectrum of compound **4** in $CDCl_3$ solution, 500 MHz.

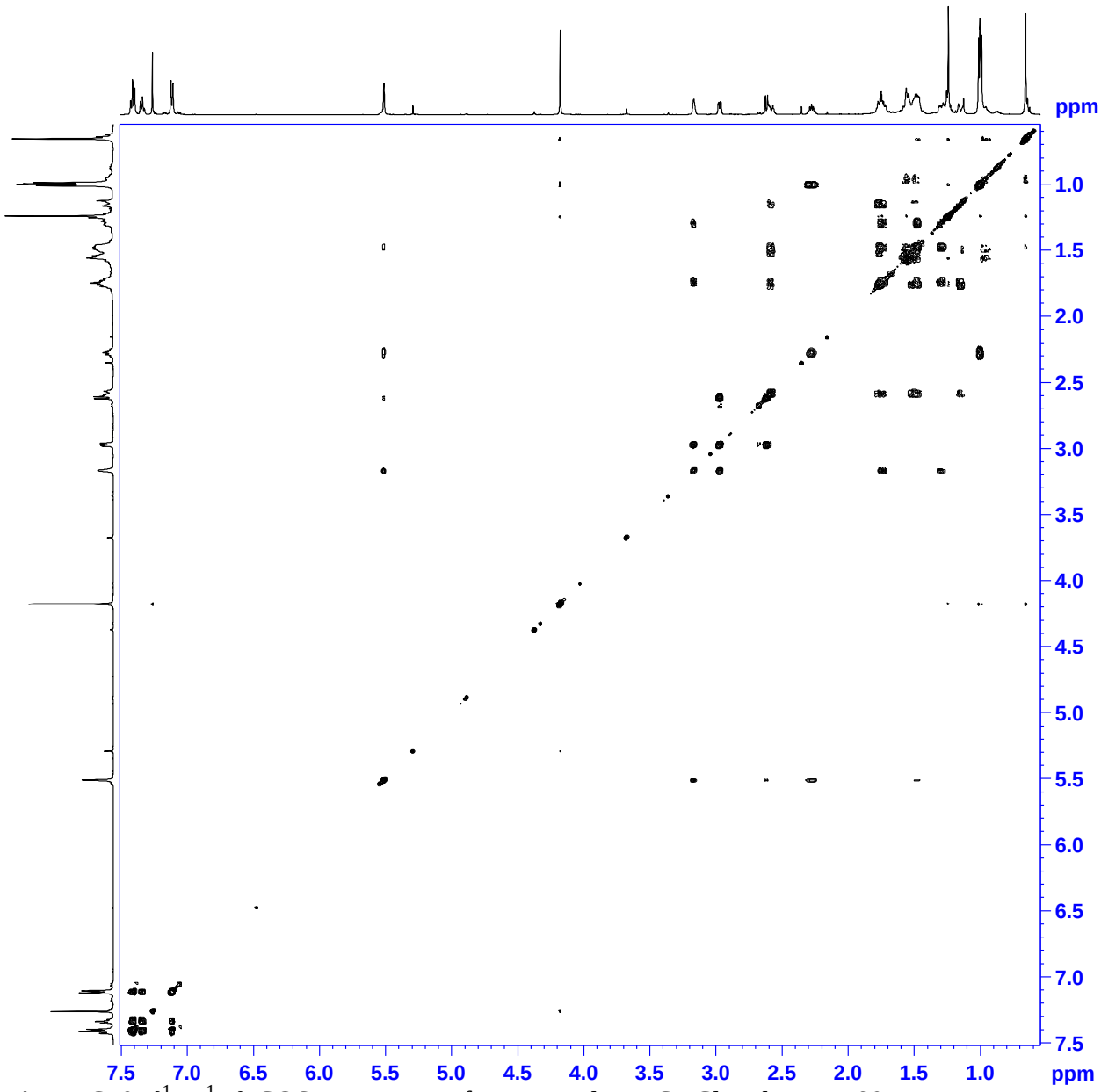

Figure S10. {^{1}H, ^{1}H} COSY spectrum of compound **4** in $CDCl_3$ solution, 500 MHz.

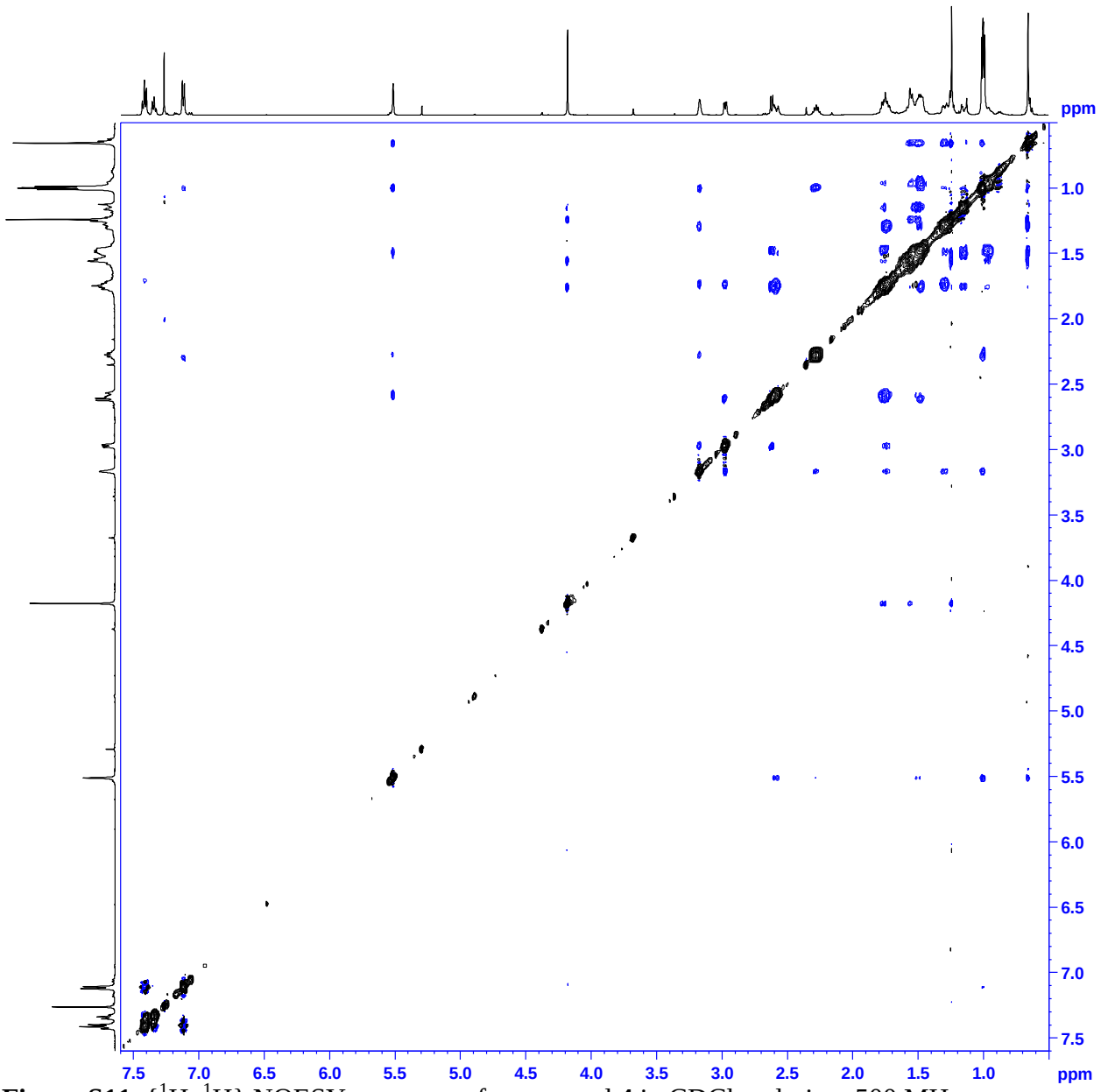

Figure S11. {^{1}H, ^{1}H} NOESY spectrum of compound **4** in $CDCl_3$ solution, 500 MHz.

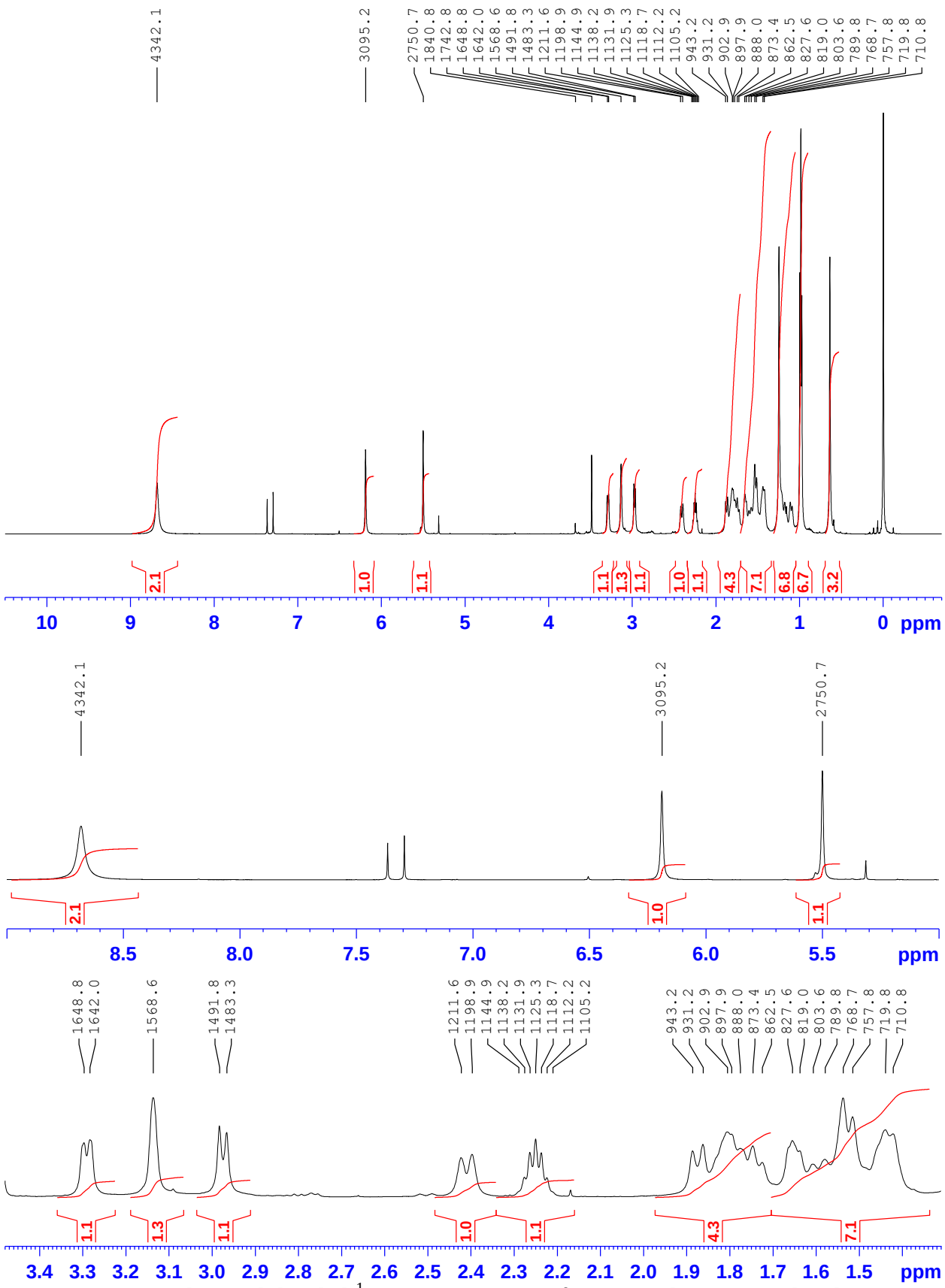

Figure S12. Complete and detailed ^{1}H NMR spectrum of compound **6a** in $CDCl_3$ solution, 500 MHz.

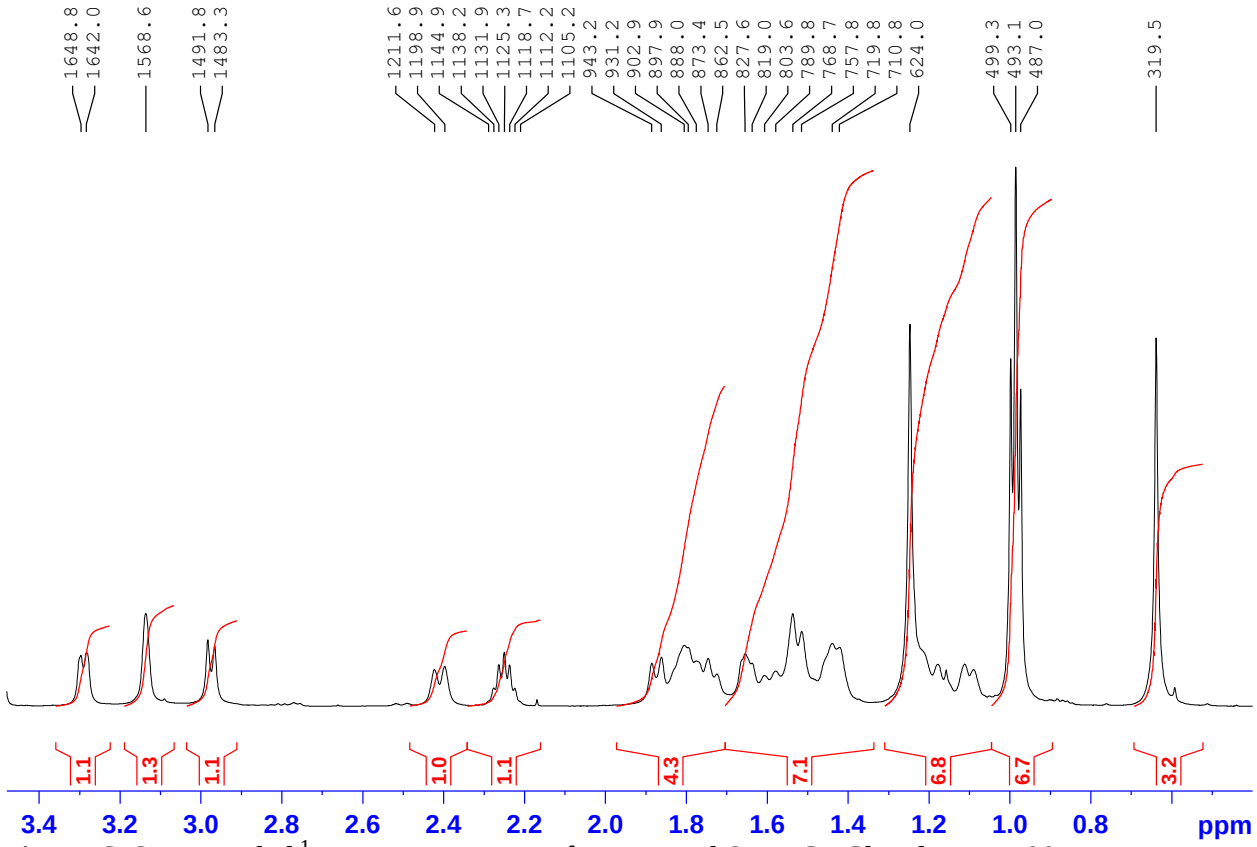

Figure S13. Expanded ^{1}H NMR spectrum of compound **6a** in $CDCl_3$ solution, 500 MHz.

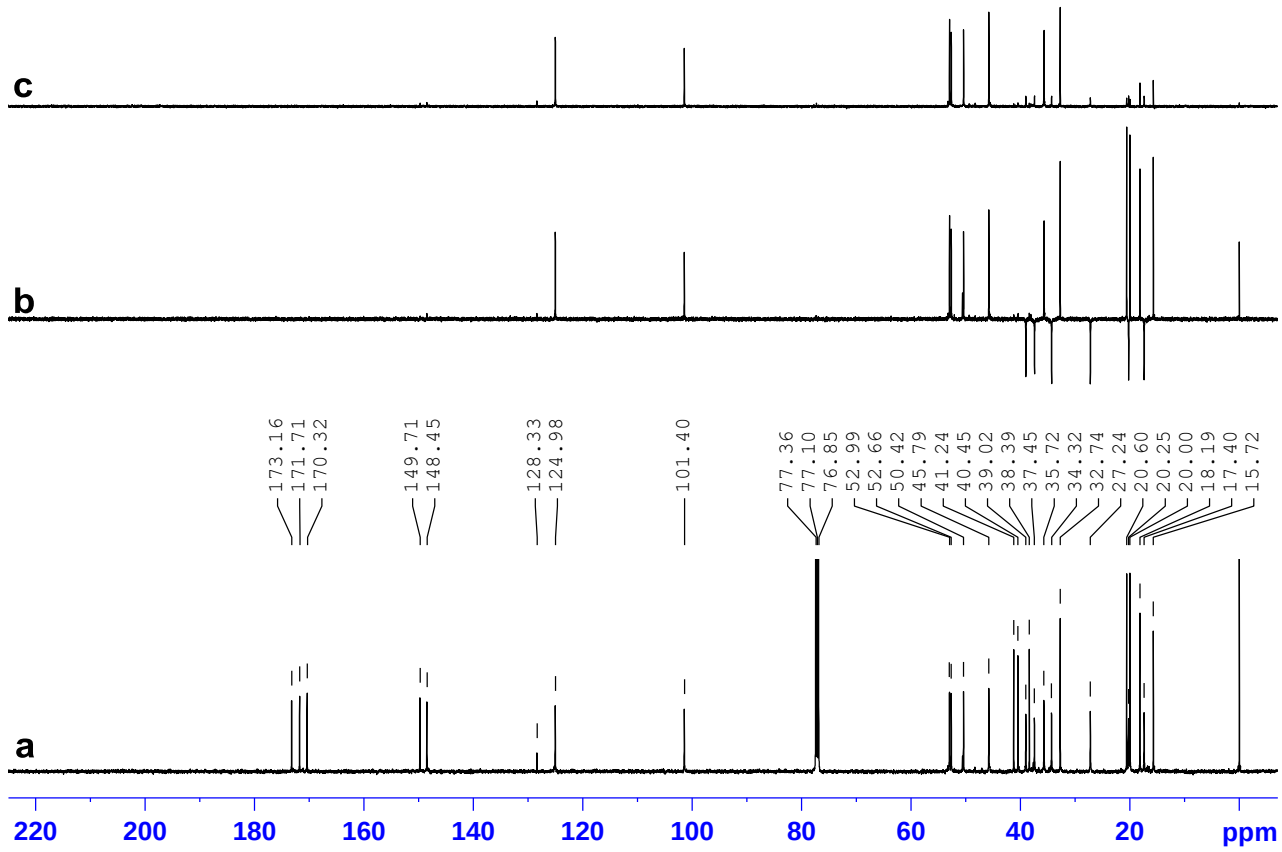

Figure S14. Complete ^{13}C{^{1}H}(**a**), DEPT-135(**b**) and DEPT-90(**c**) spectra of compound **6a** in $CDCl_3$ solution, 500 MHz.

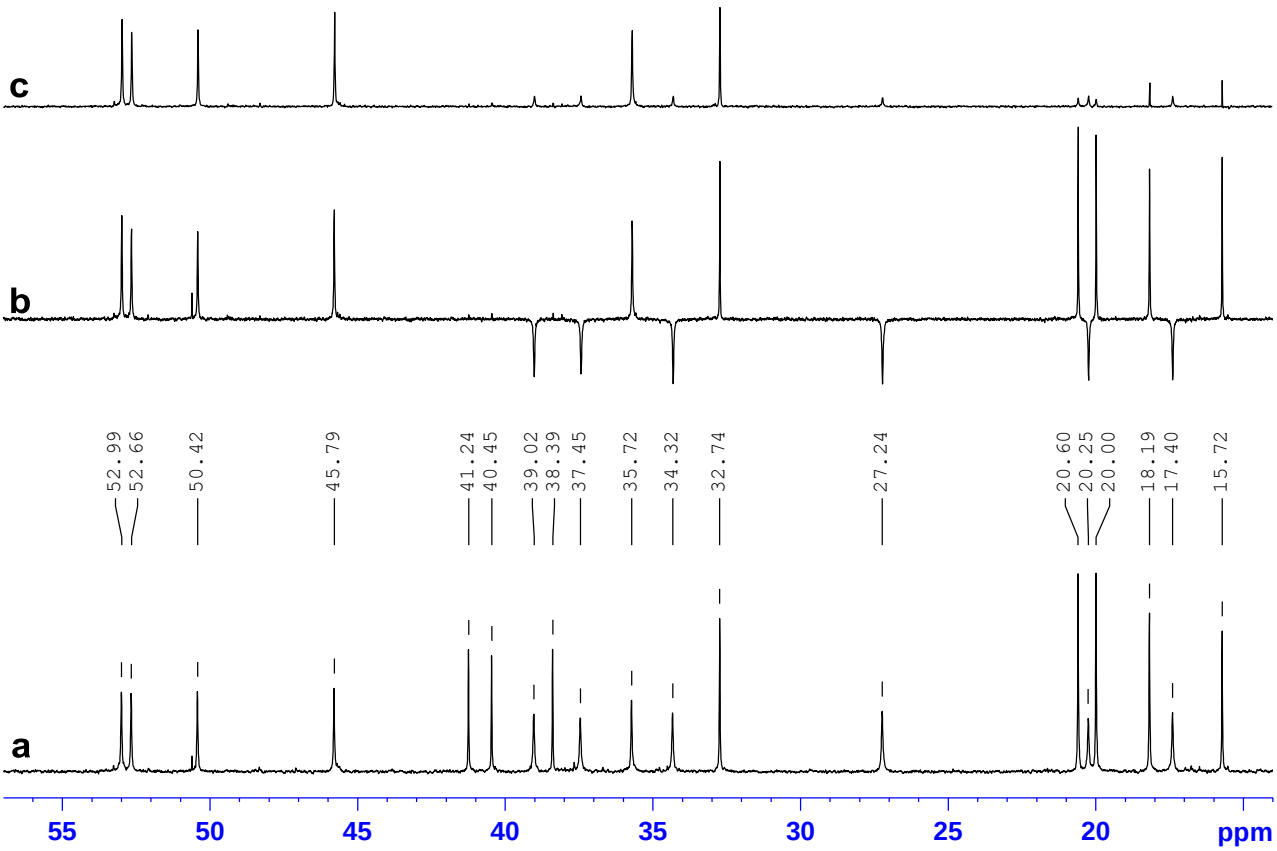

Figure S15. Expanded $^{13}C\{^{1}H\}$(**a**), DEPT-135(**b**) and DEPT-90(**c**) spectra of compound **6a** in $CDCl_3$ solution, 500 MHz.

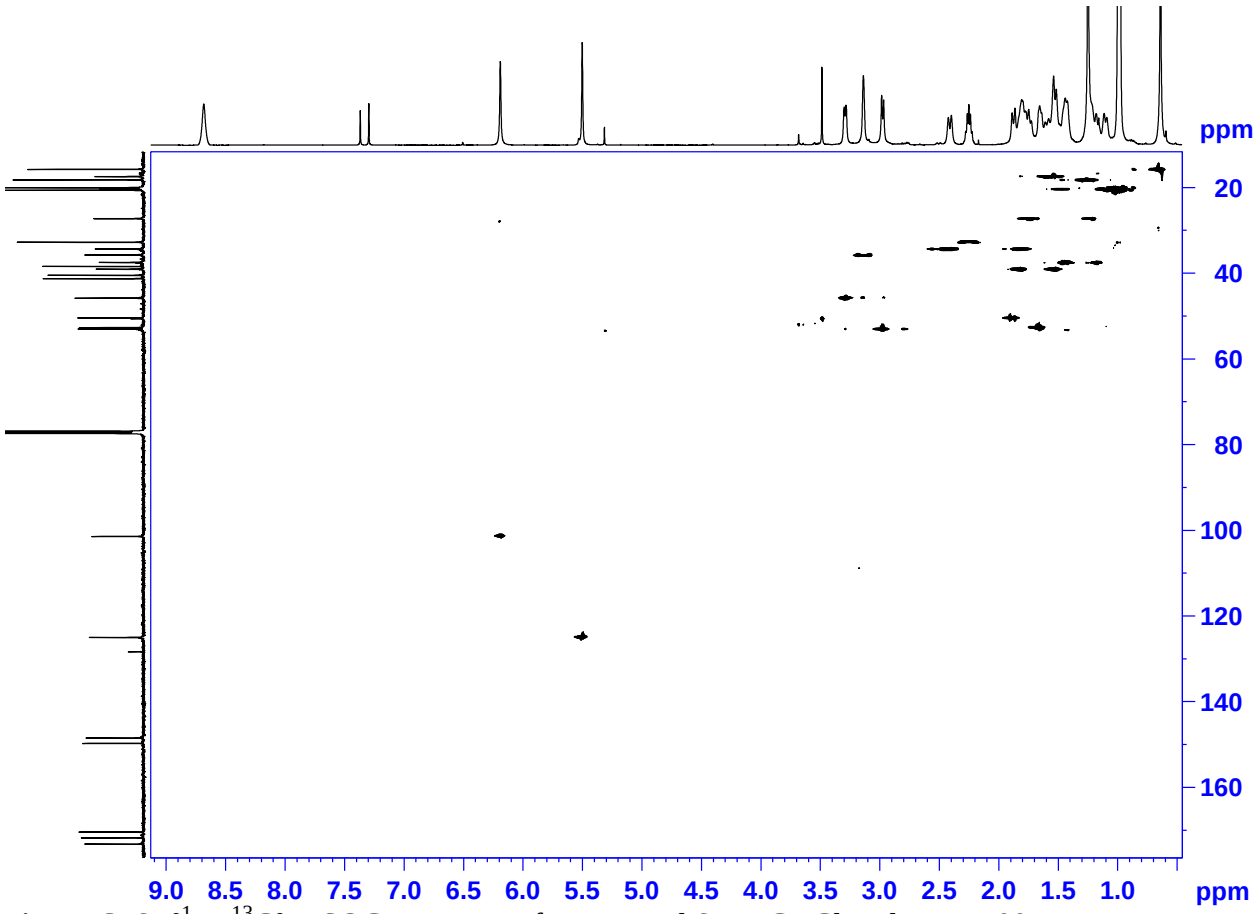

Figure S16. $\{^{1}H, ^{13}C\}$ HSQC spectrum of compound **6a** in $CDCl_3$ solution, 500 MHz.

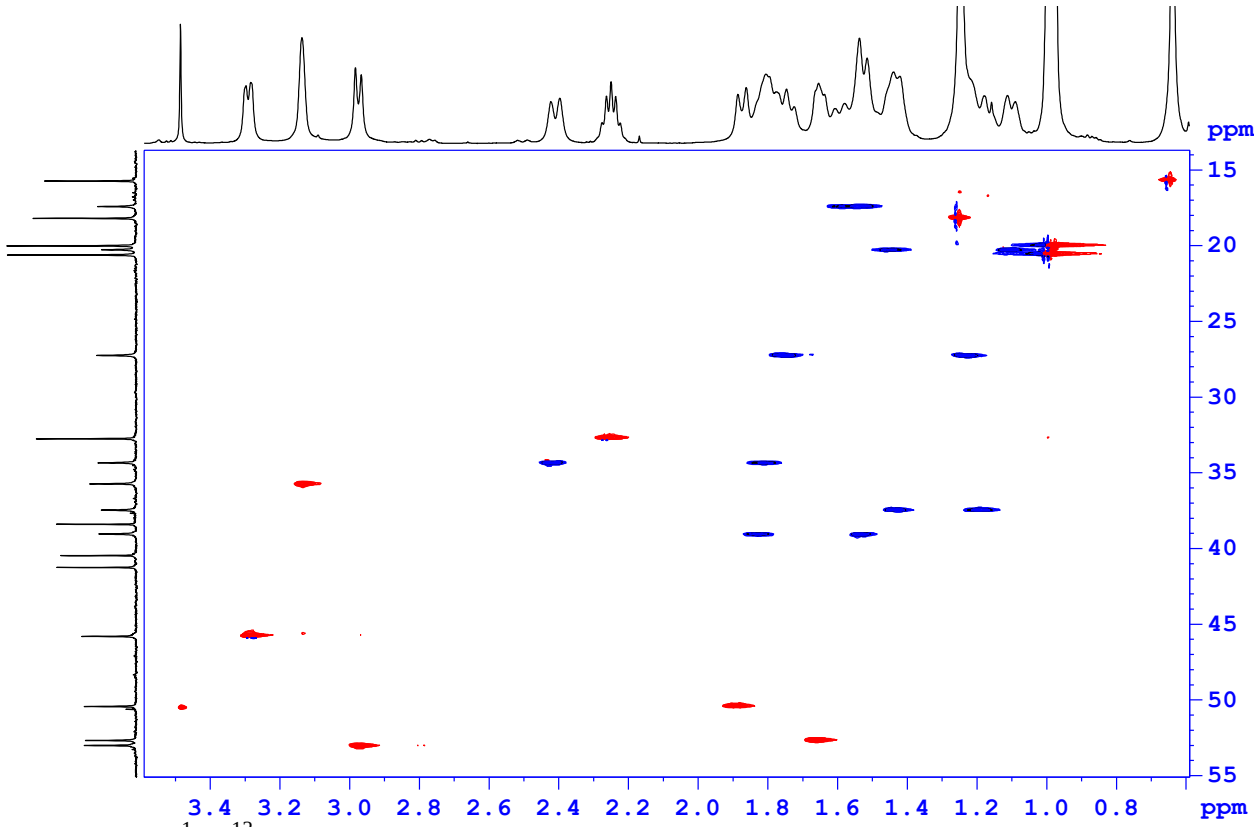

Figure S17. {^{1}H, ^{13}C} HSQCed spectrum of compound **6a** in $CDCl_3$ solution, 500 MHz.

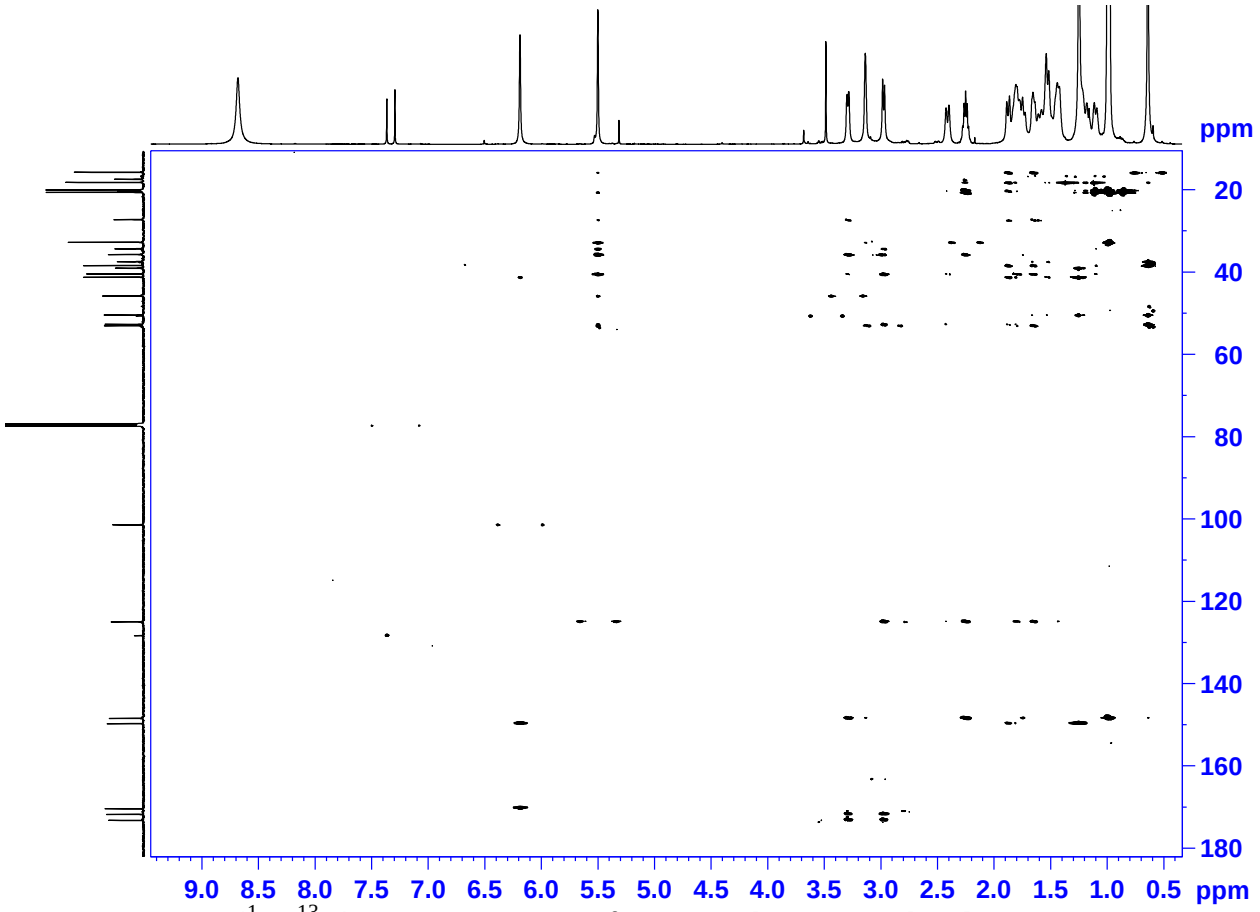

Figure S18. {^{1}H, ^{13}C} HMBC spectrum of compound **6a** in $CDCl_3$ solution, 500 MHz.

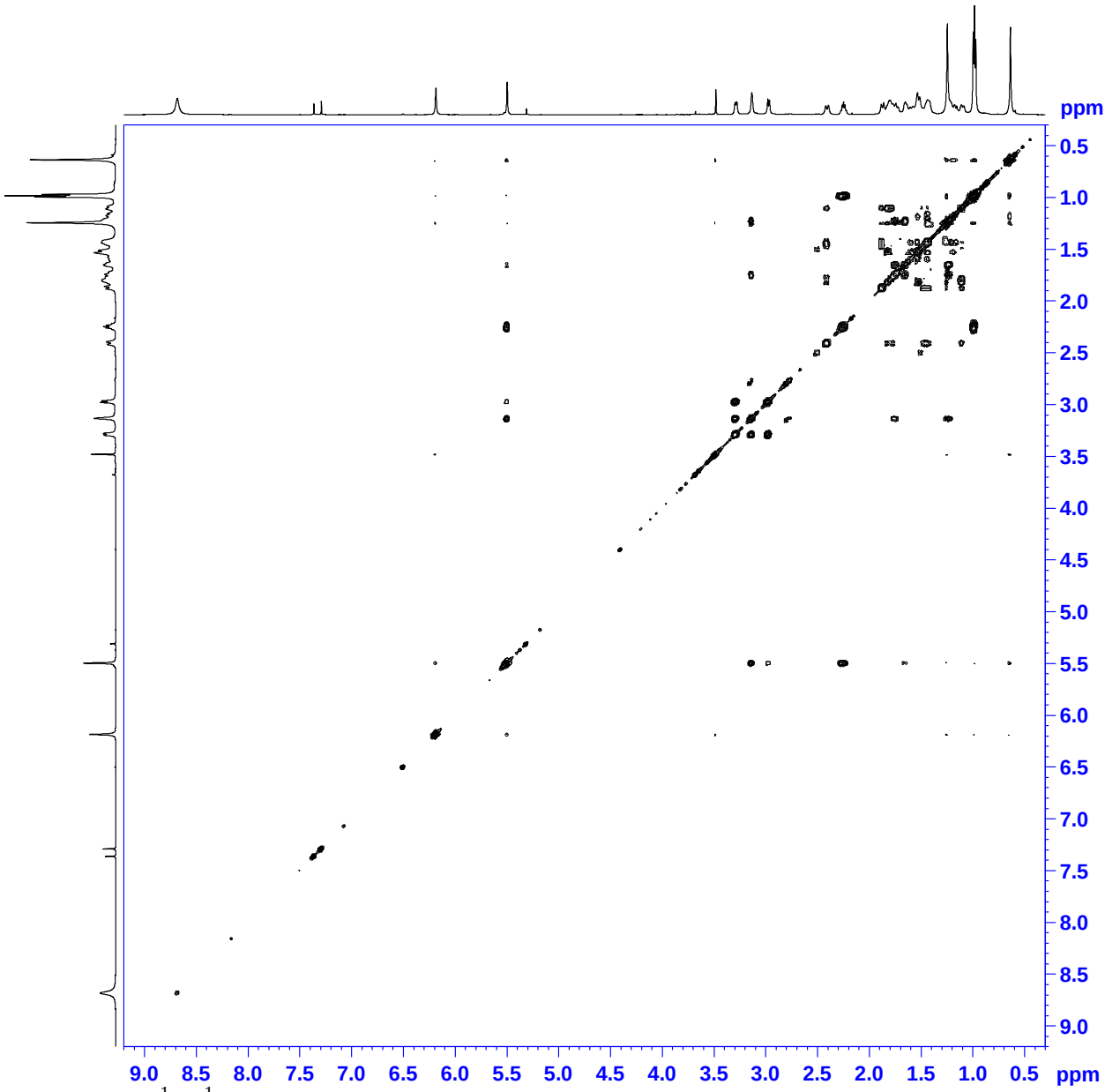

Figure S19. {^{1}H, ^{1}H} COSY spectrum of compound **6a** in $CDCl_3$ solution, 500 MHz.

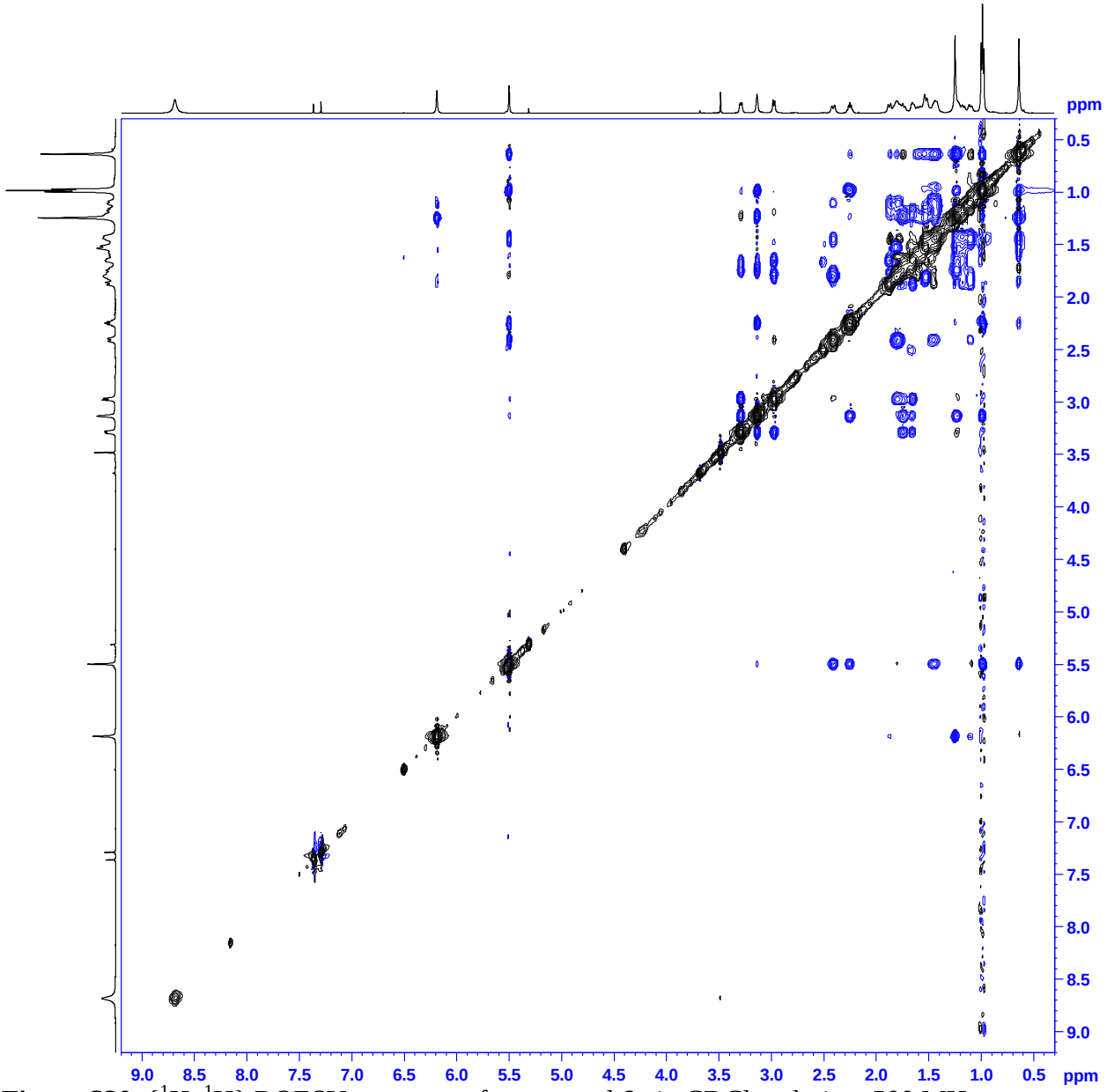

Figure S20. {^{1}H, ^{1}H} ROESY spectrum of compound **6a** in $CDCl_3$ solution, 500 MHz.

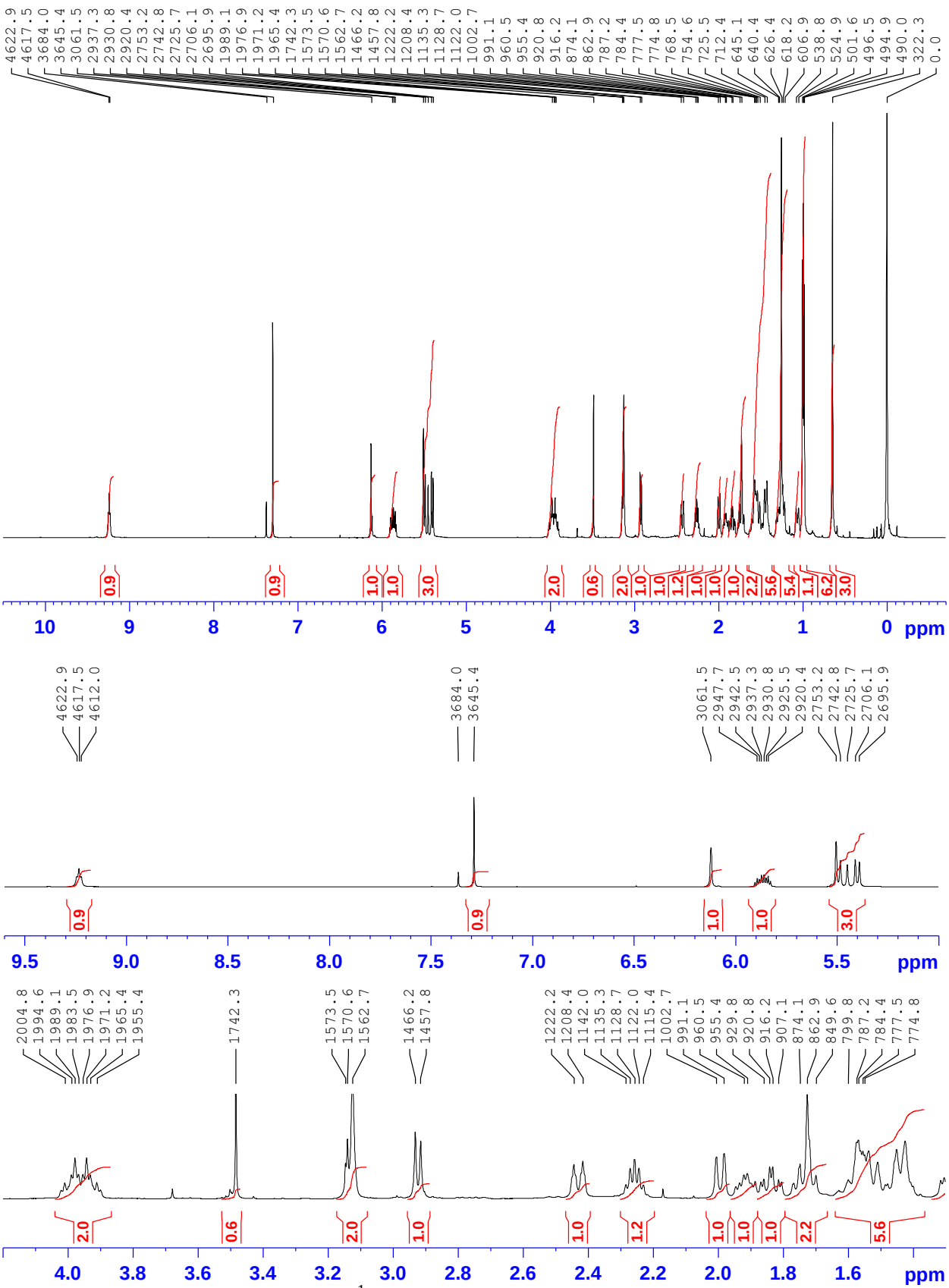

Figure S21. Complete and detailed ^{1}H NMR spectrum of compound **6c** in $CDCl_3$ solution, 500 MHz.

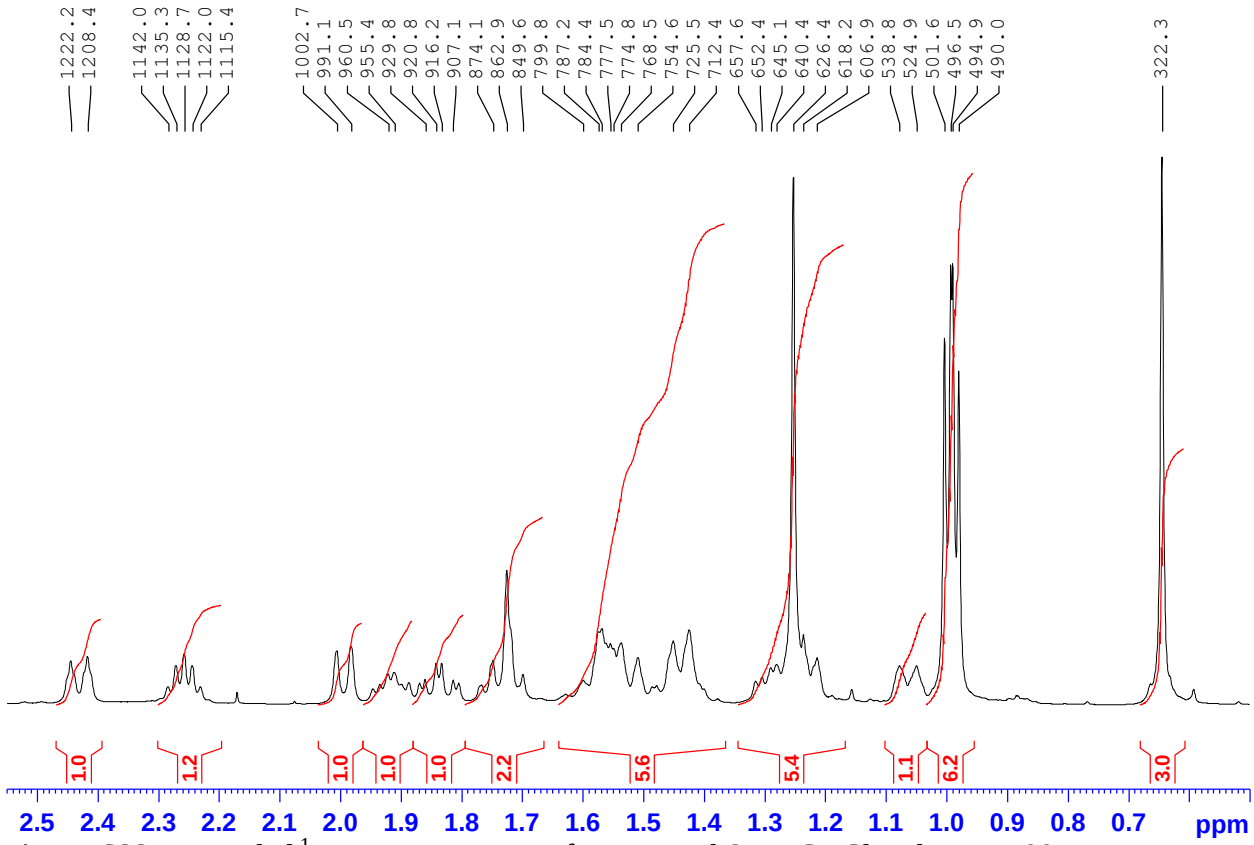

Figure S22. Expanded ^{1}H NMR spectrum of compound **6c** in $CDCl_3$ solution, 500 MHz.

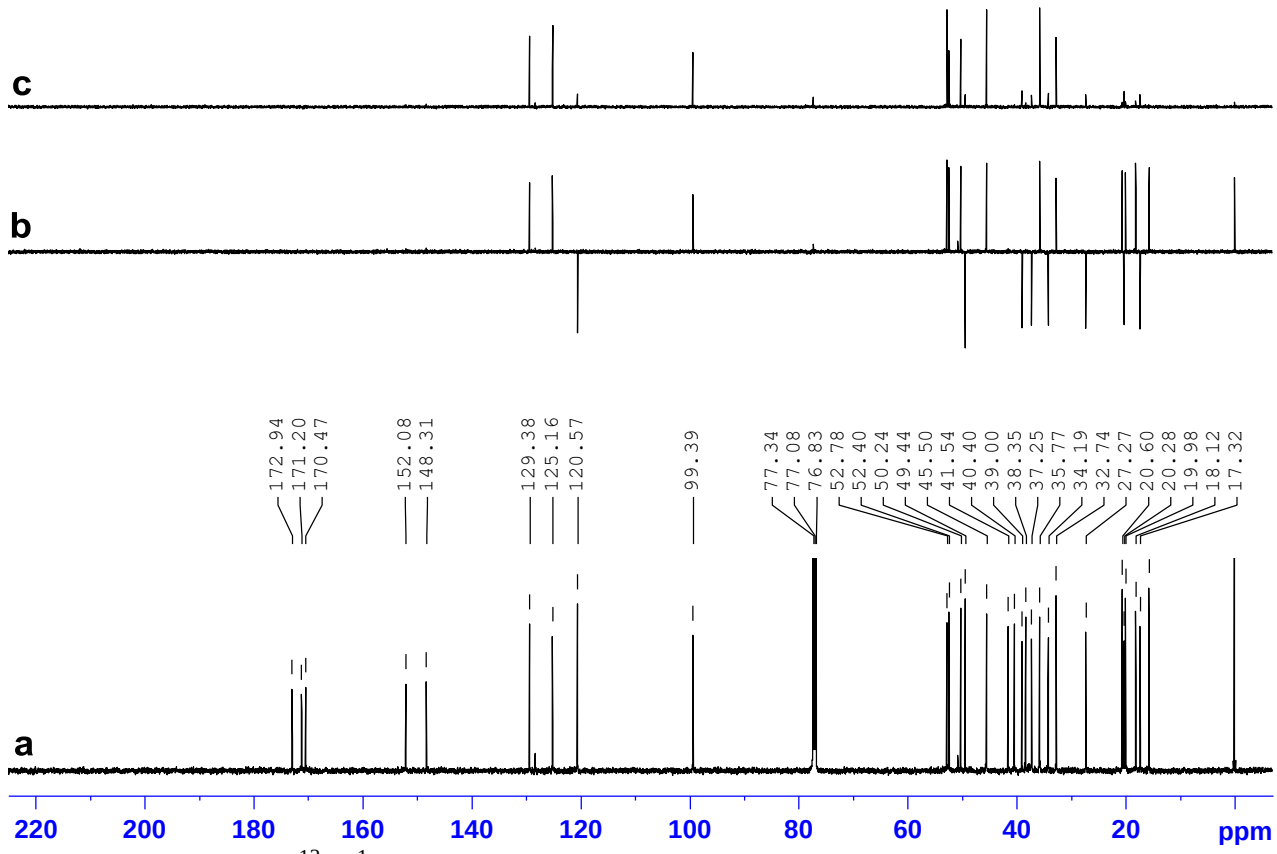

Figure S23. Complete $^{13}C\{^{1}H\}$(**a**), DEPT-135(**b**) and DEPT-90(**c**) spectra of compound **6c** in $CDCl_3$ solution, 500 MHz.

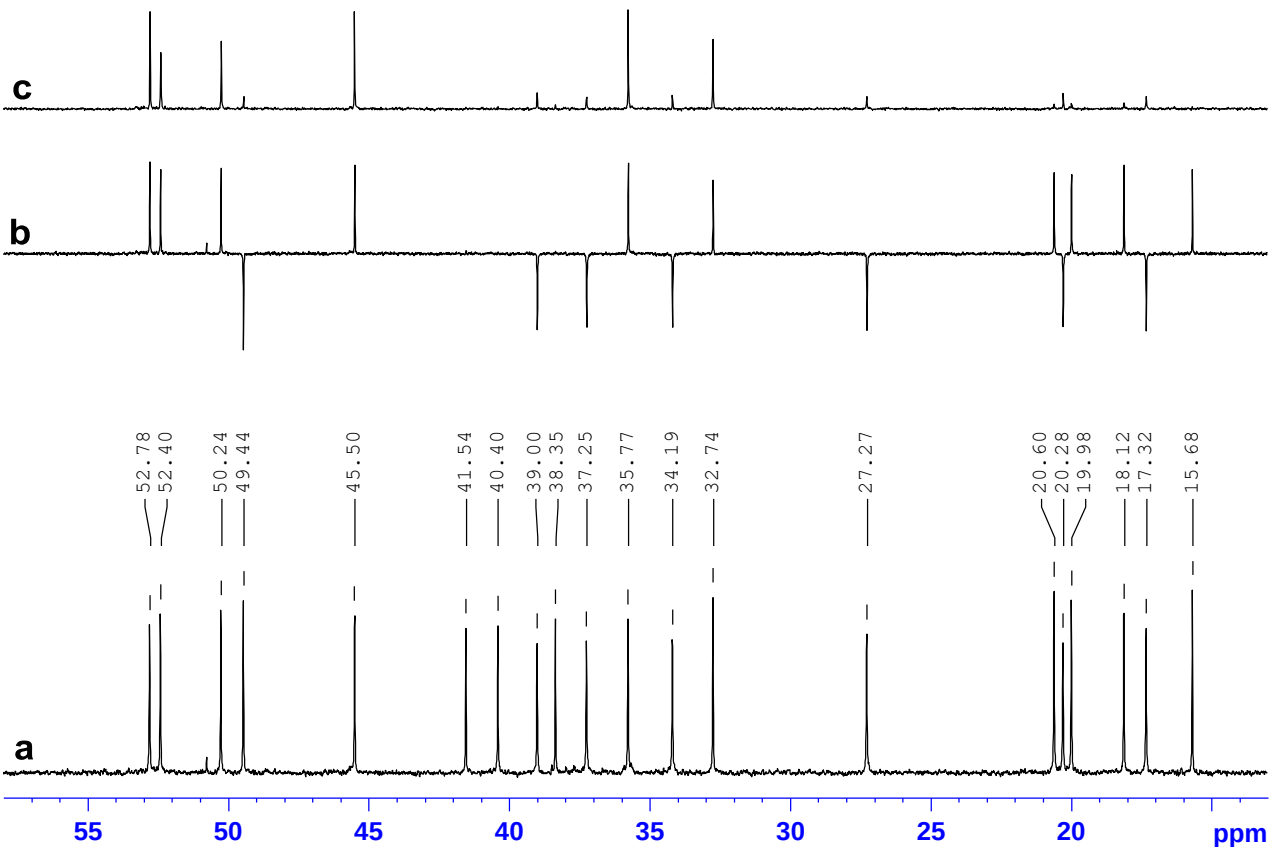

Figure S24. Expanded $^{13}C\{^{1}H\}$(**a**), DEPT-135(**b**) and DEPT-90(**c**) spectra of compound **6c** in $CDCl_3$ solution, 500 MHz.

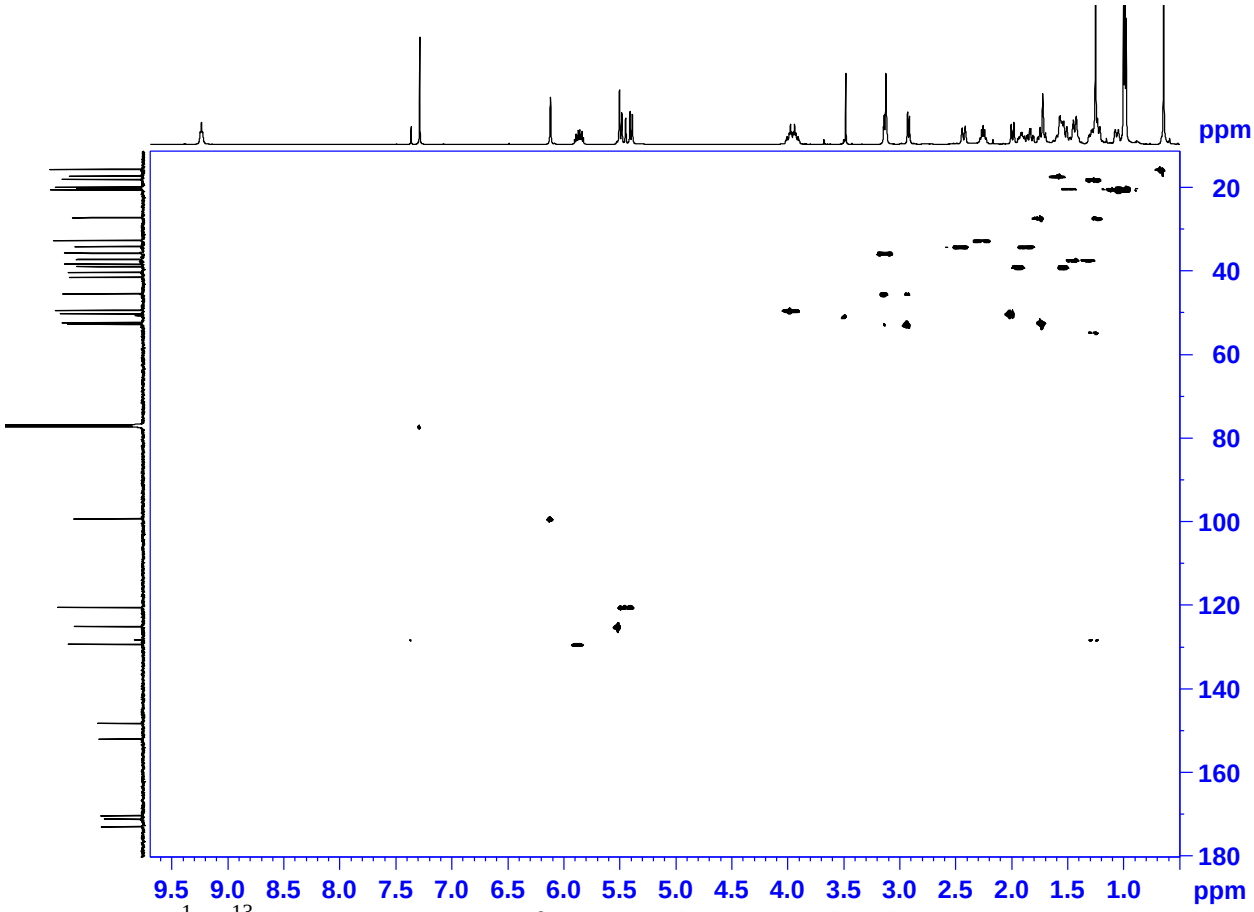

Figure S25. $\{^{1}H, ^{13}C\}$ HSQC spectrum of compound **6c** in $CDCl_3$ solution, 500 MHz.

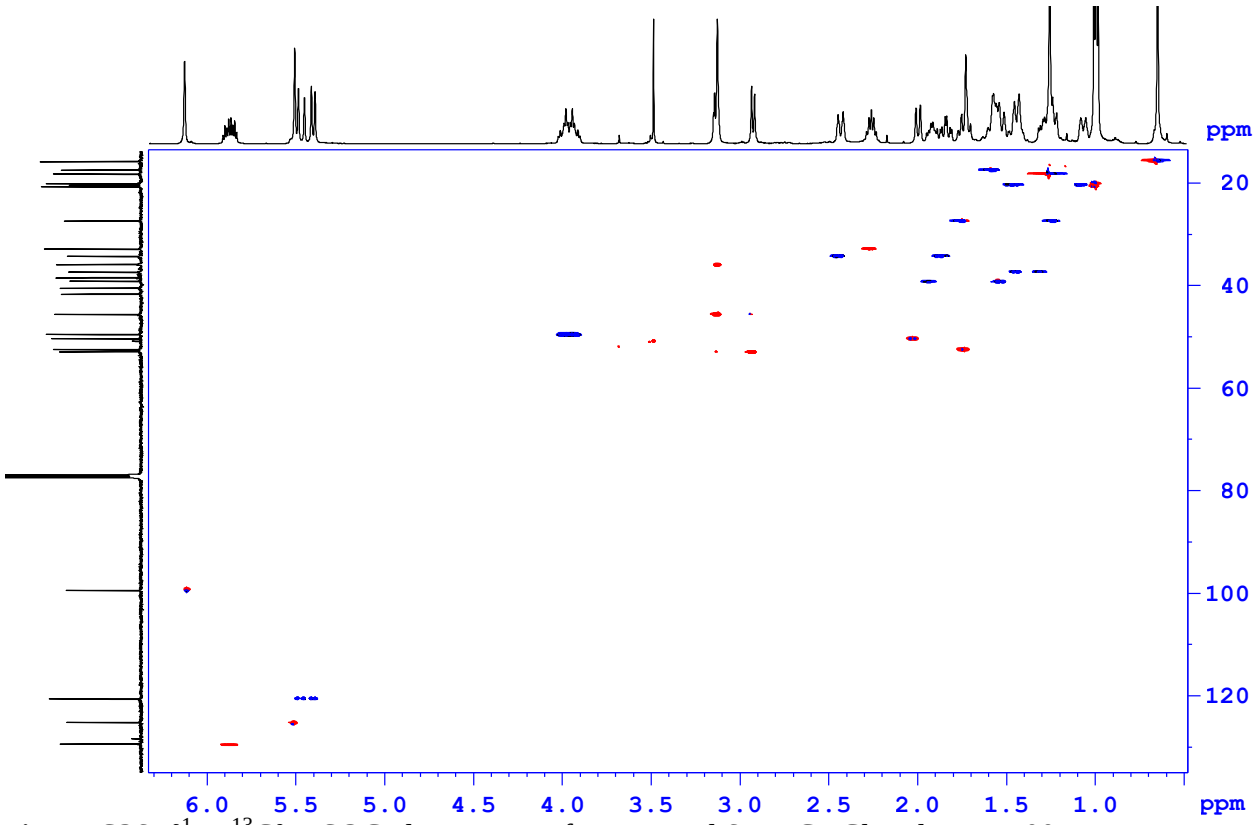

Figure S26. {^{1}H, ^{13}C} HSQCed spectrum of compound **6c** in $CDCl_3$ solution, 500 MHz.

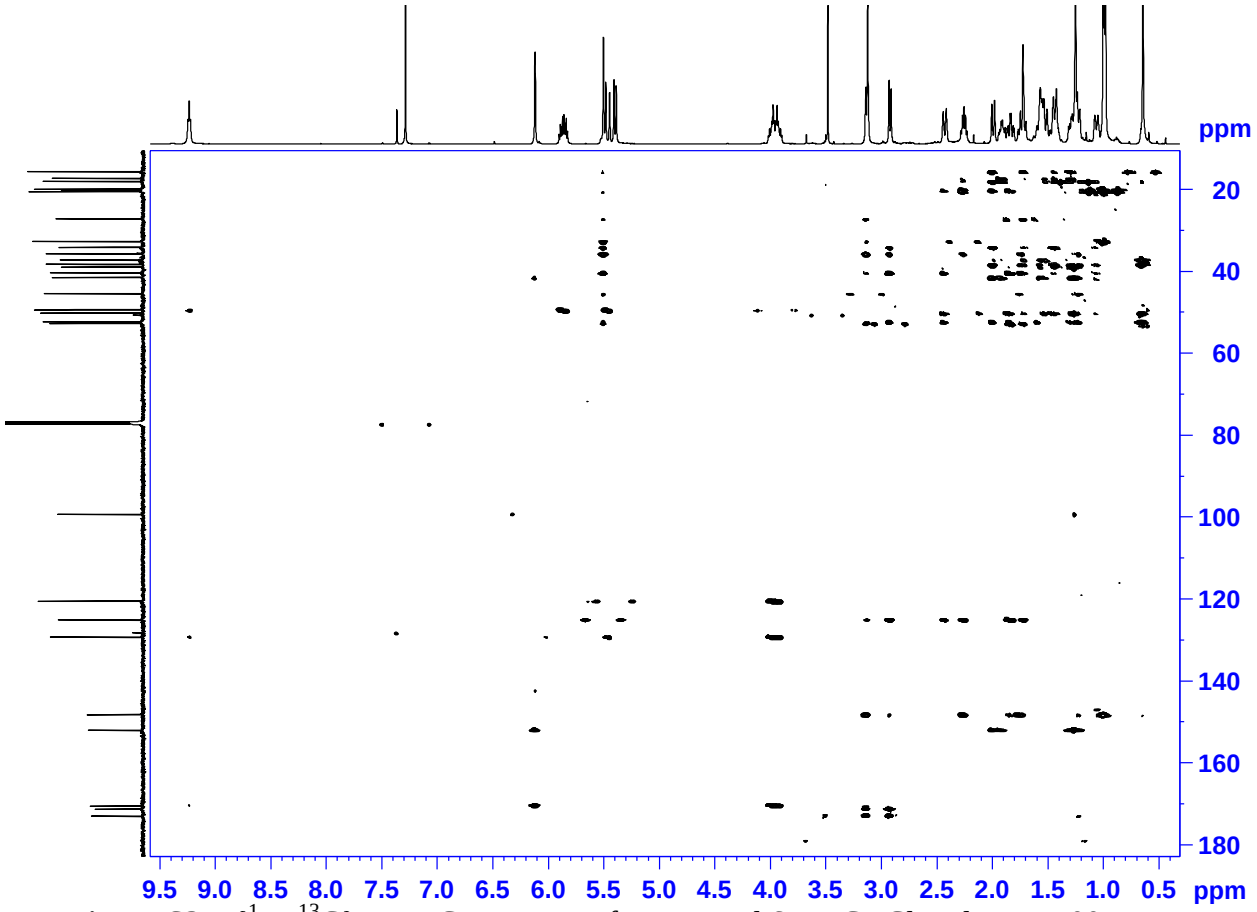

Figure S27. {^{1}H, ^{13}C} HMBC spectrum of compound **6c** in $CDCl_3$ solution, 500 MHz.

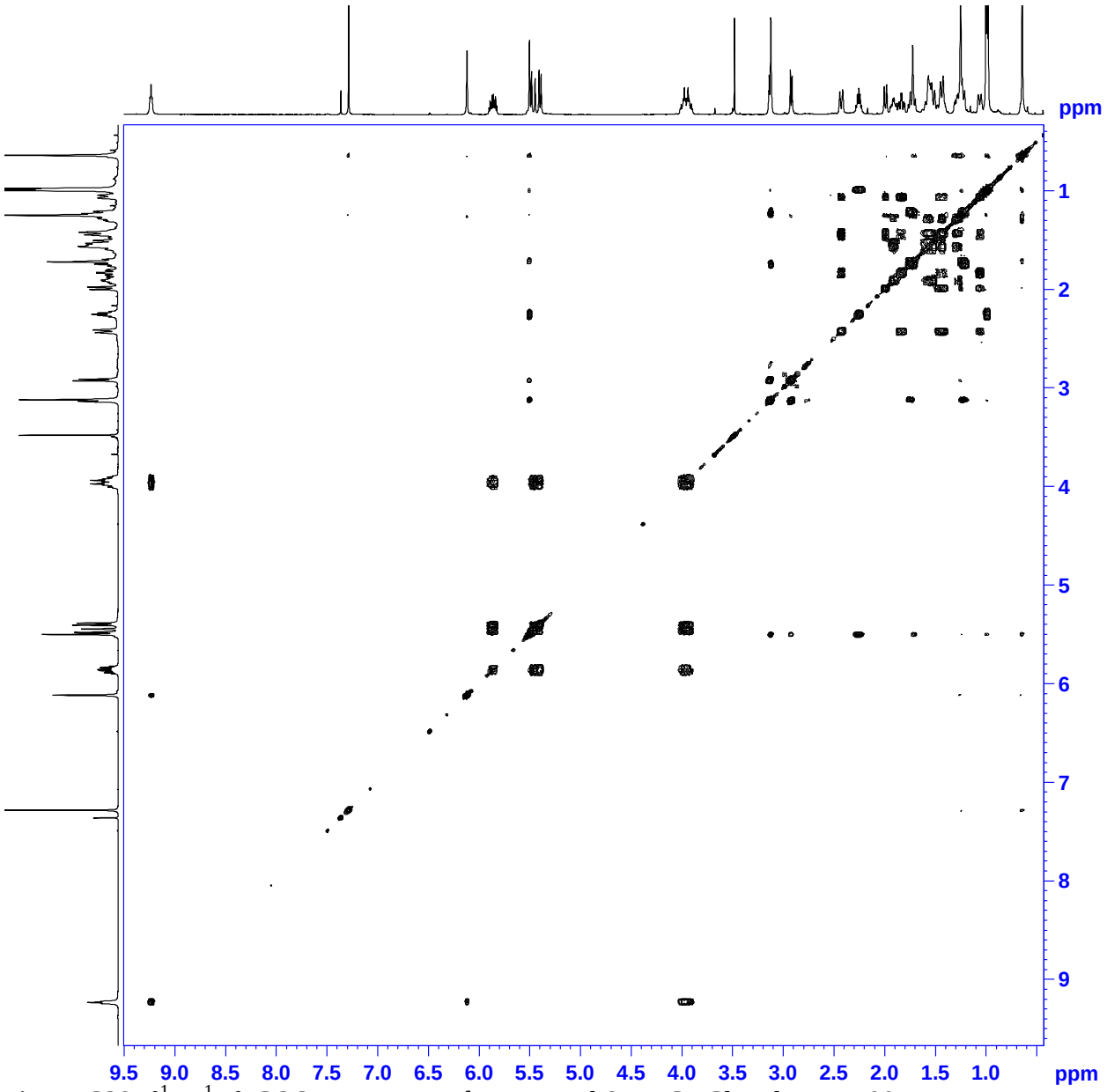

Figure S28. {^{1}H, ^{1}H} COSY spectrum of compound **6c** in $CDCl_3$ solution, 500 MHz.

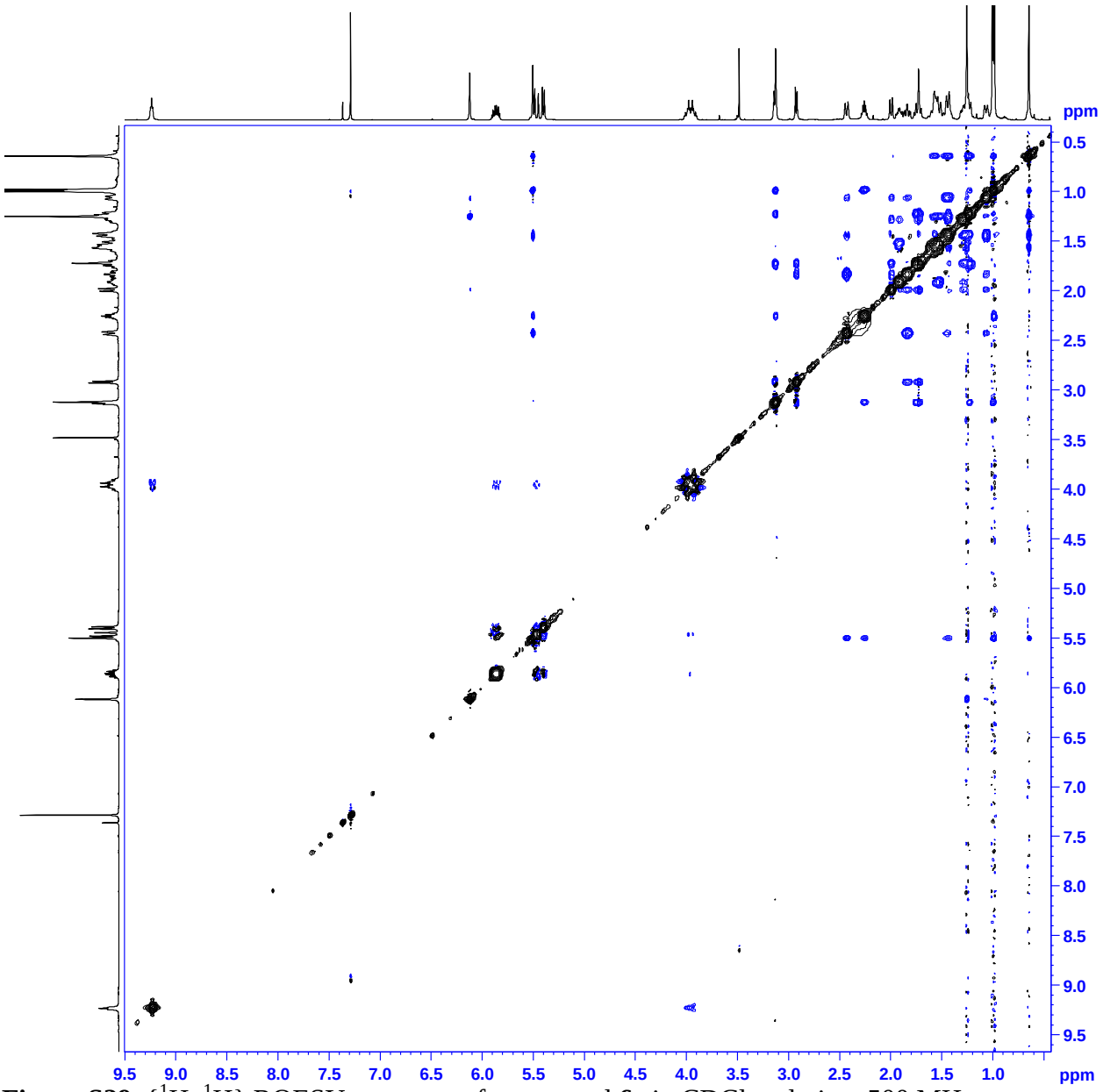

Figure S29. {^{1}H, ^{1}H} ROESY spectrum of compound **6c** in $CDCl_3$ solution, 500 MHz.

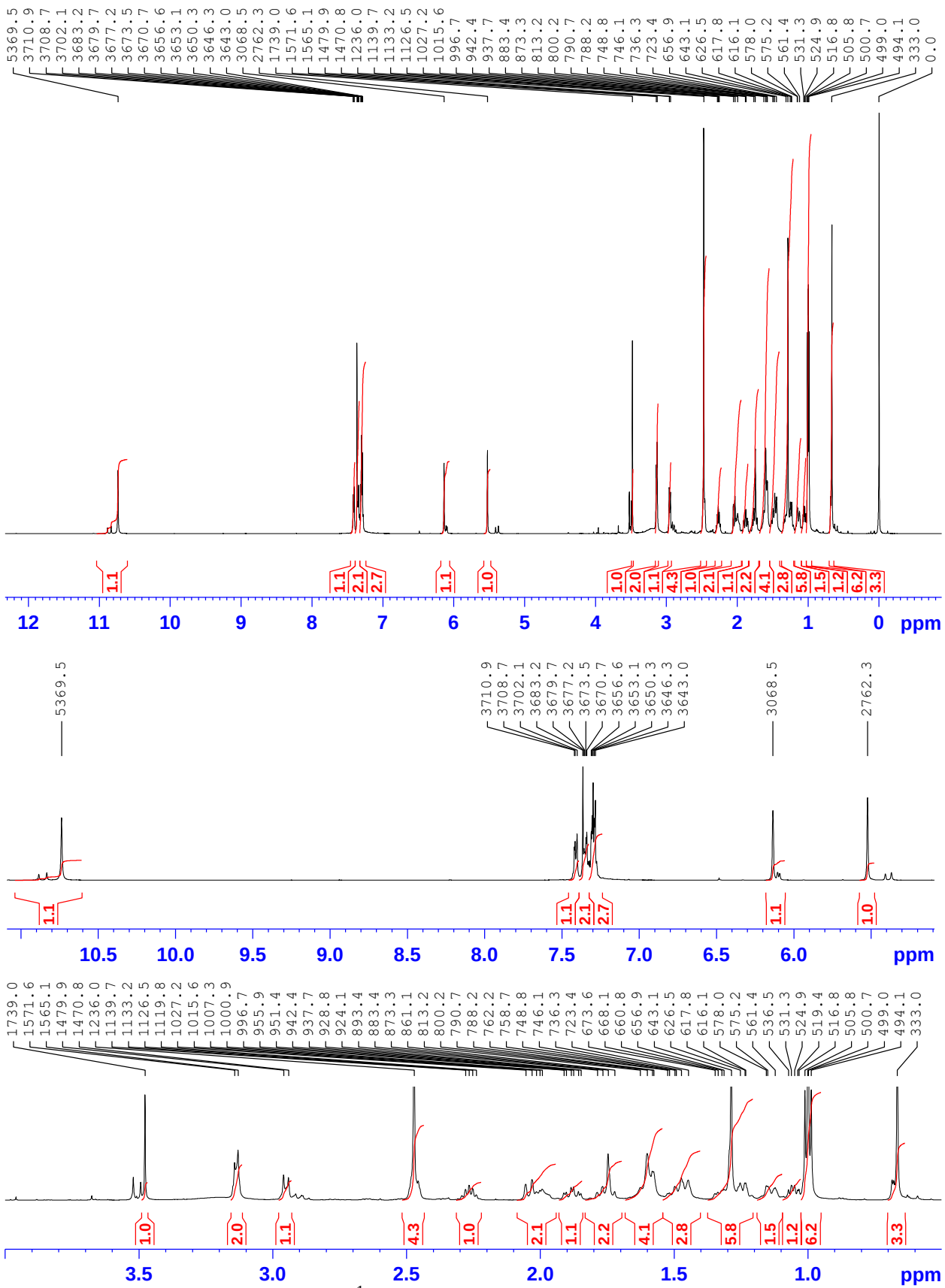

Figure S30. Complete and detailed ^{1}H NMR spectrum of compound **6e** in $CDCl_3$ solution, 500 MHz.

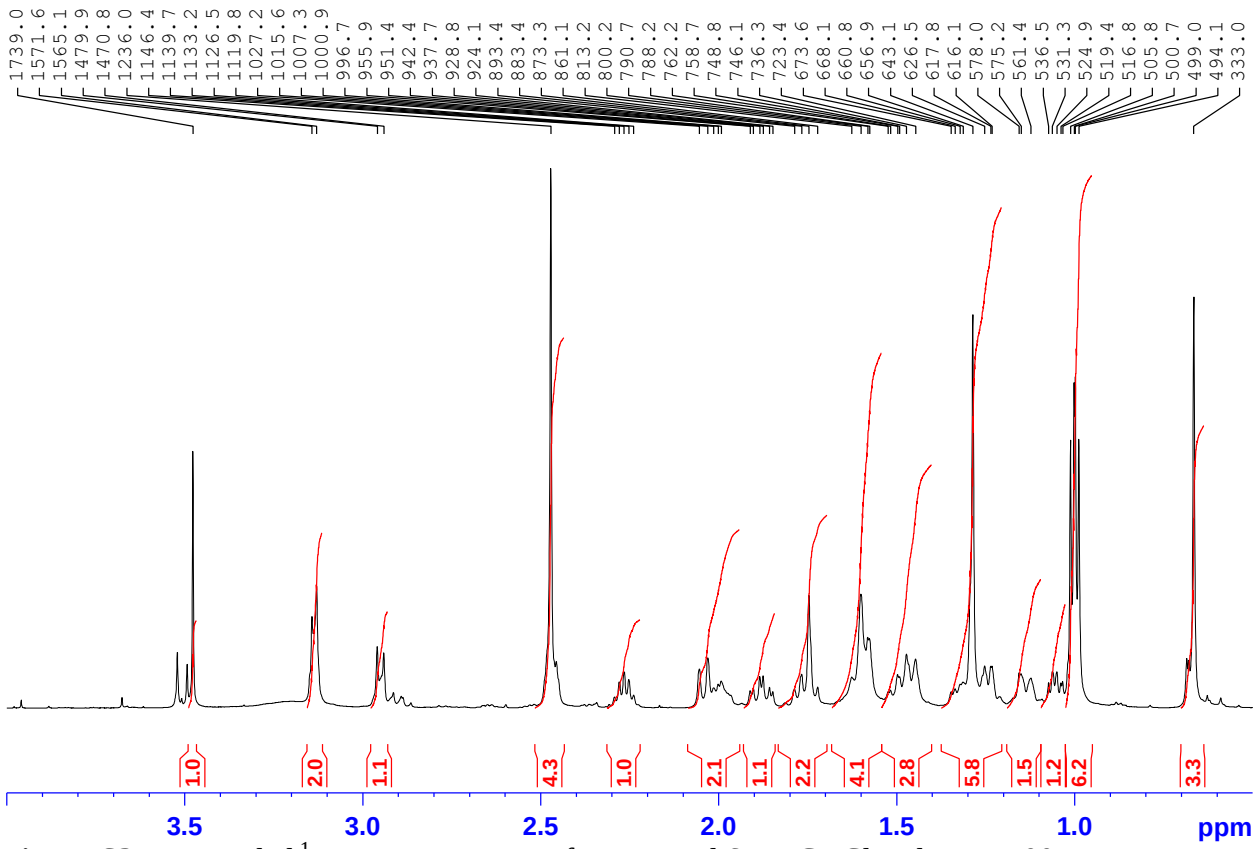

Figure S31. Expanded ^{1}H NMR spectrum of compound **6e** in $CDCl_3$ solution, 500 MHz.

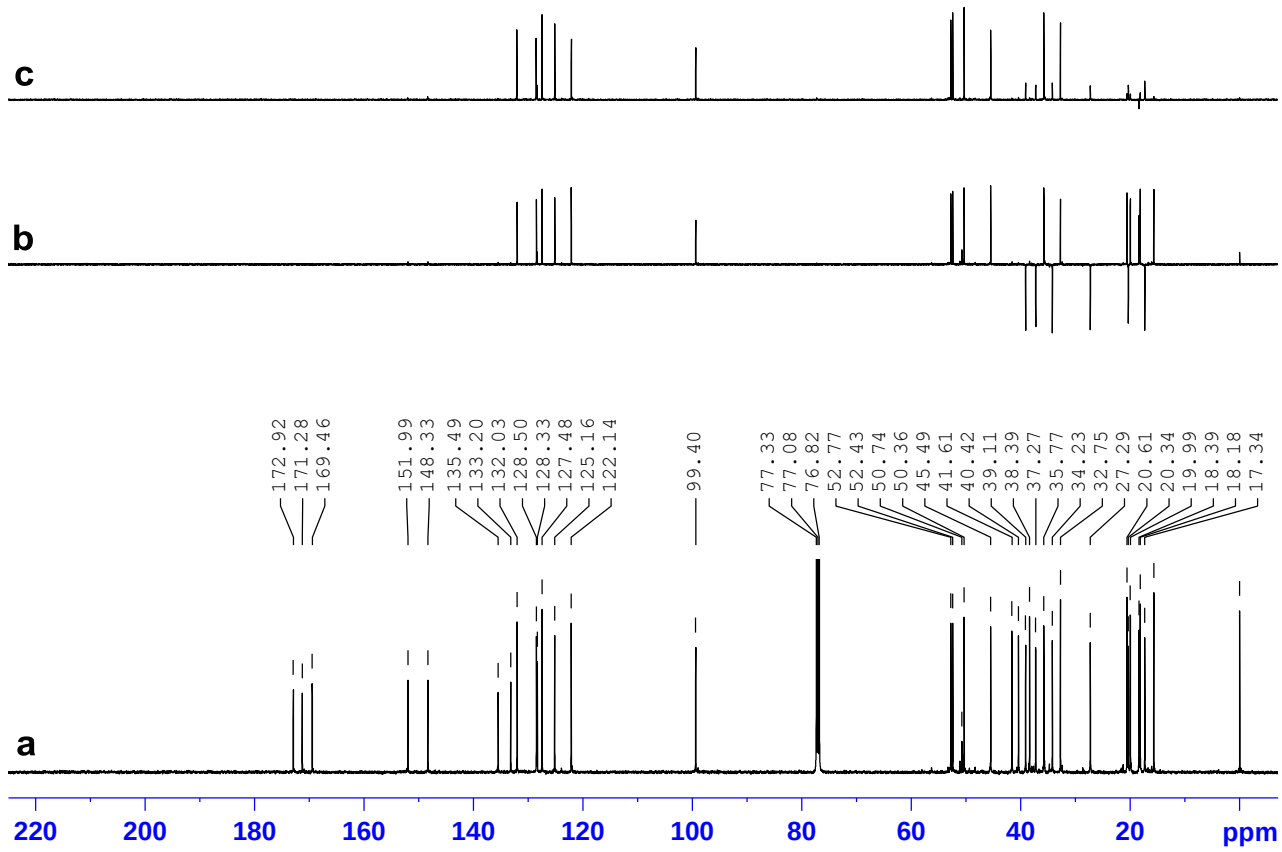

Figure S32. Complete ^{13}C{^{1}H}(**a**), DEPT-135(**b**) and DEPT-90(**c**) spectra of compound **6e** in $CDCl_3$ solution, 500 MHz.

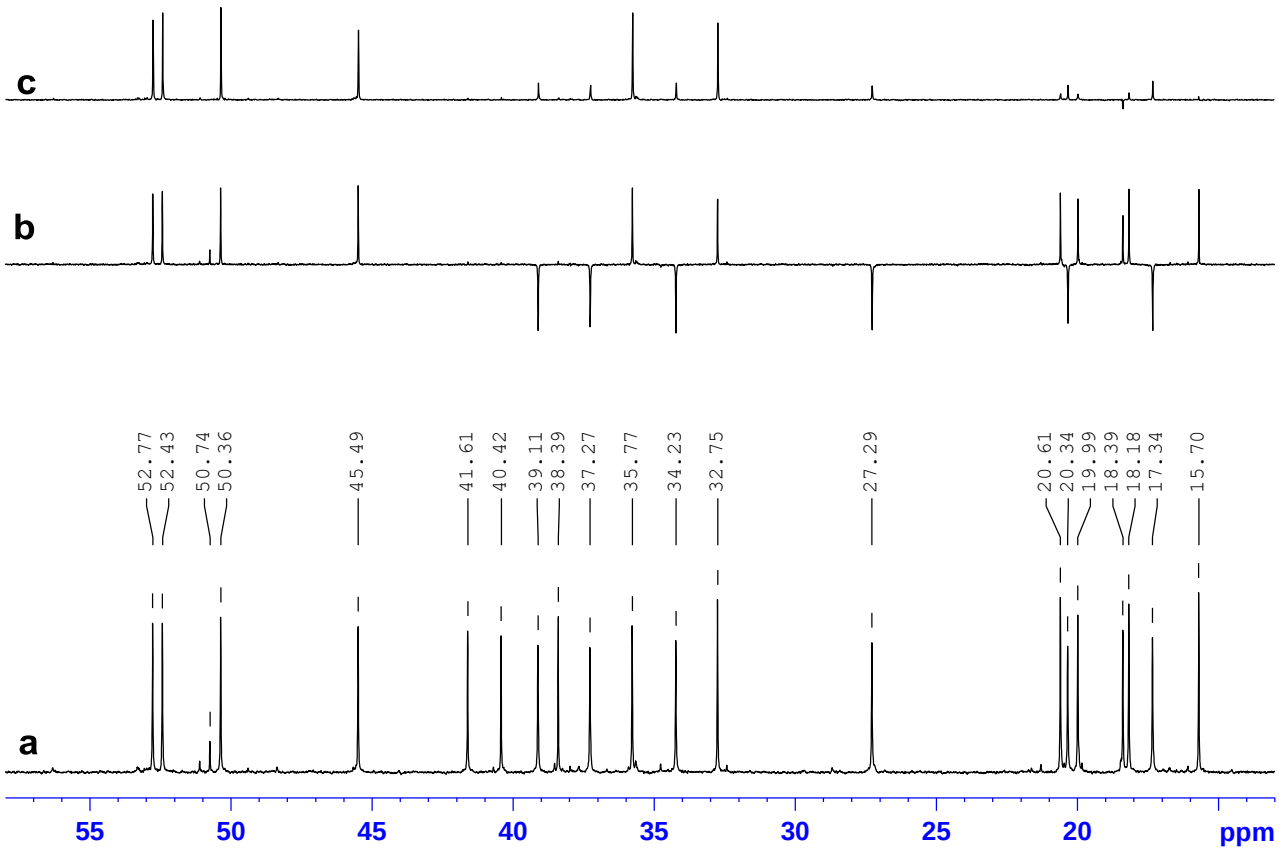

Figure S33. Expanded $^{13}C\{^{1}H\}$(**a**), DEPT-135(**b**) and DEPT-90(**c**) spectra of compound **6e** in $CDCl_3$ solution, 500 MHz.

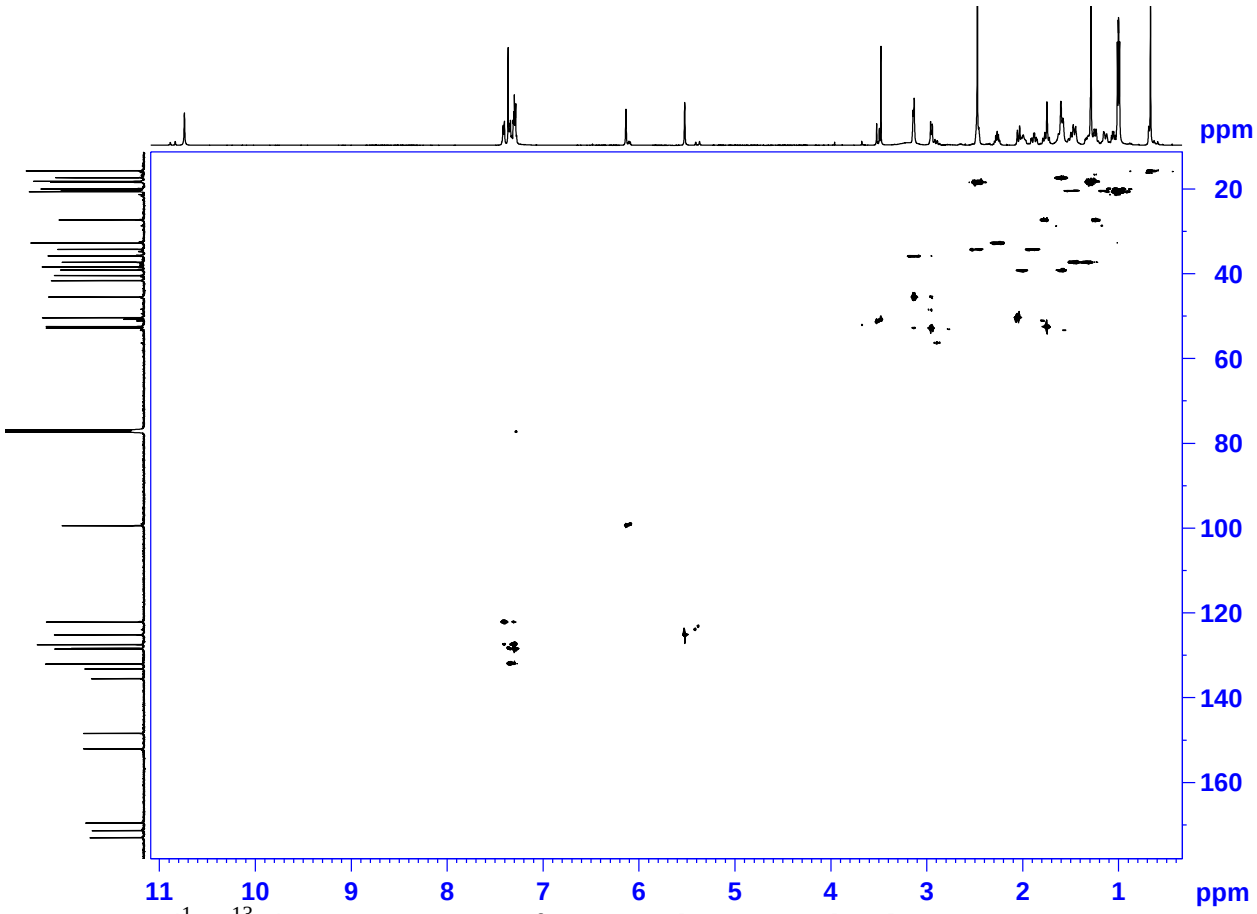

Figure S34. $\{^{1}H, ^{13}C\}$ HSQC spectrum of compound **6e** in $CDCl_3$ solution, 500 MHz.

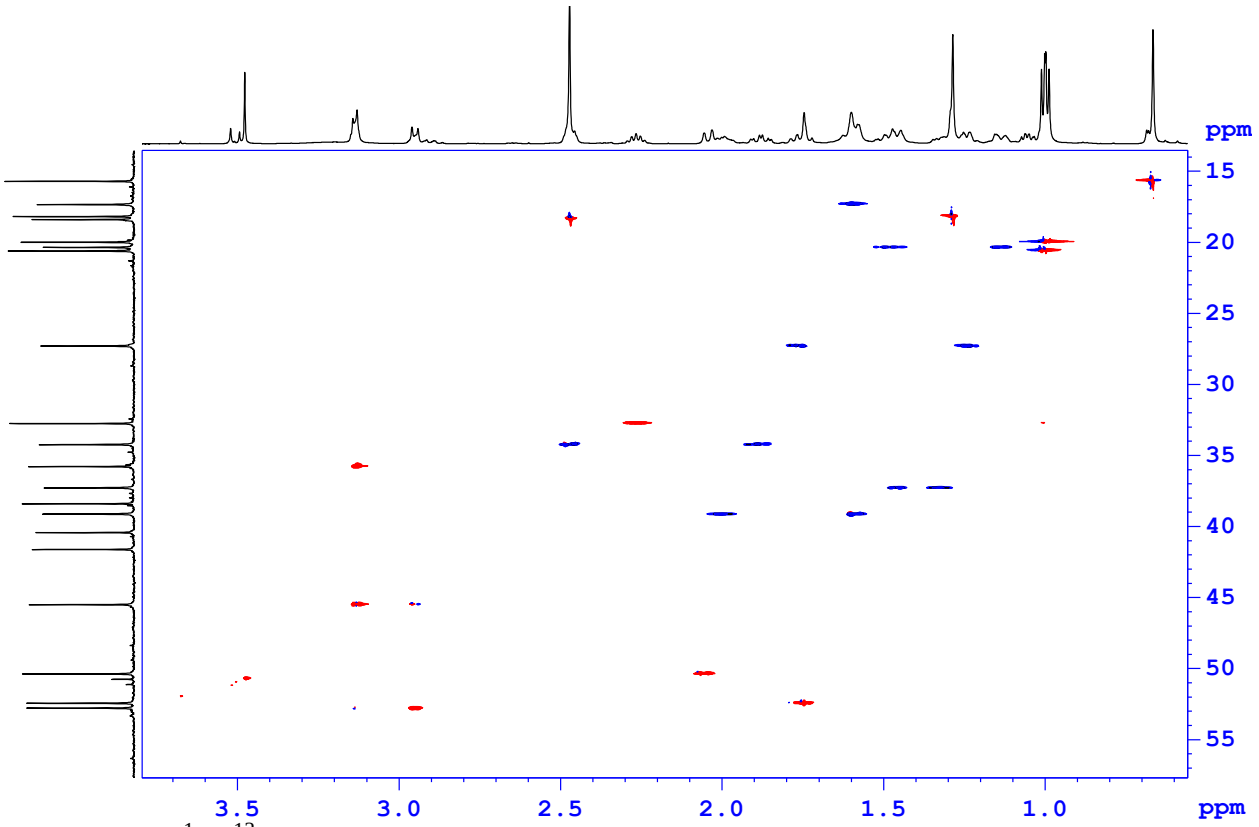

Figure S35. {^{1}H, ^{13}C} HSQCed spectrum of compound **6e** in $CDCl_3$ solution, 500 MHz.

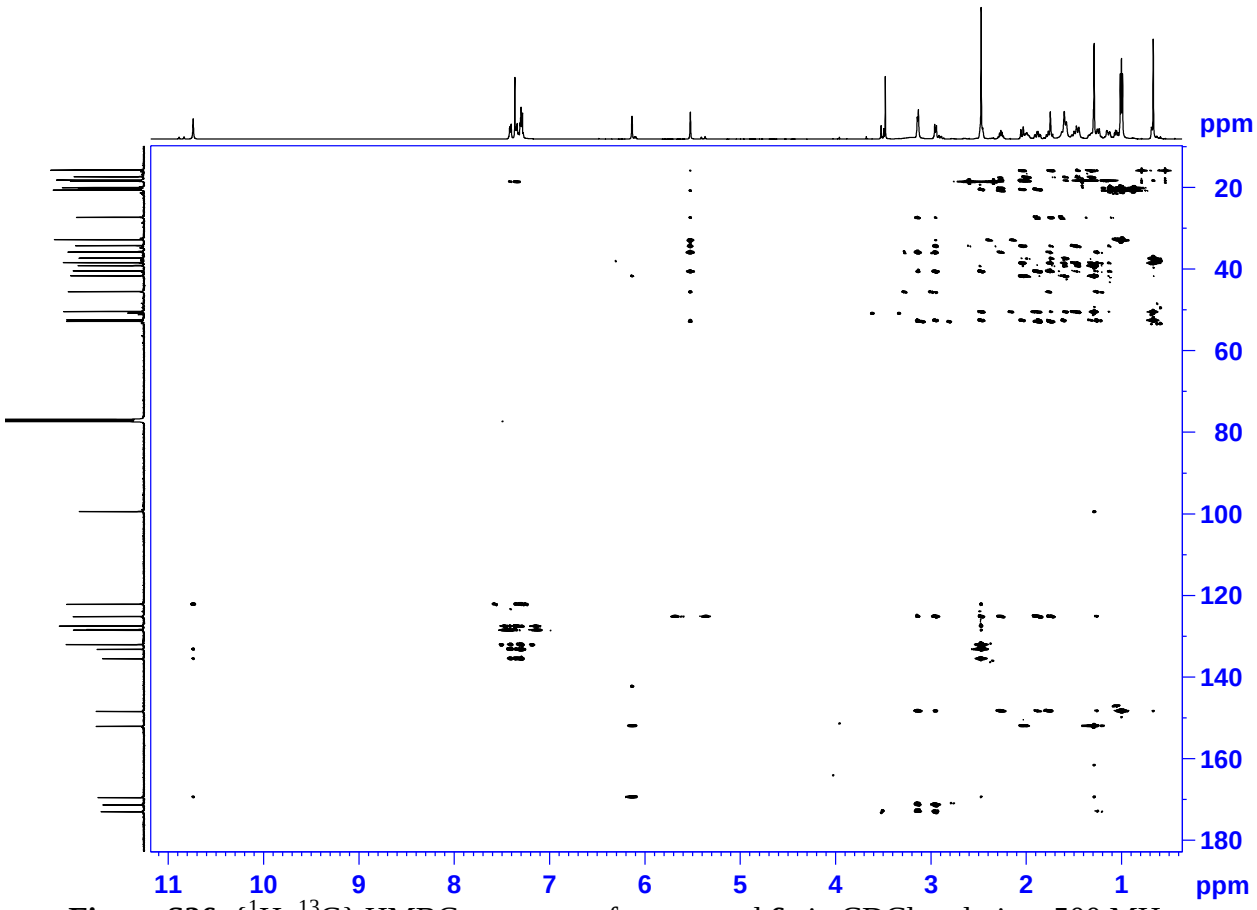

Figure S36. {^{1}H, ^{13}C} HMBC spectrum of compound **6e** in $CDCl_3$ solution, 500 MHz.

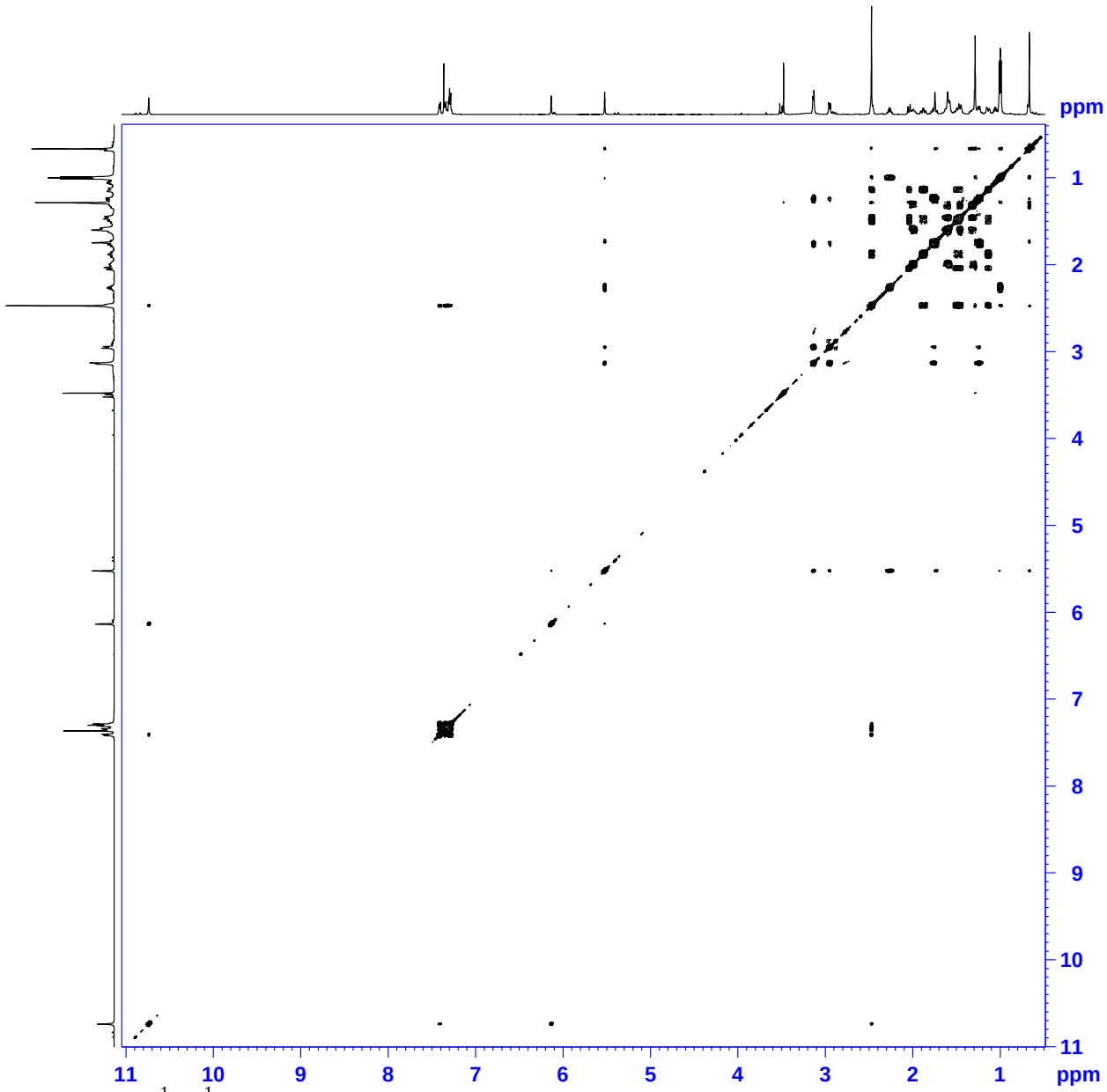

Figure S37. {^{1}H, ^{1}H} COSY spectrum of compound **6e** in $CDCl_3$ solution, 500 MHz.

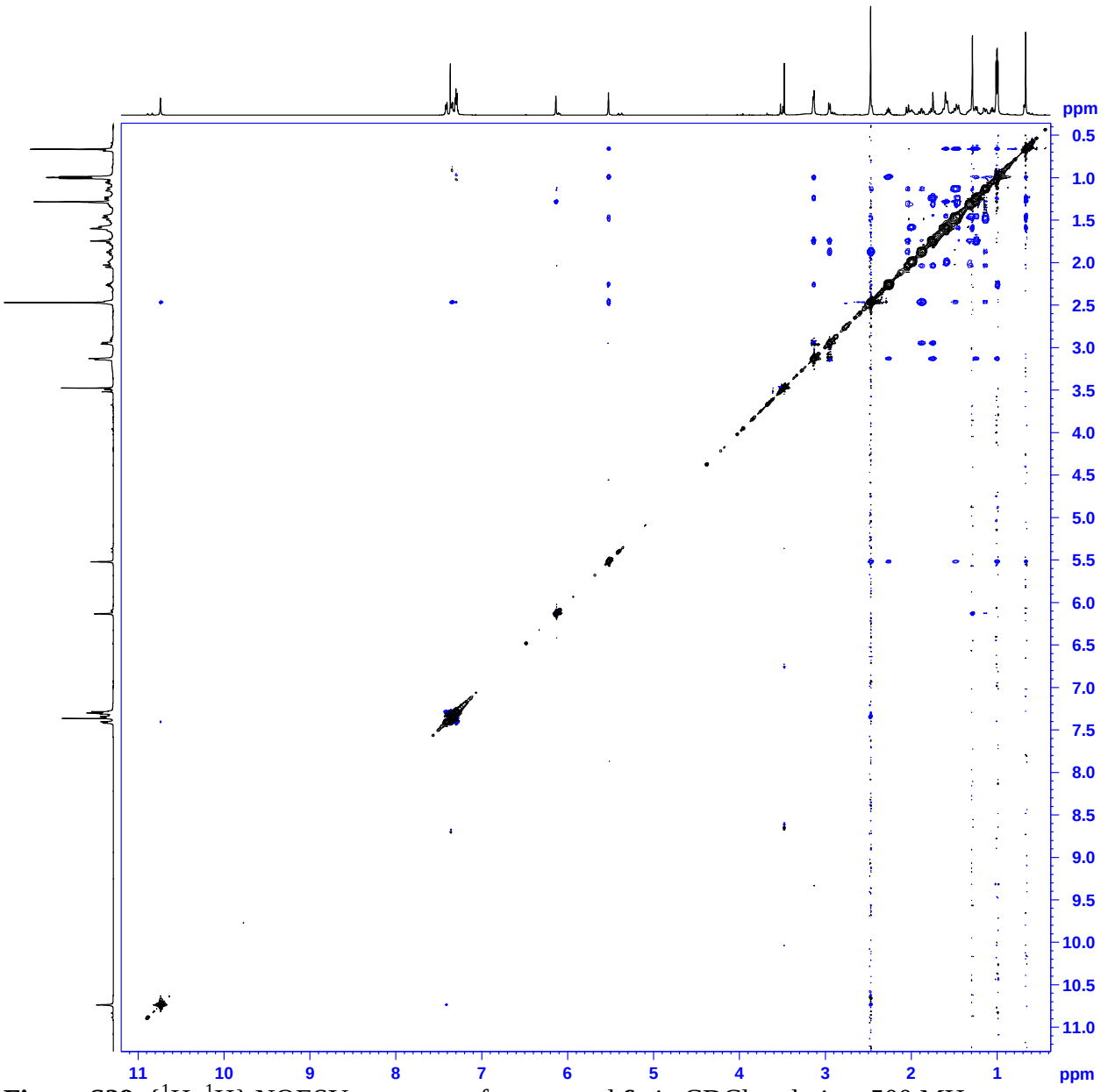

Figure S38. {^{1}H, ^{1}H} NOESY spectrum of compound **6e** in $CDCl_3$ solution, 500 MHz.

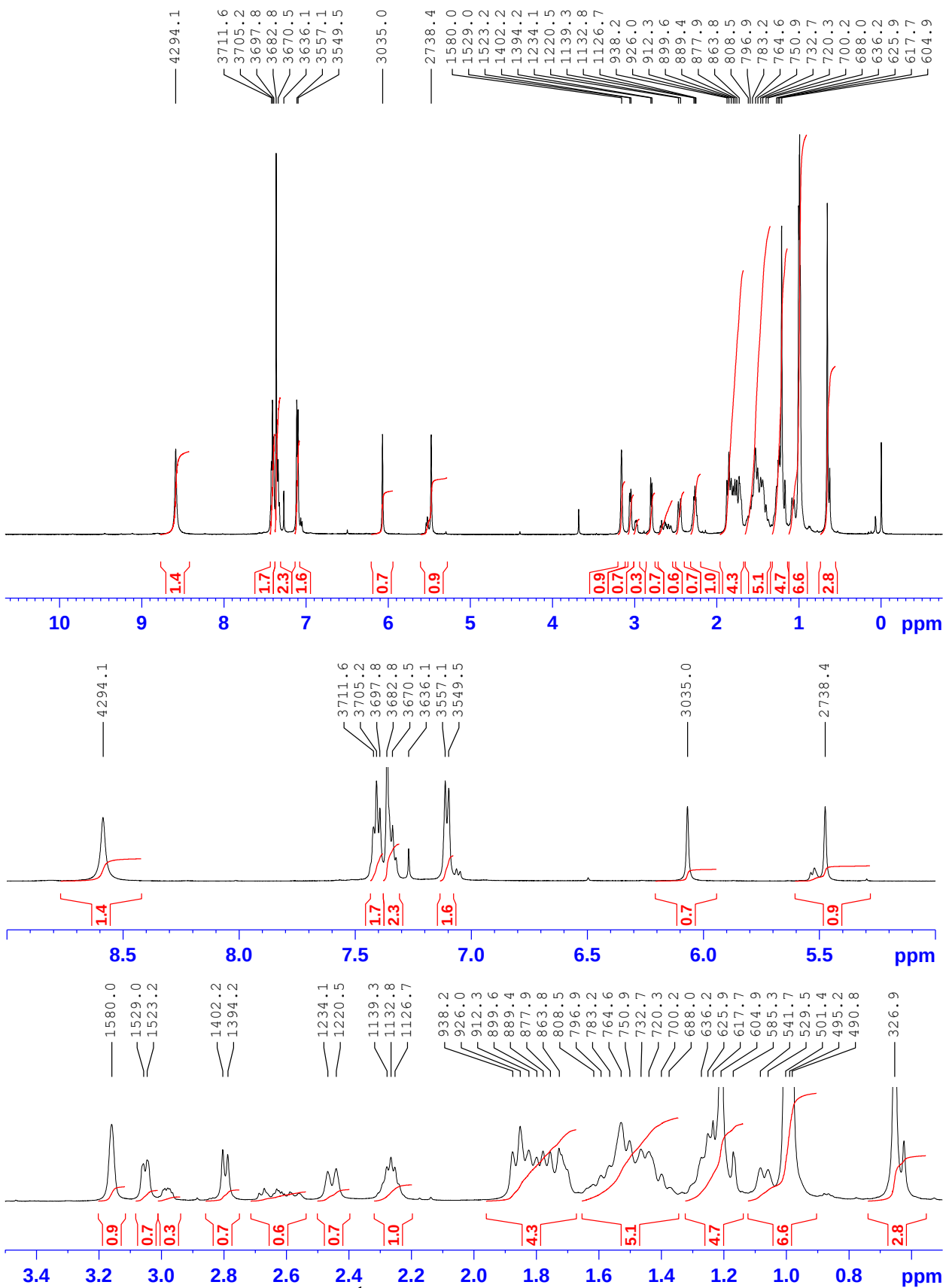

Figure S39. Complete and detailed ^{1}H NMR spectrum of compound **7a** in $CDCl_3$ solution, 500 MHz.

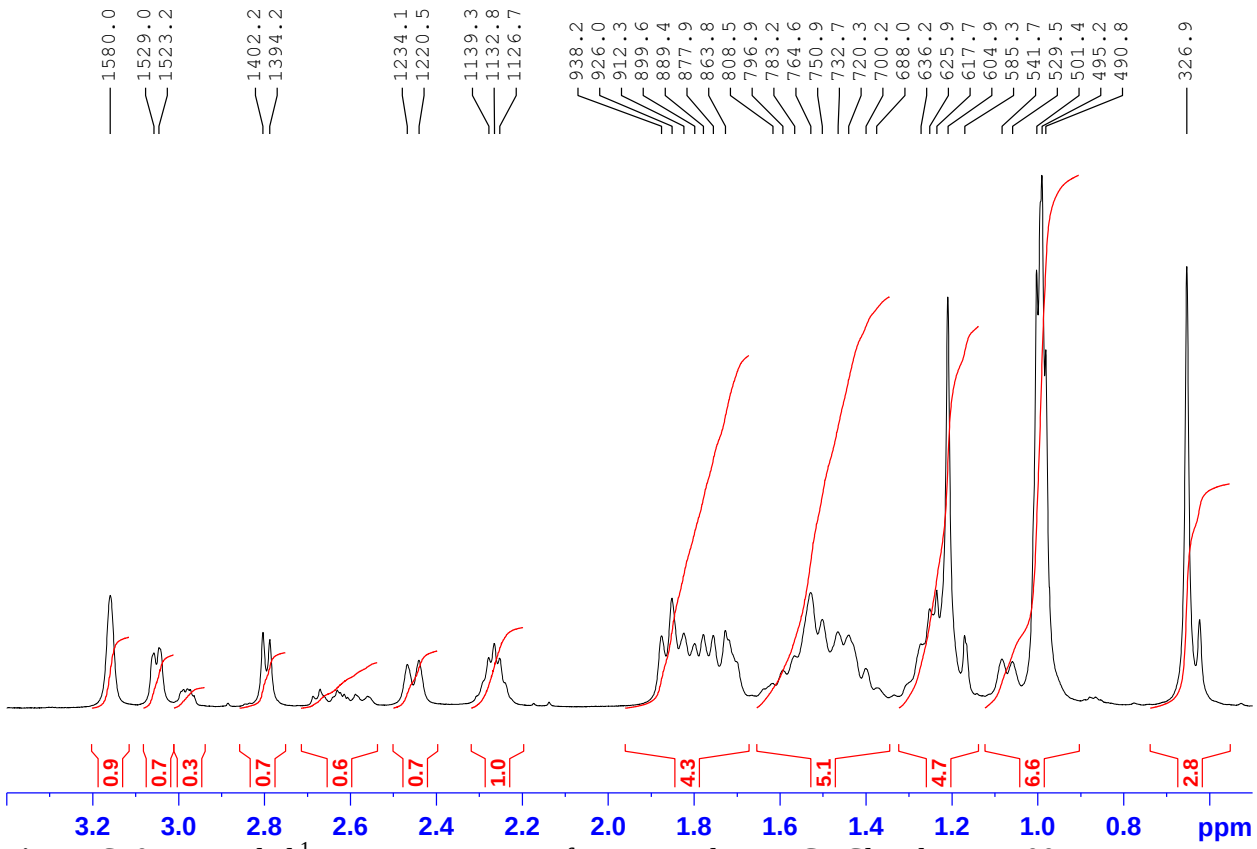

Figure S40. Expanded ^{1}H NMR spectrum of compound **7a** in $CDCl_3$ solution, 500 MHz.

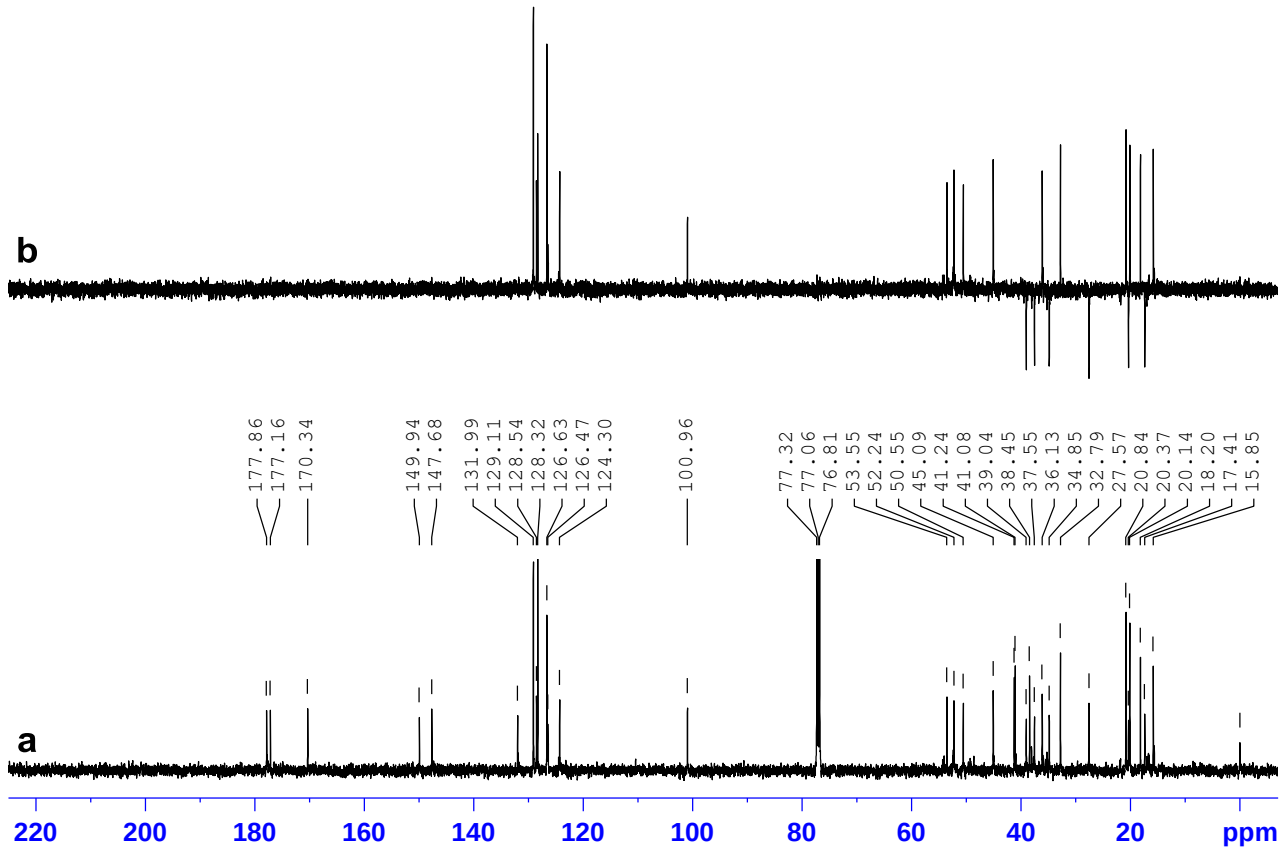

Figure S41. Complete $^{13}C\{^{1}H\}$(**a**) and DEPT-135(**b**) spectra of compound **7a** in $CDCl_3$ solution, 500 MHz.

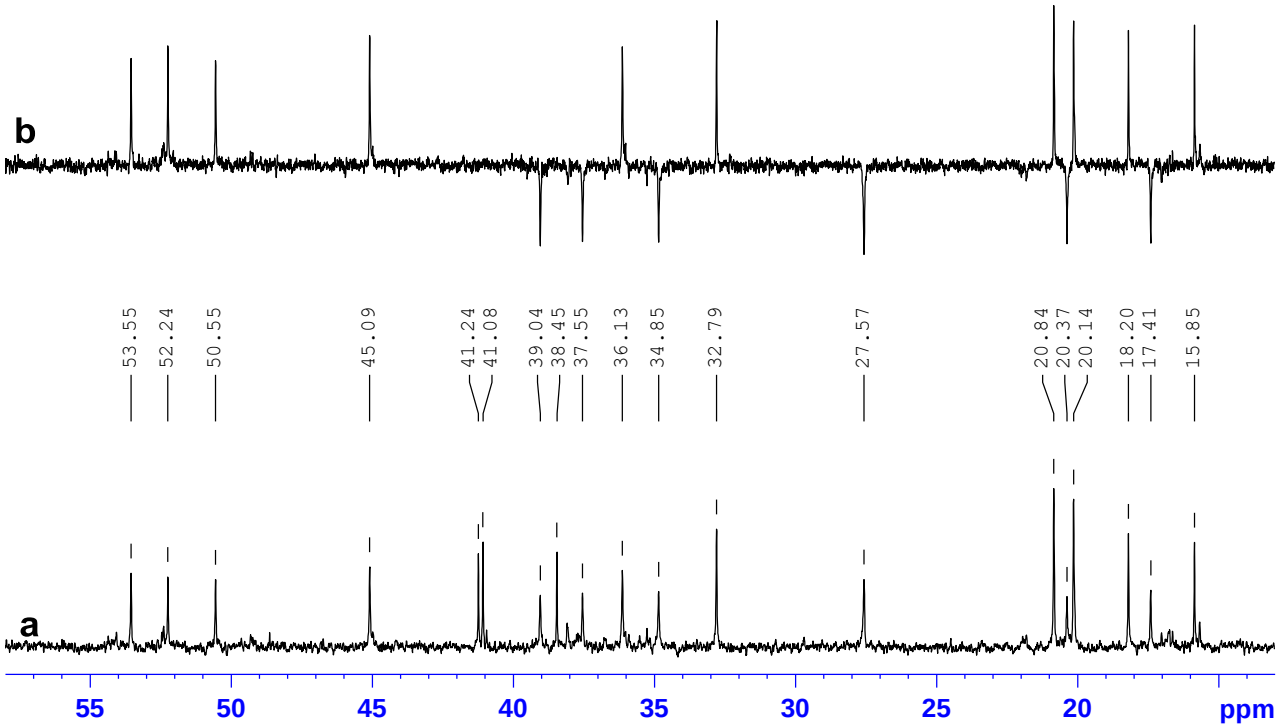

Figure S42. Expanded $^{13}C\{^{1}H\}$(**a**) and DEPT-135(**b**) spectra of compound **7a** in $CDCl_3$ solution, 500 MHz.

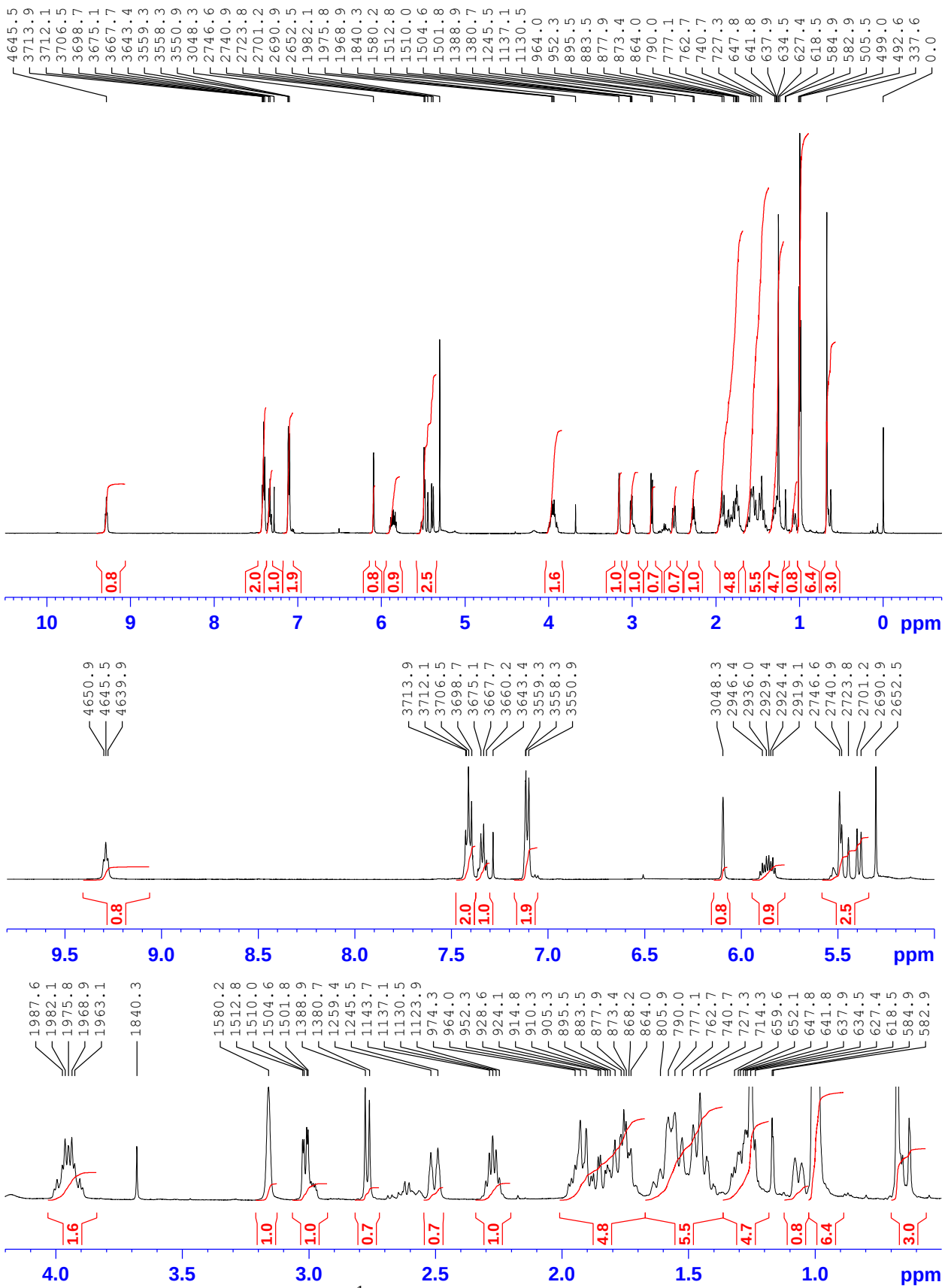

Figure S43. Complete and detailed ^{1}H NMR spectrum of compound **7c** in $CDCl_3$ solution, 500 MHz.

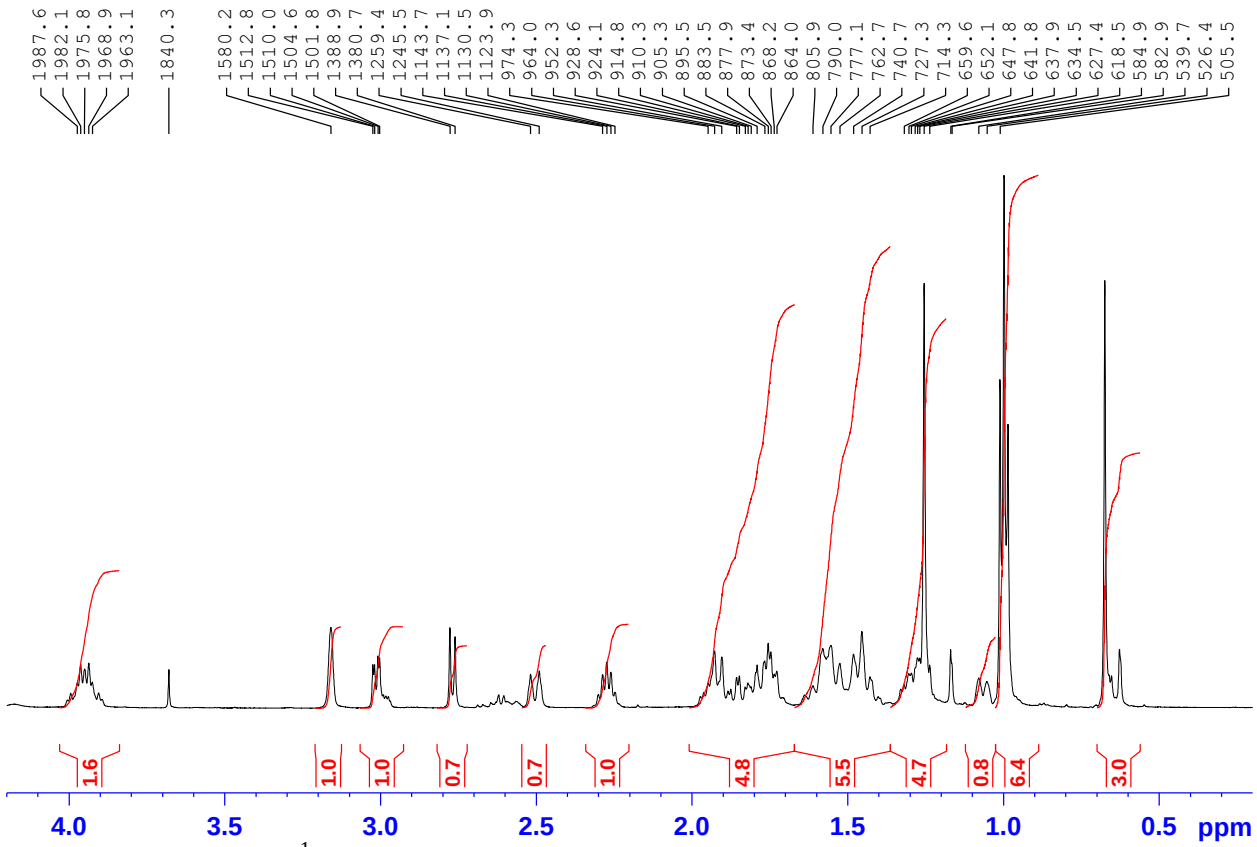

Figure S44. Expanded ^{1}H NMR spectrum of compound **7c** in $CDCl_3$ solution, 500 MHz.

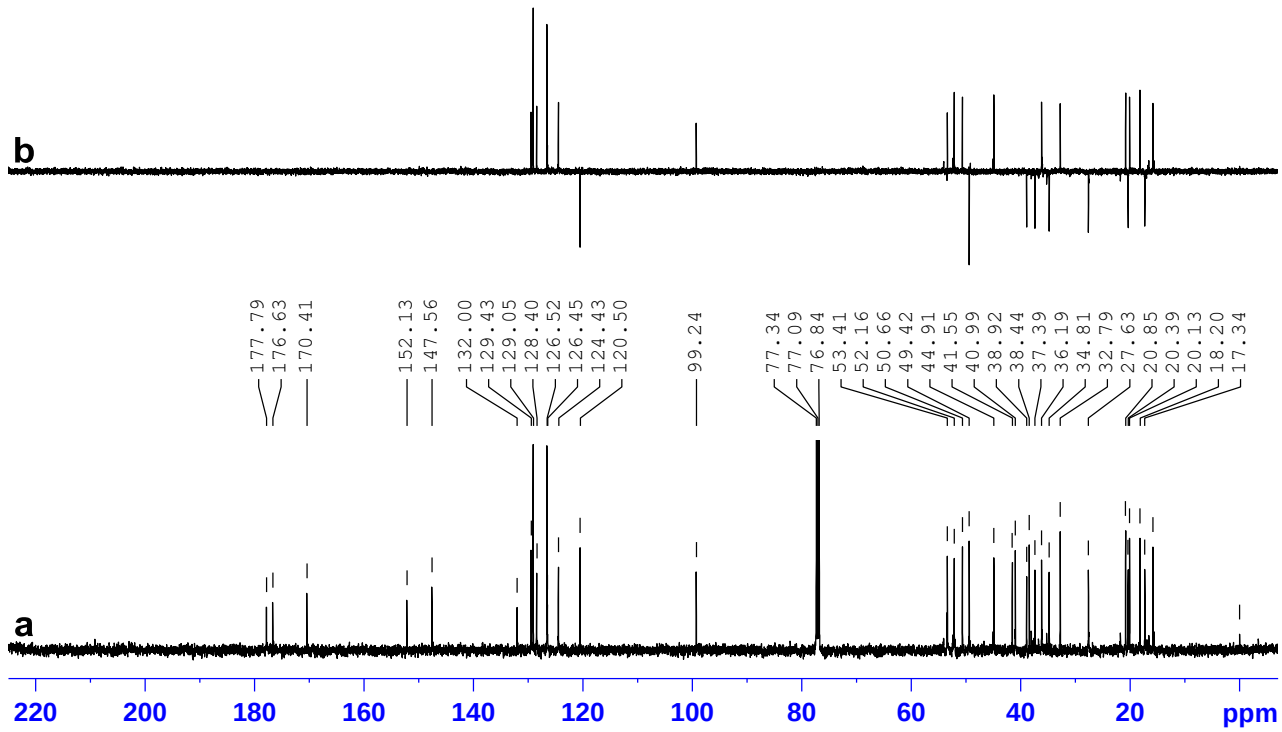

Figure S45. Complete $^{13}C\{^{1}H\}$(**a**) and DEPT-135(**b**) spectra of compound **7c** in $CDCl_3$ solution, 500 MHz.

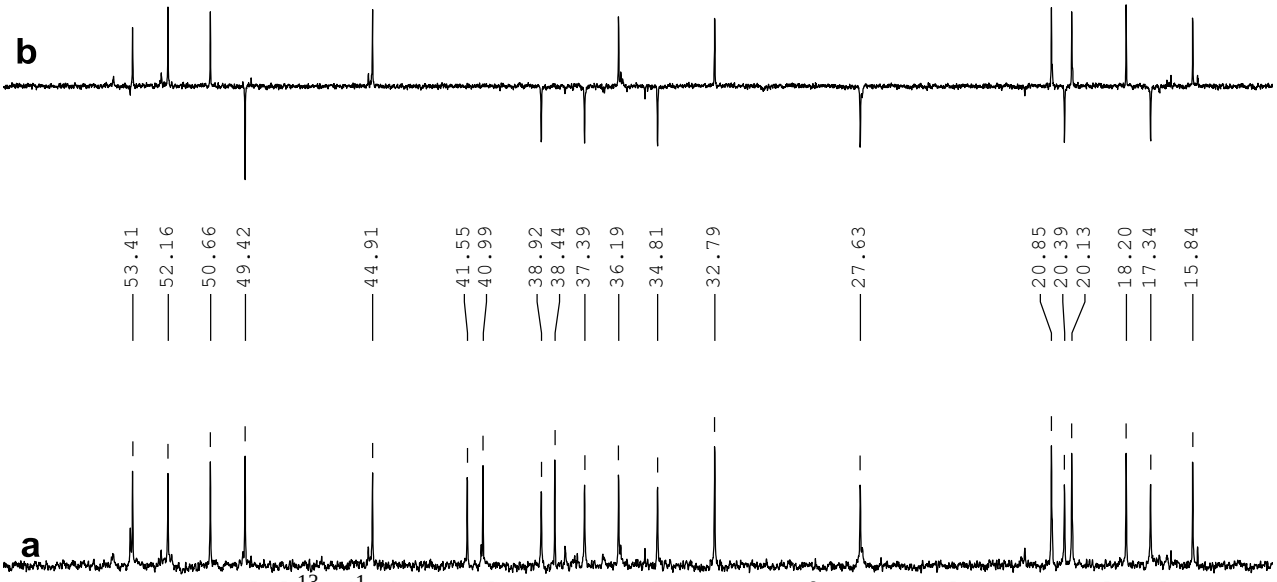

Figure S46. Expanded $^{13}C\{^{1}H\}$(**a**) and DEPT-135(**b**) spectra of compound **7c** in $CDCl_3$ solution, 500 MHz.

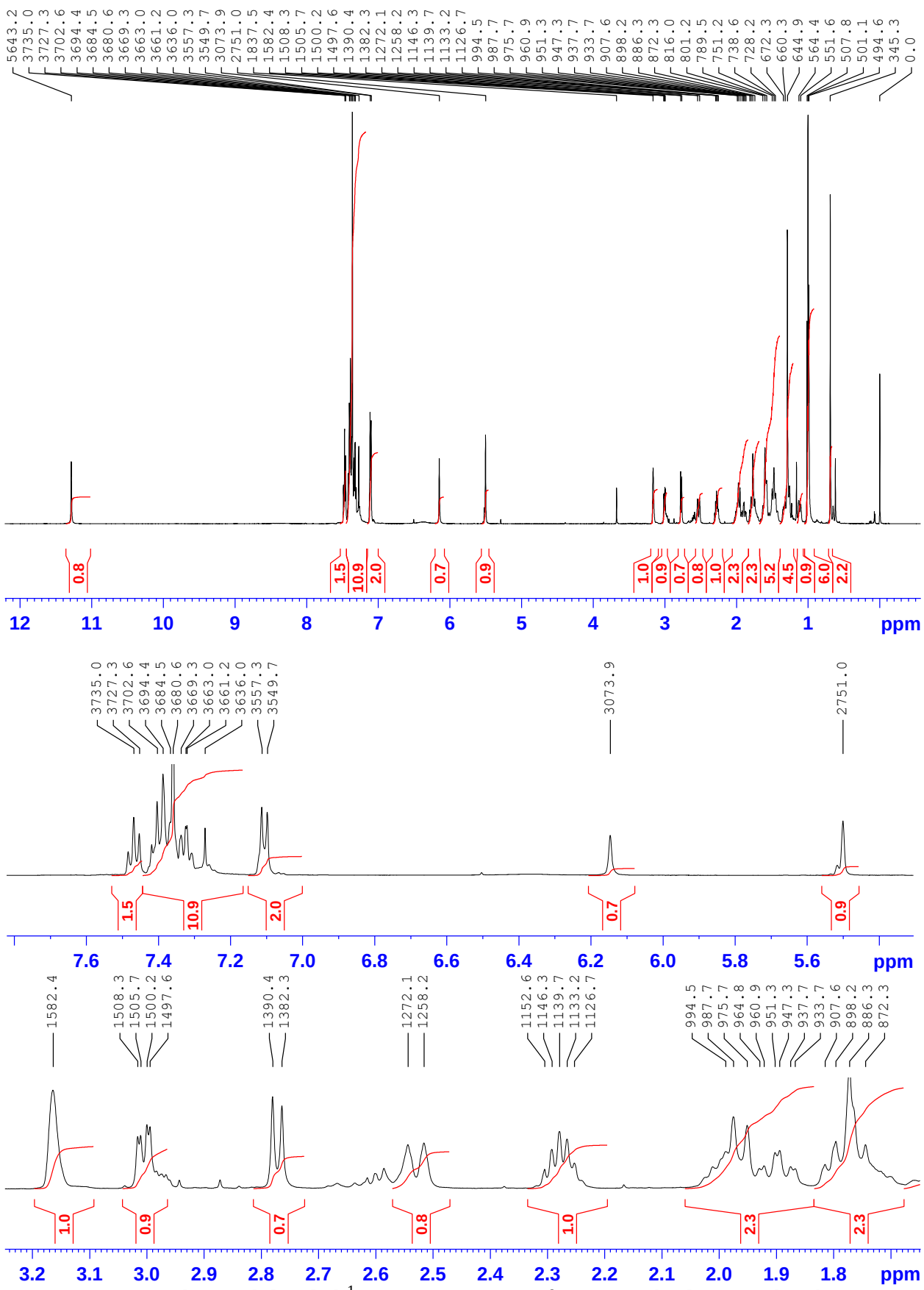

Figure S47. Complete and detailed ^{1}H NMR spectrum of compound **7d** in $CDCl_3$ solution, 500 MHz.

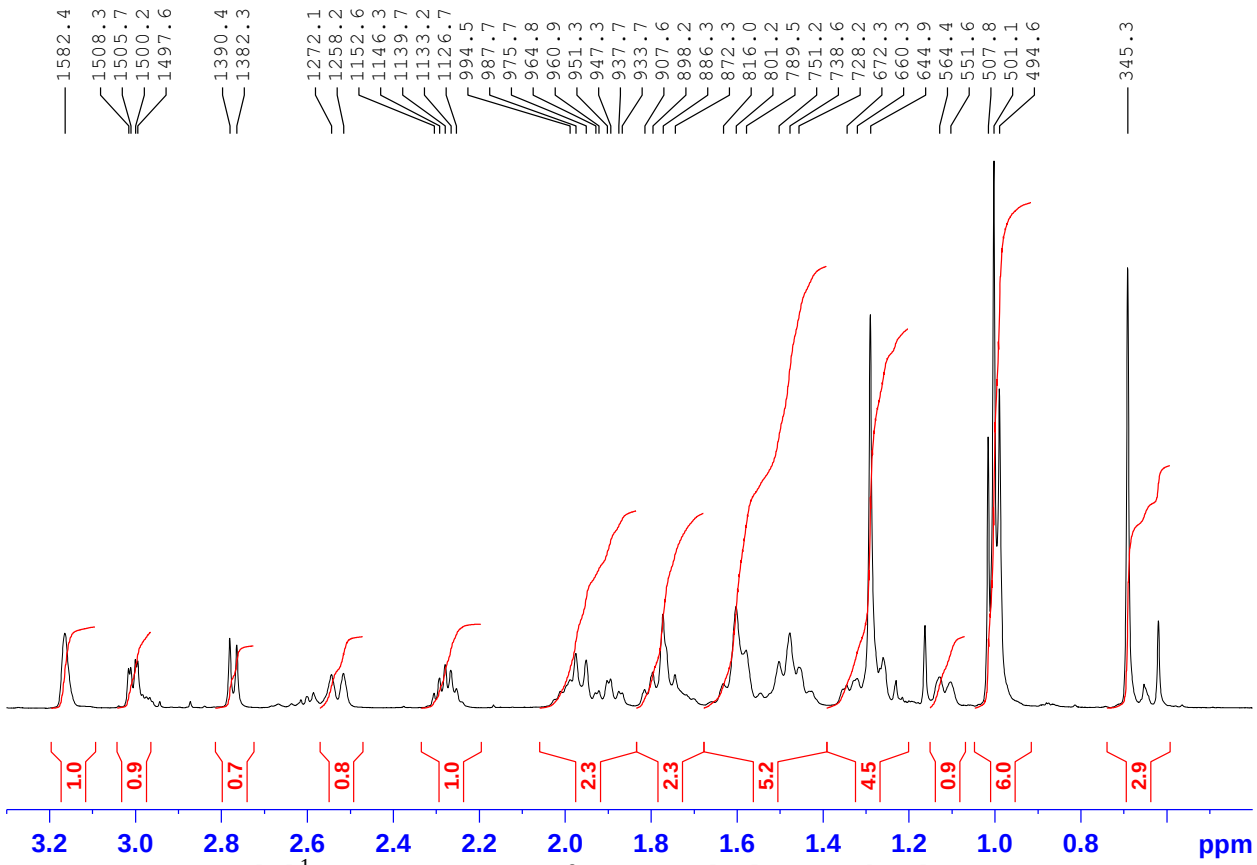

Figure S48. Expanded ^{1}H NMR spectrum of compound **7d** in $CDCl_3$ solution, 500 MHz.

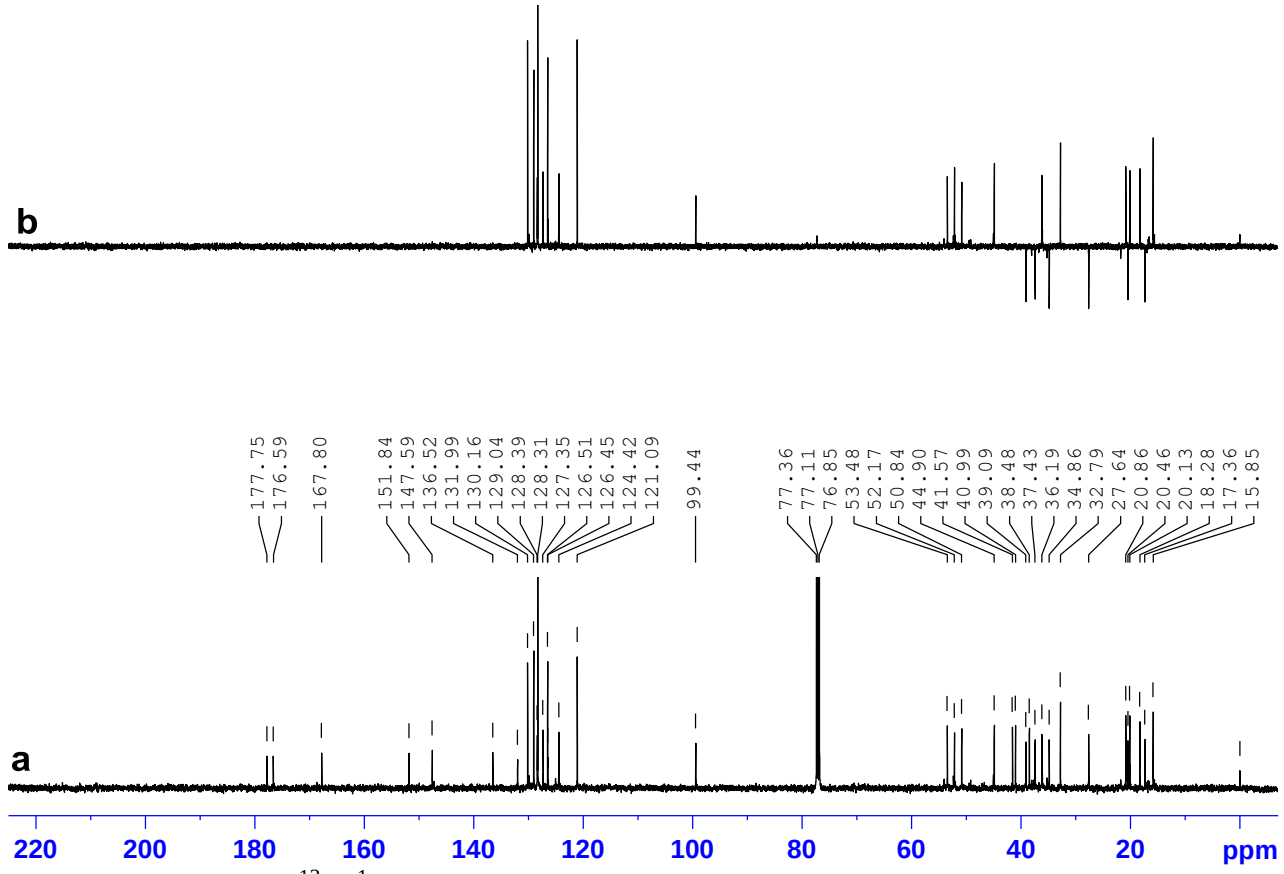

Figure S49. Complete ^{13}C{^{1}H}(**a**) and DEPT-135(**b**) spectra of compound **7d** in $CDCl_3$ solution, 500 MHz.

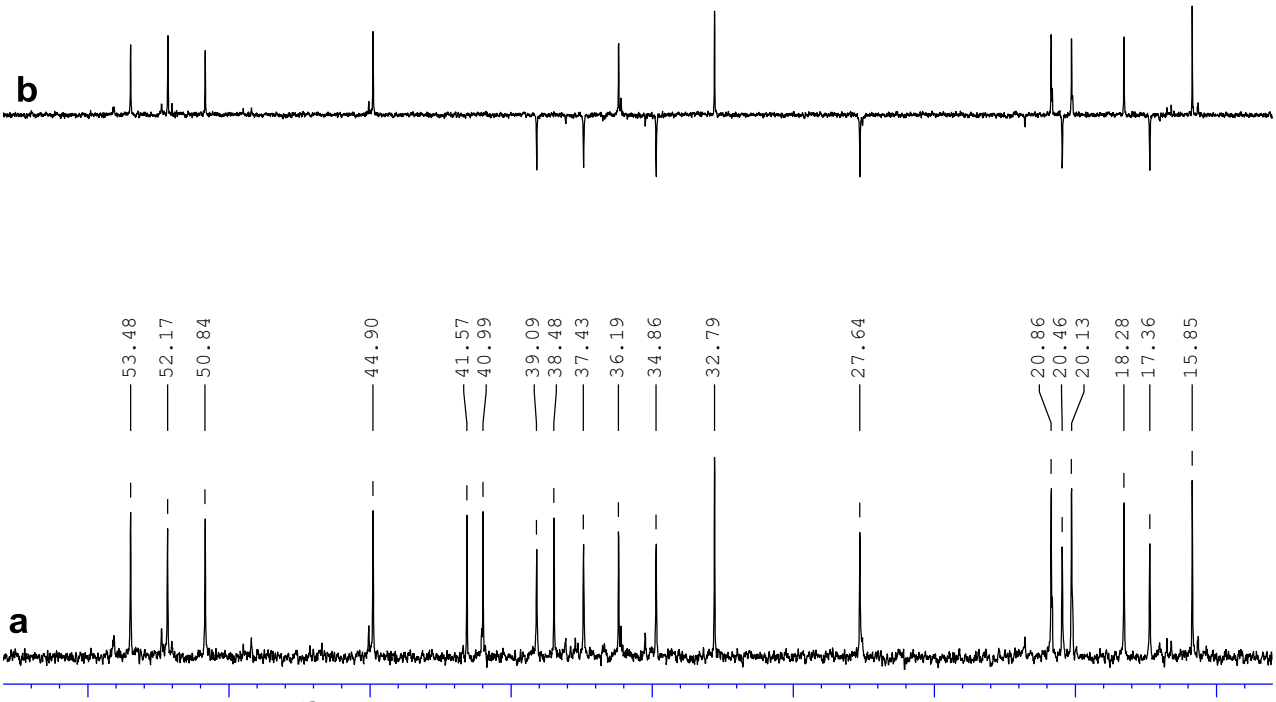

Figure S50. Expanded $^{13}C\{^{1}H\}$(**a**) and DEPT-135(**b**) spectra of compound **7d** in $CDCl_3$ solution, 500 MHz.

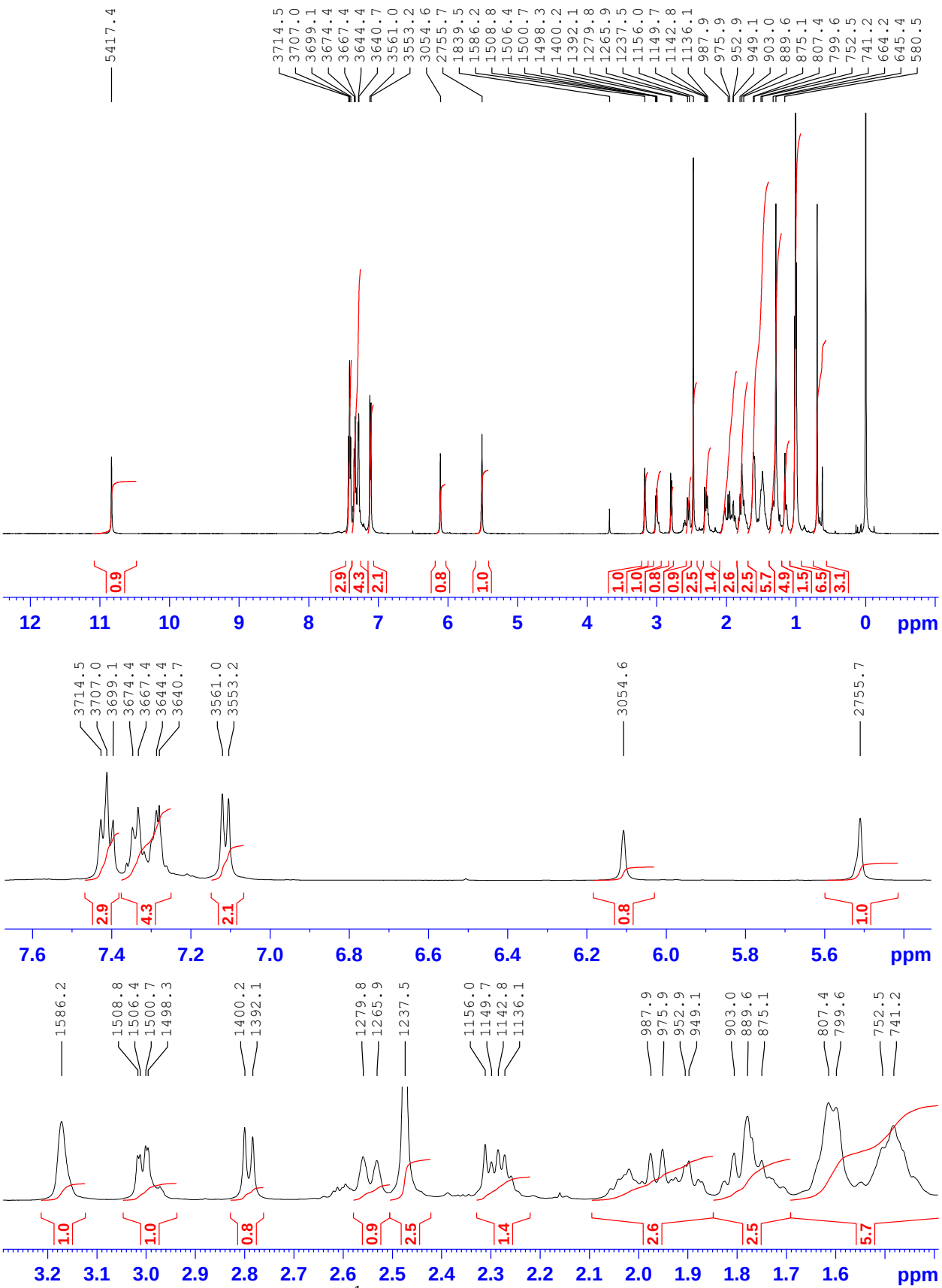

Figure S51. Complete and detailed ^{1}H NMR spectrum of compound **7e** in $CDCl_3$ solution, 500 MHz.

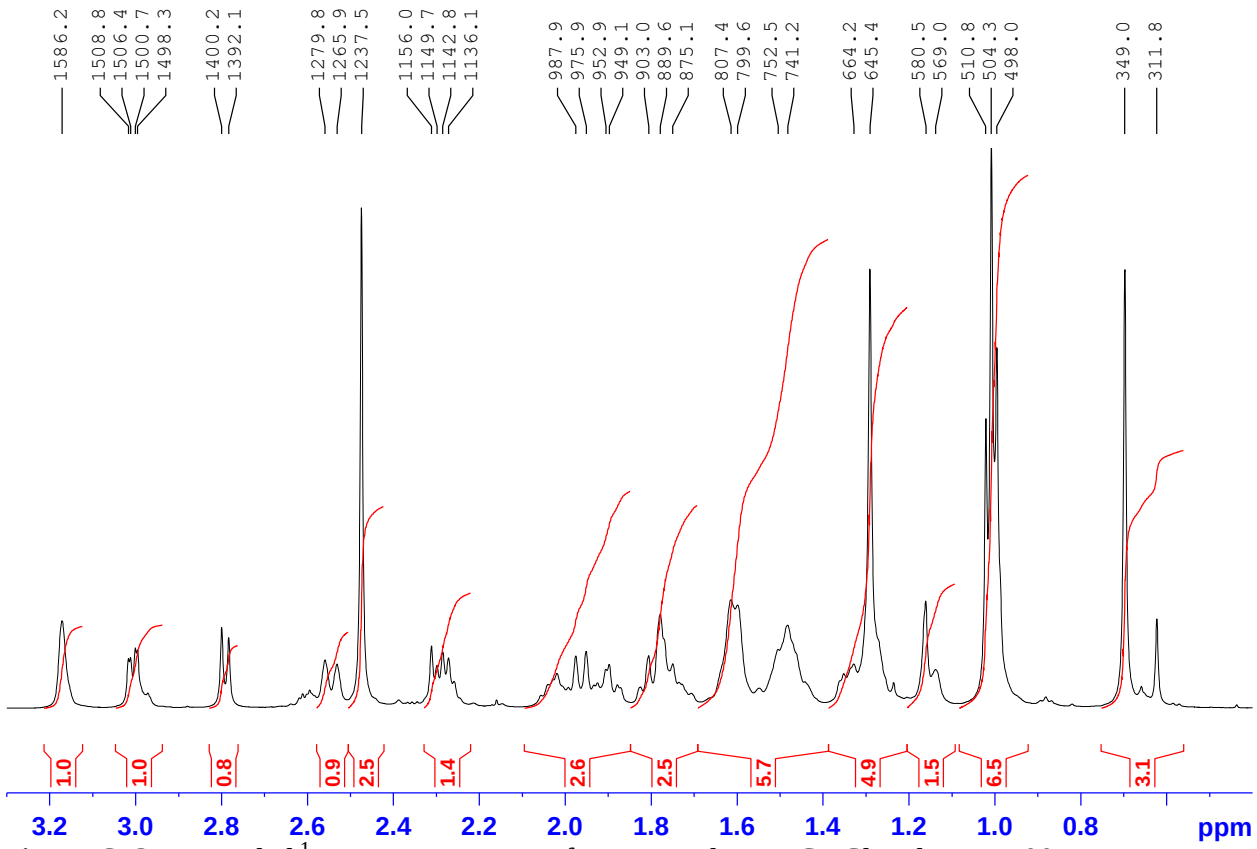

Figure S52. Expanded ^{1}H NMR spectrum of compound **7e** in $CDCl_3$ solution, 500 MHz.

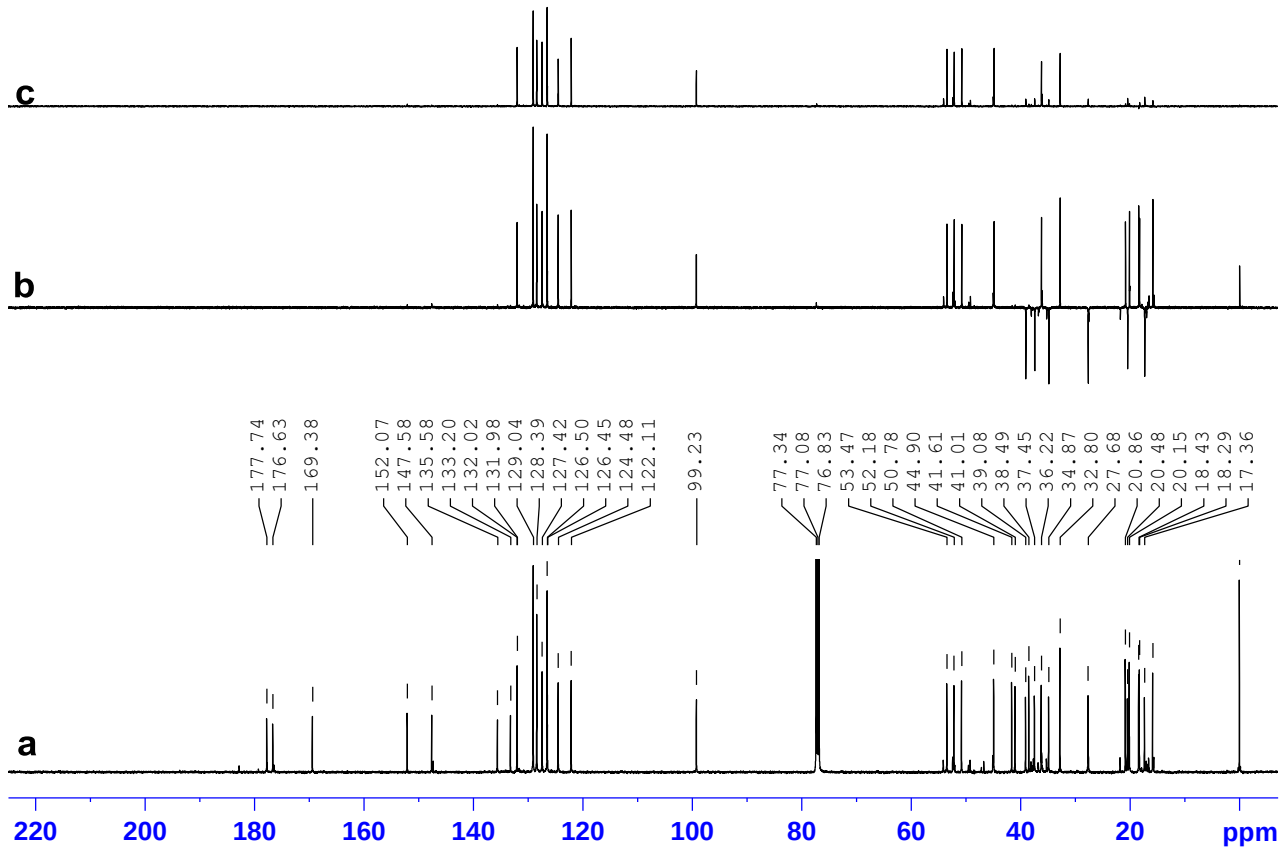

Figure S53. Complete $^{13}C\{^{1}H\}$(**a**), DEPT-135(**b**) and DEPT-90(**c**) spectra of compound **7e** in $CDCl_3$ solution, 500 MHz.

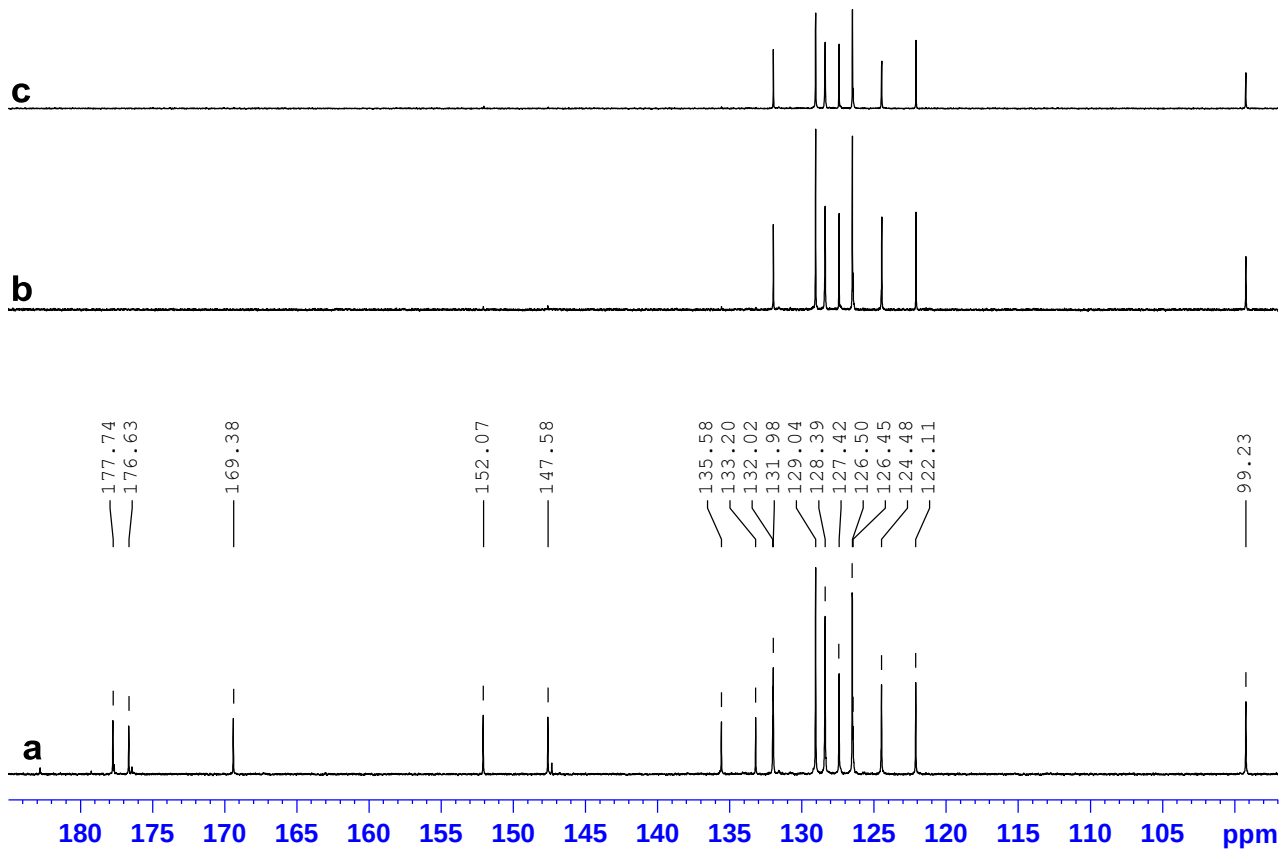

Figure S54. Expanded $^{13}C\{^{1}H\}$(**a**), DEPT-135(**b**) and DEPT-90(**c**) spectra of compound **7e** in $CDCl_3$ solution, 500 MHz.

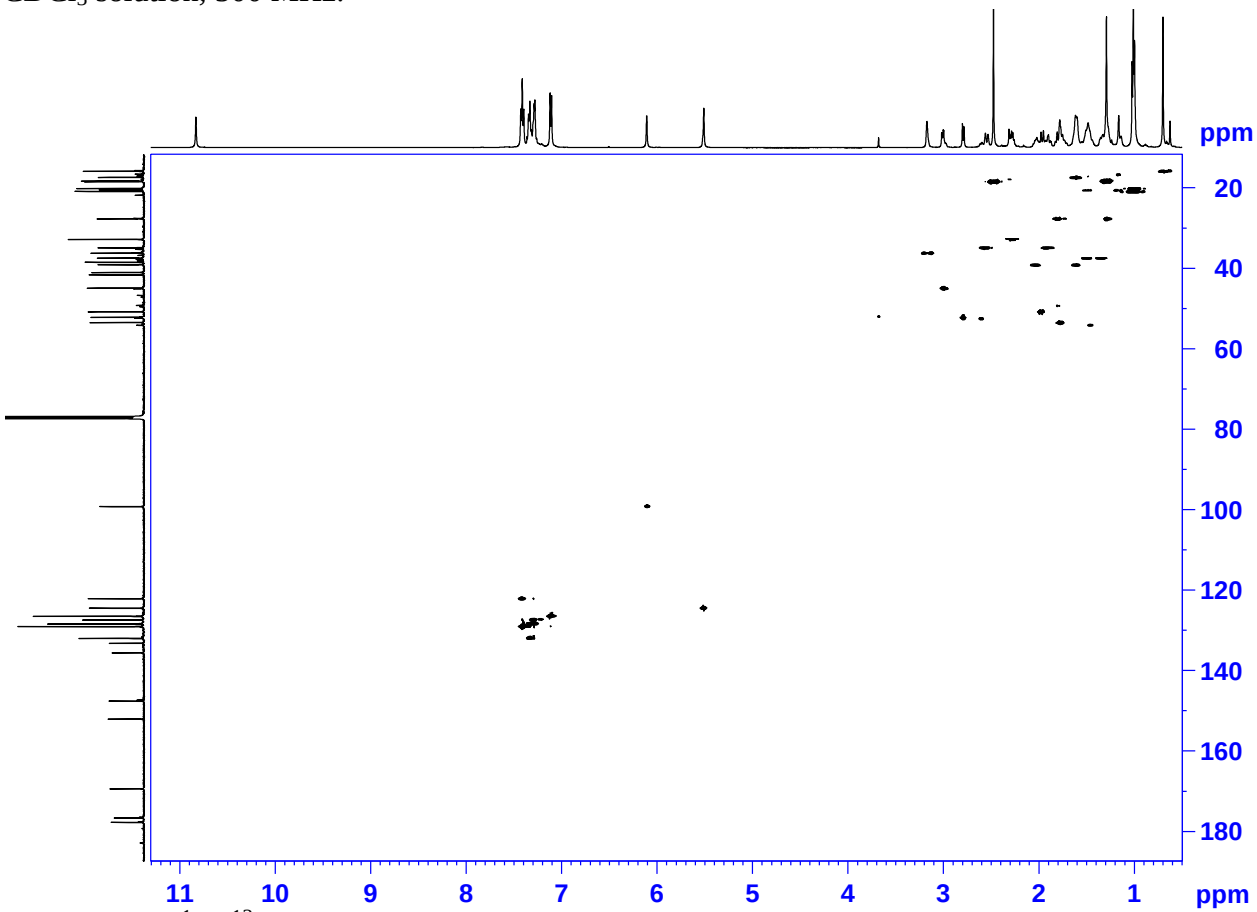

Figure S56. $\{^{1}H, ^{13}C\}$ HSQC spectrum of compound **7e** in $CDCl_3$ solution, 500 MHz.

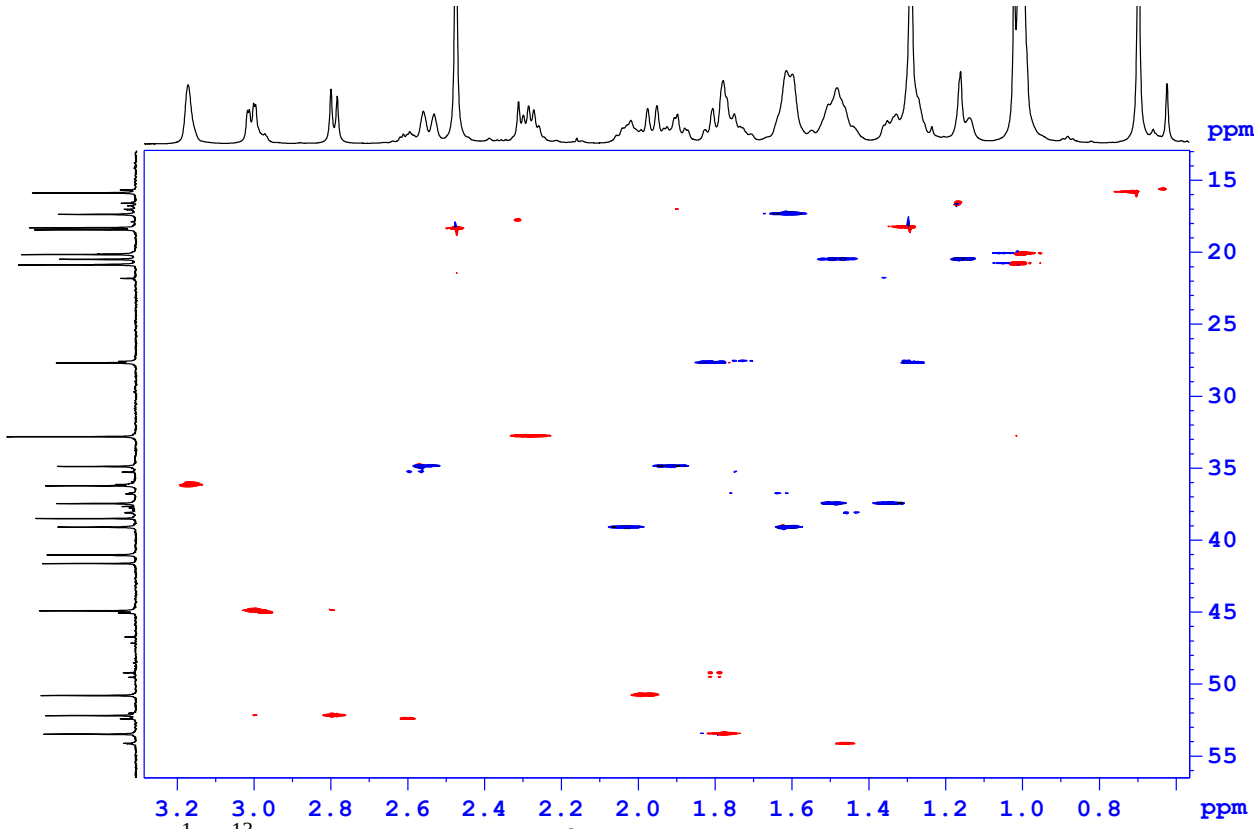

Figure S57. {^{1}H, ^{13}C} HSQCed spectrum of compound **7e** in $CDCl_3$ solution, 500 MHz.

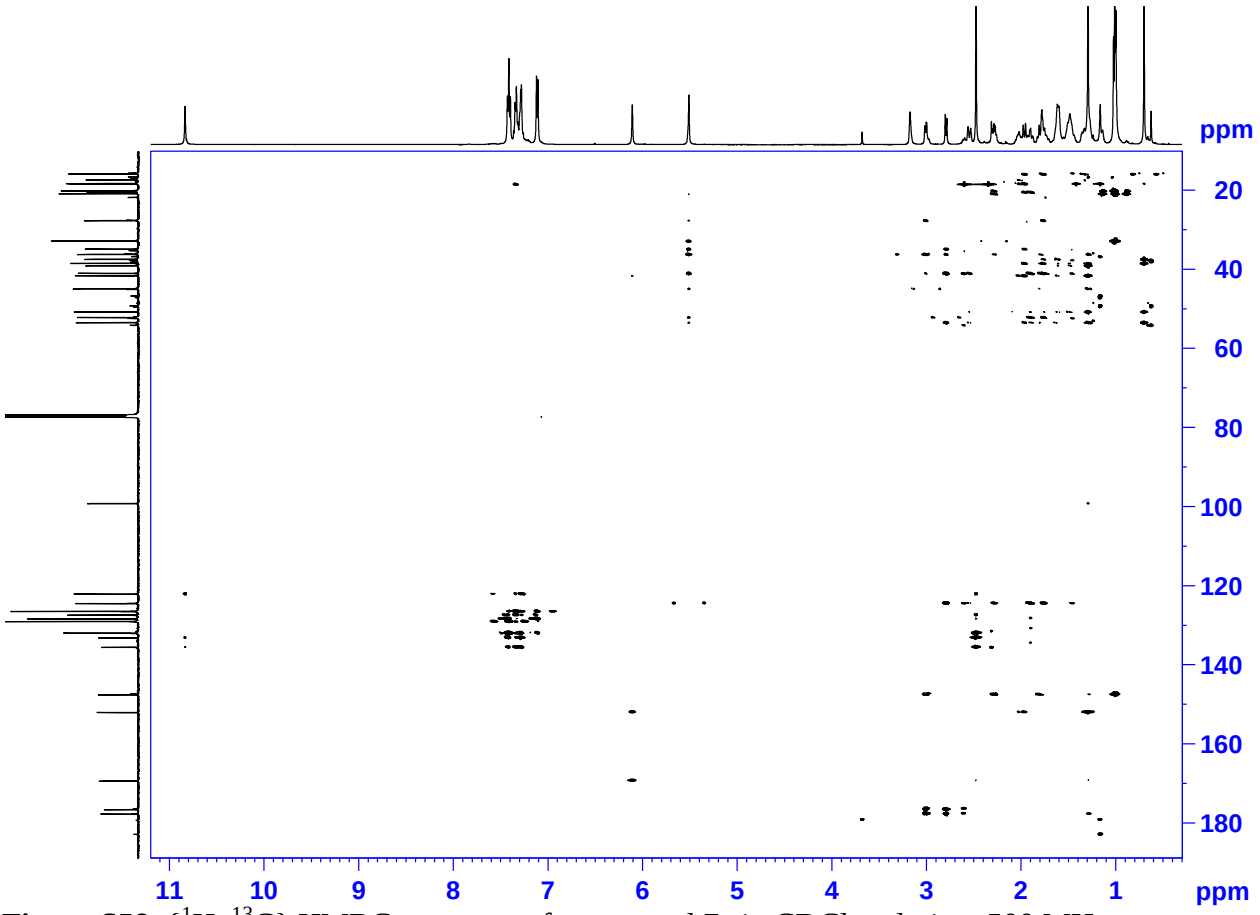

Figure S58. {^{1}H, ^{13}C} HMBC spectrum of compound **7e** in $CDCl_3$ solution, 500 MHz.

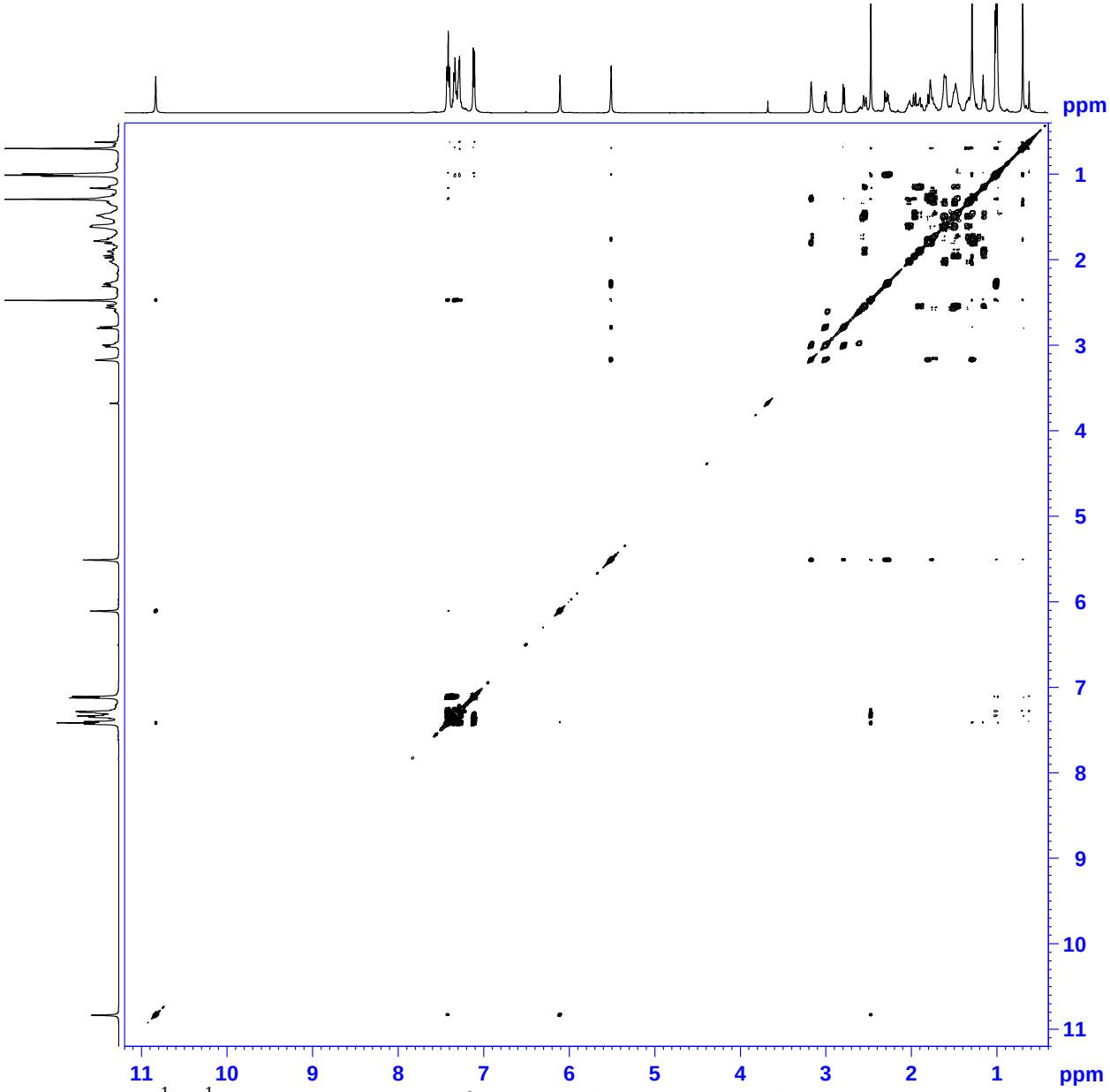

Figure S59. {^{1}H, ^{1}H} COSY spectrum of compound **7e** in $CDCl_3$ solution, 500 MHz.

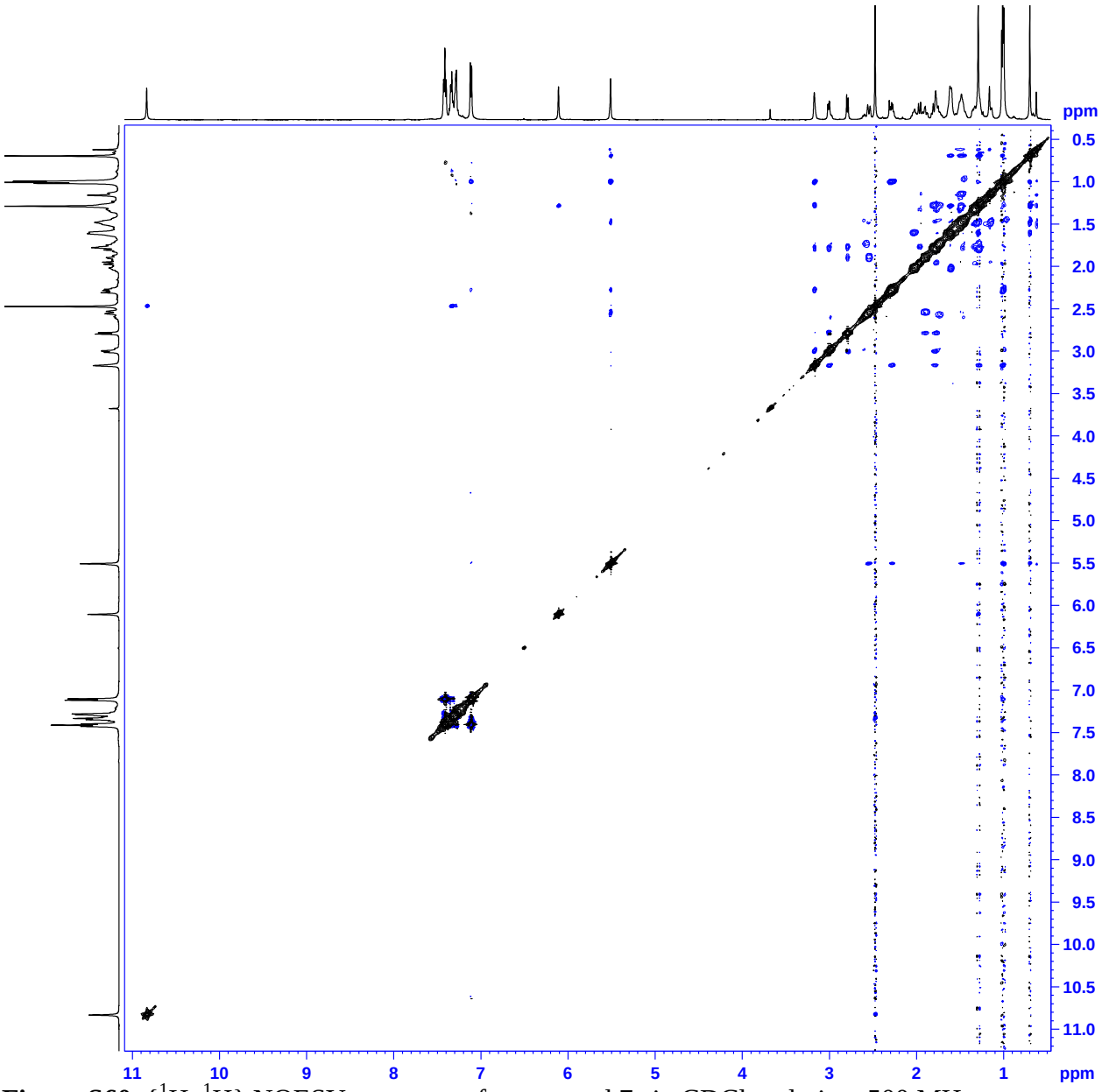

Figure S60. {^{1}H, ^{1}H} NOESY spectrum of compound **7e** in $CDCl_3$ solution, 500 MHz.