



Supporting Information

for

α -Ketoglutaric acid in Ugi reactions and Ugi/aza-Wittig tandem reactions

Vladyslav O. Honcharov, Yana I. Sakhno, Olena H. Shvets, Vyacheslav E. Saraev, Svitlana V. Shishkina, Tetyana V. Shcherbakova and Valentyn A. Chebanov

Beilstein J. Org. Chem. **2025**, 21, 2021–2029. doi:10.3762/bjoc.21.157

General synthetic procedures, characterization of compounds, ^1H and ^{13}C NMR spectra and X-ray data

General

^1H and ^{13}C NMR spectra were recorded with Varian MR-400, Bruker Avance III, Bruker Avance DRX, and Varian Unity INOVA spectrometers (400 and 100 MHz, respectively) in $\text{DMSO}-d_6$. Mass spectra were recorded with a Shimadzu LCMS-2020 spectrometer. Elemental analysis was performed using an EuroVector EA-3000 automatic elemental analyzer. The melting points were measured with a Stuart SMP10 electronic melting point apparatus and are uncorrected. The progress of the reactions and the purity of the compounds obtained were monitored by thin-layer chromatography on ALUGRAM Xtra SIL G UV254 plates developed with mixtures of EtOAc and hexane. The starting *o*-azidoanilines were obtained according to the methods described in the literature [1,2]. Aromatic aldehydes, aromatic amines, α -ketoglutaric acid, and *tert*-butyl isocyanide were commercially available.

X-ray experimental part

The colorless crystals of compound **9e** ($\text{C}_{26}\text{H}_{31}\text{N}_3\text{O}_5$, $\text{C}_2\text{H}_6\text{O}$) are triclinic. At 173 K $a = 9.1980(13)$, $b = 9.5476(13)$, $c = 15.400(3)$ Å, $\alpha = 92.334(9)^\circ$, $\beta = 94.801(10)^\circ$, $\gamma = 90.029(9)^\circ$, $V = 1346.5(3)$ Å³, $M_r = 511.60$, $Z = 2$, space group $P\bar{1}$, $d_{\text{calc}} = 1.262$ g/cm³, $\mu(\text{Mo K}) = 0.089$ mm⁻¹, $F(000) = 548$. Intensities of 15385 reflections (14137 independent, $R_{\text{int}} = 0.0859$) were measured on a Bruker APEX II diffractometer (graphite monochromated Mo K α radiation, CCD detector, φ - and ω -scanning, $2\theta_{\text{max}} = 50^\circ$). The structure was solved by direct method using OLEX2 [3] package with SHELXT [4] and SHELXL modules [5]. Positions of the hydrogen atoms were located from electron density difference maps and refined using “riding” model with $U_{\text{iso}} = nU_{\text{eq}}$ ($n = 1.5$ for methyl group and $n = 1.2$ for other hydrogen atoms) of the carrier atom. Full-matrix least-squares refinement against F^2 in anisotropic approximation for non-

hydrogen atoms using 14137 reflections was converged to $wR_2 = 0.2360$ ($R_1 = 0.0774$ for 7589 reflections with $F > 4\sigma(F)$, $S = 1.005$). The final atomic coordinates, and crystallographic data for molecule **9e** have been deposited to with the Cambridge Crystallographic Data Centre, 12 Union Road, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk) and are available on request quoting the deposition numbers CCDC 2464193).

Synthetic procedures

Synthesis of compounds 5

General procedure for the synthesis of compounds 5a–l. Amines **3a–c** (0.68 mmol) and aldehydes **2a–d** (0.68 mmol) were dissolved in 2 mL of methanol in a round-bottomed flask and stirred at 25 °C for 30 minutes. Then, α -ketoglutaric acid (**1**, 0.68 mmol, 100 mg) was added to the reaction mixture and stirred for 30 minutes. Then, *tert*-butyl isocyanide (**4**, 0.68 mmol, 77 μ L) was added and the reaction mixture was stirred at 45 °C for 24 hours. The completeness of the reaction was determined by thin-layer chromatography (hexane/ethyl acetate 1:2). The reaction mixture was cooled, and a small amount of water was added until it became cloudy. The precipitate of compounds **5a–l** formed after the addition of water was filtered and dried in vacuo.

5-((2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2-oxoethyl)(4-chlorophenyl)amino)-4,5-dioxopentanoic acid (5a). Yield 81% (265 mg), white solid, m.p. = 169-171 °C, $R_f = 0.57$.

^1H NMR spectrum (400 MHz, DMSO- d_6), δ , ppm: 12.17 (s, 1H, COOH), 7.97 (s, 1H, NH), 6.98-7.35 (m, 8H, ArH), 6.04 (s, 1H, CH), 2.88 (t, $J = 6.5$ Hz, 2H, CH₂), 2.26 (t, $J = 6.6$ Hz, 2H, CH₂), 1.24 (s, 9H, *t*-Bu).

^{13}C NMR spectrum (100 MHz, DMSO- d_6), δ , ppm: 198.8, 172.9, 167.6, 166.3, 136.3, 133.3, 132.7, 132.6, 132.2, 131.9, 128.3, 128.1, 62.8, 50.6, 35.0, 28.3, 26.6.

Mass spectrum (ESI), m/z : 477 (100) $[\text{M-H}]^-$.

Elemental analysis calcd for $\text{C}_{23}\text{H}_{24}\text{Cl}_2\text{N}_2\text{O}_5$: C 57.63, H 5.05, N 5.84; found: C 57.51, H 5.14, N 5.93.

5-((2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2-oxoethyl)(*p*-tolyl)amino)-4,5-dioxopentanoic acid (5b) Yield 64% (200 mg), white solid, m.p. = 150-152 °C, R_f = 0.65.

^1H NMR spectrum (400 MHz, DMSO- d_6), δ , ppm: 7.89 (s, 1H, NH), 6.84-7.33 (m, 8H, ArH), 6.00 (s, 1H, CH), 2.76 (t, J = 6.8 Hz, 2H, CH_2), 2.19 (t, J = 6.4 Hz, 2H, CH_2), 2.16 (s, 3H, CH_3), 1.24 (s, 9H, *t*-Bu).

^{13}C NMR spectrum (100 MHz, DMSO- d_6), δ , ppm: 199.1, 172.8, 167.6, 166.9, 137.5, 134.4, 133.6, 132.5, 131.8, 130.3, 128.9, 128.0, 62.7, 50.5, 35.1, 28.3, 26.7, 20.6.

Mass spectrum (ESI), m/z : 457 (100) $[\text{M-H}]^-$.

Elemental analysis calcd for $\text{C}_{24}\text{H}_{27}\text{ClN}_2\text{O}_5$: C 62.81, H 5.93, N 6.10; found: C 62.71, H 6.02, N 6.17.

5-((2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2-oxoethyl)(4-methoxyphenyl)amino)-4,5-dioxopentanoic acid (5c). Yield 68% (220 mg), white solid, m.p. = 155-157 °C, R_f = 0.36.

^1H NMR spectrum (400 MHz, DMSO- d_6), δ , ppm: 12.15 (s, 1H, COOH), 7.89 (s, 1H, NH), 6.61-7.33 (m, 8H, ArH), 5.98 (s, 1H, CH), 3.64 (s, 3H, OCH_3), 2.75 (t, J = 7.1 Hz, 2H, CH_2), 2.20 (t, J = 6.6 Hz, 2H, CH_2), 1.24 (s, 9H, *t*-Bu).

^{13}C NMR spectrum (100 MHz, DMSO- d_6), δ , ppm: 199.2, 172.8, 167.8, 167.0, 158.6, 133.6, 132.5, 132.0, 131.9, 129.3, 128.0, 113.4, 62.7, 55.1, 50.5, 35.1, 28.3, 26.7.

Mass spectrum (ESI), m/z : 473 (100) $[\text{M-H}]^-$.

Elemental analysis calcd for C₂₄H₂₇ClN₂O₆: C 60.70, H 5.73, N 5.90; found: C 60.61, H 5.79, N 5.99.

5-((2-(*tert*-Butylamino)-1-(4-methoxyphenyl)-2-oxoethyl)(4-chlorophenyl)amino)-4,5-dioxopentanoic acid (5d). Yield 50% (160 mg), white solid, m.p. = 144-146 °C, R_f = 0.45.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.14 (s, 1H, COOH), 7.85 (s, 1H, NH), 6.63-7.40 (m, 8H, ArH), 5.99 (s, 1H, CH), 3.65 (s, 3H, OCH₃), 2.85 (t, *J* = 6.5 Hz, 2H, CH₂), 2.25 (t, *J* = 6.4 Hz, 2H, CH₂), 1.25 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 198.9, 172.9, 168.3, 166.3, 158.8, 136.5, 132.3, 131.4, 128.1, 125.9, 113.5, 63.0, 55.0, 50.5, 35.0, 28.4, 26.6.

Mass spectrum (ESI), *m/z*: 473 (100) [M-H]⁻.

Elemental analysis calcd for C₂₄H₂₇ClN₂O₆: C 60.70, H 5.73, N 5.90; found: C 60.59, H 5.78, N 5.98.

5-((2-(*tert*-Butylamino)-1-(4-methoxyphenyl)-2-oxoethyl)(*p*-tolyl)amino)-4,5-dioxopentanoic acid (5e). Yield 54% (165 mg), white solid, m.p. = 131-133 °C, R_f = 0.38.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.13 (s, 1H, COOH), 7.78 (s, 1H, NH), 6.58-7.30 (m, 8H, ArH), 5.96 (s, 1H, CH), 3.64 (s, 3H, OCH₃), 2.74 (t, *J* = 5.9 Hz, 2H, CH₂), 2.04-2.28 (m, 2H, CH₂), 2.15 (s, 3H, CH₃), 1.25 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 199.2, 172.8, 168.4, 166.9, 158.6, 137.2, 134.6, 131.3, 130.4, 128.7, 126.2, 113.3, 62.8, 55.0, 50.4, 35.1, 28.4, 26.7, 20.6.

Mass spectrum (ESI), *m/z*: 453 (100) [M-H]⁻.

Elemental analysis calcd for C₂₅H₃₀N₂O₆: C 66.06, H 6.65, N 6.16; found: C 65.92, H 6.71, N 6.28.

5-((2-(*tert*-Butylamino)-1-(4-methoxyphenyl)-2-oxoethyl)(4-

methoxyphenyl)amino)-4,5-dioxopentanoic acid (5f). Yield 52% (165 mg), white solid, m.p. = 135-137 °C, R_f = 0.40.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.10 (s, 1H, COOH), 7.74 (s, 1H, NH), 6.58-7.25 (m, 8H, ArH), 5.93 (s, 1H, CH), 3.65 (s, 3H, OCH₃), 3.64 (s, 3H, OCH₃), 2.71 (t, *J* = 6.0 Hz, 2H, CH₂), 2.18 (t, *J* = 6.6 Hz, 2H, CH₂), 1.25 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 199.4, 172.8, 168.5, 167.1, 158.7, 158.4, 132.1, 131.3, 129.5, 126.3, 113.4, 113.2, 62.8, 55.1, 55.0, 50.4, 35.1, 28.4, 26.7.

Mass spectrum (ESI), *m/z*: 469 (100) [M-H]⁻.

Elemental analysis calcd for C₂₅H₃₀N₂O₇: C 63.82, H 6.43, N 5.95; found: C 63.75, H 6.49, N 6.07.

5-((2-(*tert*-Butylamino)-1-(4-(methoxycarbonyl)phenyl)-2-oxoethyl)(4-

chlorophenyl)amino)-4,5-dioxopentanoic acid (5g). Yield 57% (195 mg), white solid, m.p. = 156-158 °C, R_f = 0.50.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.15 (s, 1H, COOH), 8.02 (s, 1H, NH), 7.04-8.15 (m, 8H, ArH), 6.12 (s, 1H, CH), 3.79 (s, 3H, COOCH₃), 2.89 (t, *J* = 6.6 Hz, 2H, CH₂), 2.26 (t, *J* = 6.3 Hz, 2H, CH₂), 1.25 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 198.8, 172.9, 167.3, 166.3, 165.8, 139.7, 136.3, 132.1, 130.4, 129.0, 128.8, 128.3, 63.1, 52.2, 50.7, 35.0, 28.3, 26.6.

Mass spectrum (ESI), *m/z*: 501 (100) [M-H]⁻.

Elemental analysis calcd for C₂₅H₂₇ClN₂O₇: C 59.70, H 5.41, N 5.57; found: C 59.61, H 5.48, N 5.67.

5-((2-(*tert*-Butylamino)-1-(4-(methoxycarbonyl)phenyl)-2-oxoethyl)(*p*-tolyl)amino)-4,5-dioxopentanoic acid (5h). Yield 72% (235 mg), white solid, m.p. = 168-170 °C, R_f = 0.52.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.15 (s, 1H, COOH), 7.95 (s, 1H, NH), 6.81-7.80 (m, 8H, ArH), 6.09 (s, 1H, CH), 3.78 (s, 3H, COOCH₃), 2.79 (t, *J* = 7.0 Hz, 2H, CH₂), 2.20 (t, *J* = 6.8 Hz, 2H, CH₂), 2.13 (s, 3H, CH₃), 1.24 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 199.0, 172.8, 167.4, 166.9, 165.8, 140.0, 137.5, 134.4, 130.4, 130.2, 128.8, 128.7, 63.1, 52.1, 50.6, 35.1, 28.3, 26.7, 20.5.

Mass spectrum (ESI), *m/z*: 481 (100) [M-H]⁻.

Elemental analysis calcd for C₂₆H₃₀N₂O₇: C 64.72, H 6.27, N 5.81; found: C 64.65, H 6.20, N 5.89.

5-((2-(*tert*-Butylamino)-1-(4-(methoxycarbonyl)phenyl)-2-oxoethyl)(4-methoxyphenyl)amino)-4,5-dioxopentanoic acid (5i). Yield 54% (185 mg), white solid, m.p. = 132-134 °C, R_f = 0.54.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.17 (s, 1H, COOH), 7.94 (s, 1H, NH), 6.52-7.82 (m, 8H, ArH), 6.06 (s, 1H, CH), 3.78 (s, 3H, COOCH₃), 3.61 (s, 3H, OCH₃), 2.76 (t, *J* = 6.8 Hz, 2H, CH₂), 2.20 (t, *J* = 6.5 Hz, 2H, CH₂), 1.24 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 199.2, 172.8, 167.5, 167.1, 165.9, 158.6, 140.0, 131.9, 130.4, 129.4, 128.9, 128.8, 113.4, 63.1, 55.1, 52.1, 50.6, 35.1, 28.3, 26.7.

Mass spectrum (ESI), *m/z*: 497 (100) [M-H]⁻.

Elemental analysis calcd for C₂₆H₃₀N₂O₈: C 62.64, H 6.07, N 5.62; found: C 62.49, H 5.99, N 5.78.

5-((1-(4-Bromophenyl)-2-(*tert*-butylamino)-2-oxoethyl)(4-chlorophenyl)amino)-4,5-dioxopentanoic acid (5j). Yield 77% (275 mg), white solid, m.p. = 157-159 °C, R_f = 0.40.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.16 (s, 1H, COOH), 7.97 (s, 1H, NH), 6.93-7.45 (m, 8H, ArH), 6.01 (s, 1H, CH), 2.88 (t, *J* = 6.5 Hz, 2H, CH₂), 2.25 (t, *J* = 6.4 Hz, 2H, CH₂), 1.24 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 198.8, 172.8, 167.5, 166.3, 136.3, 133.7, 132.5, 132.1, 131.0, 128.3, 121.3, 62.8, 50.6, 35.0, 28.3, 26.6.

Mass spectrum (ESI), *m/z*: 521 (77) [M-H]⁻.

Elemental analysis calcd for C₂₃H₂₄BrClN₂O₅: C 52.74, H 4.62, N 5.35; found: C 52.62, H 4.71, N 5.43.

5-((1-(4-Bromophenyl)-2-(*tert*-butylamino)-2-oxoethyl)(*p*-tolyl)amino)-4,5-dioxopentanoic acid (5k). Yield 73% (250 mg), white solid, m.p. = 133-135 °C, R_f = 0.63.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 7.90 (s, 1H, NH), 6.87-7.45 (m, 8H, ArH), 5.98 (s, 1H, CH), 2.76 (t, *J* = 6.8 Hz, 2H, CH₂), 2.10-2.24 (m, 2H, CH₂), 2.16 (s, 3H, CH₃), 1.23 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 199.1, 172.9, 167.6, 166.9, 137.5, 134.4, 134.0, 132.2, 130.9, 130.3, 128.9, 121.2, 62.8, 50.5, 35.2, 28.3, 26.9, 20.6.

Mass spectrum (ESI), *m/z*: 501 (99) [M-H]⁻.

Elemental analysis calcd for C₂₄H₂₇BrN₂O₅: C 57.26, H 5.41, N 5.57; found: C 57.18, H 5.52, N 5.66.

5-((1-(4-Bromophenyl)-2-(*tert*-butylamino)-2-oxoethyl)(4-methoxyphenyl)amino)-4,5-dioxopentanoic acid (5l**).** Yield 61% (215 mg), white solid, m.p. = 133-135 °C, R_f = 0.55.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.13 (s, 1H, COOH), 7.88 (s, 1H, NH), 6.61-7.44 (m, 8H, ArH), 5.96 (s, 1H, CH), 3.64 (s, 3H, OCH₃), 2.75 (t, *J* = 6.1 Hz, 2H, CH₂), 2.20 (t, *J* = 6.7 Hz, 2H, CH₂), 1.24 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 199.2, 172.8, 167.7, 167.0, 158.6, 134.0, 132.2, 132.0, 130.9, 129.3, 121.2, 113.4, 62.7, 55.1, 50.5, 35.1, 28.3, 26.7

Mass spectrum (ESI), *m/z*: 517 (98) [M-H]⁻.

Elemental analysis calcd for C₂₄H₂₇BrN₂O₆: C 55.50, H 5.24, N 5.39; found: C 55.41, H 5.29, N 5.48.

Synthesis of compounds **6**

General procedure for the synthesis of compounds **6a–d from acid **5a**.** Amines **3a–c** (0.2 mmol) and aldehydes **2a,c** (0.2 mmol) were dissolved in 2 mL of methanol in a round-bottomed flask and stirred at 25 °C for 30 minutes. Subsequently, 5-((2-(*tert*-butylamino)-1-(4-chlorophenyl)-2-oxoethyl)(4-chlorophenyl)amino)-4,5-dioxopentanoic acid (**5a**, 0.2 mmol, 100 mg) was added to the reaction mixture and stirred for 30 minutes. Then, *tert*-butyl isocyanide (**4**, 0.2 mmol, 24 μL) was added and the reaction mixture was stirred at 45 °C for 48 hours until a precipitate was formed. The resulting precipitate of compounds **6a–d** was filtered and dried in vacuo.

Synthesis of compound **6a from α-ketoglutaric acid.** 4-Chloroaniline (**3a**, 1.36 mmol, 175 mg) and 4-chlorobenzaldehyde (**2a**, 1.36 mmol, 190 mg) were dissolved in 4 mL of methanol and stirred at 25 °C for 30 min. Subsequently, α-ketoglutaric acid (**1**, 0.68 mmol, 100 g) was added to the reaction mixture and stirred for 30 minutes. Then, *tert*-butyl isocyanide (**4**, 1.36 mmol, 154 μL) was added and the

reaction mixture was stirred at 45 °C for 24 hours until a precipitate was formed. The resulting precipitate of compound **6a** was filtered and dried in vacuo.

***N*¹,*N*⁵-bis(2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2-oxoethyl)-*N*¹,*N*⁵-bis(4-chlorophenyl)-2-oxopentanediamide (**6a**).** Yield 45% (75 mg) from acid **5a**, 55% (305 mg) from α-ketoglutaric acid, white solid, m.p. = 199-201 °C.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 7.96 (s, 1H, NH), 7.76 (s, 1H, NH), 6.47-7.53 (m, 16H, ArH), 6.01 (s, 1H, CH), 5.99 (s, 1H, CH), 2.65-2.96 (m, 2H, CH₂), 1.80-2.06 (m, 2H, CH₂), 1.24 (s, 9H, *t*-Bu), 1.22 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 199.1, 199.0, 169.9, 168.6, 168.5, 167.5, 166.1, 138.2, 136.2, 134.5, 133.2, 132.7, 132.6, 132.5, 132.3, 132.2, 132.1, 131.8, 131.7, 128.5, 128.2, 128.1, 127.9, 62.7, 50.6, 50.4, 35.3, 28.4, 28.3, 27.8.

Mass spectrum (ESI), *m/z*: 813 (30) [M+H]⁺, 811 (74) [M-H]⁻.

Elemental analysis calcd for C₄₁H₄₂Cl₄N₄O₅: C 60.60, H 5.21, N 6.89; found: C 60.52, H 5.28, N 6.95.

***N*¹,*N*⁵-bis(2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2-oxoethyl)-*N*¹-(4-chlorophenyl)-*N*⁵-(4-methoxyphenyl)-2-oxopentanediamide (**6b**).** Yield 41% (65 mg), white solid, m.p. = 211-213 °C.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 7.91 (s, 1H, NH), 7.61 (s, 1H, NH), 6.40-7.30 (m, 16H, ArH), 6.01 (s, 1H, CH), 5.96 (s, 1H, CH), 3.66 (s, 3H, OCH₃), 2.69-2.92 (m, 2H, CH₂), 1.82-2.02 (m, 2H, CH₂), 1.24 (s, 9H, *t*-Bu), 1.22 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 199.0, 170.4, 168.6, 167.4, 166.2, 158.2, 136.2, 134.9, 133.2, 132.6, 132.5, 132.1, 132.0, 131.8, 131.7, 128.1, 128.0, 127.7, 113.5, 62.8, 62.6, 55.0, 50.5, 50.2, 35.3, 28.3, 28.2, 27.7.

Mass spectrum (ESI), *m/z*: 807 (38) [M+H]⁺, 843 (100) [M+K-2H]⁻.

Elemental analysis calcd for C₄₂H₄₅Cl₃N₄O₆: C 62.42, H 5.61, N 6.93; found: C 62.31, H 5.72, N 7.04.

***N*¹,*N*⁵-bis(2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2-oxoethyl)-*N*¹-(4-chlorophenyl)-2-oxo-*N*⁵-(*p*-tolyl)pentanediamide (6c).** Yield 61% (95 mg), white solid, m.p. = 187-189 °C.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 7.95 (s, 1H, NH), 7.66 (s, 1H, NH), 6.28-7.34 (m, 16H, ArH), 6.01 (s, 1H, CH), 5.96 (s, 1H, CH), 2.64-2.96 (m, 2H, CH₂), 2.18 (s, 3H, CH₃), 1.79-2.05 (m, 2H, CH₂), 1.24 (s, 9H, *t*-Bu), 1.22 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 199.0, 170.2, 168.5, 167.4, 166.2, 136.9, 136.7, 136.2, 134.8, 133.2, 132.6, 132.5, 132.1, 132.0, 131.7, 130.4, 128.9, 128.1, 128.0, 127.7, 62.9, 62.6, 50.5, 50.3, 35.3, 28.3, 28.2, 27.8, 20.5.

Mass spectrum (ESI), *m/z*: 791 (39) [M+H]⁺, 789 (39) [M-H]⁻.

Elemental analysis calcd for C₄₂H₄₅Cl₃N₄O₅: C 63.68, H 5.73, N 7.07; found: C 63.76, H 5.78, N 7.18.

Methyl 4-(12,13-bis(4-chlorophenyl)-2,2,16,16-tetramethyl-4,7,10,11,14-pentaoxo-6-(*p*-tolyl)-3,6,12,15-tetraazaheptadecan-5-yl)benzoate (6d). Yield 42% (70 mg), white solid, m.p. = 214-216 °C.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 7.95 (s, 1H, NH), 7.72 (s, 1H, NH), 6.43-7.81 (m, 16H, ArH), 6.05 (s, 1H, CH), 6.01 (s, 1H, CH), 3.78 (s, 3H, COOCH₃), 2.67-2.96 (m, 2H, CH₂), 2.16 (s, 3H, CH₃), 1.78-2.03 (m, 2H, CH₂), 1.24 (s, 9H, *t*-Bu), 1.21 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 199.1, 170.3, 168.3, 167.5, 166.2, 165.9, 141.3, 137.0, 136.7, 136.2, 136.1, 133.3, 132.7, 132.5, 132.2, 131.8, 130.5, 130.3, 129.0, 128.6, 128.2, 128.1, 63.3, 62.7, 52.1, 50.6, 50.4, 35.3, 28.4, 28.3, 27.8, 20.5.

Mass spectrum (ESI), *m/z*: 815 (25) [M+H]⁺, 813 (23) [M-H]⁻.

Elemental analysis calcd for C₄₄H₄₈Cl₂N₄O₇: C 64.78, H 5.93, N 6.87; found: C 64.72, H 5.98, N 6.96.

Tandem Ugi/aza-Wittig reaction

General procedure for the synthesis of compounds 8a–h. Aldehydes **2a,b,e** (0.68 mmol) and *o*-azidoanilines **7a–c** (0.68 mmol) were dissolved in 2 mL of methanol in a round-bottomed flask and stirred at 25 °C for 30 minutes. Then, α -ketoglutaric acid (**1**, 0.68 mmol, 100 mg) was added to the reaction mixture and stirred for 30 minutes. Then, *tert*-butyl isocyanide (**4**, 0.68 mmol, 77 μ L) was added and the reaction mixture was stirred at 45 °C for 24 hours. The completeness of the reaction was determined by thin-layer chromatography (hexane/ethyl acetate 1:2). The reaction mixture was cooled and poured onto ice, the precipitate of compounds **8a–h** was filtered and dried in vacuo. If necessary, the crude product was purified by column chromatography, eluting with gradient hexane/ethyl acetate 3:1 to hexane/ethyl acetate 1:2 + 0.1% formic acid.

5-((2-Azido-4-chlorophenyl)(2-(*tert*-butylamino)-1-(4-chlorophenyl)-2-

oxoethyl)amino)-4,5-dioxopentanoic acid (8a). Yield 57% (200 mg), white solid, m.p. = 137-139 °C, R_f = 0.62.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ , ppm: 12.15 (s, 1H, COOH), 7.95 (s, 1H, NH), 7.02–7.82 (m, 7H, ArH), 5.95 (s, 1H, CH), 2.95 (t, *J* = 6.2 Hz, 2H, CH₂), 2.32 (t, *J* = 6.0 Hz, 2H, CH₂), 1.25 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ , ppm: 197.8, 172.9, 167.7, 165.6, 139.3, 133.9, 133.7, 133.0, 132.0, 131.9, 127.8, 127.5, 124.7, 118.9, 63.2, 50.6, 33.9, 28.3, 26.5.

Mass spectrum (ESI), *m/z*: 518 (92) [M-H][–].

Elemental analysis calcd for C₂₃H₂₃Cl₂N₅O₅: C 53.09, H 4.46, N 13.46; found: C 52.97, H 4.59, N 13.57.

5-((2-Azidophenyl)(2-(*tert*-butylamino)-1-(4-chlorophenyl)-2-oxoethyl)amino)-4,5-dioxopentanoic acid (8b). Yield 54% (180 mg), white solid, m.p. = 127-129 °C, R_f = 0.56.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 7.92 (s, 1H, NH), 6.89–7.82 (m, 8H, ArH), 5.91 (s, 1H, CH), 2.91 (t, *J* = 6.5 Hz, 2H, CH₂), 2.26 (t, *J* = 6.4 Hz, 2H, CH₂), 1.24 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 198.0, 172.9, 167.8, 166.0, 137.8, 132.9, 132.8, 132.2, 132.0, 130.5, 130.2, 128.4, 128.2, 127.6, 124.8, 119.0, 63.4, 50.5, 34.2, 28.3, 26.5.

Mass spectrum (ESI), *m/z*: 484 (69) [M-H][−].

Elemental analysis calcd for C₂₃H₂₄ClN₅O₅: C 56.85, H 4.98, N 14.41; found: C 56.78, H 5.12, N 14.52.

5-((2-Azidophenyl)(2-(*tert*-butylamino)-1-(4-methoxyphenyl)-2-oxoethyl)amino)-4,5-dioxopentanoic acid (8d). Yield 35% (115 mg), white solid, m.p. = 63-65 °C (with decomposition), R_f = 0.69.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.12 (s, 1H, COOH), 7.79 (s, 1H, NH), 6.54-7.33 (m, 8H, ArH), 5.85 (s, 1H, CH), 3.61 (s, 3H, OCH₃), 2.90 (t, *J* = 6.0 Hz, 2H, CH₂), 2.25 (t, *J* = 6.1 Hz, 2H, CH₂), 1.24 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 198.2, 172.9, 168.4, 166.1, 158.8, 137.8, 132.9, 131.4, 130.0, 128.7, 124.9, 124.6, 119.0, 112.9, 63.7, 55.0, 50.4, 34.1, 28.4, 26.5.

Mass spectrum (ESI), *m/z*: 480 (100) [M-H][−].

Elemental analysis calcd for C₂₄H₂₇N₅O₆: C 59.87, H 5.65, N 14.54; found: C 59.67, H 5.73, N 14.68

5-((2-Azido-4-chlorophenyl)(2-(*tert*-butylamino)-2-oxo-1-phenylethyl)amino)-4,5-dioxopentanoic acid (8f). Yield 78% (255 mg), white solid, m.p. = 129-131 °C, R_f = 0.67.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.15 (s, 1H, COOH), 7.93 (s, 1H, NH), 6.94-7.85 (m, 8H, ArH), 5.96 (s, 1H, CH), 2.87-3.04 (m, 2H, CH₂), 2.31 (t, *J* = 6.2 Hz, 2H, CH₂), 1.25 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 197.9, 172.9, 168.0, 165.6, 139.2, 134.0, 133.5, 133.0, 130.1, 128.3, 127.8, 127.7, 124.5, 118.7, 64.1, 50.5, 33.9, 28.3, 26.5.

Mass spectrum (ESI), *m/z*: 484 (100) [M-H]⁻.

Elemental analysis calcd for C₂₃H₂₄ClN₅O₅: C 56.85, H 4.98, N 14.41; found: C 56.72, H 5.08, N 14.52

5-((2-Azidophenyl)(2-(*tert*-butylamino)-2-oxo-1-phenylethyl)amino)-4,5-dioxopentanoic acid (8g). Yield 71% (220 mg), white solid, m.p. = 121-123 °C (with decomposition), R_f = 0.55.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.15 (s, 1H, COOH), 7.87 (s, 1H, NH), 6.76-7.84 (m, 9H, ArH), 5.93 (s, 1H, CH), 2.92 (t, *J* = 6.4 Hz, 2H, CH₂), 2.26 (t, *J* = 6.4 Hz, 2H, CH₂), 1.25 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 198.0, 172.8, 168.0, 166.0, 137.7, 133.0, 132.8, 130.1, 129.9, 128.6, 128.0, 127.4, 124.6, 118.8, 64.2, 50.4, 34.1, 28.3, 26.5.

Mass spectrum (ESI), *m/z*: 450 (100) [M-H]⁻.

Elemental analysis calcd for C₂₃H₂₅N₅O₅: C 61.19, H 5.58, N 15.51; found: C 61.07, H 5.64, N 15.62

5-((2-Azido-4,6-dimethylphenyl)(2-(*tert*-butylamino)-2-oxo-1-phenylethyl)amino)-4,5-dioxopentanoic acid (8h). Mixture of rotamers. Yield 64% (210 mg), white solid, m.p. = 83-85 °C, R_f = 0.66.

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.11 (s, 1H, COOH), 7.94 (s, 1H, NH), 7.72 (s, 1H, NH), 6.50-7.54 (m, 7H, ArH), 5.43-5.75 (m, 1H, CH), 2.60-3.06 (m, 2H, CH₂), 2.42 (s, 3H, CH₃), 2.14-2.35 (m, 2H, CH₂), 2.18 (s, 3H, CH₃), 2.09 (s, 3H, CH₃), 2.00 (s, 3H, CH₃) 1.20 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 198.0, 172.8, 167.9, 167.5, 167.1, 166.5, 140.6, 139.9, 139.3, 138.3, 138.2, 134.5, 133.3, 129.4, 128.9, 128.2, 128.0, 127.8, 127.7, 127.5, 127.4, 125.1, 116.8, 116.2, 66.5, 65.8, 50.1, 50.0, 33.7, 28.3, 28.1, 26.5, 20.5, 20.4, 18.4, 17.9.

Mass spectrum (ESI), m/z: 478 (100) [M-H]⁻.

Elemental analysis calcd for C₂₅H₂₉N₅O₅: C 62.62, H 6.10, N 14.60; found: C 62.51, H 6.17, N 14.71

General procedure for the synthesis of compounds 9a–h.

The azidated derivatives **8a–h** (0.2 mmol) were dissolved in 3 mL of dichloromethane in a round-bottomed flask. Triphenylphosphine (0.2 mmol, 52 mg) was added to the solution and the reaction mixture was stirred at 20 °C for 12 hours. Then, the solvent was evaporated under vacuum and the crude product of compounds **9a–h** was purified by column chromatography, eluting with gradient hexane/ethyl acetate 3:1 to hexane/ethyl acetate 1:2 + 0.1% formic acid.

General procedure for the one-pot synthesis of compounds **9c–e**

The corresponding benzaldehyde **2a** or **2b** (0.68 mmol) and *o*-azidoaniline **7b,c** (0.68 mmol) were dissolved in 2 mL of methanol in a round-bottomed flask and stirred at 25 °C for 30 minutes. Then, α -ketoglutaric acid (**1**, 0.68 mmol, 100 mg) was added to the reaction mixture and stirred for 30 minutes. Then, *tert*-butyl isocyanide (**4**, 0.68 mmol, 77 μ L) was added and the reaction mixture was stirred at 45 °C for 24 hours. Then, the solvent was evaporated, and the dry residue was dissolved in 4 mL of dichloromethane. Triphenylphosphine (0.68 mmol, 180 mg) was added to the solution and the reaction mixture was stirred at 20 °C for 12 hours. Then, the solvent was evaporated under vacuum and the crude product of compounds **9c–e** was purified by column chromatography, elution gradient hexane/ethyl acetate 3:1 to hexane/ethyl acetate 1:2 + 0.1% formic acid.

3-(4-(2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2-oxoethyl)-7-chloro-3-oxo-3,4-dihydroquinoxalin-2-yl)propanoic acid (9a**)**. Yield 82% (80 mg), white solid, m.p. = 78-80 °C, R_f = 0.67 (hexane/ethyl acetate 1:2 + 0.1% formic acid).

^1H NMR spectrum (400 MHz, DMSO- d_6), δ , ppm: 7.99 (s, 1H, NH), 7.18-7.76 (m, 7H, ArH), 6.86 (s, 1H, CH), 3.12 (t, J = 7.0 Hz, 2H, CH₂), 2.75 (t, J = 7.0 Hz, 2H, CH₂), 1.26 (s, 9H, *t*-Bu).

^{13}C NMR spectrum (100 MHz, DMSO- d_6), δ , ppm: 173.9, 165.2, 160.5, 154.4, 134.2, 133.2, 132.3, 130.9, 129.8, 128.4, 128.1, 127.7, 127.2, 119.0, 59.2, 51.1, 29.5, 28.4.

Mass spectrum (ESI), m/z : 474 (40) $[\text{M-H}]^-$.

Elemental analysis calcd for C₂₃H₂₃Cl₂N₃O₄: C 57.99, H 4.87, N 8.82; found: C 57.89; H 4.96; N 8.89.

3-(4-(2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2-oxoethyl)-3-oxo-3,4-

dihydroquinoxalin-2-yl)propanoic acid (9b). Yield 93% (80 mg), white solid, m.p. = 62-64 °C, R_f = 0.46 (hexane/ethyl acetate 1:2 + 0.1% formic acid).

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 7.86 (s, 1H, NH), 7.21-7.75 (m, 8H, ArH), 6.84 (s, 1H, CH), 3.12 (t, *J* = 6.5 Hz, 2H, CH₂), 2.76 (t, *J* = 7.0 Hz, 2H, CH₂), 1.25 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 174.0, 165.3, 158.8, 154.6, 134.5, 132.5, 132.2, 131.9, 130.0, 129.0, 128.5, 128.3, 123.3, 117.0, 59.2, 51.1, 29.6, 28.4.

Mass spectrum (ESI), *m/z*: 440 (39) [M-H]⁻.

Elemental analysis calcd for C₂₃H₂₄ClN₃O₄: C 62.51, H 5.47, N 9.51; found: C 62.42; H 5.57; N 9.62

3-(4-(2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2-oxoethyl)-5,7-dimethyl-3-oxo-3,4-

dihydroquinoxalin-2-yl)propanoic acid (9c). Yield 46% (45 mg) in terms of KGA using the one-pot method, white solid, m.p. = 184-186 °C (decomposition), R_f = 0.62 (hexane/ethyl acetate 1:2 + 0.1% formic acid).

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.11 (s, 1H, COOH), 7.42 (s, 1H, NH), 6.74-7.41 (m, 6H, ArH), 6.10 (s, 1H, CH), 2.90 (t, *J* = 7.3 Hz, 2H, CH₂), 2.63 (t, *J* = 6.6 Hz, 2H, CH₂), 2.41 (s, 3H, CH₃), 2.34 (s, 3H, CH₃), 1.25 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 173.8, 165.9, 159.0, 156.1, 135.4, 135.0, 134.1, 132.9, 132.4, 131.9, 130.7, 127.8, 127.4, 124.5, 66.7, 51.0, 29.4, 28.3, 27.8, 21.8, 19.7.

Mass spectrum (ESI), *m/z*: 468 (100) [M-H]⁻.

Elemental analysis calcd for C₂₅H₂₈ClN₃O₄: C 63.89, H 6.01, N 8.94; found: C 63.76, H 6.05, N 8.98

3-(4-(2-(*tert*-Butylamino)-1-(4-methoxyphenyl)-2-oxoethyl)-3-oxo-3,4-dihydroquinoxalin-2-yl)propanoic acid (9d). Yield 75% (65 mg), 51% (150 mg) in terms of KGA using the one-pot method, white solid, m.p. = 77-79 °C, R_f = 0.48 (hexane/ethyl acetate 1:2 + 0.1% formic acid).

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.15 (s, 1H, COOH), 7.78 (s, 1H, NH), 6.67-7.74 (m, 9H, ArH+CH), 3.71 (s, 3H, OCH₃), 3.12 (t, *J* = 6.1 Hz, 2H, CH₂), 2.76 (t, *J* = 7.1 Hz, 2H, CH₂), 1.28 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 173.8, 165.9, 158.6, 158.5, 154.6, 132.4, 131.9, 129.2, 128.7, 128.2, 127.4, 123.0, 117.5, 113.8, 59.4, 55.0, 50.9, 29.6, 28.4.

Mass spectrum (ESI), *m/z*: 436 (100) [M-H]⁻.

Elemental analysis calcd for C₂₄H₂₇N₃O₅: C 65.89, H 6.22, N 9.60; found: C 65.77, H 6.28, N 9.71

3-(4-(2-(*tert*-Butylamino)-1-(4-methoxyphenyl)-2-oxoethyl)-5,7-dimethyl-3-oxo-3,4-dihydroquinoxalin-2-yl)propanoic acid (9e). Yield 35% (110 mg) in terms of KGA using the one-pot method, white solid, m.p. = 152-154 °C, R_f = 0.56 (hexane/ethyl acetate 1:2 + 0.1% formic acid).

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.10 (s, 1H, COOH), 7.41 (s, 1H, NH), 6.40-7.29 (m, 6H, ArH), 6.00 (s, 1H, CH), 3.74 (s, 3H, OCH₃), 2.91 (t, *J* = 7.2 Hz, 2H, CH₂), 2.63 (br t, 2H, CH₂), 2.41 (s, 3H, CH₃), 2.34 (s, 3H, CH₃), 1.24 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 173.7, 166.7, 159.0, 158.4, 156.2, 134.9, 134.0, 132.7, 132.6, 130.0, 127.9, 127.2, 124.6, 113.4, 67.5, 55.0, 50.8, 29.5, 28.2, 27.9, 21.8, 19.7.

Mass spectrum (ESI), *m/z*: 464 (100) [M-H]⁻.

Elemental analysis calcd for C₂₆H₃₁N₃O₅: C 67.08, H 6.71, N 9.03; found: C 67.01, H 6.74, N 9.11

3-(4-(2-(*tert*-Butylamino)-2-oxo-1-phenylethyl)-7-chloro-3-oxo-3,4-dihydroquinoxalin-2-yl)propanoic acid (9f). Yield 83% (75 mg), white solid, m.p. = 97-99 °C, R_f = 0.62 (hexane/ethyl acetate 1:2 + 0.1% formic acid).

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.17 (s, 1H, COOH), 8.07 (s, 1H, NH), 7.11-7.77 (m, 8H, ArH), 6.98 (s, 1H, CH), 3.14 (t, *J* = 7.1 Hz, 2H, CH₂), 2.76 (t, *J* = 7.1 Hz, 2H, CH₂), 1.29 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 173.8, 165.5, 160.3, 154.5, 135.4, 133.2, 130.9, 128.5, 127.8, 127.6, 127.0, 119.6, 59.7, 51.1, 29.5, 28.5, 28.4.

Mass spectrum (ESI), *m/z*: 440 (100) [M-H]⁻.

Elemental analysis calcd for C₂₃H₂₄ClN₃O₄: C 62.51, H 5.47, N 9.51; found: C 62.42, H 5.52, N 9.59

3-(4-(2-(*tert*-Butylamino)-2-oxo-1-phenylethyl)-3-oxo-3,4-dihydroquinoxalin-2-yl)propanoic acid (9g). Yield 59% (50 mg), white solid, m.p. = 78-80 °C, R_f = 0.69 (hexane/ethyl acetate 1:2 + 0.1% formic acid).

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.15 (s, 1H, COOH), 7.92 (s, 1H, NH), 7.12-7.76 (m, 9H, ArH), 6.95 (s, 1H, CH), 3.12 (t, *J* = 6.9 Hz, 2H, CH₂), 2.77 (t, *J* = 7.0 Hz, 2H, CH₂), 1.28 (s, 9H, *t*-Bu).

¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 173.8, 165.6, 158.6, 154.6, 135.6, 132.4, 131.9, 128.7, 128.4, 128.1, 127.7, 127.4, 123.1, 117.6, 59.7, 51.0, 29.6, 28.4.

Mass spectrum (ESI), *m/z*: 406 (100) [M-H]⁻.

Elemental analysis calcd for C₂₃H₂₅N₃O₄: C 67.80, H 6.18, N 10.31; found: C 67.73, H 6.37, N 10.36

3-(4-(2-(*tert*-Butylamino)-2-oxo-1-phenylethyl)-5,7-dimethyl-3-oxo-3,4-dihydroquinoxalin-2-yl)propanoic acid (9h). Yield 47% (40 mg), white solid, m.p. = 186-188°C, R_f = 0.68 (hexane/ethyl acetate 1:2 + 0.1% formic acid).

¹H NMR spectrum (400 MHz, DMSO-*d*₆), δ, ppm: 12.10 (s, 1H, COOH), 7.42 (s, 1H, NH), 6.56-7.39 (m, 7H, ArH), 6.09 (s, 1H, CH), 2.91 (t, *J* = 7.2 Hz, 2H, CH₂), 2.63 (br t, 2H, CH₂), 2.40 (s, 3H, CH₃), 2.34 (s, 3H, CH₃), 1.24 (s, 9H, *t*-Bu).

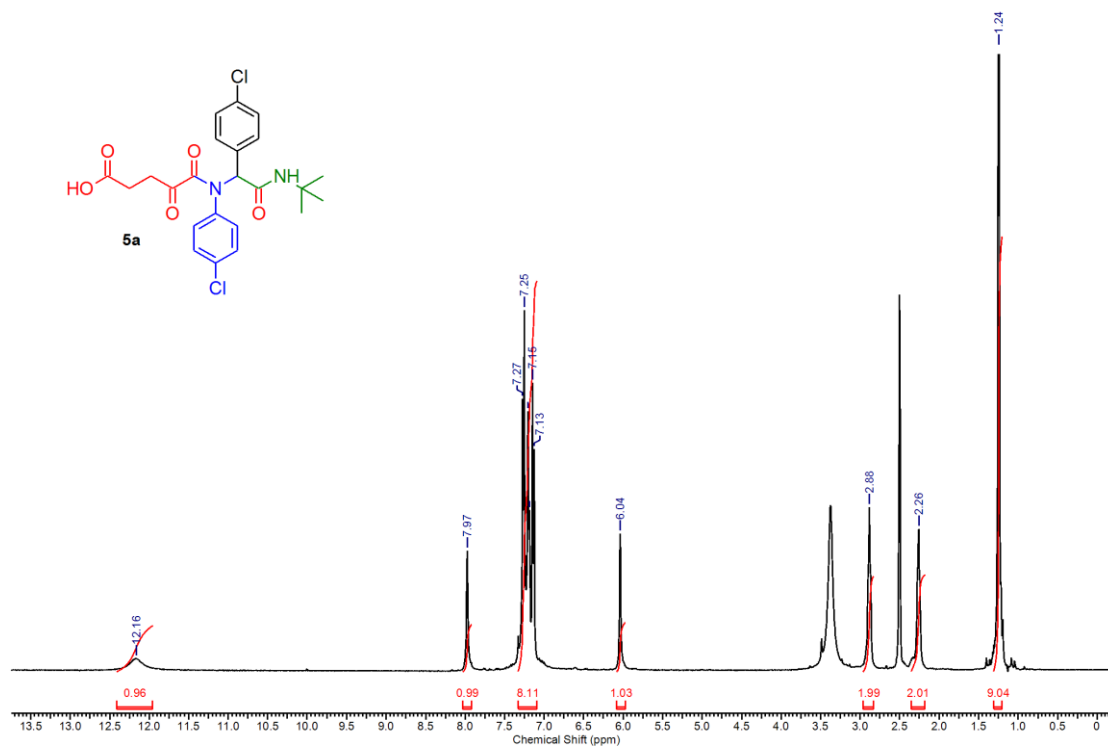
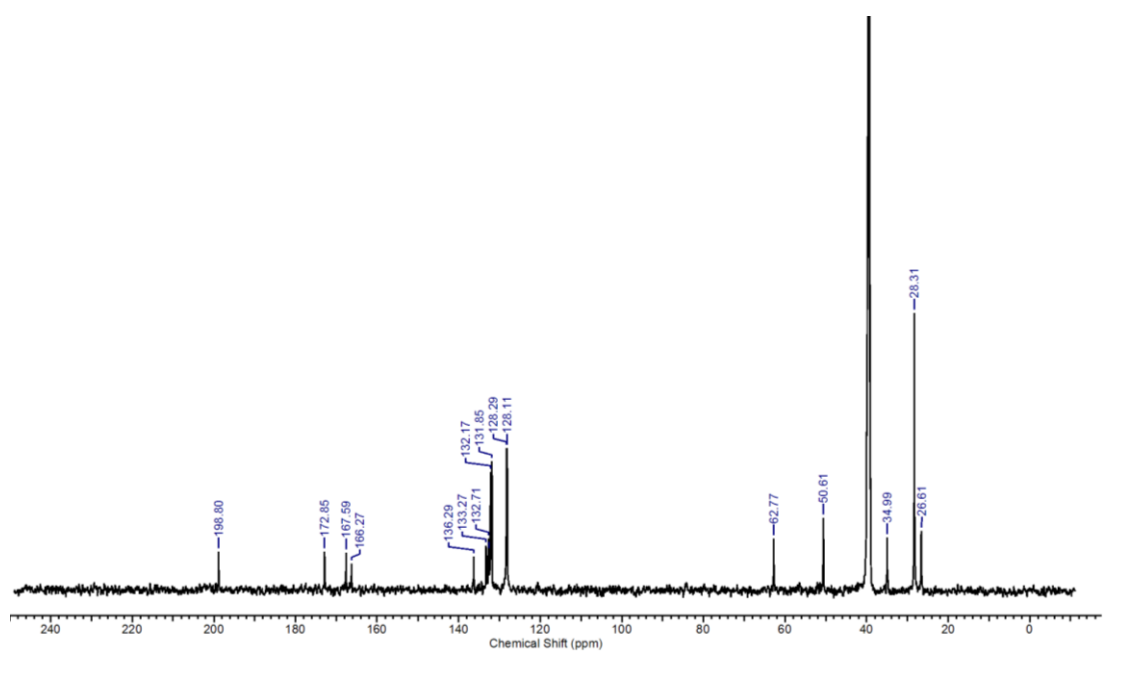
¹³C NMR spectrum (100 MHz, DMSO-*d*₆), δ, ppm: 173.8, 166.3, 159.1, 156.2, 136.3, 135.0, 134.0, 132.8, 132.6, 128.6, 128.0, 127.4, 127.3, 124.6, 67.7, 50.9, 29.5, 28.3, 27.9, 21.9, 19.7.

Mass spectrum (ESI), *m/z*: 434 (100) [M-H]⁻.

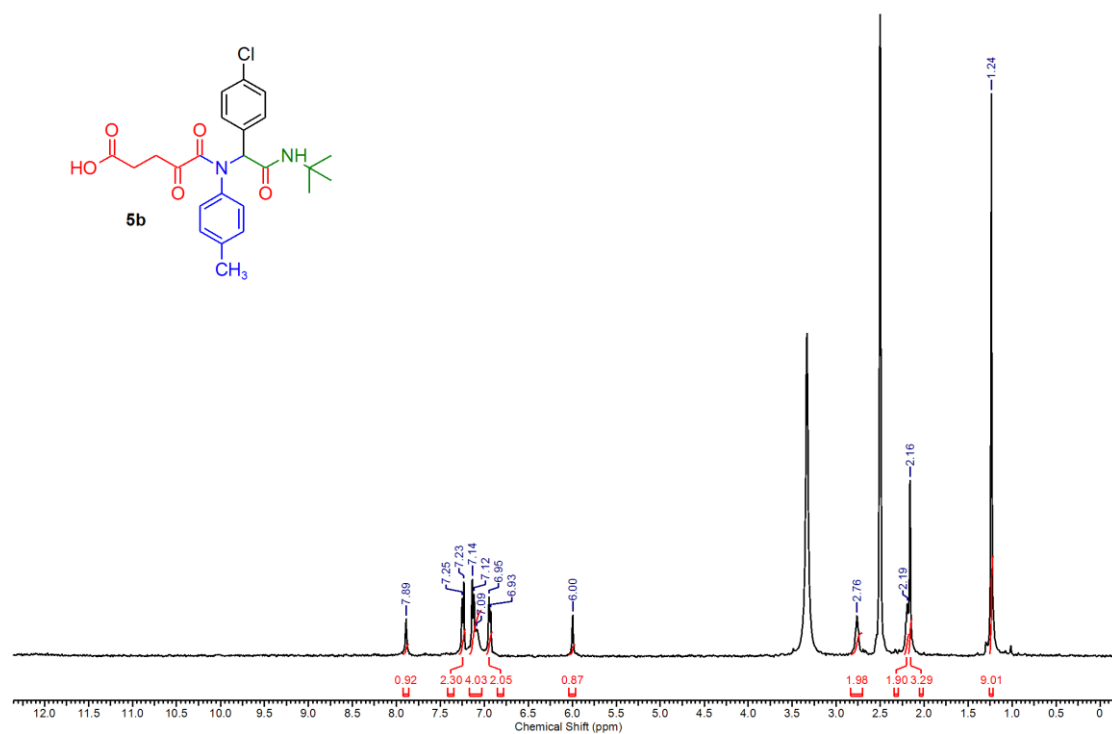
Elemental analysis calcd for C₂₅H₂₉N₃O₄: C 68.95, H 6.71, N 9.65; found: C 68.82, H 6.80, N 9.73

¹H NMR and ¹³C NMR spectra

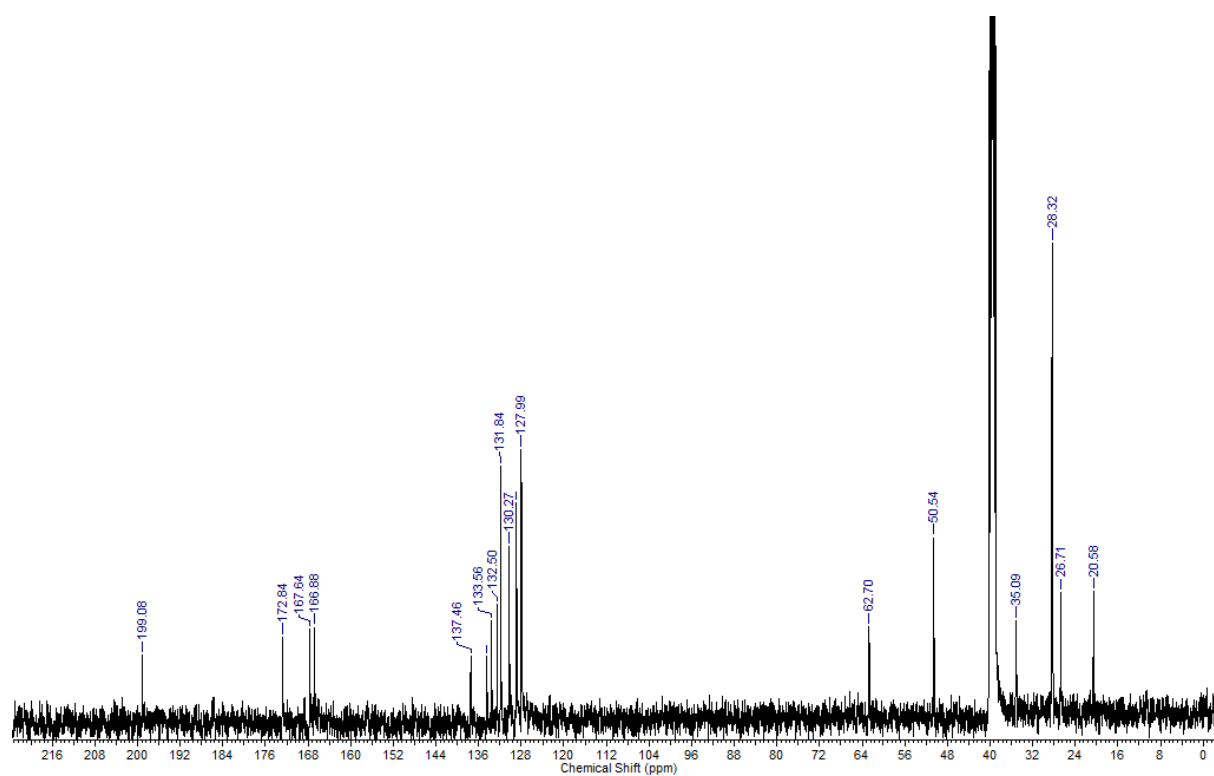
¹H NMR spectrum of compound **5a**

 ^{13}C NMR spectrum of compound **5a**

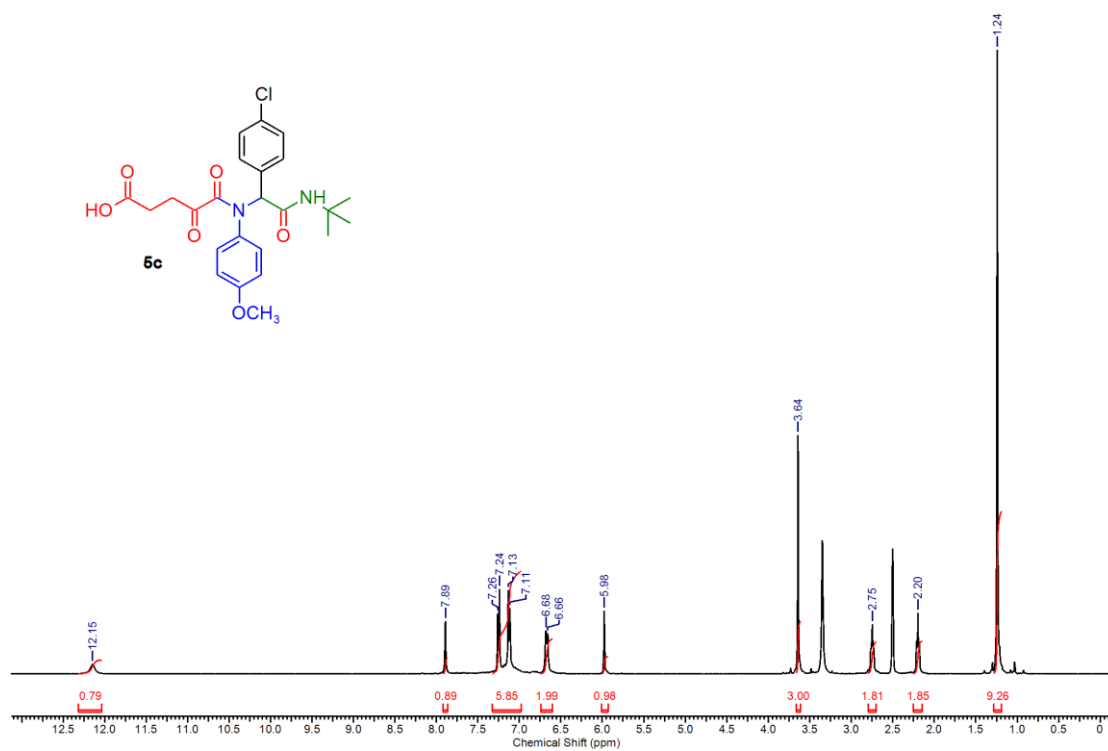
¹H NMR spectrum of compound **5b**



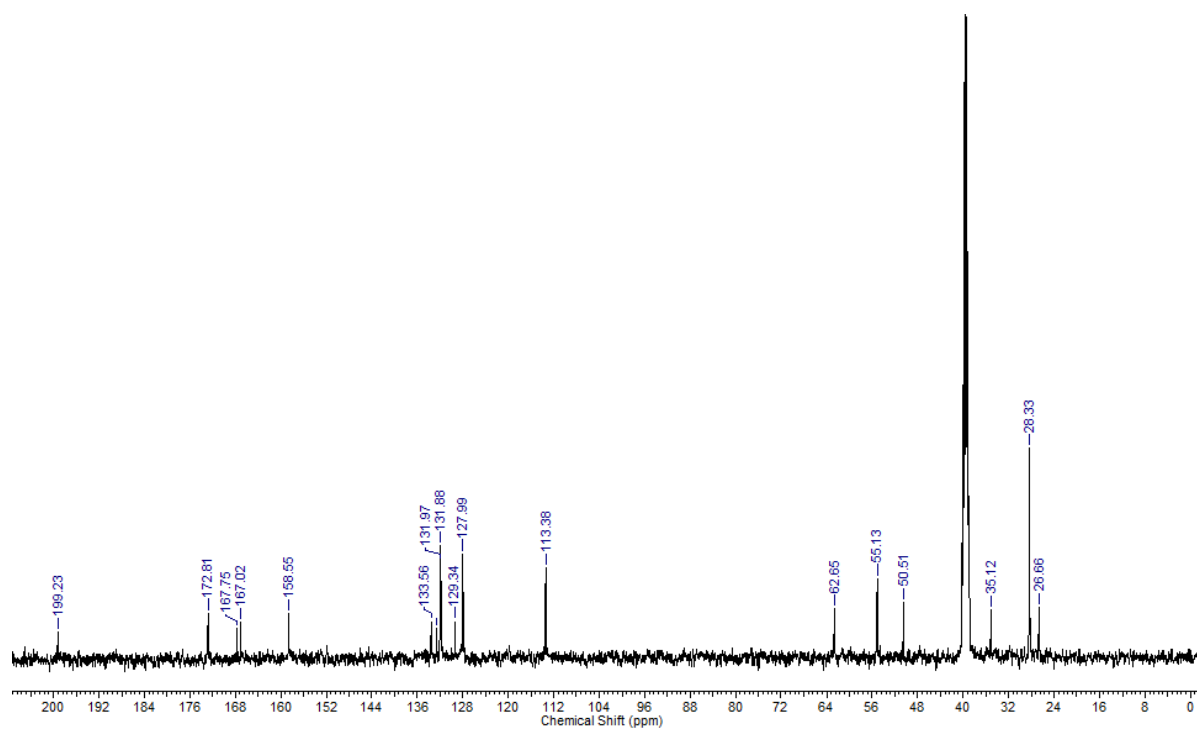
¹³C NMR spectrum of compound **5b**



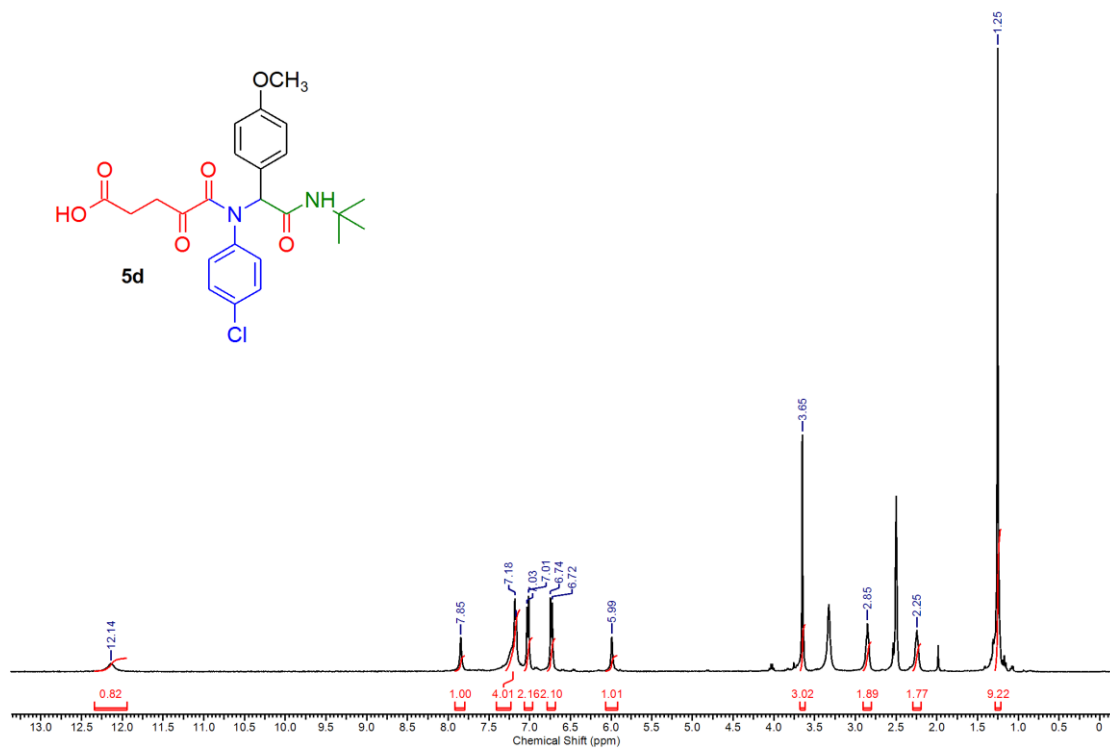
¹H NMR spectrum of compound **5c**



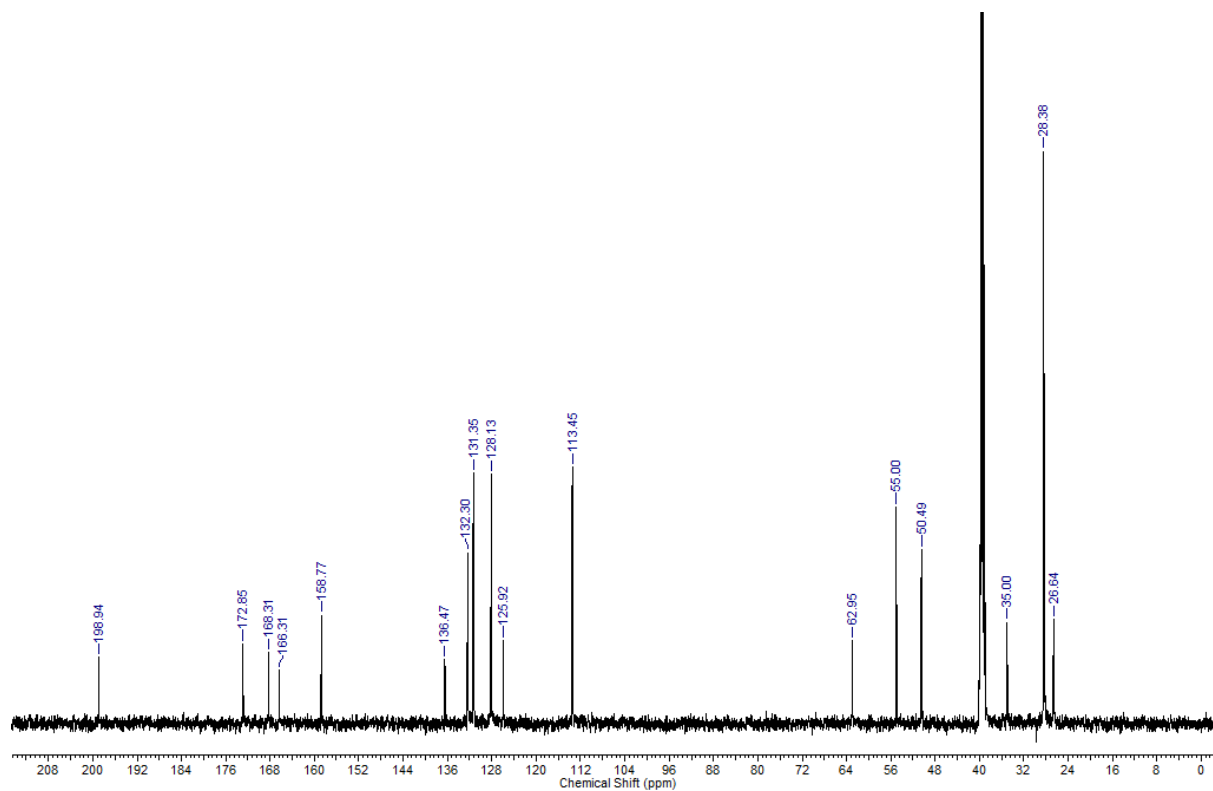
¹³C NMR spectrum of compound **5c**



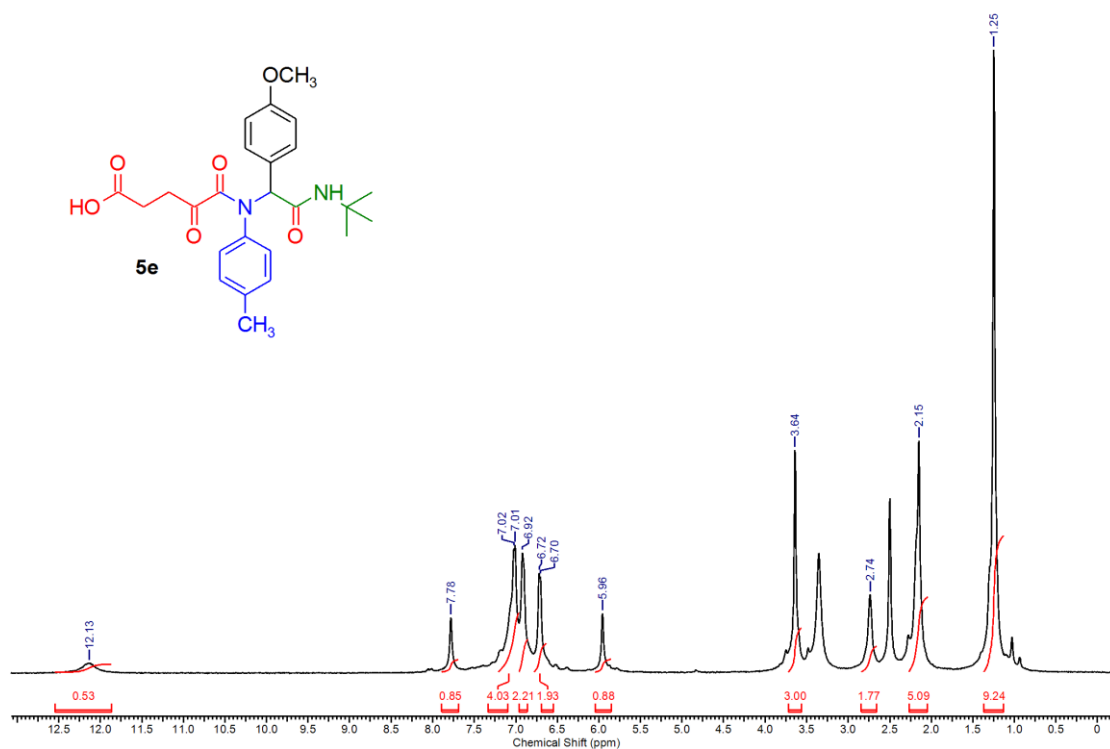
¹H NMR spectrum of compound **5d**



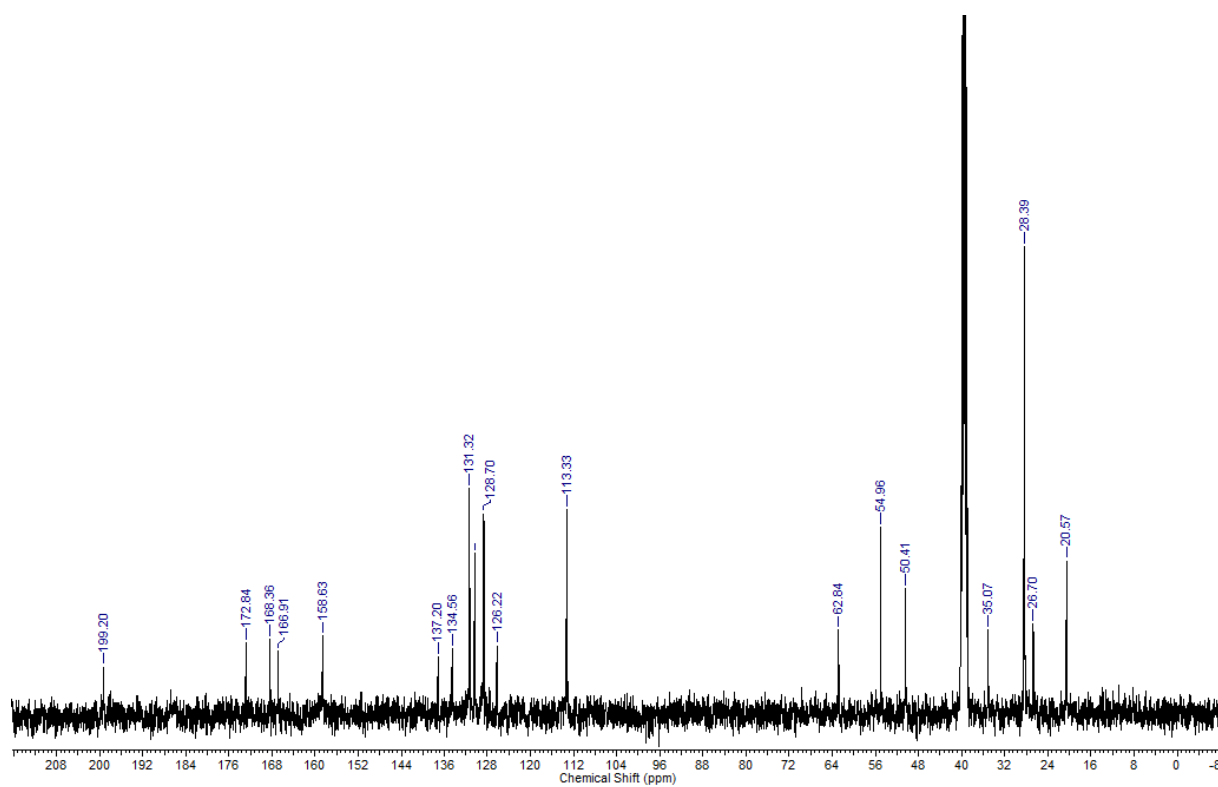
¹³C NMR spectrum of compound **5d**



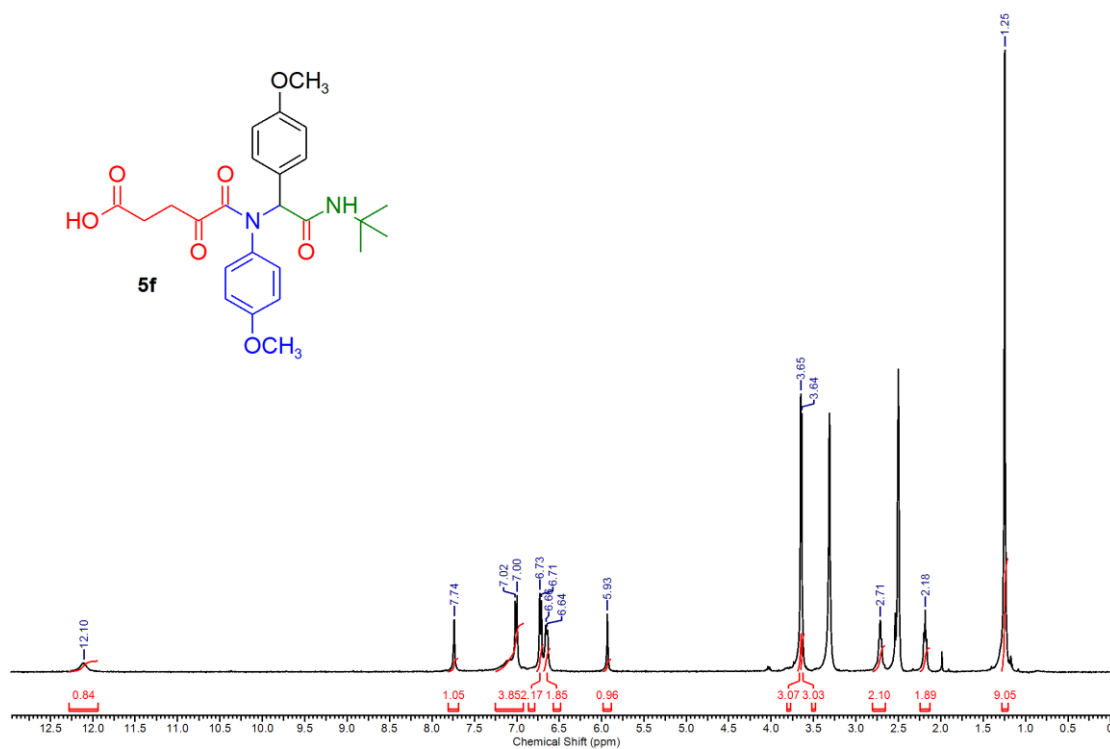
¹H NMR spectrum of compound **5e**



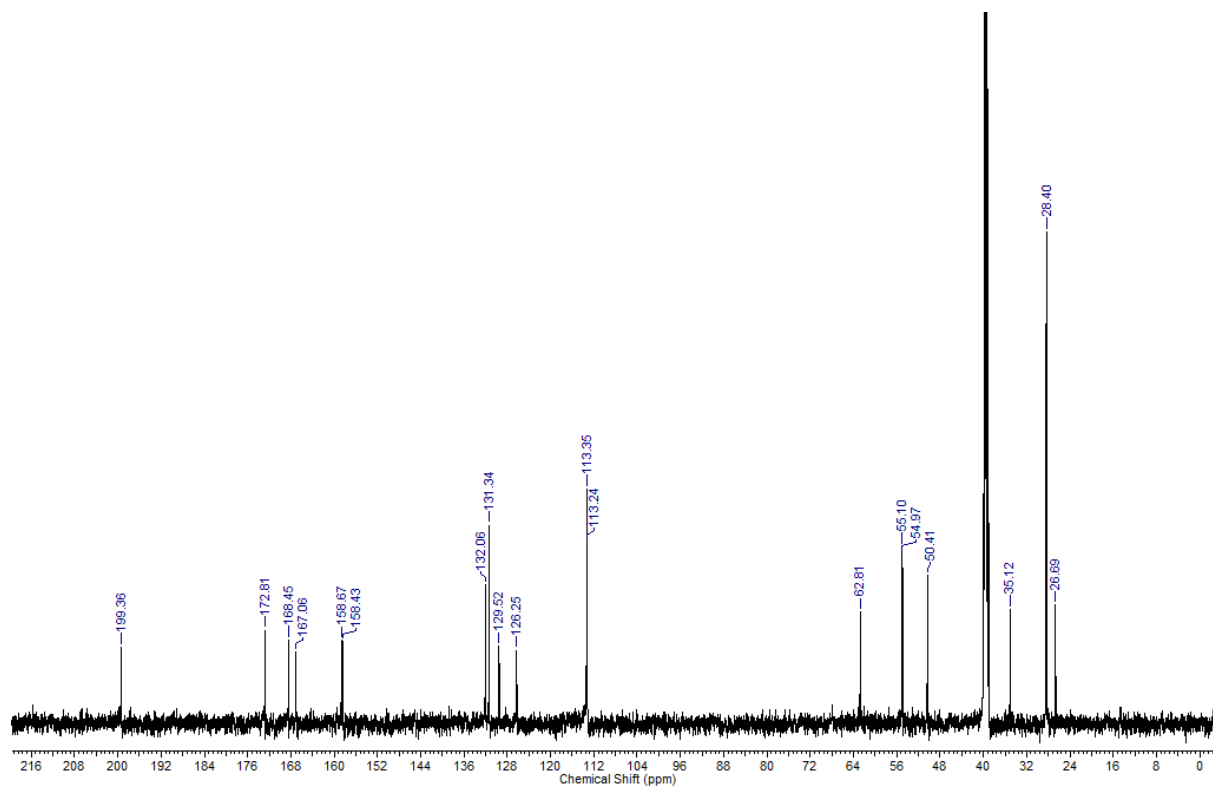
¹³C NMR spectrum of compound **5e**



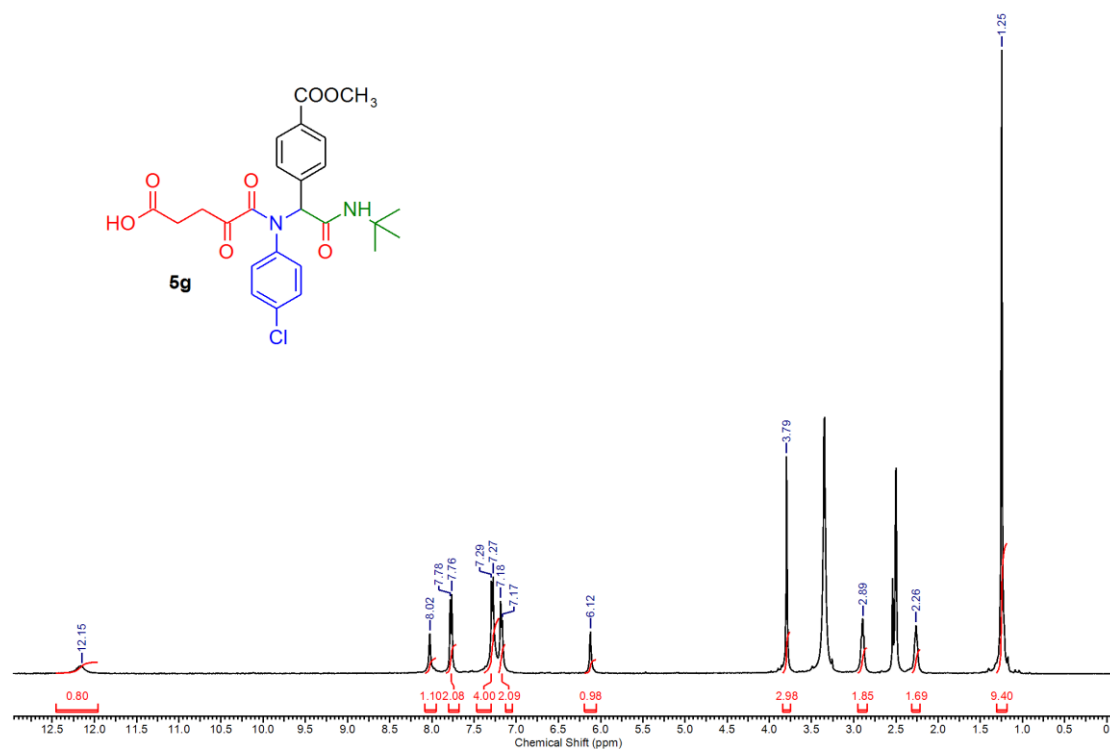
¹H NMR spectrum of compound **5f**



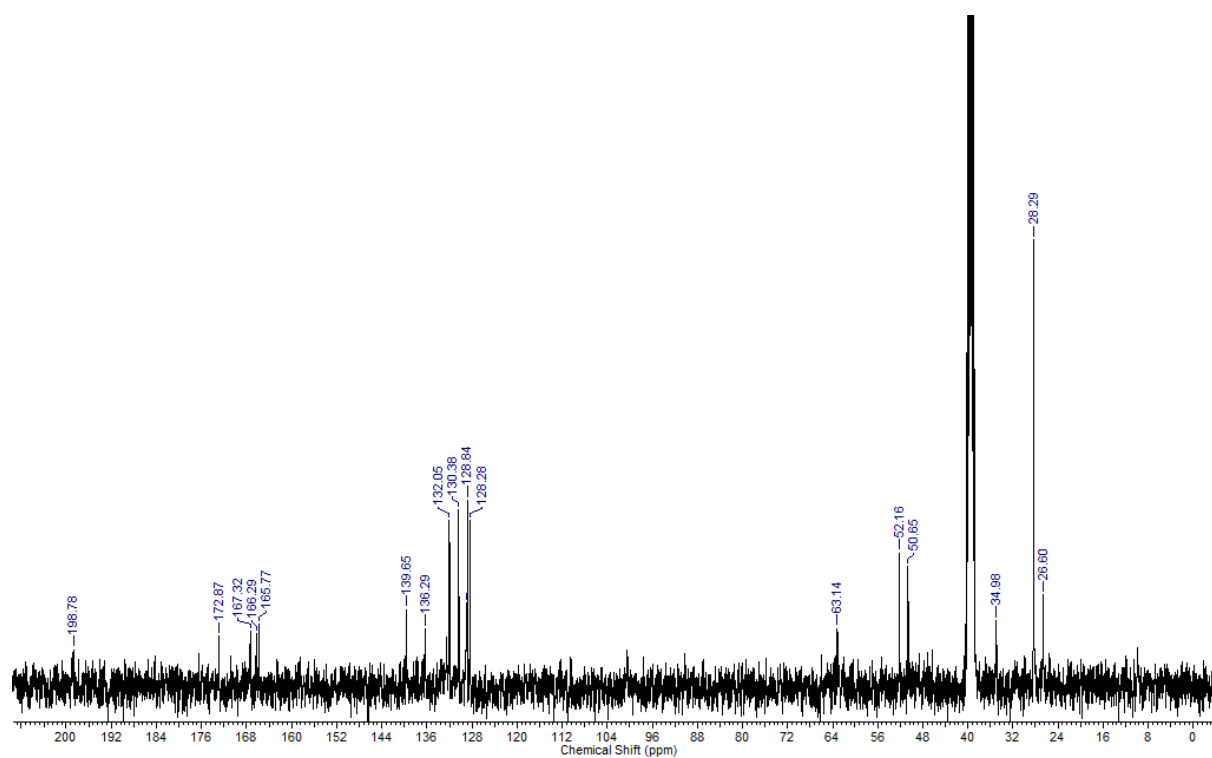
¹³C NMR spectrum of compound **5f**



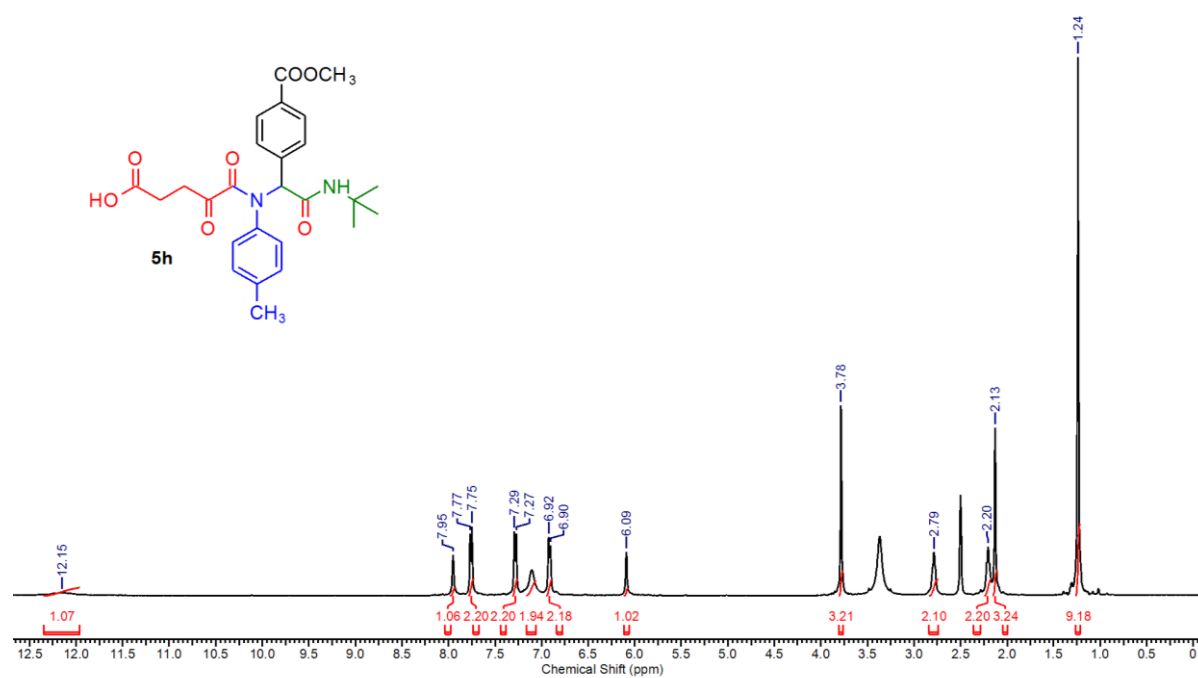
¹H NMR spectrum of compound **5g**



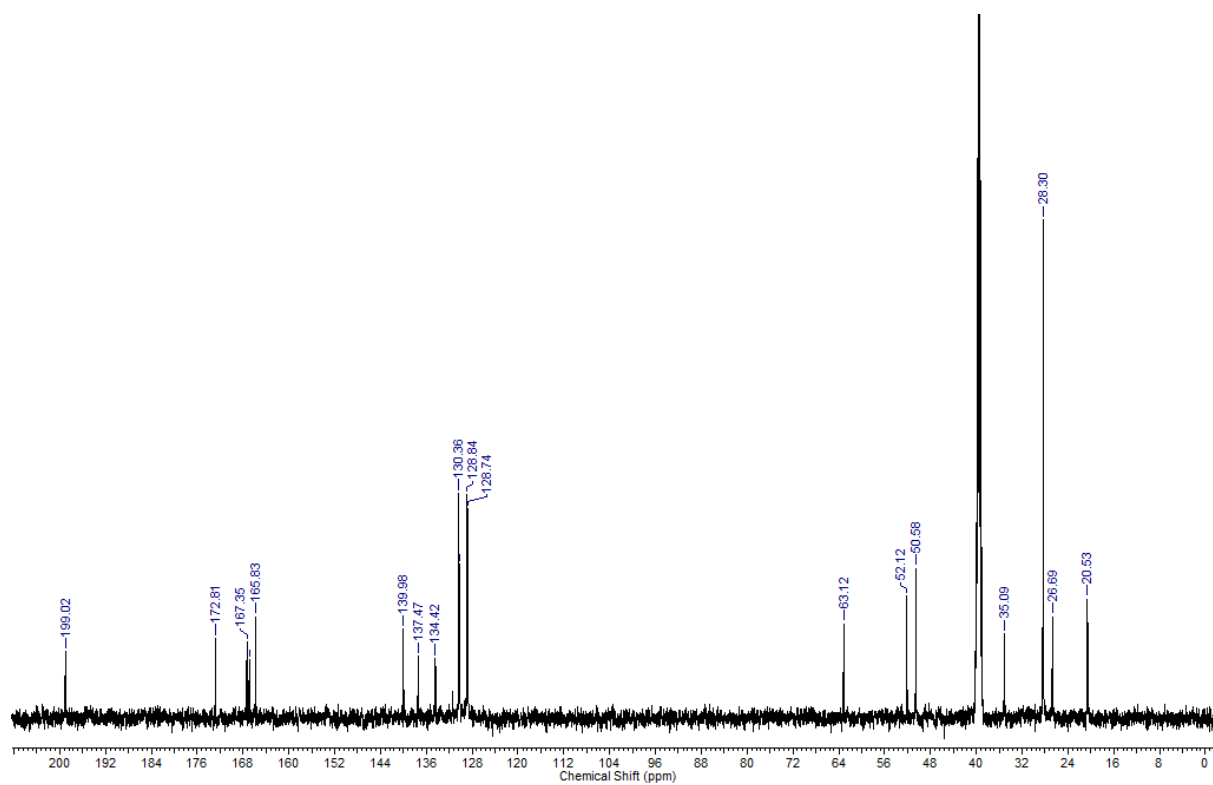
¹³C NMR spectrum of compound **5g**



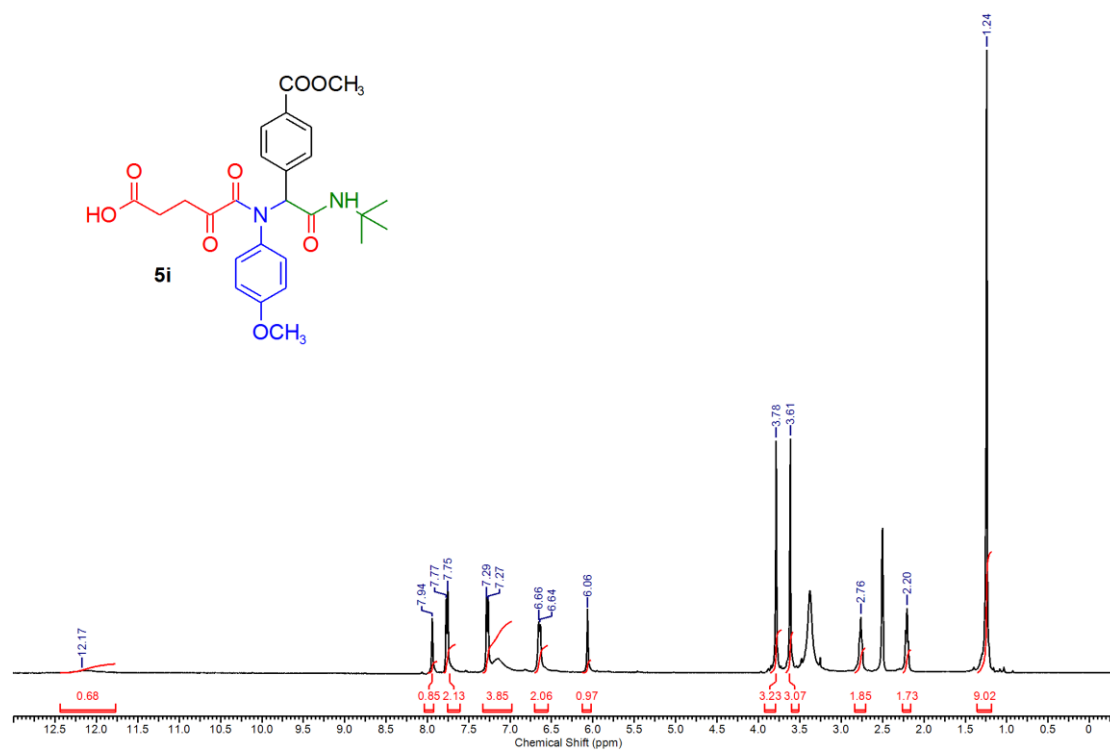
¹H NMR spectrum of compound **5h**



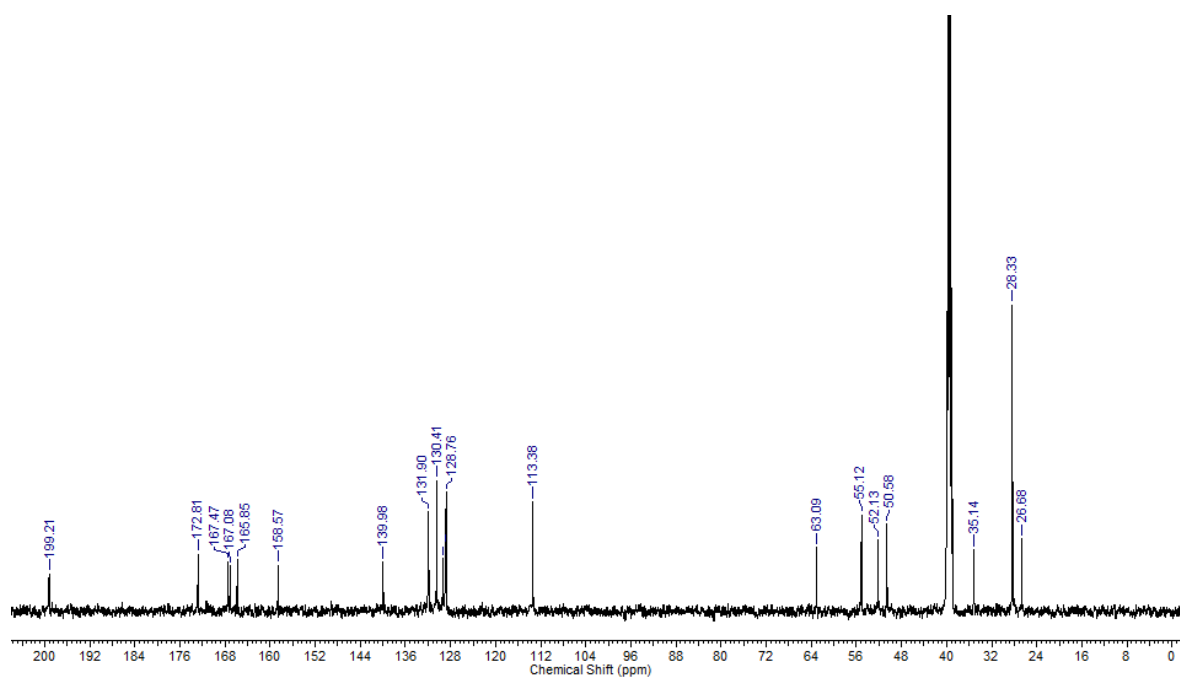
¹³C NMR spectrum of compound **5h**



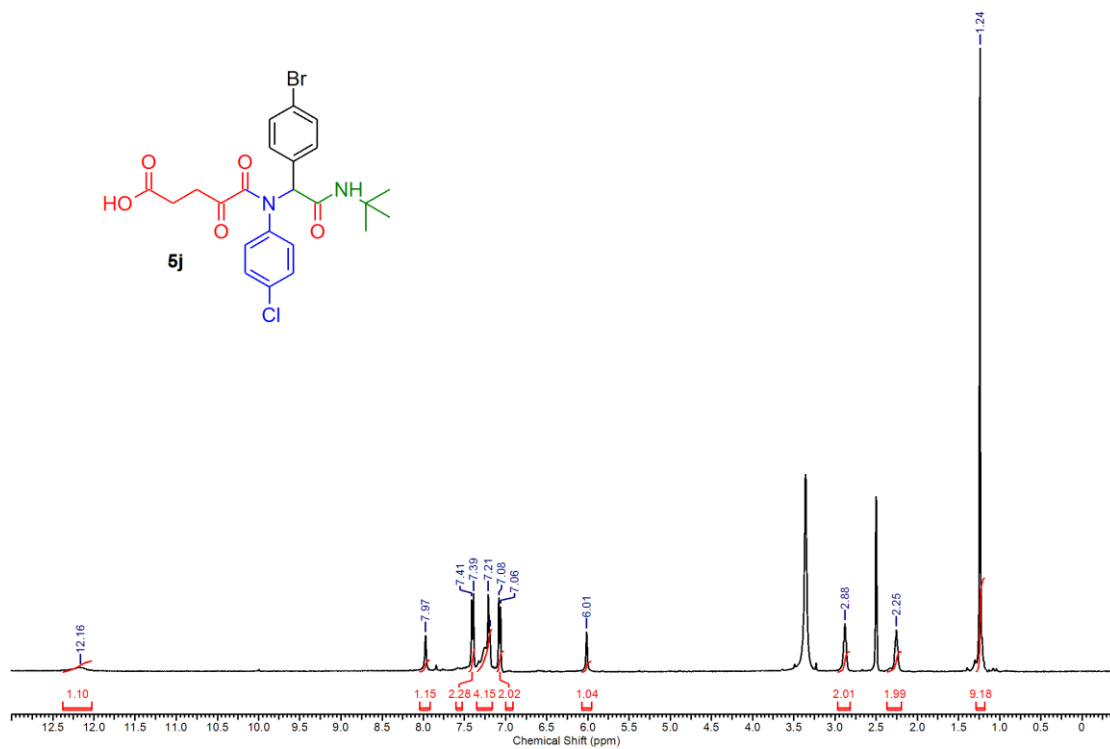
¹H NMR spectrum of compound **5i**



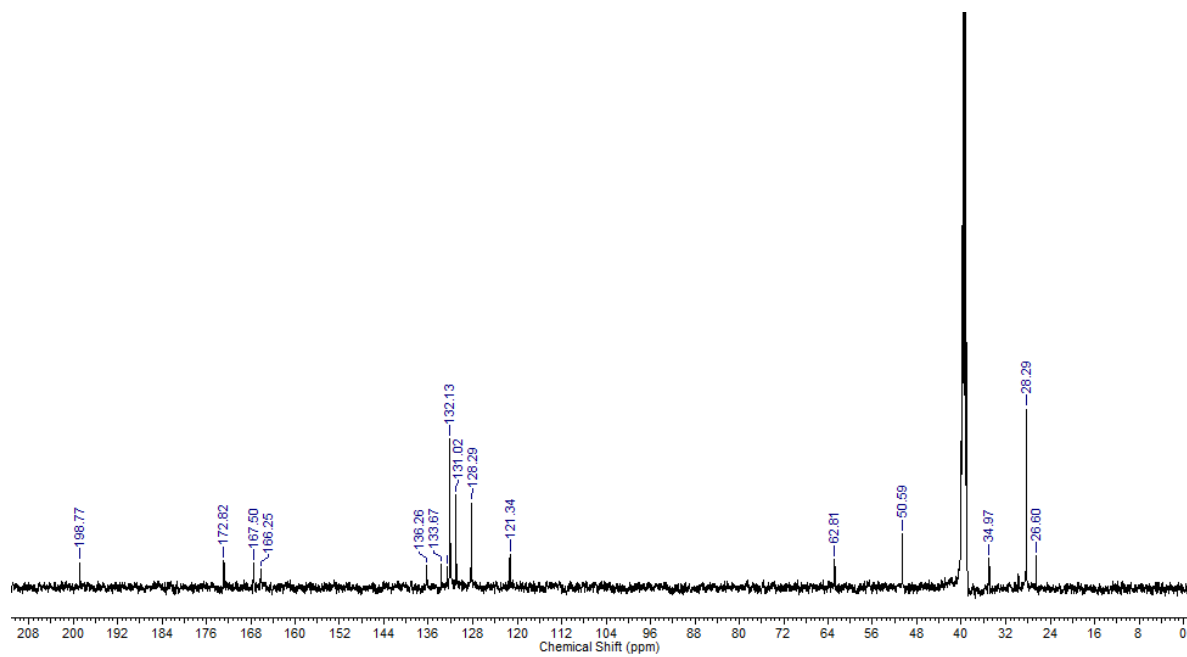
¹³C NMR spectrum of compound **5i**



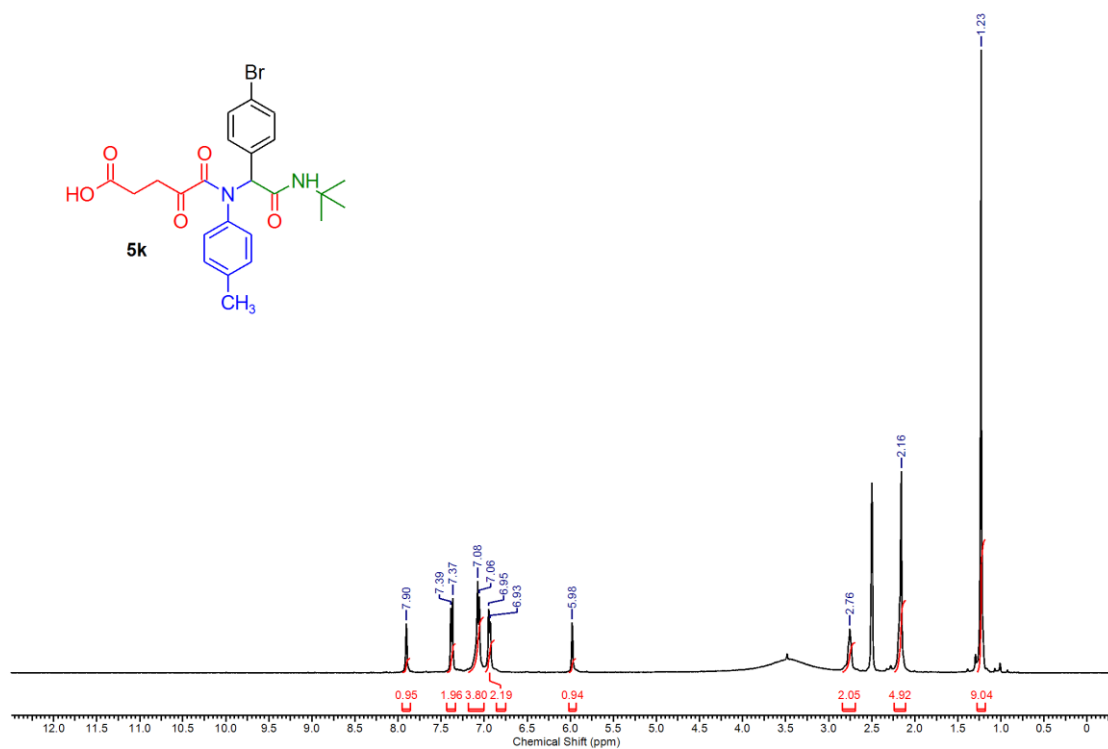
¹H NMR spectrum of compound **5j**



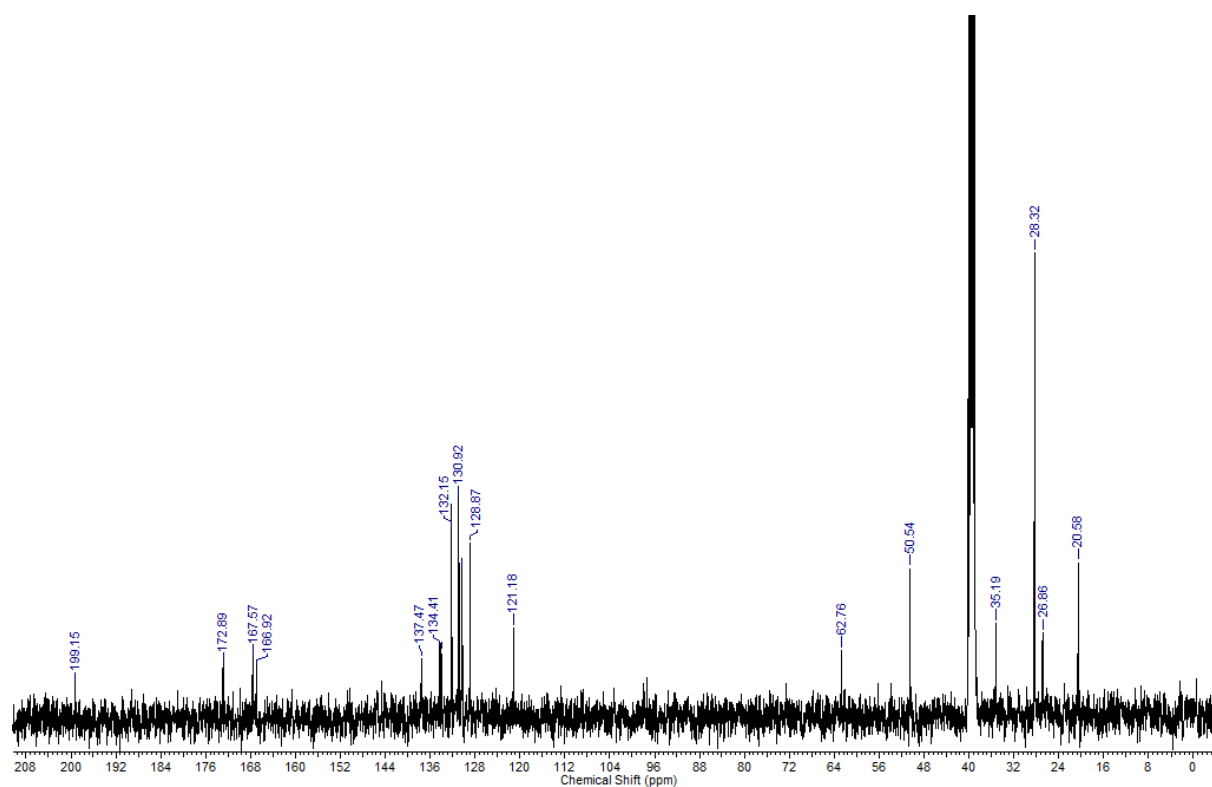
¹³C NMR spectrum of compound **5j**



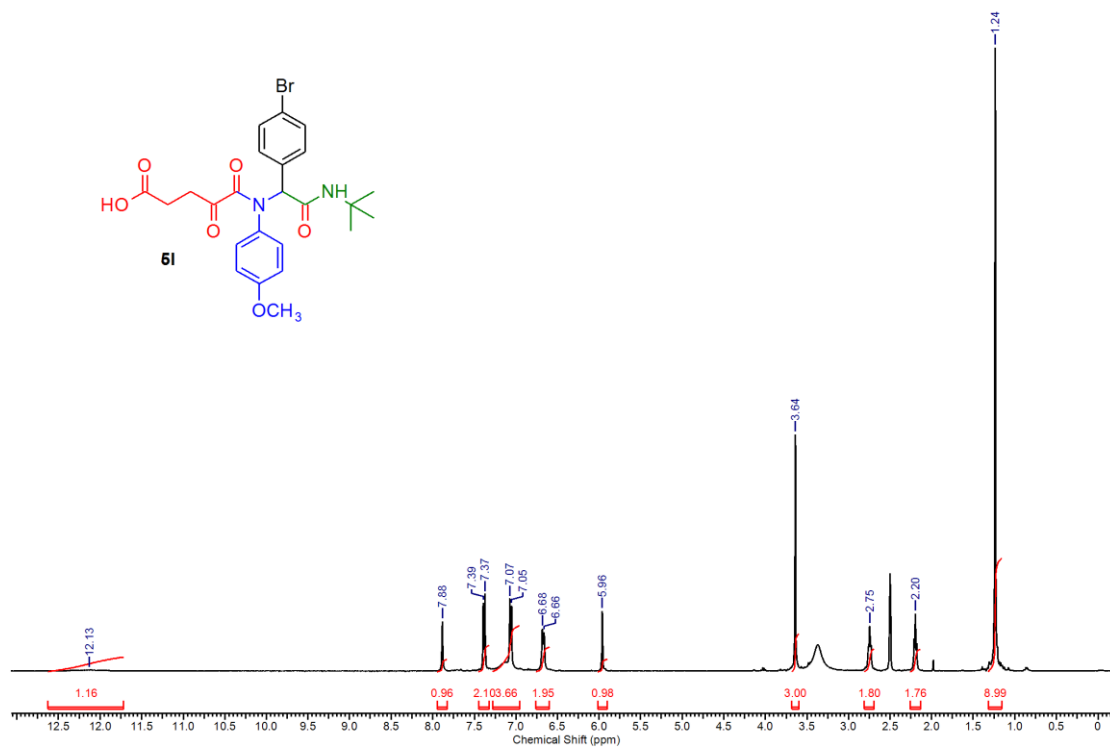
¹H NMR spectrum of compound **5k**



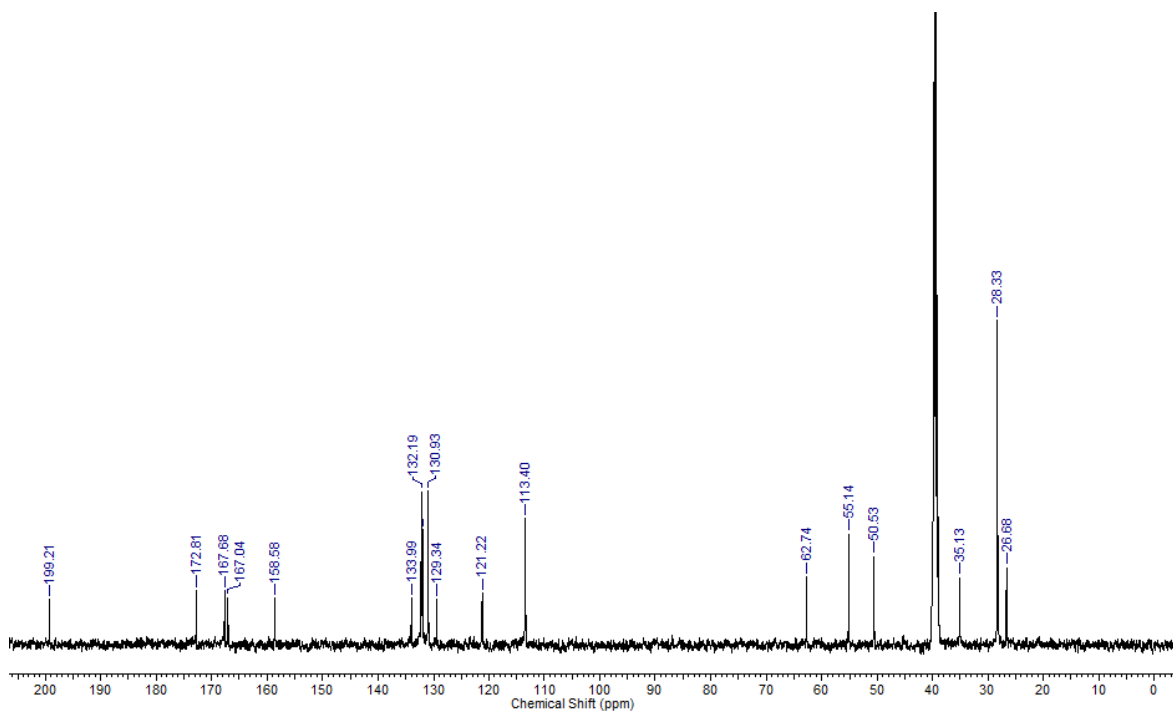
¹³C NMR spectrum of compound **5k**



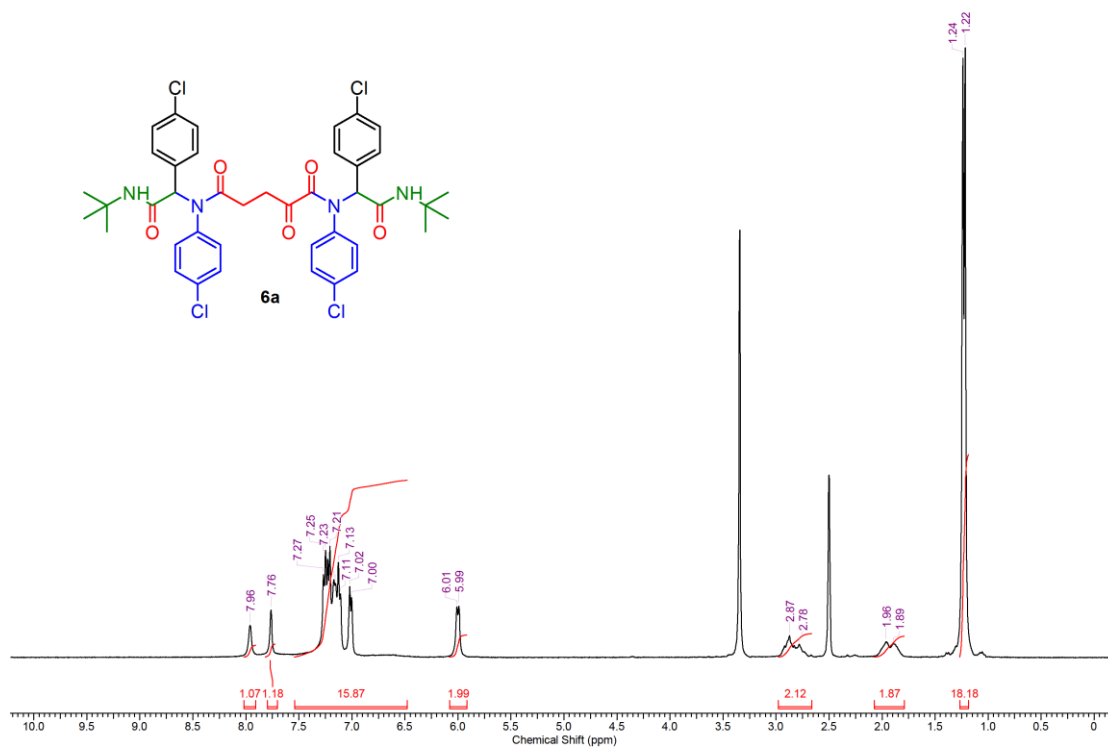
¹H NMR spectrum of compound **5I**



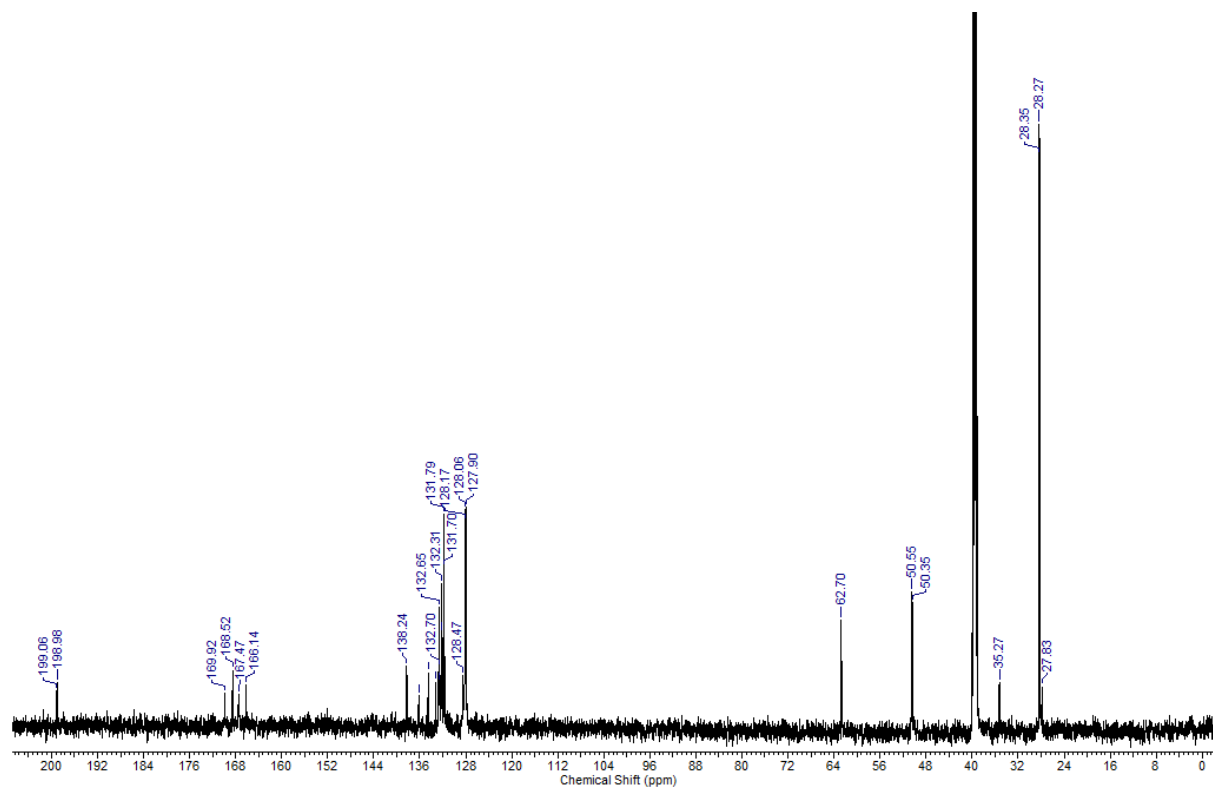
¹³C NMR spectrum of compound **5I**



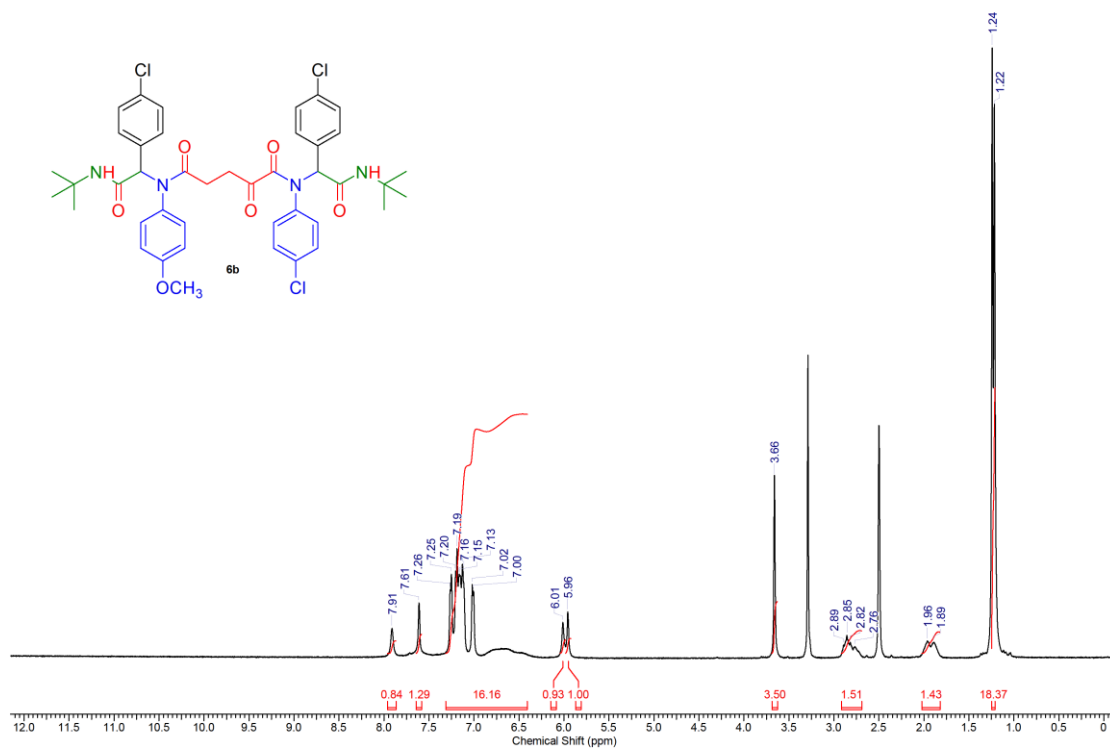
^1H NMR spectrum of compound **6a**



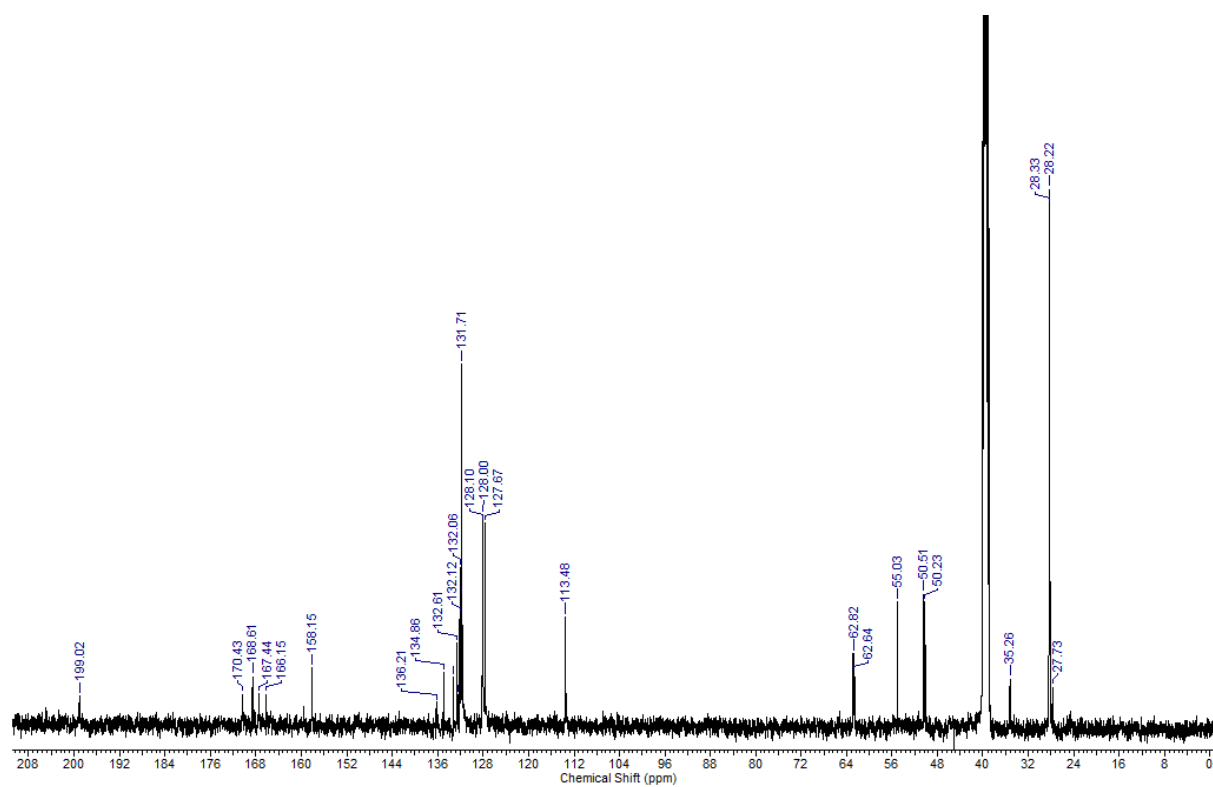
^{13}C NMR spectrum of compound **6a**



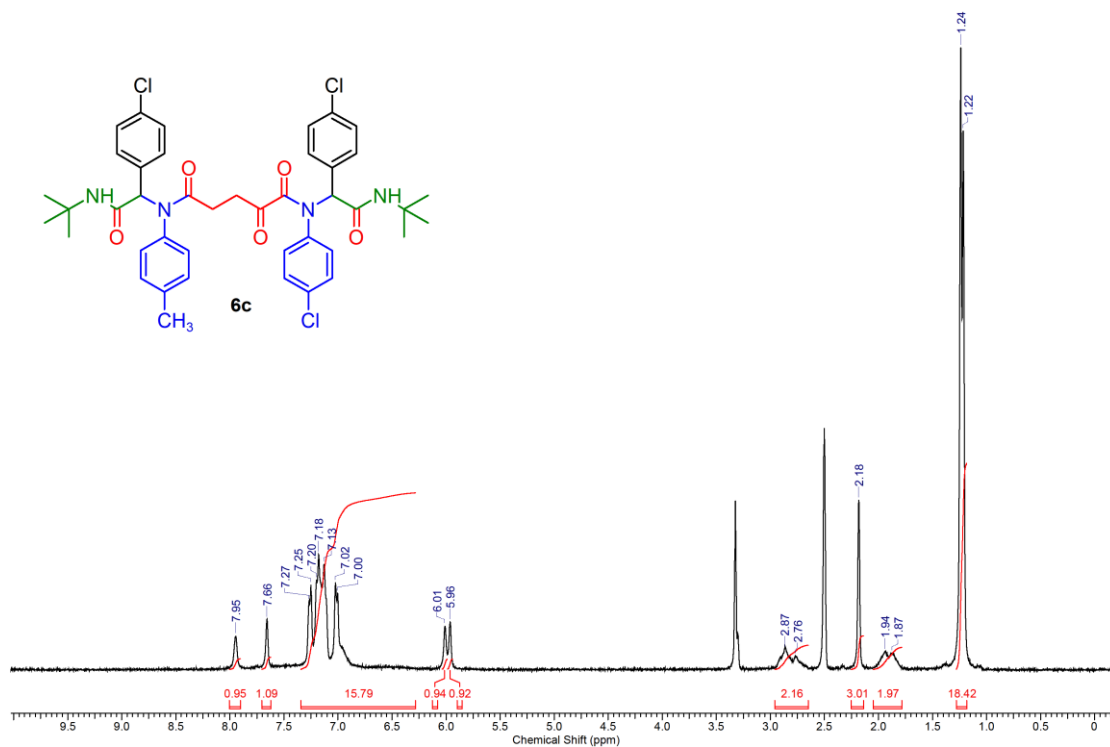
¹H NMR spectrum of compound **6b**



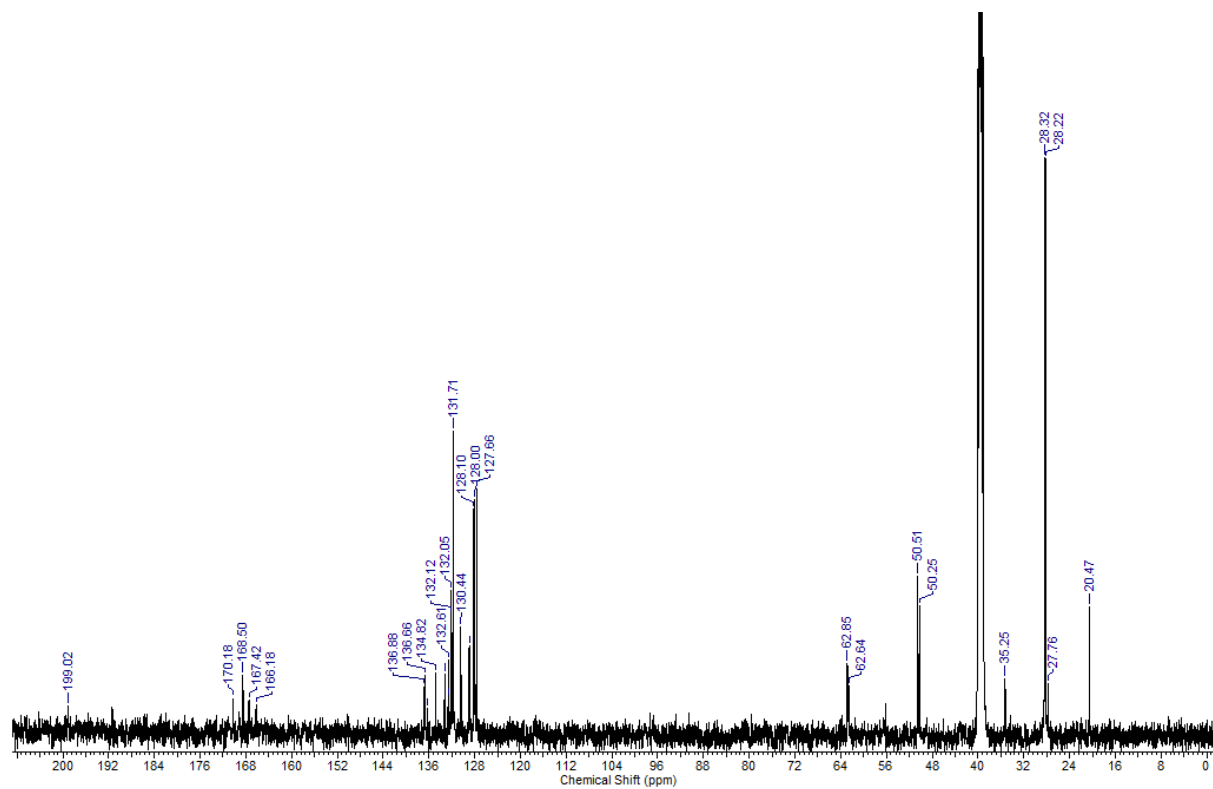
¹³C NMR spectrum of compound **6b**



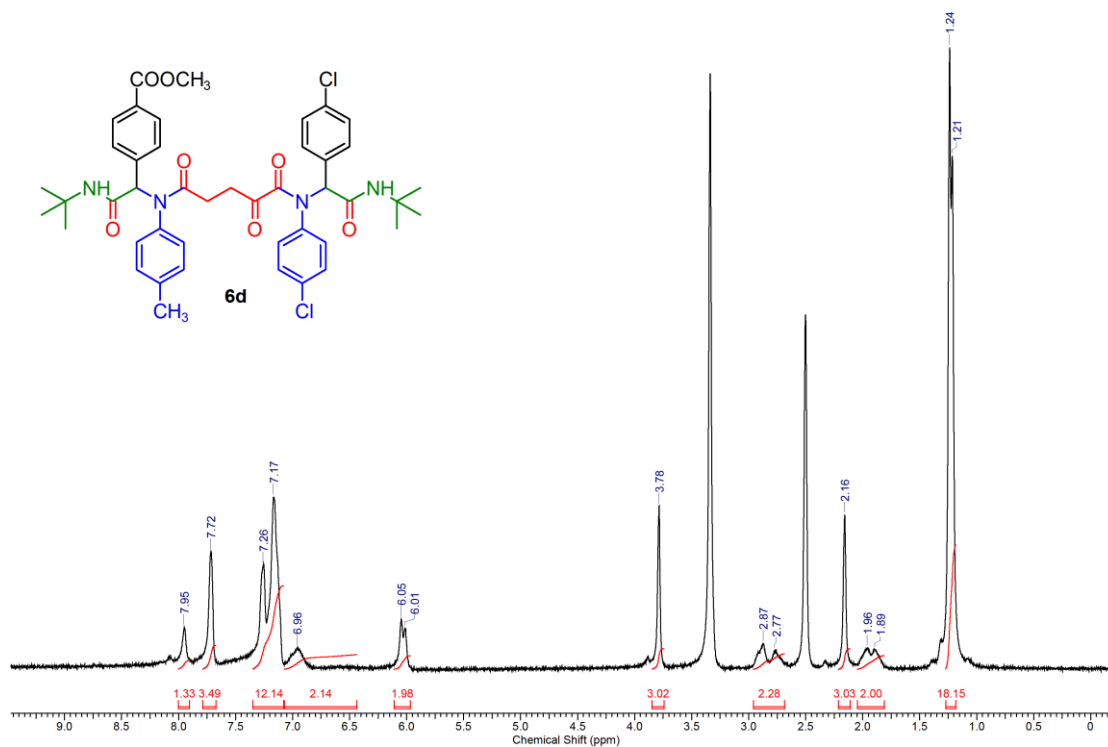
¹H NMR spectrum of compound **6c**



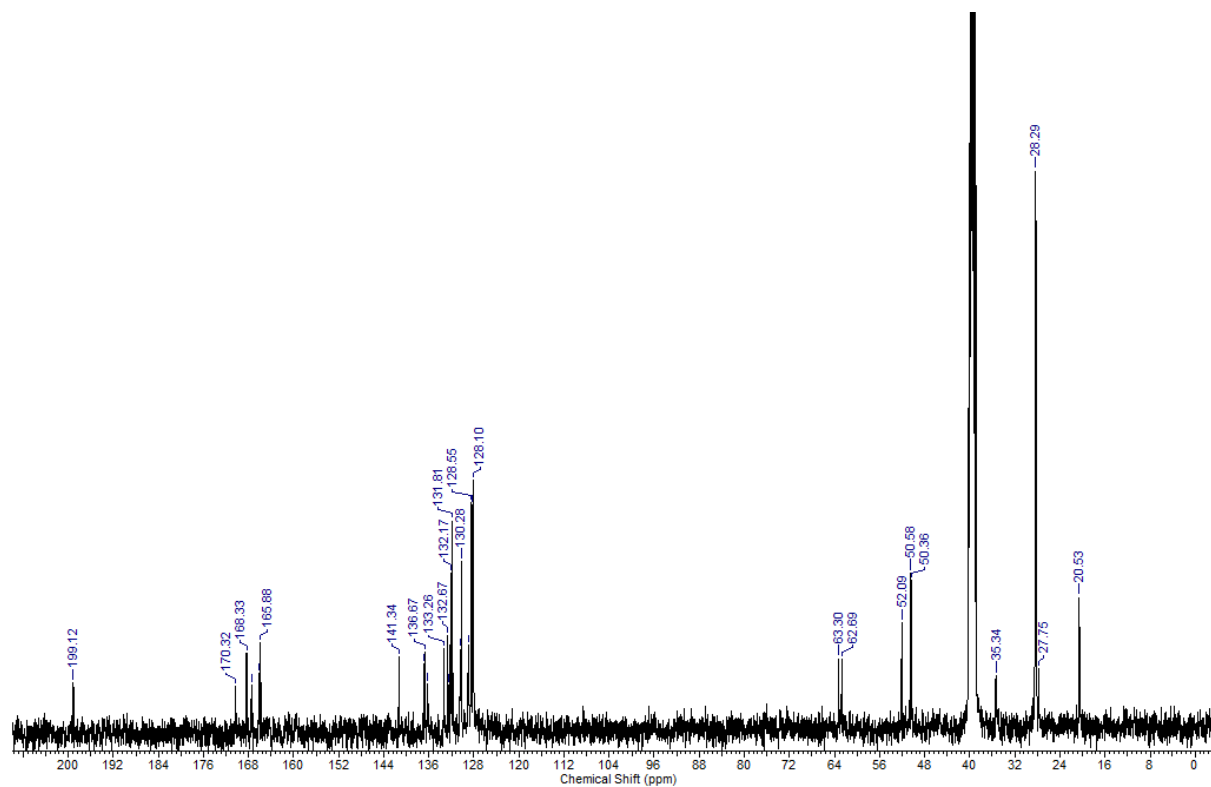
¹³C NMR spectrum of compound **6c**



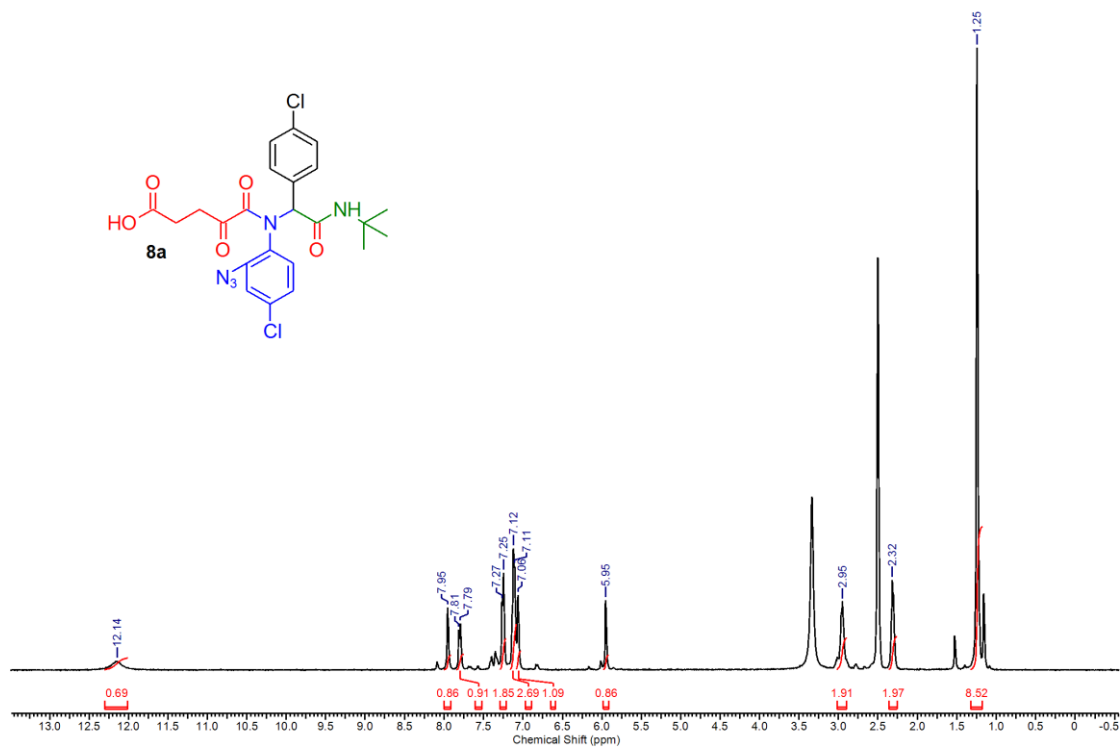
¹H NMR spectrum of compound **6d**



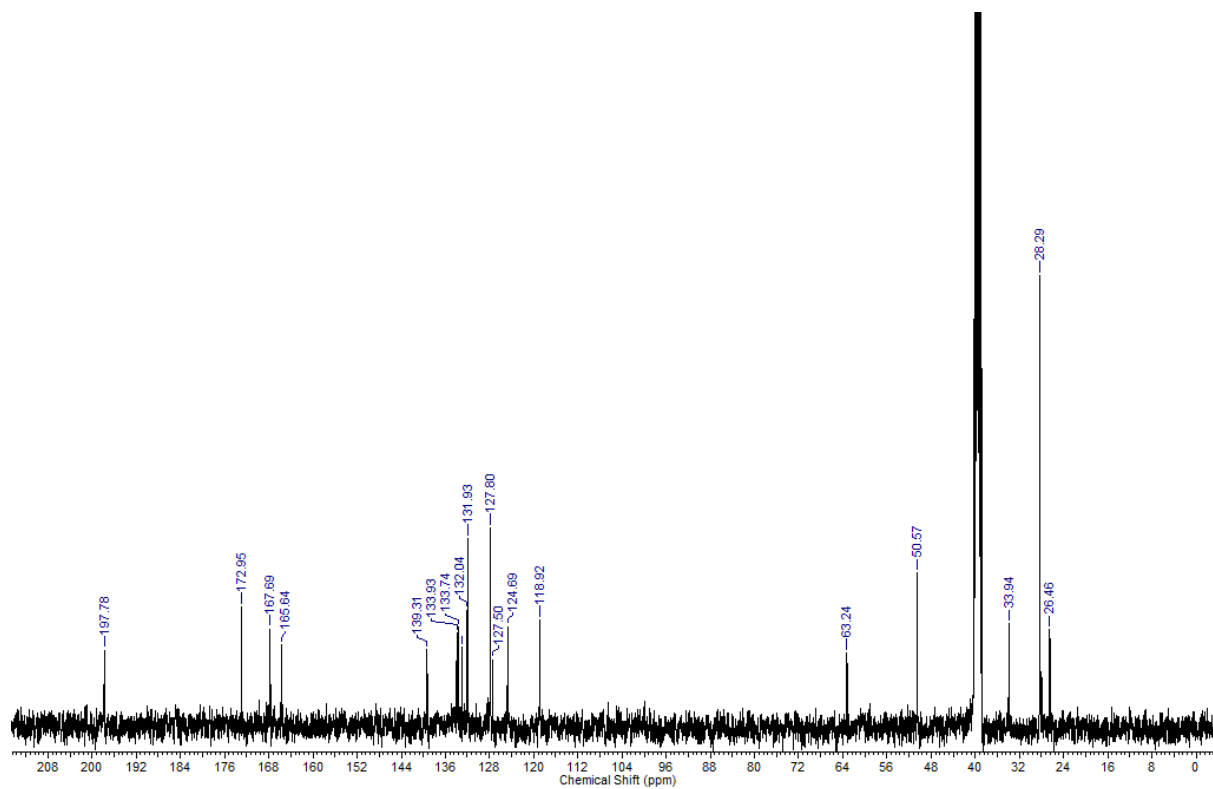
¹³C NMR spectrum of compound **6d**



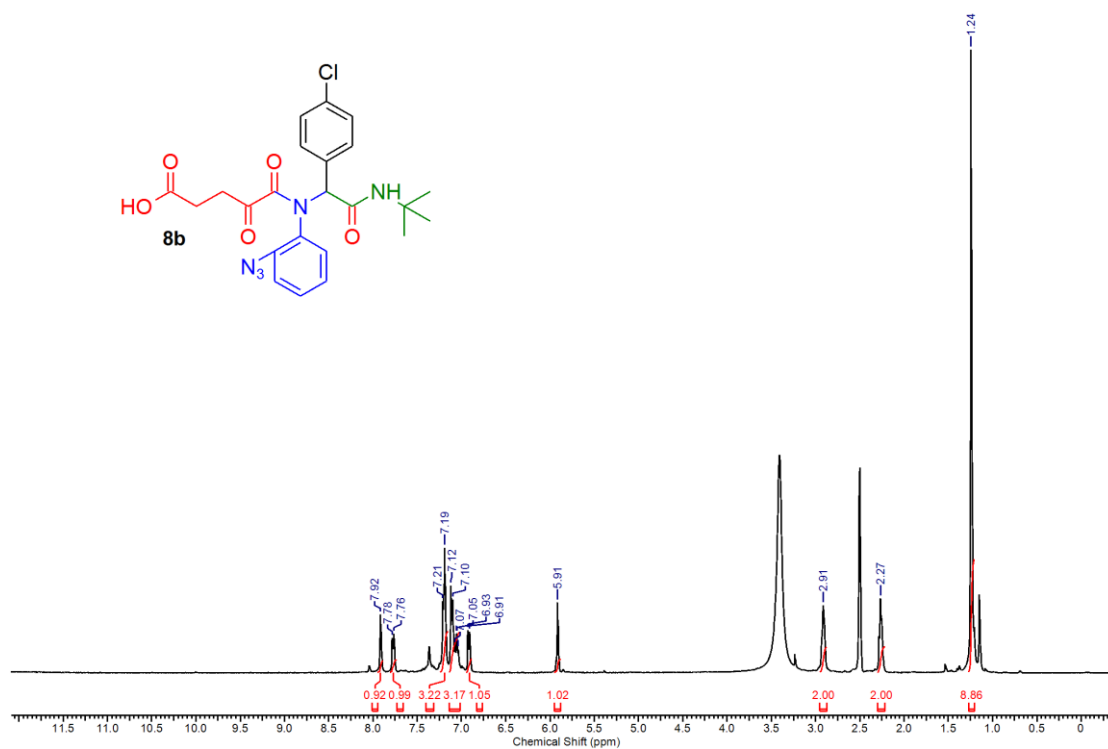
¹H NMR spectrum of compound **8a**



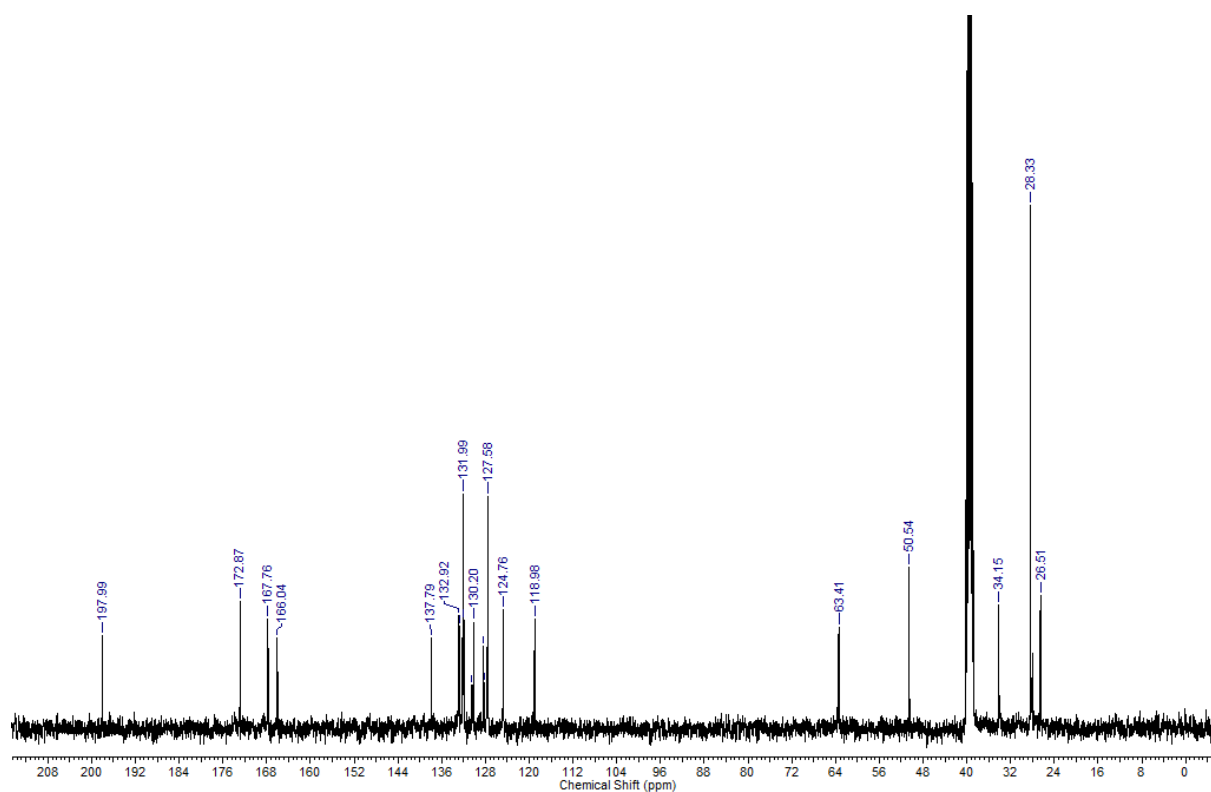
¹³C NMR spectrum of compound **8a**



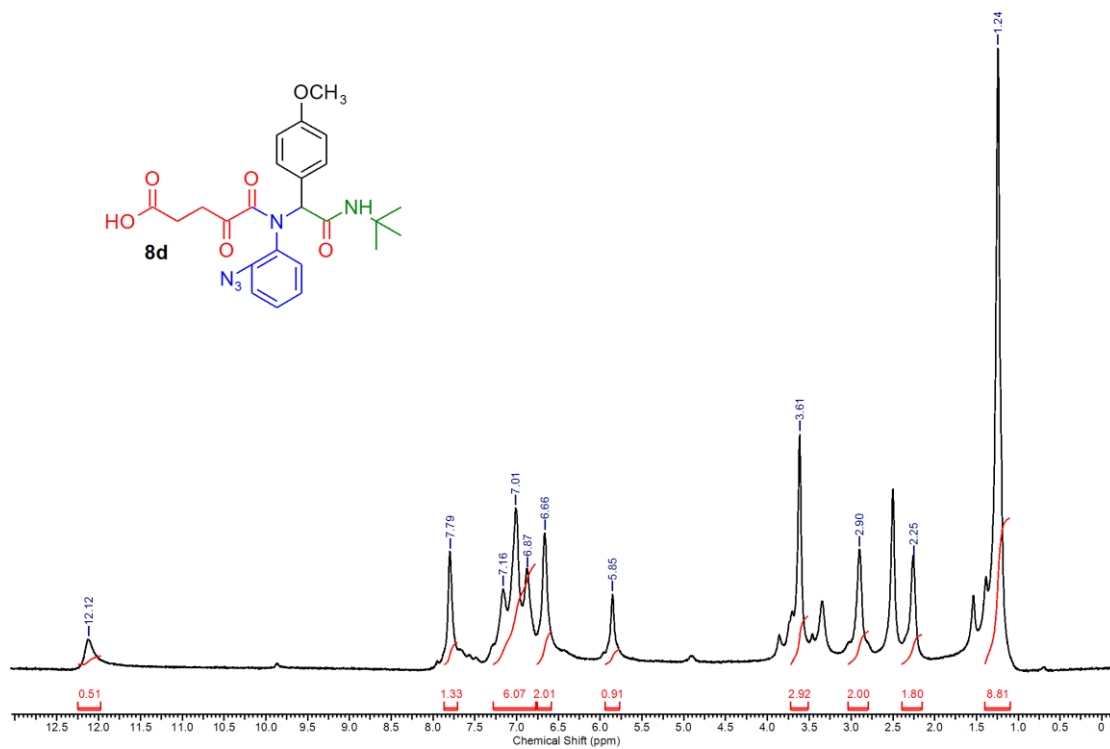
¹H NMR spectrum of compound **8b**



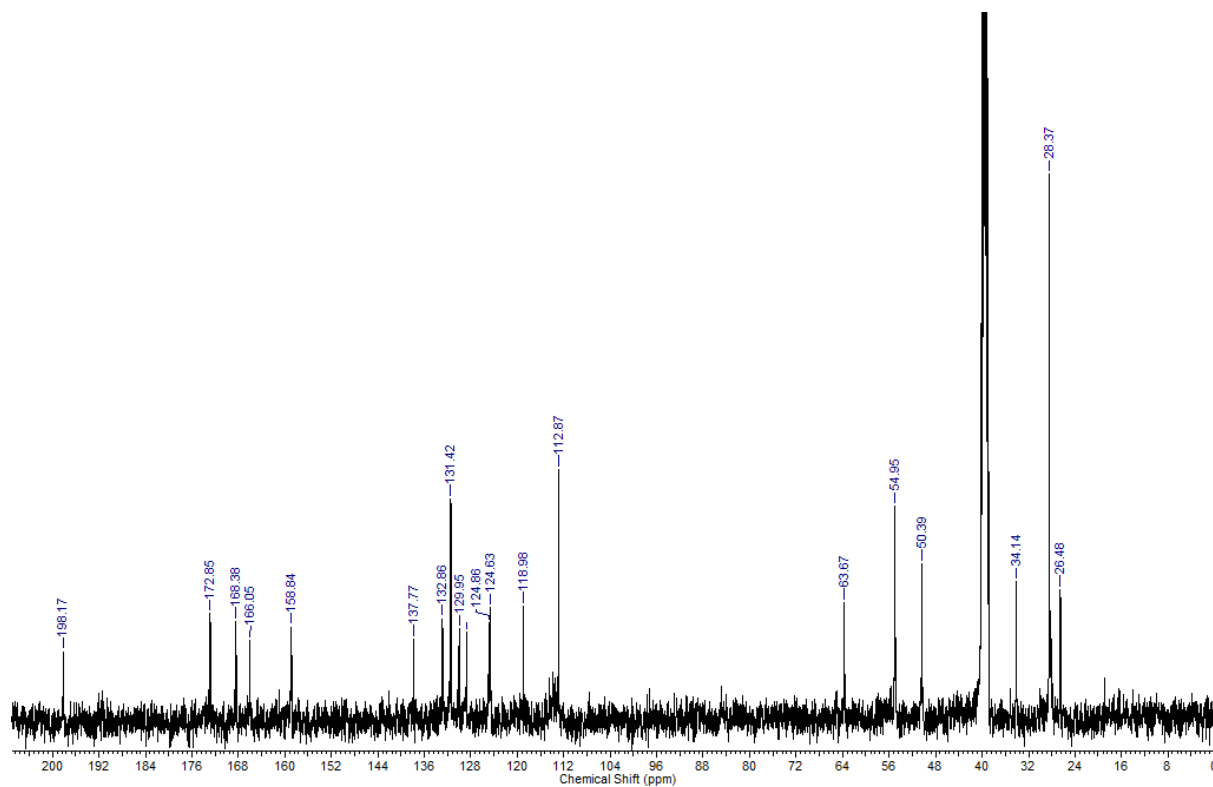
¹³C NMR spectrum of compound **8b**

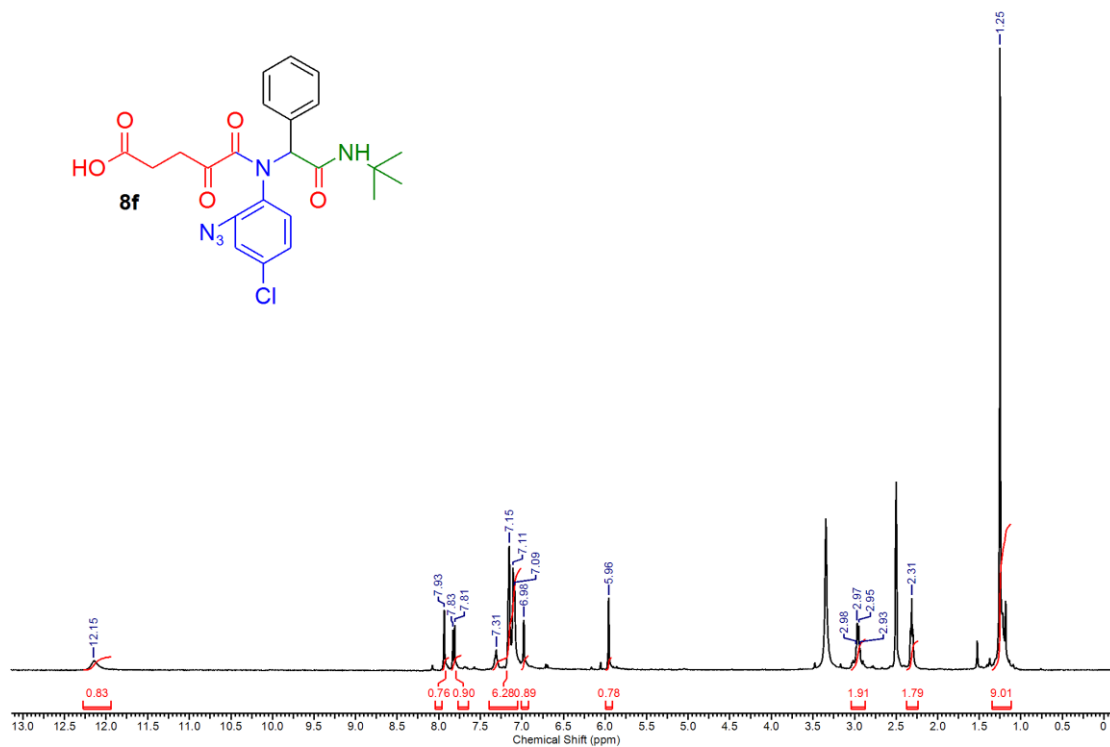
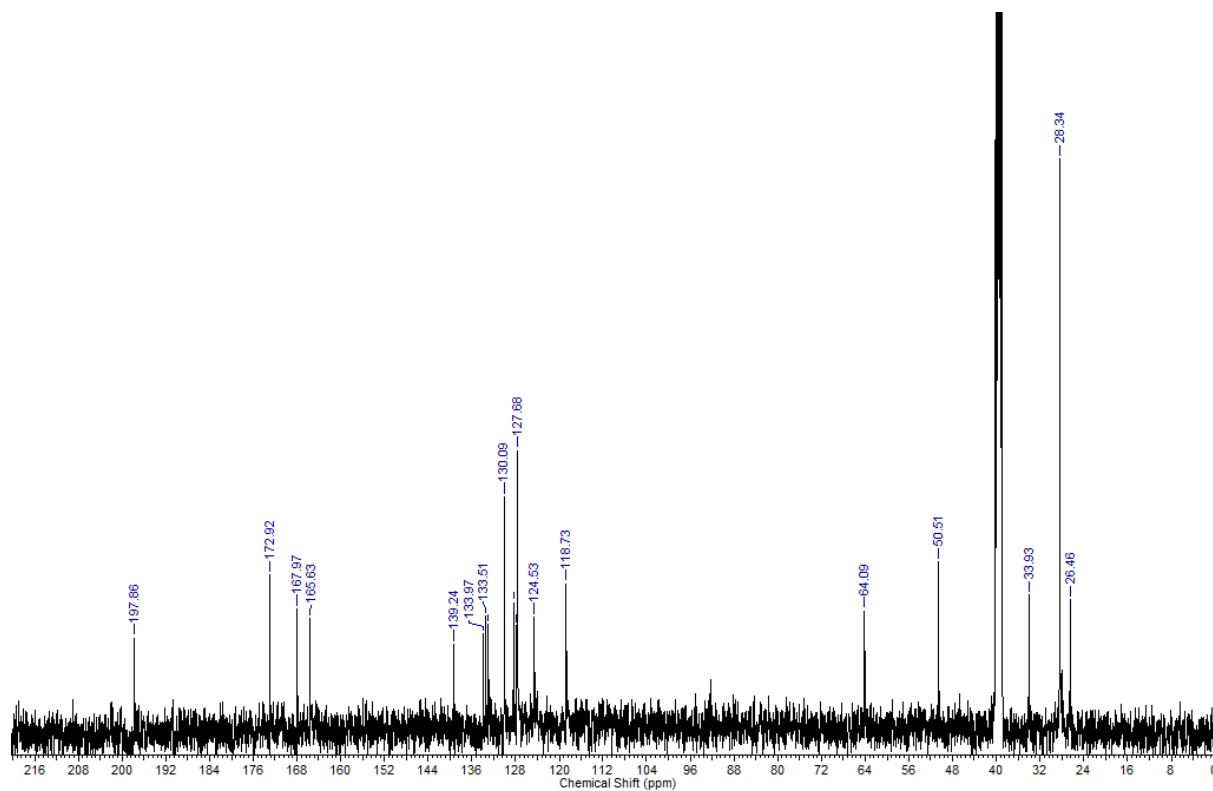


¹H NMR spectrum of compound **8d**

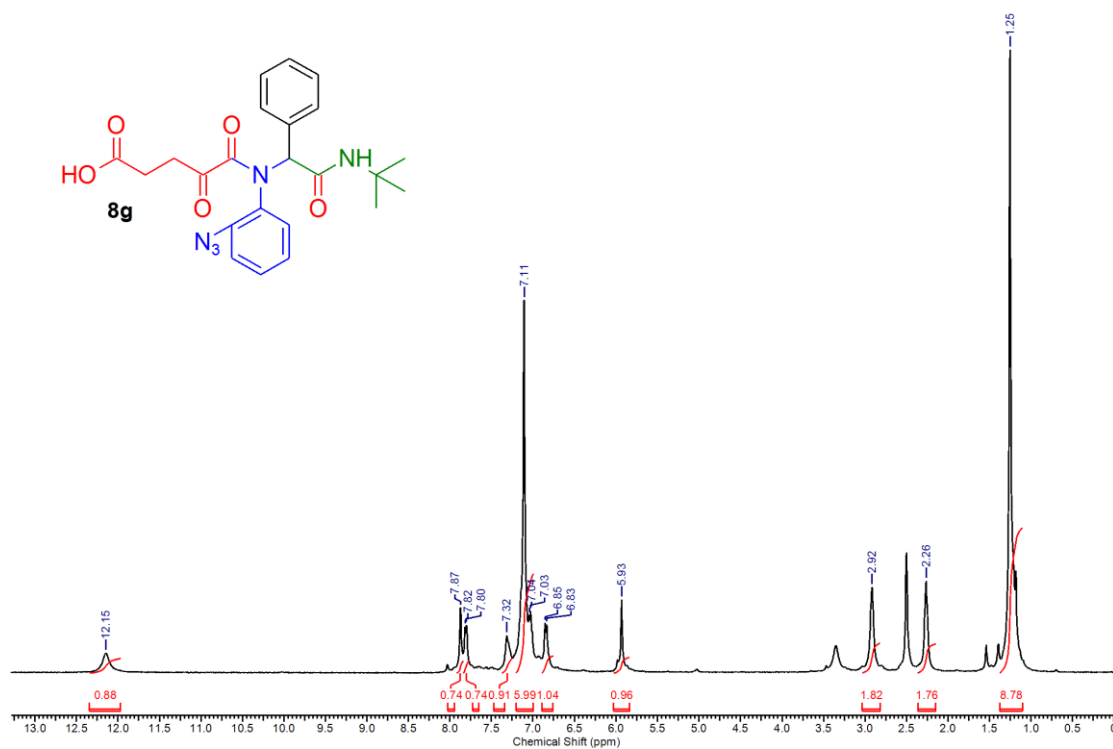


¹³C NMR spectrum of compound **8d**

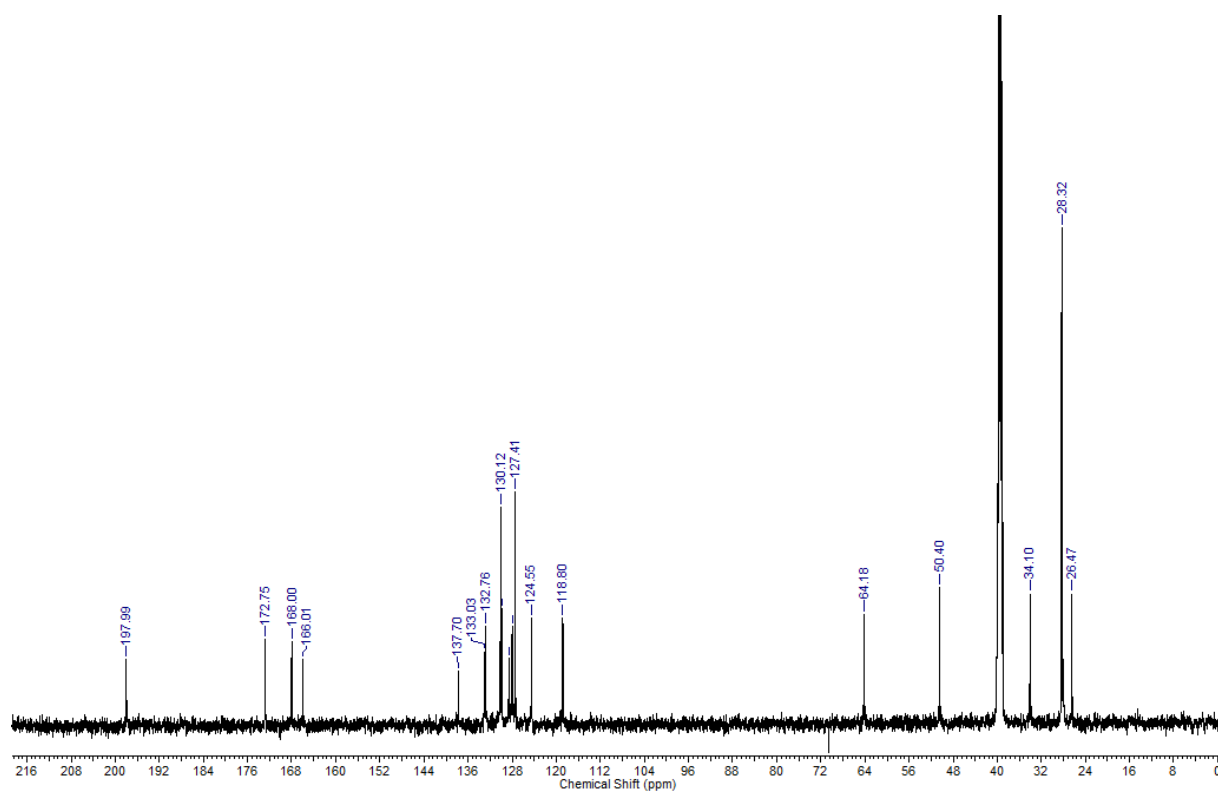


¹H NMR spectrum of compound **8f** ^{13}C NMR spectrum of compound **8f**

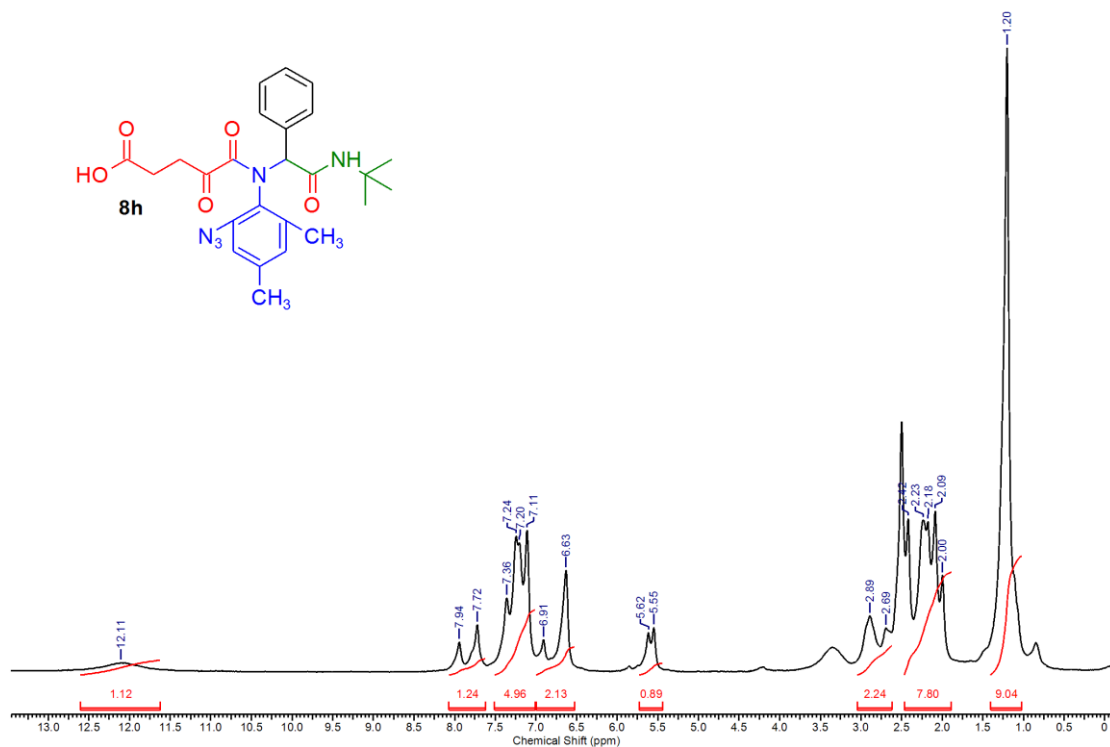
^1H NMR spectrum of compound **8g**



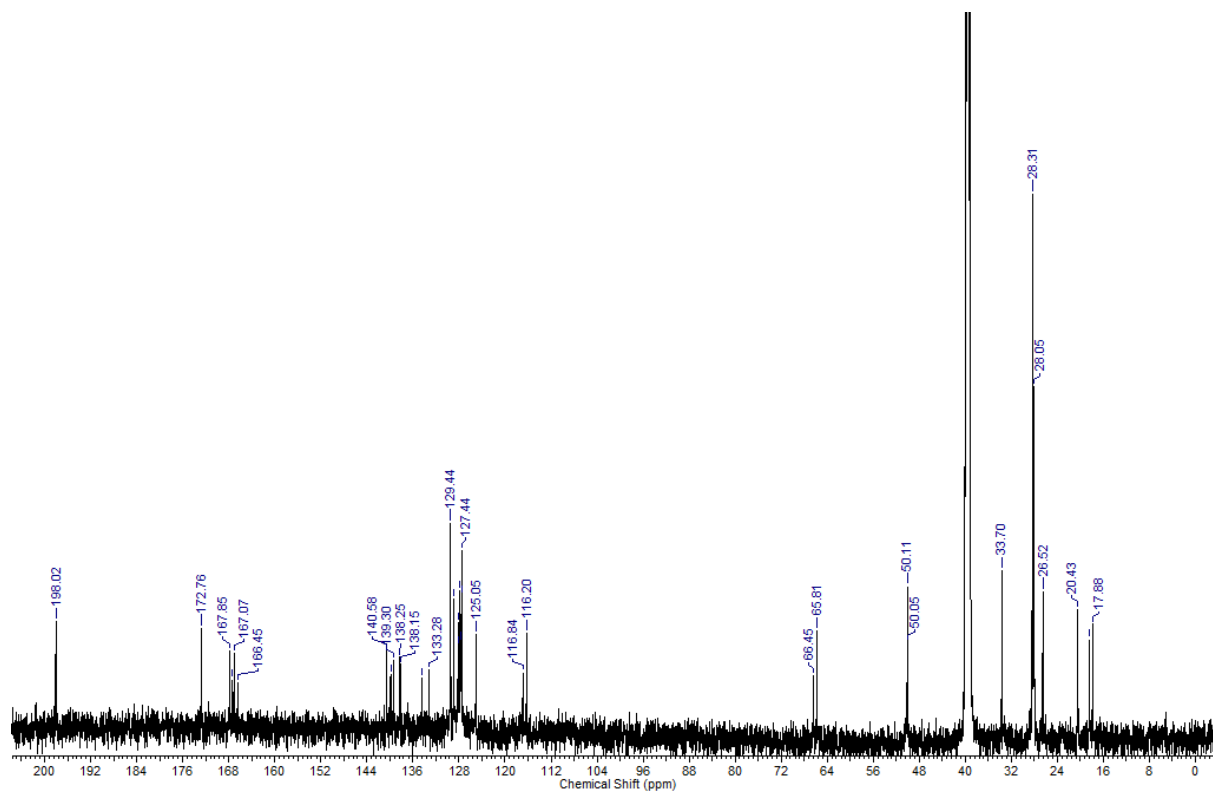
^{13}C NMR spectrum of compound **8g**



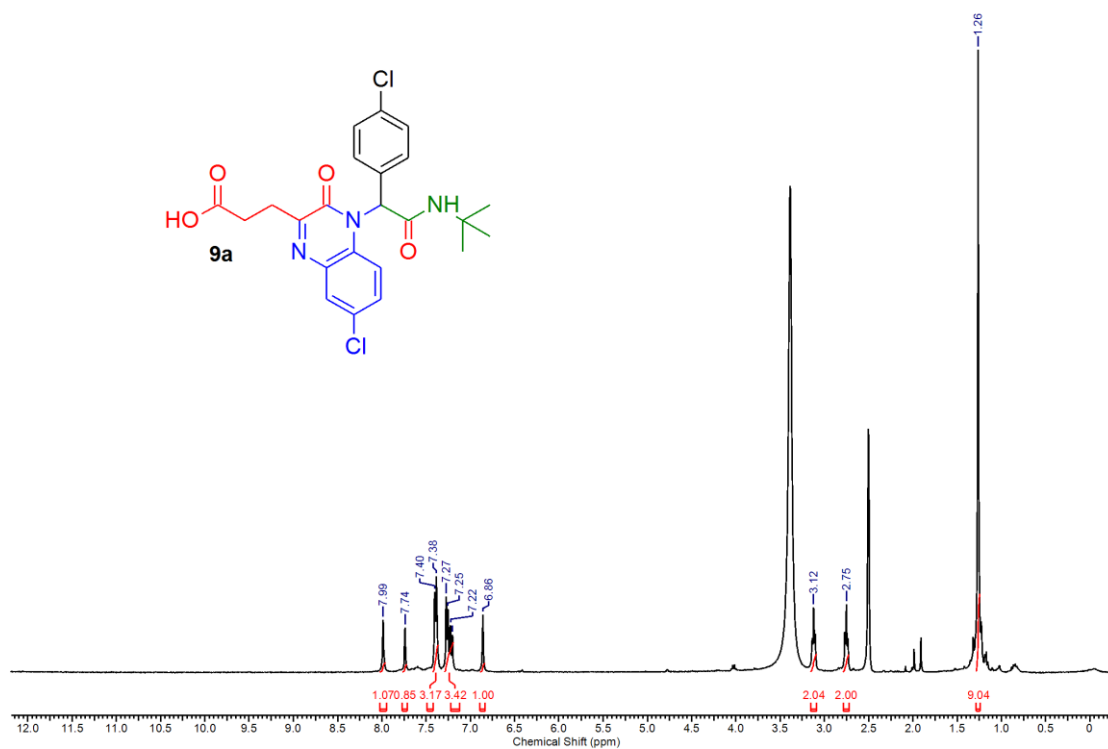
¹H NMR spectrum of compound **8h**



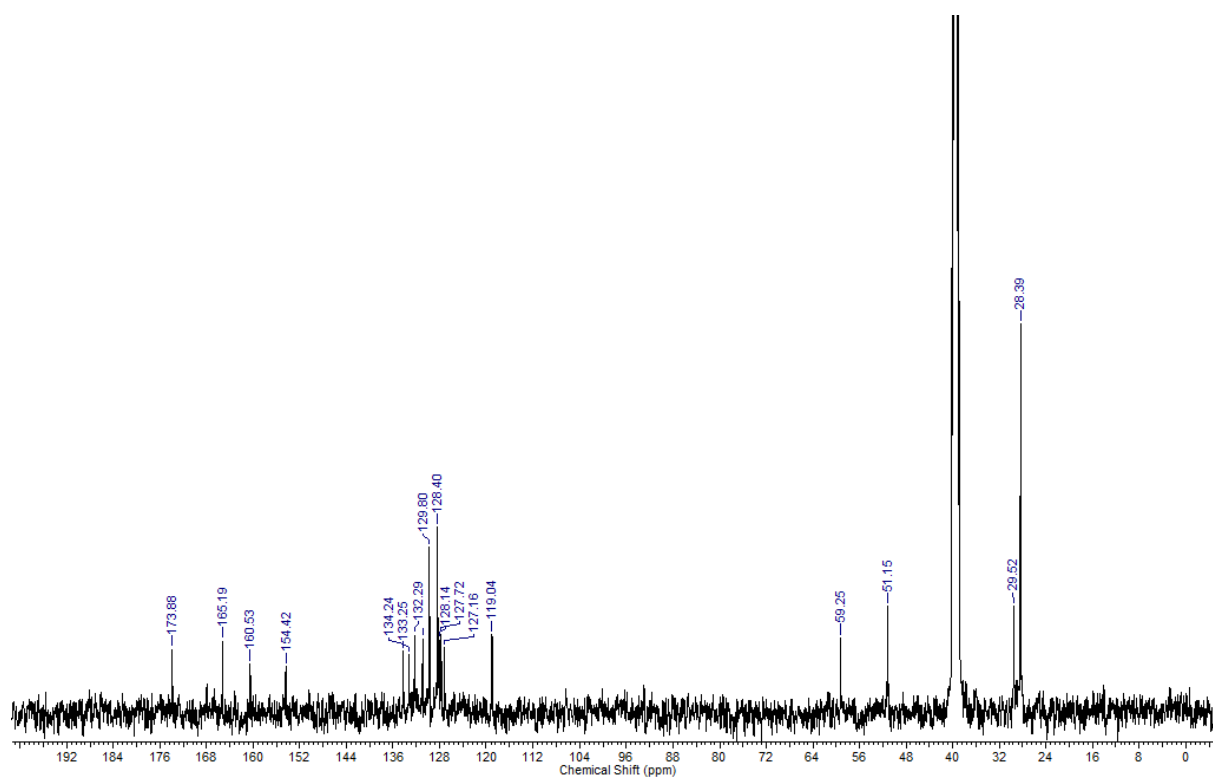
¹³C NMR spectrum of compound **8h**



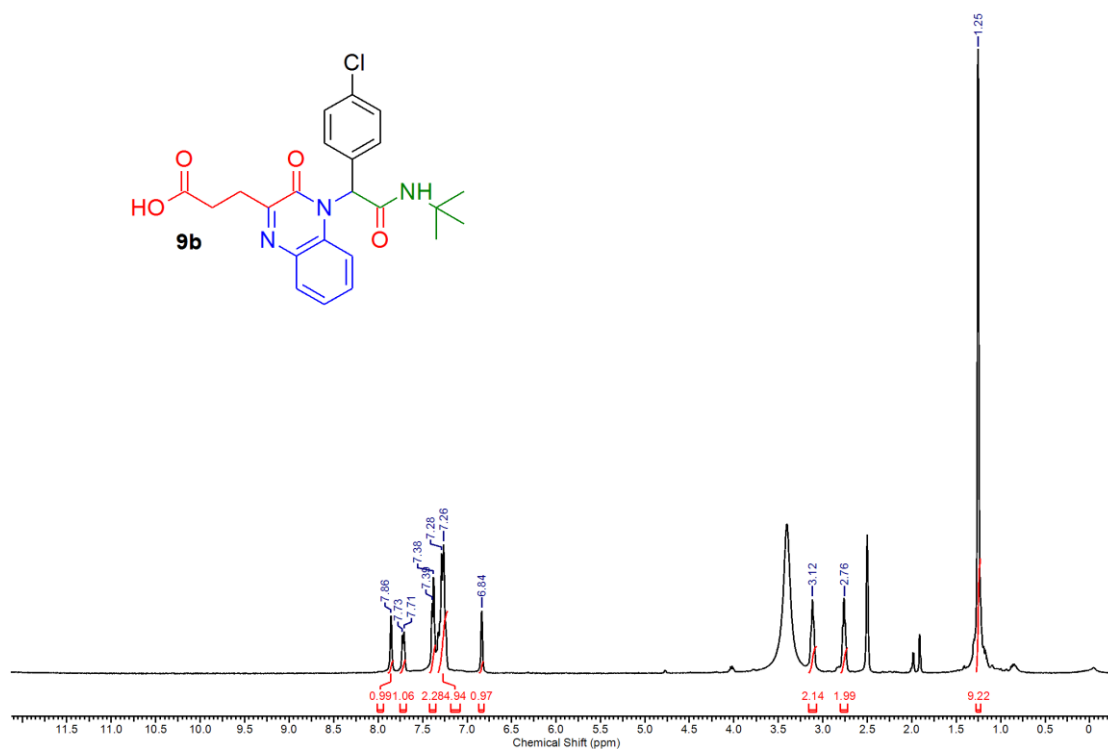
¹H NMR spectrum of compound **9a**



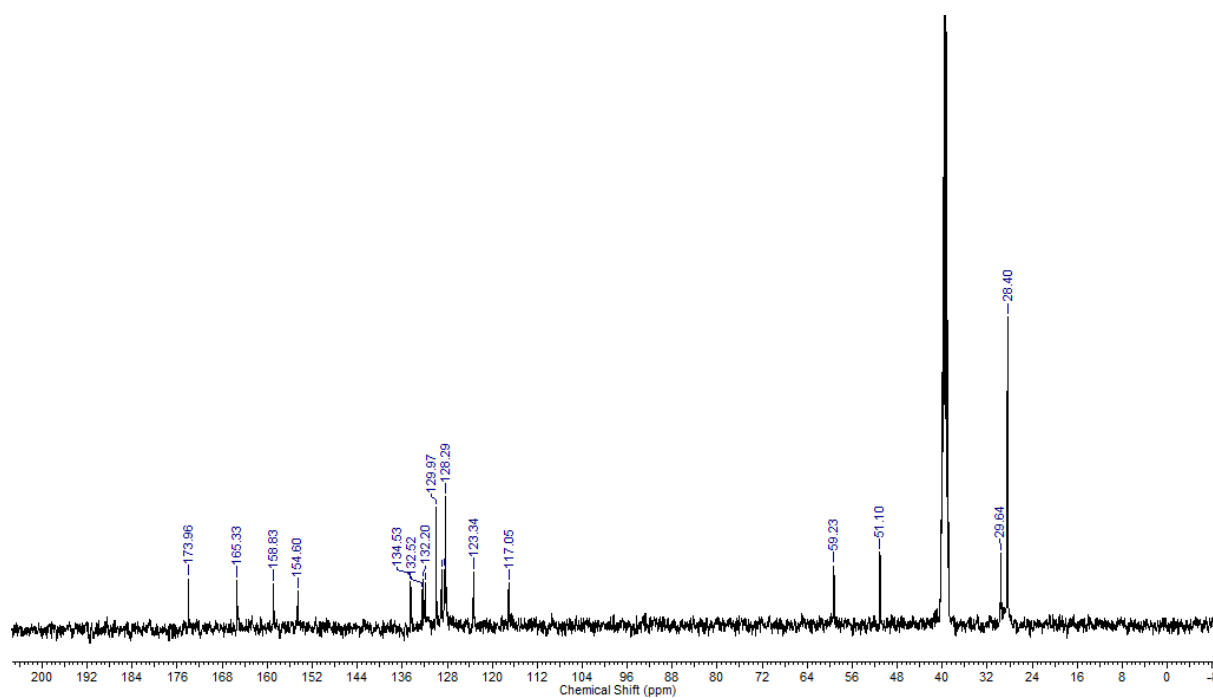
¹³C NMR spectrum of compound **9a**



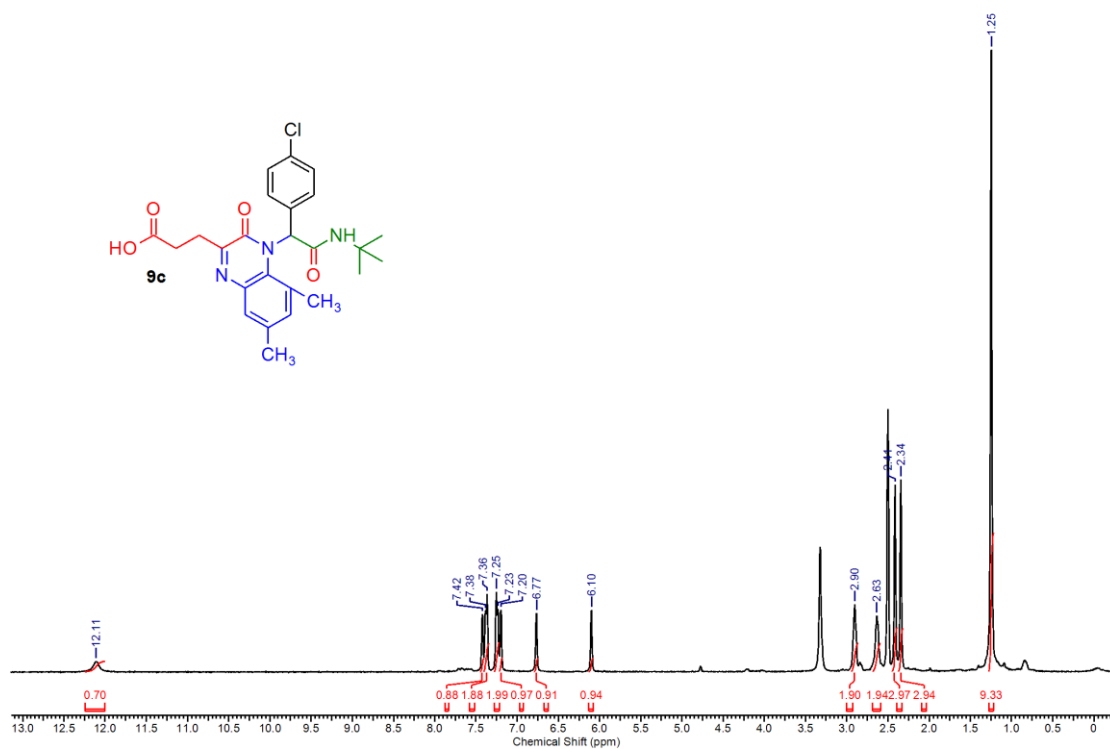
¹H NMR spectrum of compound **9b**



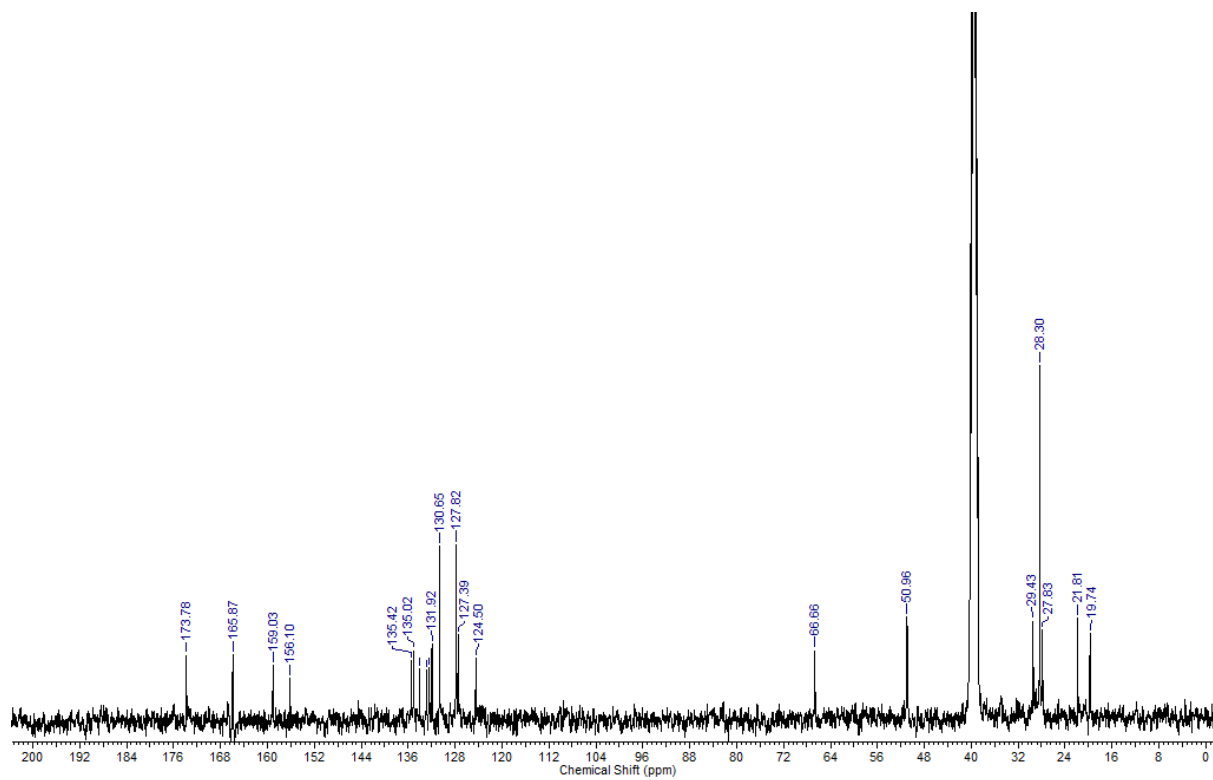
¹³C NMR spectrum of compound **9b**



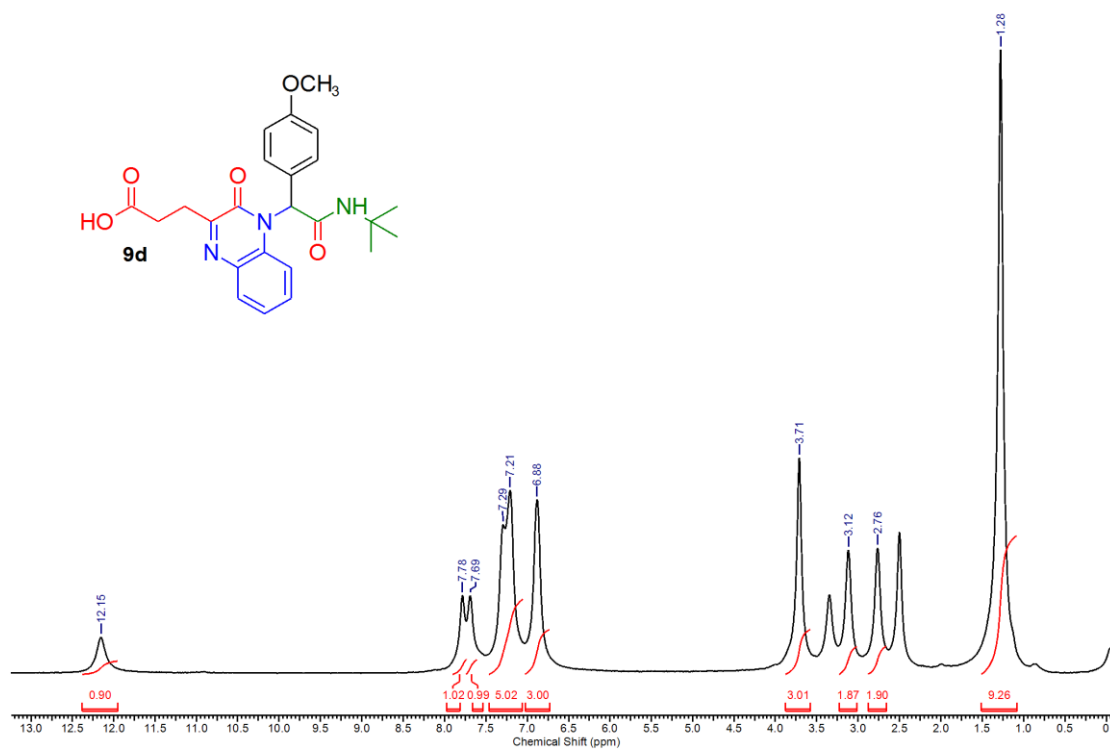
¹H NMR spectrum of compound **9c**



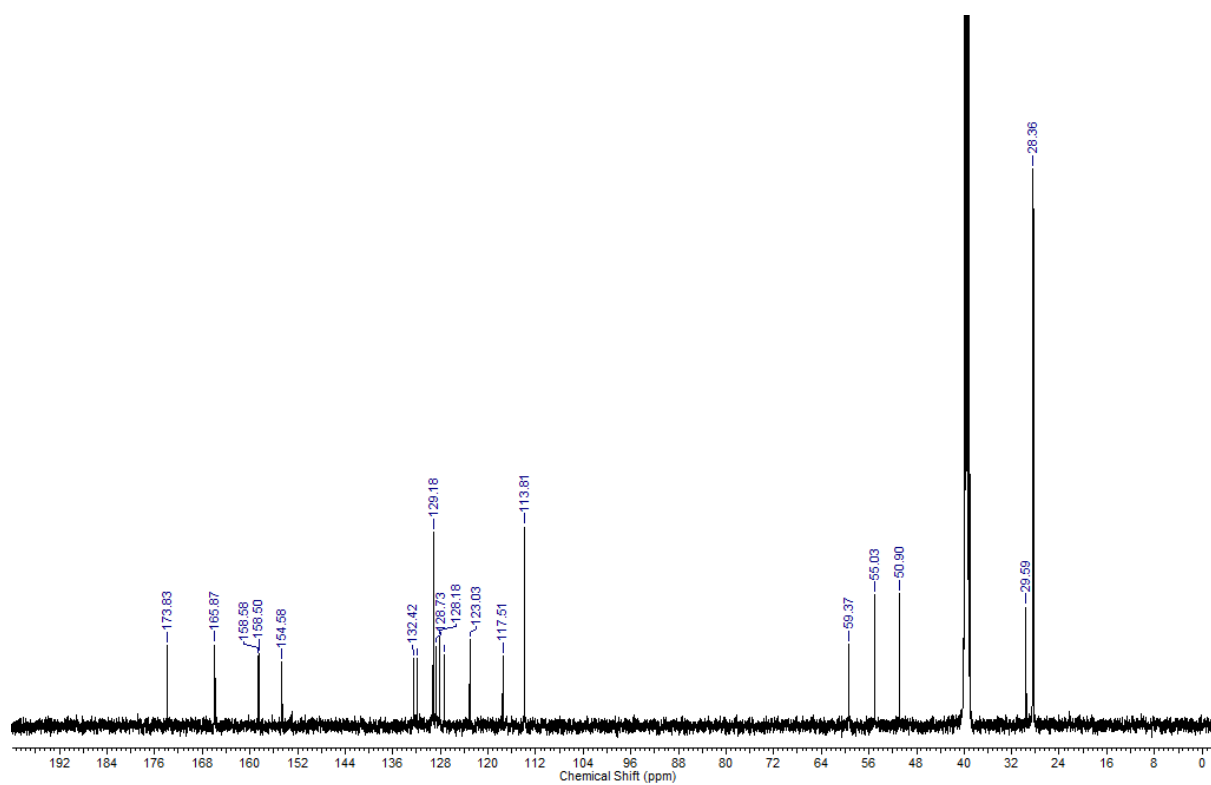
¹³C NMR spectrum of compound **9c**



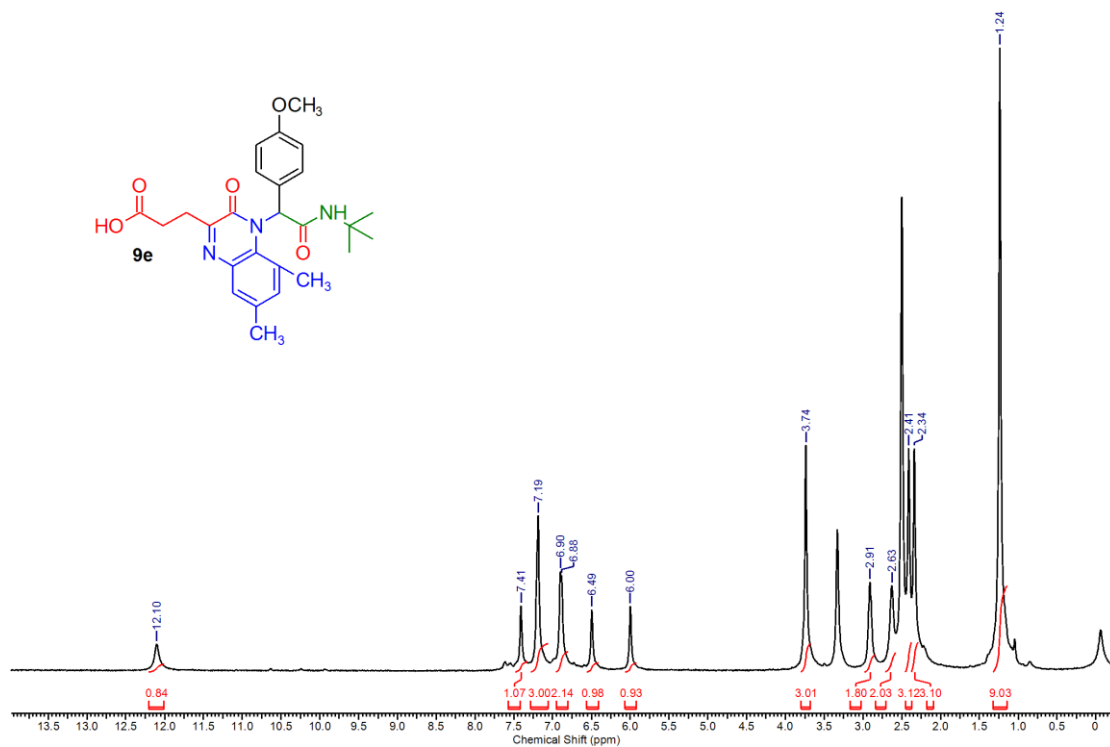
¹H NMR spectrum of compound **9d**



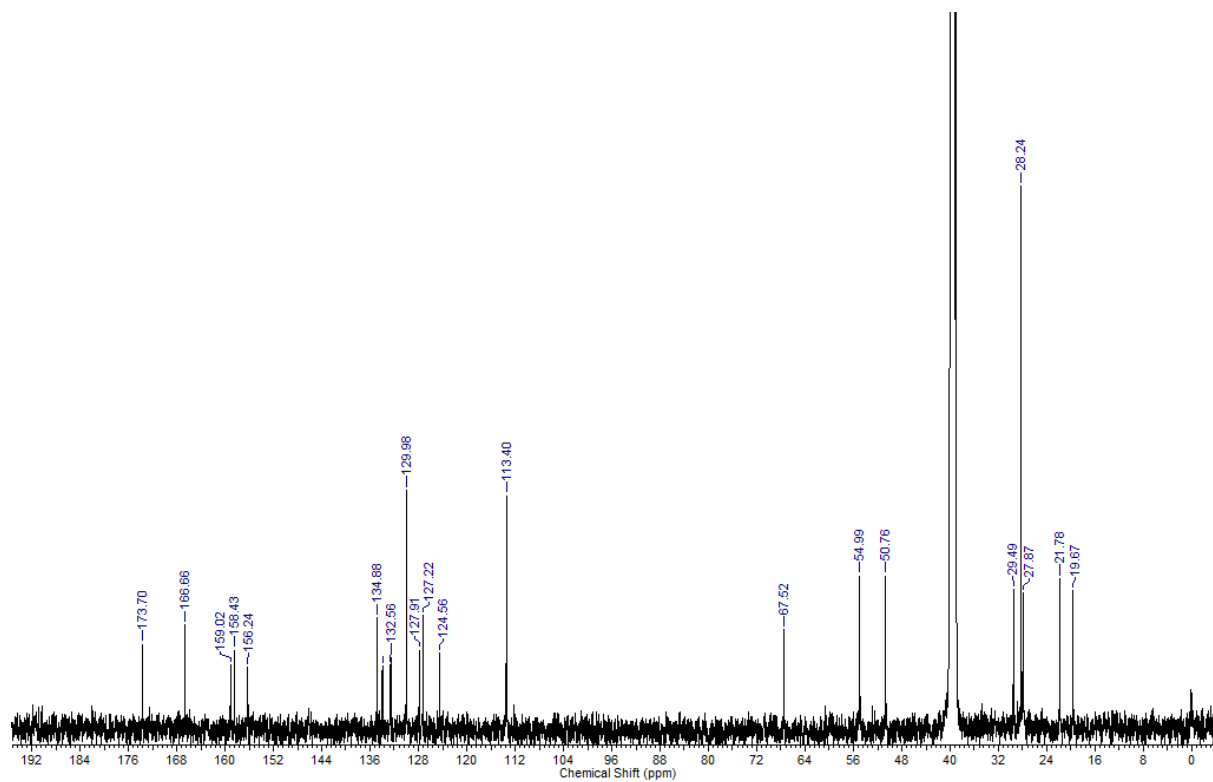
¹³C NMR spectrum of compound **9d**



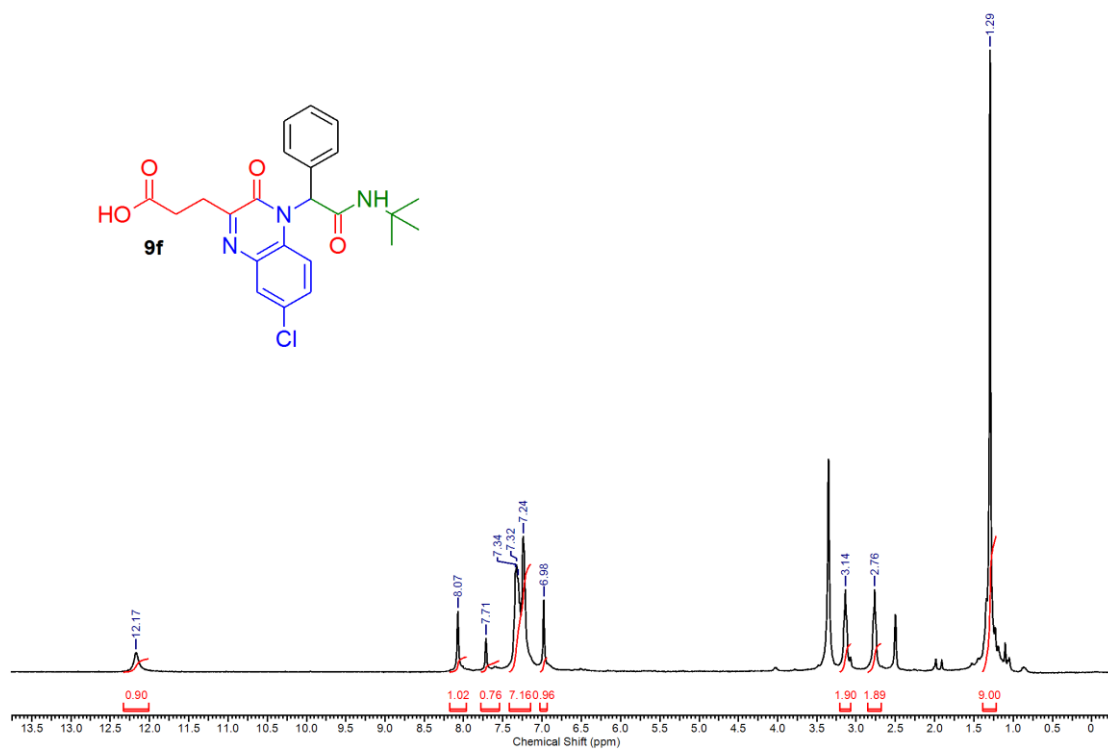
¹H NMR spectrum of compound **9e**



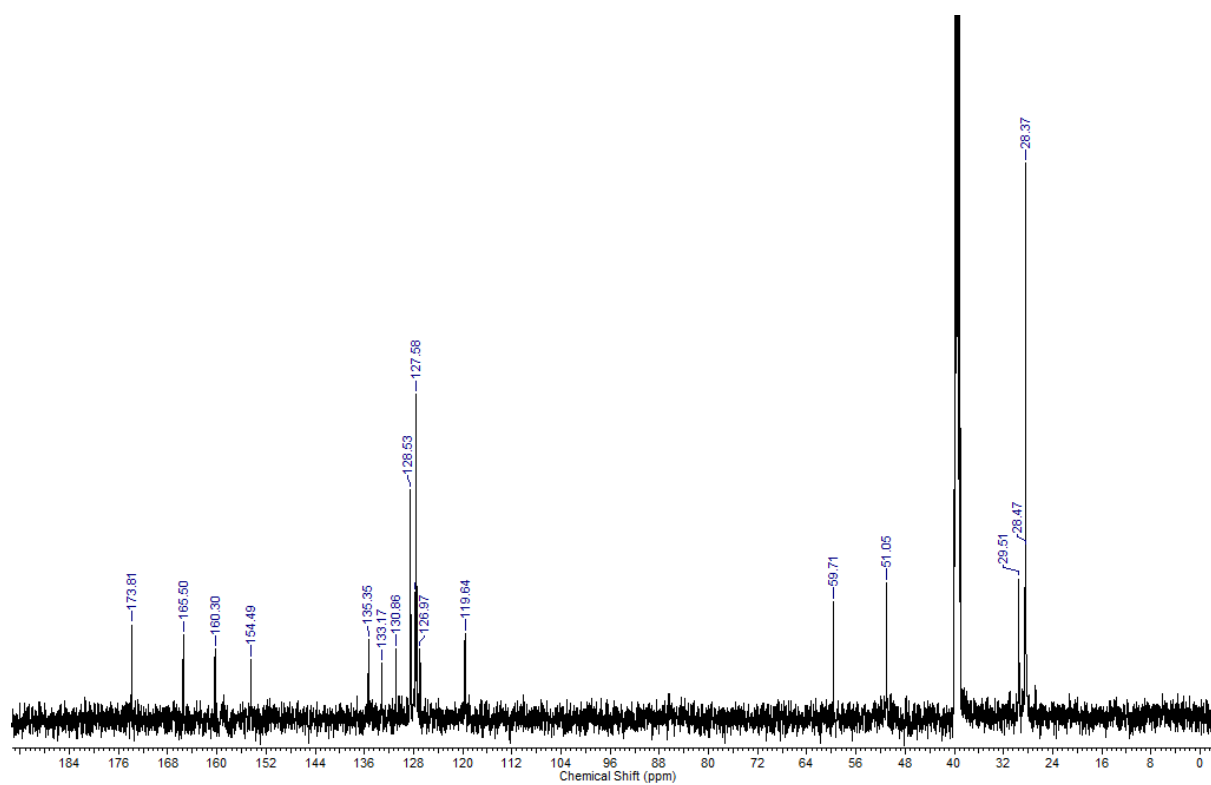
¹³C NMR spectrum of compound **9e**



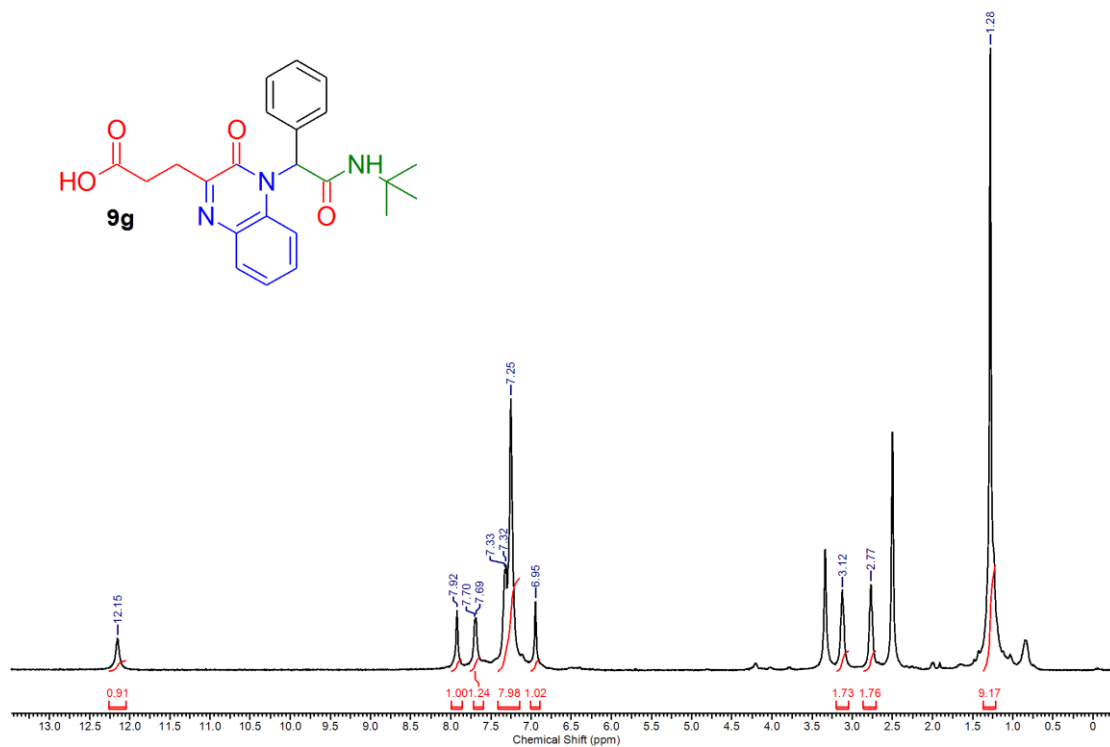
^1H NMR spectrum of compound **9f**



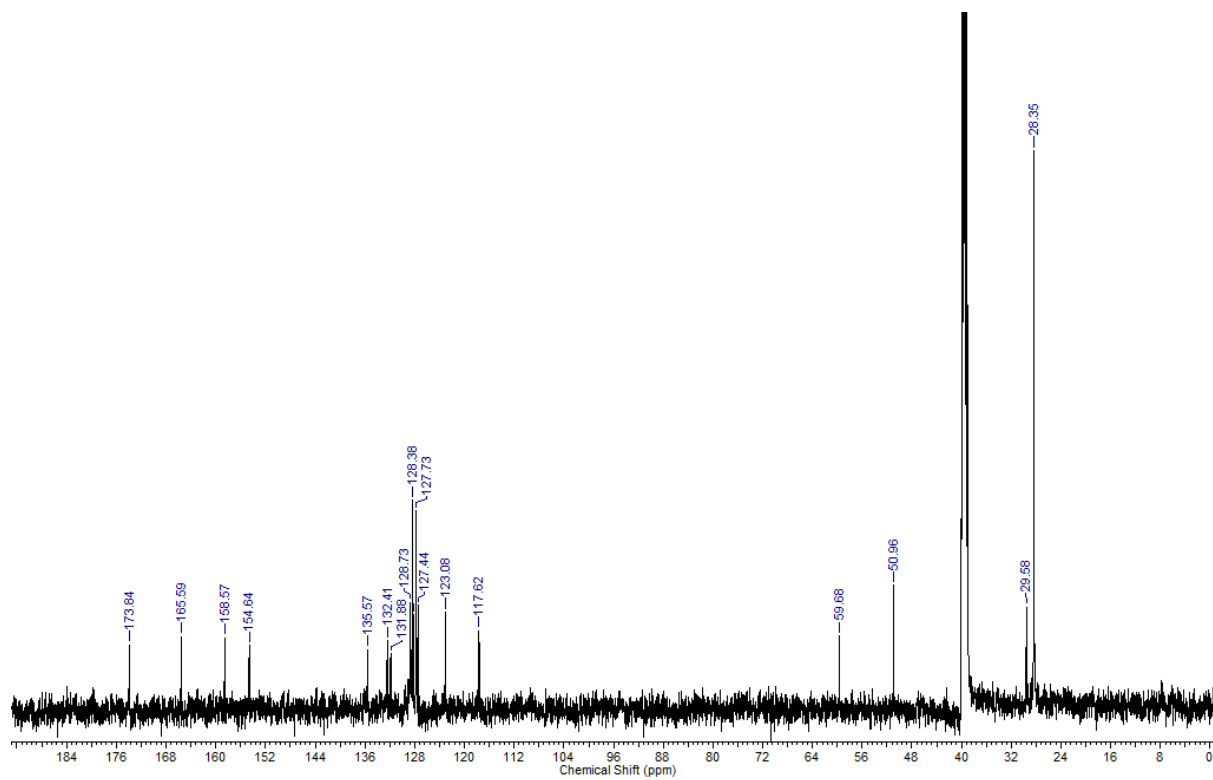
^{13}C NMR spectrum of compound **9f**



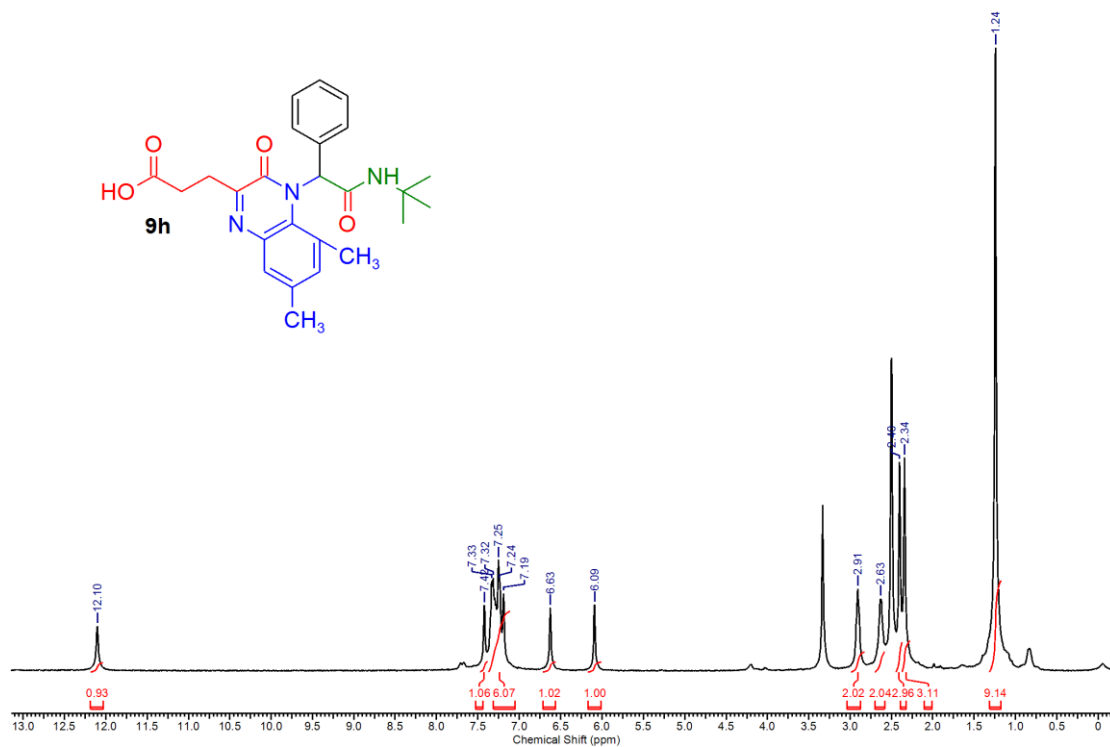
¹H NMR spectrum of compound **9g**



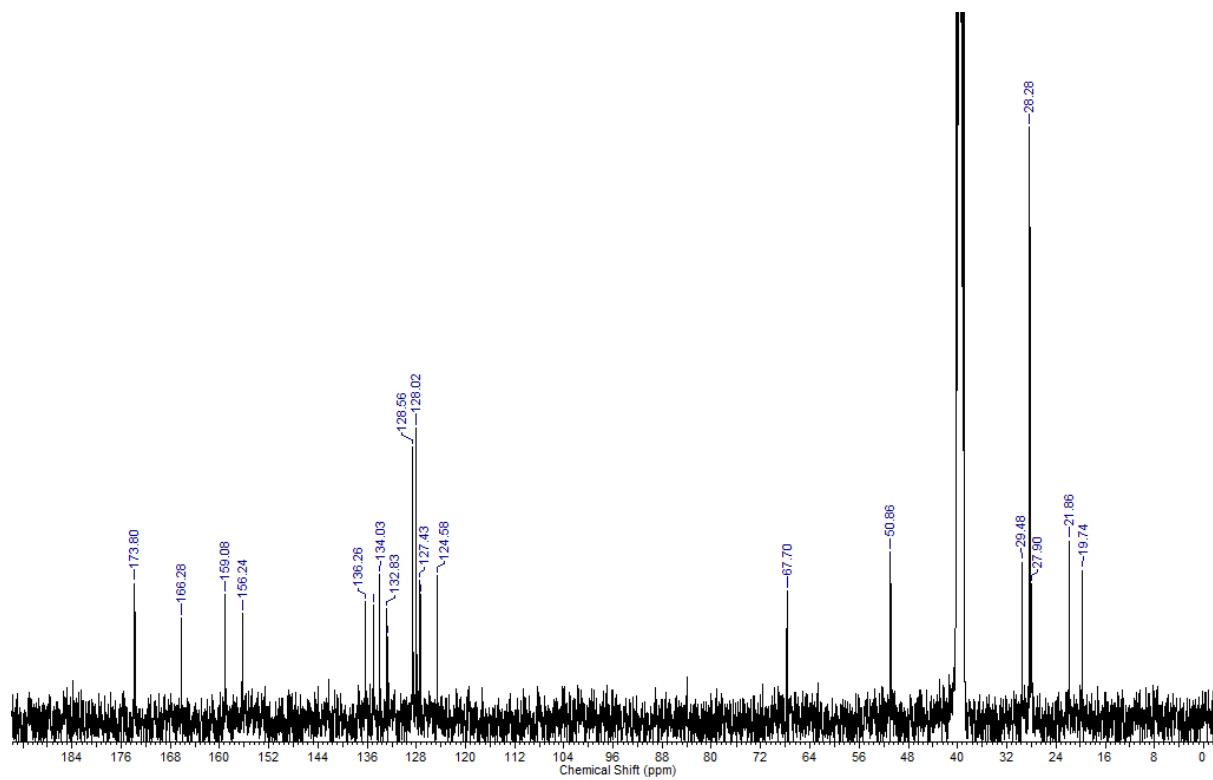
¹³C NMR spectrum of compound **9g**



¹H NMR spectrum of compound **9h**



¹³C NMR spectrum of compound **9h**



References

1. Seki, M.; Takahashi, Y. *J. Org. Chem.* **2021**, *86*, 7842–7848. doi:10.1021/acs.joc.1c00734
2. Fang, H.; Dou, Y.; Ge, J.; Chhabra, M.; Sun, H.; Zhang, P.; Zheng, Y.; Zhu, Q. *J. Org. Chem.* **2017**, *82*, 11212–11217. doi:10.1021/acs.joc.7b01594
3. Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Crystallogr.* **2009**, *42*, 339–341. doi:10.1107/S0021889808042726
4. Sheldrick, G. M. *Acta Crystallogr. Sect. A Found. Adv.* **2015**, *71*, 3–8. doi:10.1107/S2053273314026370
5. Sheldrick, G. M. *Acta Crystallogr. Sect. C Struct. Chem.* **2015**, *71*, 3–8. doi:10.1107/S2053229614024218