Electronic Supplementary Material (ESI) for MedChemComm.

Supporting Information for

Antitrypanosomal and antileishmanial activity of prenyl-1,2,3-triazoles.

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List of Supporting Information

Material and Methods

General Information

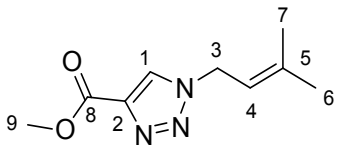
^{1}H and ^{13}C NMR spectra were acquired on a Bruker Avance II 300 MHz (75.13 MHz) using $CDCl_3$ as solvent. Chemical shifts (δ) were reported in ppm downfield from tetramethylsilane (TMS) at 0 ppm as internal standard and coupling constants (*J*) are in hertz (Hz). Chemical shifts for carbon nuclear magnetic resonance (^{13}C NMR) spectra are reported in parts per million relative to the center line of the $CDCl_3$ triplet at 76.9 ppm. The following abbreviations are used to indicate NMR signal multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, p = pentuplet, br = broad signal. Atmospheric Pressure Chemical Ionization tandem High-resolution mass spectra (APCI-HRMS) were recorded on a Bruker MicroTOF II with lock spray source. IR spectra were obtained using an FTIR Shimadzu spectrometer and only partial spectral data are listed. Chemical reagents were purchased from commercial suppliers and used without further purification, unless otherwise noted. Solvents were analytical grade or were purified by standard procedures prior to use. Yields were calculated for material judged homogeneous by thin layer chromatography (TLC) and nuclear magnetic resonance (^{1}H-NMR). All reactions were monitored by thin layer chromatography performed on silica gel 60 F_{254} pre-coated aluminum sheets, visualized by a 254 nm UV lamp, and stained with an ethanolic solution of 4-anisaldehyde. Column flash chromatography was performed using silica gel 60 (230–400 mesh).

General procedure for the Cu(I) mediated 1.3-dipolar cycloaddition

Alkyne (1 eq) and the azide (1.1 eq) were suspended in 10 mL/eq of *t*BuOH:H_2O (1:1) and then 1 M $CuSO_4$ solution, finally 1 M sodium ascorbate solution were added and the mixture was stirred overnight at room temperature. Brine was added and the solution was extracted with dichloromethane. Combined organic extracts were dried over sodium sulphate and evaporated. Products were purified by column chromatography in silica gel with increasing ethyl acetate/methanol gradients.

Synthesis of methyl 1-(3-methylbut-2-en-1-yl)-1H-1.2.3-triazole-4-carboxylate (IT-1).

Following the general reaction conditions for the CuAAC reaction, a 6% w/w prenyl azide solution in toluene (75 μL; 0.68 mmol) and methyl propiolate (178 mg, 2.03 mmol) was dissolved in *t*BuOH:H_2O (1:1, 4 mL). Then, a solution 1M of $CuSO_4$ was added (34 μL, 0.034 mmol) followed by the addition of a solution 1M of sodium ascorbate (135 μL; 0.135 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 109 mg of white solid (isolated yield: 83%).

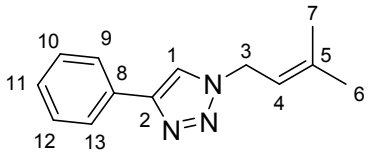


^{1}H NMR ($CDCl_3$): δ = 8.04 ppm (s, 1H, H triazole, C1–H); 5.45 (tq, 1H, $^{3}J_{H4\text{-}H3}$= 7.4 Hz and $^{4}J_{H4\text{-}H7}$=1.4 Hz, C4–H); 5.00 (d, 2H, $^{3}J_{H3\text{-}H4}$=7.3 Hz, C3–H); 3.95 (s, 3H, OMe, O–C9–H); 1.83 (s, 3H, methyl, C6–H) and 1.80 (s, 3H, methyl, C7–H). **^{13}C NMR** ($CDCl_3$): δ =161.2 (C8, carbonyl); 141.2 (C2, quaternary

triazole); 139.8 (C5, quaternary olefinic); 126.8 (C1, CH triazole); 116.2 (C4, CH olefinic); 52.1 (C9, OCH_3); 48.1 (C3, CH_2); 25.7 (C6, CH_3) and 18.1 (C7, CH_3). **HRMS** calculated for $C_9H_{14}N_3O_2$ 196.1081; found m/z 196.1084.

Synthesis of 1-(3-methylbut-2-en-1-yl)-4-phenyl-1*H*-1.2.3-triazole (IT-2).

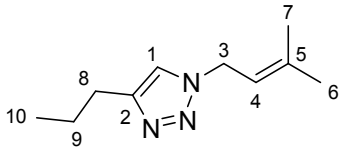
Following the general reaction conditions for the CuAAC reaction, a 6% w/w prenyl azide solution in toluene (75 μL; 0.68 mmol) and phenylacetylene (138 mg, 1.35 mmol) was dissolved in *t*BuOH:H_2O (1:1, 4 mL). Then, a solution 1M of $CuSO_4$ was added (34 μL, 0.034 mmol) followed by the addition of a solution 1M of sodium ascorbate (135 μL; 0.135 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 133 mg of white solid (isolated yield: 93%).



^{1}H NMR ($CDCl_3$): δ =7.82 ppm (m, 2H, *ortho* aromatic protons, Ar9–H and Ar13–H); 7.71 (s, 1H, H triazole, C1–H); 7.42 (m, 2H, *meta* aromatic protons, Ar10–H and Ar12–H); 7.32 (m, 1H, *para* aromatic proton, Ar11–H); 5.49 (tq, 1H, $^3J_{H4\text{-}H3}$= 7.3 Hz, $^4J_{H4\text{-}H7}$= 1.4 Hz, C4–H); 5.00 (d, 2H, $^3J_{H3\text{-}H4}$=7.3 Hz, C3–H) and 1.83 (s, 6H, methyl, C7–H and C6–H). **^{13}C NMR** ($CDCl_3$): δ = 147.7 (C2, quaternary triazole); 139.7 (C5, quaternary olefinic); 130.8 (C8, *ipso* aromatic); 128.8 (C10 and C12, *meta* aromatic); 128.0 (C11, *para* aromatic); 125.6 (C9 and C13, *ortho* aromatic); 119.2 (C1, CH triazole); 117.3 (C4, CH olefinic); 48.0 (C3, CH_2); 25.7 (C6, CH_3) and 18.1 (C7, CH_3). **HRMS** calculated for $C_{13}H_{16}N_3$ 214.1336; found m/z 214.1344.

Synthesis of 1-(3-methylbut-2-en-1-yl)-4-propyl-1H-1.2.3-triazole (IT-3).

Following the general reaction conditions for the CuAAC reaction, a 6% w/w prenyl azide solution in toluene (75 μL; 0.68 mmol) and 1-pentyne (138 mg, 2.03 mmol) was dissolved in *t*BuOH:H_2O (1:1, 4 mL). Then, a solution 1M of $CuSO_4$ was added (34 μL, 0.034 mmol) followed by the addition of a solution 1M of sodium ascorbate (135 μL; 0.135 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 89 mg of white solid (isolated yield: 74%).

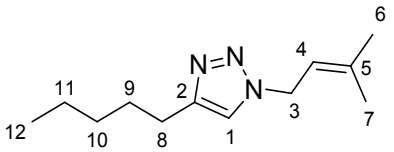


^{1}H NMR ($CDCl_3$): δ = 7.22 ppm (s, 1H, H triazole, C1–H); 5.41 (tq, 1H, $^3J_{H4\text{-}H3}$= 7.4 Hz and $^4J_{H4\text{-}H7}$=1.4 Hz, C4–H); 4.90 (d, 2H, $^3J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.67 (t, 2H, $^3J_{H8\text{-}H9}$ = 7.6 Hz, C8–H); 1.79 (s, 3H, methyl, C6–H); 1.78 (s, 3H, methyl, C7–H); 1.68 (h, 2H, ^3J = 7.6 Hz, C9–H) and 0.96 (t, 3H, ^3J = 7.5 Hz, methyl C10–H). **^{13}C NMR** ($CDCl_3$): δ =148.2 ppm (C2, quaternary triazole); 139.2 (C5, quaternary olefinic); 119.9 (C1, CH triazole); 117.6 (C4, CH olefinic); 47.8 (C3, CH_2); 27.7 (C8, CH_2); 25.6 (C6, CH_3); 22.7 (C9, CH_2); 18.0 (C7, CH_3) and 13.8 (C10, CH_3). **HRMS** calculated for $C_{10}H_{17}N_3$ 180.1494; found m/z 180.1501.

Synthesis of 1-(3-methylbut-2-en-1-yl)-4-pentyl-1H-1.2.3-triazole (IT-4).

Following the general reaction conditions for the CuAAC reaction, a 6% w/w prenyl azide solution in toluene (75 μL; 0.68 mmol) and 1-heptine (130 mg, 1.35 mmol) was dissolved in *t*BuOH:H_2O (1:1, 4

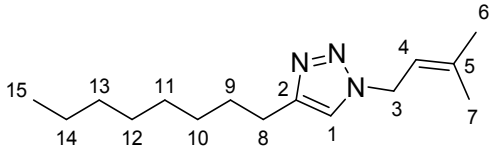
mL). Then, a solution 1M of $CuSO_4$ was added (34 μL, 0.034 mmol) followed by the addition of a solution 1M of sodium ascorbate (135 μL; 0.135 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 116 mg of white solid (isolated yield: 83%).



^{1}H NMR ($CDCl_3$): δ = 7.22 ppm (s, 1H, H triazole, C1–H); 5.42 (tq, 1H, $^3J_{H4\text{-}H3}$= 7.4 Hz and $^4J_{H4\text{-}H7}$=1.4 Hz, C4–H); 4.91 (d, 2H, $^3J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.69 (t, 2H, $^3J_{H8\text{-}H9}$= 7.6 Hz, C8–H); 1.80 (s, 3H, methyl, C6–H); 1.79 (s, 3H, methyl, C7–H); 1.66 (m, 2H, C9–H); 1.33 (m, 4H, C10–H and C11–H) and 0.89 (t, ^3J= 7.4 Hz, methyl, C12–H). **^{13}C NMR** ($CDCl_3$): δ =148.5 (C2, quaternary triazole); 139.2 (C5, quaternary olefinic); 119.8 (C1, CH triazole); 117.6 (C4, CH olefinic); 47.8 (C3, CH_2); 31.4 (C8, CH_2); 29.2 and 25.7 (C10 and C11, CH_2); 25.6 (C6, CH_3); 22.4 (C9, CH_2); 18.0 (C7, CH_3) and 14.0 (C12, CH_3). **HRMS** calculated for $C_{12}H_{22}N_3$ 208.1808; found m/z 208.1808.

Synthesis of 1-(3-methylbut-2-en-1-yl)-4-octyl-1H-1.2.3-triazole (IT-5).

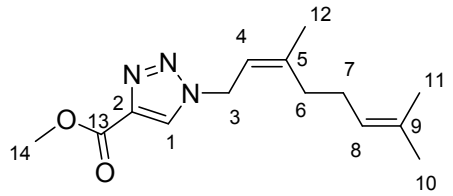
Following the general reaction conditions for the CuAAC reaction, a 6% w/w prenyl azide solution in toluene (75 μL mg; 0.68 mmol) and 1-decyne (95 mg, 0.75 mmol) was dissolved in *t*BuOH:H_2O (1:1, 4 mL). Then, a solution 1M of $CuSO_4$ was added (34 μL, 0.034 mmol) followed by the addition of a solution 1M of sodium ascorbate (135 μL; 0.135 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 134 mg of white solid (isolated yield: 80%).



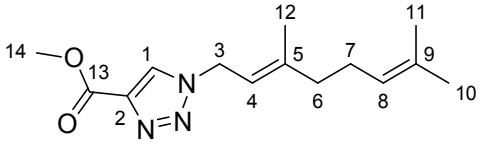
^{1}H NMR ($CDCl_3$): δ = 7.21 ppm (s, 1H, H triazole, C1–H); 5.41 (tq, 1H, $^3J_{H4\text{-}H3}$= 7.4 Hz and $^4J_{H4\text{-}H7}$=1.4 Hz, C4–H); 4.90 (d, 2H, $^3J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.69 (t, 2H, $^3J_{H8\text{-}H9}$ = 7.6 Hz, C8–H); 1.80 (s, 3H, methyl, C6–H); 1.78 (s, 3H, methyl, C7–H); 1.65 (m, 2H, C9–H); 1.29 (m, 10H, C10–H to C14–H) and 0.87 (t, $^3J_{H15\text{-}H14}$ = 7.4 Hz, methyl, C15–H); **^{13}C NMR** ($CDCl_3$): δ =148.4 ppm (C2, quaternary triazole); 139.0 (C5, quaternary olefinic); 119.8 (C1, CH triazole); 117.6 (C4, CH olefinic); 47.7 (C3, CH_2); 31.8 (C8, CH_2); 29.5, 29.3, 29.2, 29.1 and 25.7 (C10 to C14, CH_2); 25.6 (C6, CH_3); 22.6 (C9, CH_2); 17.9 (C7, CH_3) and 14.0 (C15, CH_3). **HRMS** calculated for $C_{15}H_{28}N_3$ 250.2278; found m/z 250.2285.

Synthesis of metil (*Z*)-methyl 1-(3.7-dimethylocta-2.6-dien-1-yl)-1H-1.2.3-triazole-4-carboxylate (IT-6) and (*E*)-methyl 1-(3.7-dimethylocta-2.6-dien-1-yl)-1H-1.2.3-triazole-4-carboxylate (IT-11).

Following the general reaction conditions for the CuAAC reaction, a mixture of monoterpene azide (50 mg; 0.28 mmol) and methyl propiolate (24 mg, 0.28 mmol) was dissolved in *t*BuOH:H_2O (1:1, 2 mL). Then, a solution 1M of $CuSO_4$ was added (12 μL, 0.01 mmol) followed by the addition of a solution 1M of sodium ascorbate (50 μL; 0.06 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 63 mg of white solid (isolated yield: 86%; ratio *E/Z*, 2:1).



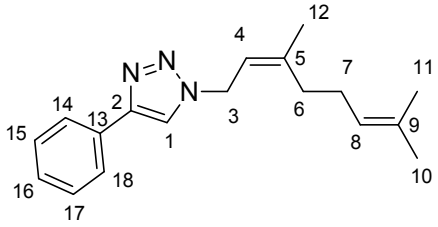
^{1}H NMR ($CDCl_3$): δ = 8.02 ppm (s, 1H, H triazole, C1–H); 5.44 (t, 1H, $^{3}J_{H4\text{-}H3}$ = 7.4 Hz, C4–H); 5.05 (m, 1H, C8–H); 4.99 (d, 2H, $^{3}J_{H3\text{-}H4}$=7.1 Hz, C3–H); 3.94 (s, 3H, OMe, O–C14–H); 2.14 (m, 4H, C6–H and C7–H); 1.83 (s, 3H, methyl, C12–H); 1.68 (s, 3H, methyl, C11–H) and 1.60 (s, 3H, methyl, C10–H). **^{13}C NMR** ($CDCl_3$): δ = 161.2 ppm (C13, carbonyl); 144.5 (C2, quaternary triazole); 139.9 (C9, quaternary olefinic); 132.2 (C5, quaternary olefinic); 126.8 (C1, CH triazole); 123.2 (C8, CH olefinic); 116.8 (C4, CH olefinic); 52.1 (C14, OCH_3); 47.9 (C3, CH_2); 32.1 (C6, CH_2); 26.1 (C7, CH_2); 25.7 (C10, CH_3); 23.4 (C12, CH_3) and 17.7 (C11, CH_3).



^{1}H NMR ($CDCl_3$): δ = 8.04 ppm (s, 1H, H triazole, C1–H); 5.44 (t, 1H, $^{3}J_{H4\text{-}H3}$ = 7.4 Hz, C4–H); 5.05 (m, 1H, C8–H); 5.00 (d, 2H, $^{3}J_{H3\text{-}H4}$=7.1. Hz, C3–H); 3.95 (s, 3H, OMe, O–C14–H); 2.15 (m, 4H, C6–H and C7–H); 1.78 (s, 3H, methyl, C12–H); 1.69 (s, 3H, methyl, C11–H) and 1.60 (s, 3H, methyl, C10–H). **^{13}C NMR** ($CDCl_3$): δ = 161.2 ppm (C13, carbonyl); 147.7 (C2, quaternary triazole); 139.8 (C9, quaternary olefinic); 132.9 (C5, quaternary olefinic); 126.7 (C1, CH triazole); 123.3 (C8, CH olefinic); 116.0 (C4, CH olefinic); 52.1 (C14, OCH_3); 48.1 (C3, CH_2); 39.3 (C6, CH_2); 26.0 (C7, CH_2); 25.6 (C10, CH_3); 17.7 (C11, CH_3) and 16.5 (C12, CH_3).

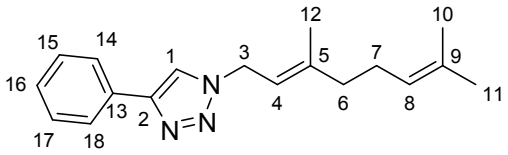
Synthesis of (*Z*)-1-(3.7-dimethylocta-2.6-dien-1-yl)-4-phenyl-1H-1.2.3-triazole (IT-7) and (*E*)-1-(3.7-dimethylocta-2.6-dien-1-yl)-4-phenyl-1H-1.2.3-triazole (IT-12).

Following the general reaction conditions for the CuAAC reaction, a mixture of monoterpene azide (50 mg; 0.28 mmol) and phenylacetylene (29 mg, 0.28 mmol) was dissolved in *t*BuOH:H_2O (1:1, 2 mL). Then, a solution 1M of $CuSO_4$ was added (12 μL, 0.01 mmol) followed by the addition of a solution 1M of sodium ascorbate (50 μL; 0.06 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 59 mg of white solid (isolated yield: 75%; ratio *E/Z*, 2:1).



^{1}H NMR ($CDCl_3$): δ = 7.81 ppm (m, 2H, *ortho* aromatic protons, Ar14–H and Ar18–H); 7.71 (s, 1H, H triazole, C1–H); 7.42 (m, 2H, *meta* aromatic protons, Ar15–H and Ar17–H); 7.32 (m, 1H, *para* aromatic próton, Ar16–H); 5.48 (t, 1H, $^{3}J_{H4\text{-}H3}$=7.3 Hz, C4–H); 5.03 (m, 1H, C8–H); *5*.00 (d, 2H, $^{3}J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.20 (m, 2H, C6–H); 2.13 (m, 2H, C7–H); 1.83 (s, 3H, methyl, C12–H); 1.68 (s, 3H, methyl, C10–H) and 1.61 (s, 3H, methyl, C11–H). **^{13}C NMR** ($CDCl_3$): δ = 147.7 ppm (C2, quaternary triazole); 143.2 (C9, quaternary olefinic); 132.6 (C5, quaternary olefinic); 130.8 (C13, *ipso* aromatic); 128.8 (C15 and C17, *meta*

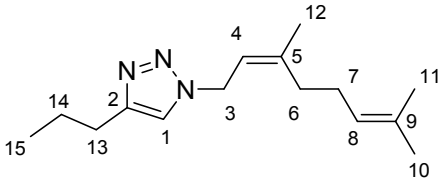
aromatic); 128.0 (C16, *para* aromatic); 125.7 (C14 and C18, *ortho* aromatic); 123.2 (C8, CH olefinic); 117.9 (C4, CH olefinic); 117.1 (C1, CH triazole); 47.8 (C3, CH_2); 32.1 (C6, CH_2); 26.2 (C7, CH_2); 25.7 (C10, CH_3); 23.4 (C12, CH_3) and 17.7 (C11, CH_3). **HRMS** calculated for $C_{18}H_{24}N_3$ 282.1970; found m/z 282.1961.



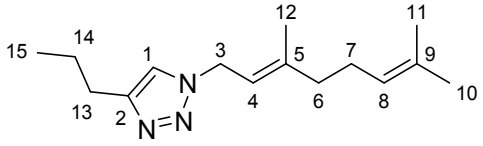
^{1}H NMR ($CDCl_3$): δ = 7.81 ppm (m, 2H, *ortho* aromatic protons, Ar14–H and Ar18–H); 7.70 (s, 1H, H triazole, C1–H); 7.42 (m, 2H, *meta* aromatic protons, Ar15–H and Ar17–H); 7.32 (m, 1H, *para* aromatic próton, Ar16–H); 5.48 (t, 1H, $^3J_{H4\text{-}H3}$=7.3 Hz, C4–H); 5.03 (m, 1H, C8–H); *5*.00 (d, 2H, $^3J_{H3\text{-}H4}$=7.0 Hz, C3–H); 2.20 (m, 2H, C6–H); 2.13 (m, 2H, C7–H); 1.81 (s, 3H, methyl, C12–H); 1.68 (s, 3H, methyl, C11–H) and 1.62 (s, 3H, methyl, C10–H). **^{13}C NMR** ($CDCl_3$): δ = 147.7 ppm (C2, quaternary triazole); 143.1 (C9, quaternary olefinic); 132.1 (C5, quaternary olefinic); 130.8 (C13, *ipso* aromatic); 128.8 (C15 and C17, *meta* aromatic); 128.0 (C16, *para* aromatic); 125.7 (C14 and C18, *ortho* aromatic); 123.4 (C8, CH olefinic); 119.0 (C4, CH olefinic); 117.1 (C1, CH triazole); 47.9 (C3, CH_2); 39.4 (C6, CH_2); 26.1 (C7, CH_2); 25.7 (C10, CH_3); 17.7 (C11, CH_3) and 16.5 (C12, CH_3). **HRMS** calculated for $C_{18}H_{24}N_3$ 282.1970; found m/z 282.1957.

Synthesis of (*Z*)-1-(3.7-dimethylocta-2.6-dien-1-yl)-4-propyl-1H-1.2.3-triazole (IT-8) and (*E*)-1-(3.7-dimethylocta-2.6-dien-1-yl)-4-propyl-1H-1.2.3-triazole (IT-13).

Following the general reaction conditions for the CuAAC reaction, a mixture of monoterpene azide (50 mg; 0.28 mmol) and 1-pentyne (19 mg, 0.28 mmol) was dissolved in *t*BuOH:H_2O (1:1, 2 mL). Then, a solution 1M of $CuSO_4$ was added (12 μL, 0.01 mmol) followed by the addition of a solution 1M of sodium ascorbate (50 μL; 0.06 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 59 mg of white solid (isolated yield: 87%; ratio *E/Z*, 2:1).



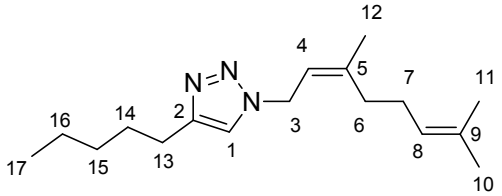
^{1}H NMR ($CDCl_3$): δ = 7.21 ppm (s, 1H, H triazole, C1–H); 5.41 (dt, 1H, $^3J_{H4\text{-}H3}$= 7.4 Hz and $^4J_{H4\text{-}H12}$=1.4 Hz, C4–H); 5.09 (dt, 1H, $^3J_{H8\text{-}H7}$= 7.2 Hz and $^4J_{H8\text{-}H10}$=1.4 Hz, C8–H); 4.90 (d, 2H, $^3J_{H3\text{-}H4}$=7.2 Hz, C3–H); 2.63 (t, 2H, $^3J_{H13\text{-}H14}$ = 7.6 Hz, C13–H); 2.13 (m, 4H, C6–H and C7–H); 1.80 (s, 3H, methyl, C12–H); 1.67 (s, 3H, methyl, C11–H); 1.68 (hexuplete, 2H, $^3J_{H15\text{-}H14\text{-}H13}$=7.5 Hz, C14–H); 1.61 (s, 3H, methyl, C10–H) and 0.96 (t, 3H, $^3J_{H15\text{-}H14}$= 7.3 Hz, methyl, C15–H). **^{13}C NMR** ($CDCl_3$): δ = 148.3 ppm (C2, quaternary triazole); 142.6 (C9, quaternary olefinic); 132.6 (C5, quaternary olefinic); 123.2 (C8, CH olefinic); 119.9 (C1, CH triazole); 118.2 (C4, CH olefinic); 47.6 (C3, CH_2); 32.0 (C6, CH_2); 27.8 (C13, CH_2); 26.3 (C7, CH_2); 25.7 (C10, CH_3); 23.4 (C12, CH_3); 22.8 (C14, CH_2); 17.7 (C11, CH_3) and 13.8 (C15, CH_3). **HRMS** calculated for $C_{15}H_{26}N_3$ 248.2127; found m/z 248.2134.



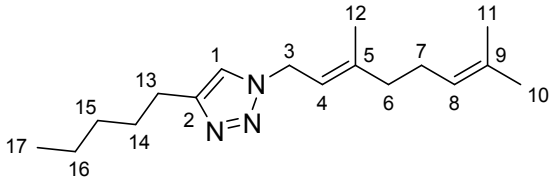
^{1}H NMR ($CDCl_3$): δ = 7.20 (s, 1H, H triazole, C1–H); 5.39 (dt, 1H, $^3J_{H4\text{-}H3}$= 7.4 Hz and $^4J_{H4\text{-}H12}$=1.4 Hz, C4–H); 5.09 (dt, 1H, $^3J_{H8\text{-}H7}$= 7.2 Hz and $^4J_{H8\text{-}H10}$=1.4 Hz, C8–H); 4.92 (d, 2H, $^3J_{H3\text{-}H4}$=7.2 Hz, C3–H); 2.67 (t, 2H, $^3J_{H13\text{-}H14}$ = 7.6 Hz, C13–H); 2.10 (m, 4H, C6–H and C7–H); 1.76 (s, 3H, methyl, C12–H); 1.69 (s, 3H, methyl, C11–H); 1.68 (hexuplete, 2H, $^3J_{H14\text{-}H15}$=7.5 Hz, C14–H); 1.59 (s, 3H, methyl, C10–H) and 0.96 (t, 3H, $^3J_{H15\text{-}H14}$= 7.3 Hz, methyl, C15–H). **^{13}C NMR** ($CDCl_3$): δ = 148.2 (C2, quaternary triazole); 142.7 (C9, quaternary olefinic); 132.6 (C5, quaternary olefinic); 123.2 (C8, CH olefinic); 119.9 (C1, CH triazole); 117.4 (C4, CH olefinic); 47.7 (C3, CH_2); 39.4 (C6, CH_2); 27.8 (C13, CH_2); 26.1 (C7, CH_2); 25.7 (C10, CH_3); 22.8 (C14, CH_2); 17.7 (C11, CH_3); 16.4 (C12, CH_3) and 13.8 (C15, CH_3). **HRMS** calculated for $C_{15}H_{26}N_3$ 248.2127; found m/z 248.2131.

Synthesis of (*Z*)-1-(3.7-dimethylocta-2.6-dien-1-yl)-4-pentyl-1H-1.2.3-triazole (IT-9) and (*E*)-1-(3.7-dimethylocta-2.6-dien-1-yl)-4-pentyl-1H-1.2.3-triazole (IT-14).

Following the general reaction conditions for the CuAAC reaction, a mixture of monoterpene azide (50 mg; 0.28 mmol) and 1-heptyne (27 mg, 0.28 mmol) was dissolved in *t*BuOH:H_2O (1:1, 2 mL). Then, a solution 1M of $CuSO_4$ was added (12 μL, 0.01 mmol) followed by the addition of a solution 1M of sodium ascorbate (50 μL; 0.06 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 65 mg of white solid (isolated yield: 85%; ratio *E/Z*, 2:1).



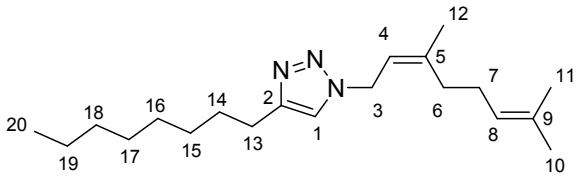
^{1}H NMR ($CDCl_3$): δ = 7.21 (s, 1H, H triazole, C1–H); 5.41 (dt, 1H, $^3J_{H4\text{-}H3}$= 7.3 Hz and $^4J_{H4\text{-}H12}$=1.4 Hz, C4–H); 5.08 (tt, 1H, $^3J_{H8\text{-}H7}$= 7.2 Hz and $^4J_{H8\text{-}H10}$=1.4 Hz, C8–H); 4.90 (d, 2H, $^3J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.68 (t, 2H, $^3J_{H13\text{-}H14}$ = 7.6 Hz, C13–H); 2.16 (m, 4H, C6–H and C7–H); 1.79 (s, 3H, methyl, C12–H); 1.67 (s, 3H, methyl, C11–H); 1.65 (m, 2H, C14–H); 1.60 (s, 3H, methyl, C10–H); 1.33 (m, 4H, C15–H and C16–H) and 0.88 (t, 3H, $^3J_{H17\text{-}H16}$ = 7.3 Hz, methyl, C17–H). **^{13}C NMR** ($CDCl_3$): δ = 148.5 (C2, quaternary triazole); 142.5 (C9, quaternary olefinic); 132.6 (C5, quaternary olefinic); 123.2 (C8, CH olefinic); 119.8 (C1, CH triazole); 118.2 (C4, CH olefinic); 47.6 (C3, CH_2); 32.1 (C6, CH_2); 31.4 (C15, CH_2); 29.6 (C14, CH_2); 26.2 (C7, CH_2); 25.7 (C10, CH_3); 25.7 (C13, CH_2); 23.4 (C12, CH_3); 22.4 (C16, CH_2); 17.7 (C11, CH_3) and 14.0 (C17, CH_3).



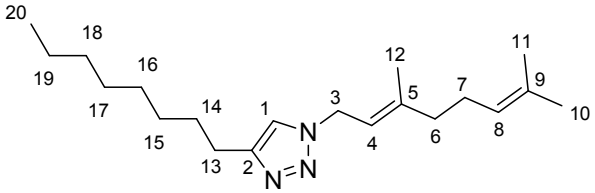
^{1}H NMR ($CDCl_3$): δ = 7.20 (s, 1H, H triazole, C1–H); 5.41 (t, 1H, $^3J_{H4\text{-}H3}$= 7.3 Hz, C4–H); 5.06 (m, 1H, C8–H); 4.92 (d, 2H, $^3J_{H3\text{-}H4}$=7.2 Hz, C3–H); 2.68 (t, 2H, $^3J_{H13\text{-}H14}$ = 7.6 Hz, C13–H); 2.10 (m, 4H, C6–H and C7–H); 1.76 (s, 3H, methyl, C12–H); 1.67 (s, 3H, methyl, C11–H); 1.65 (m, 2H, C14–H); 1.59 (s, 3H, methyl, C10–H); 1.34 (m, 4H, C15–H and C16–H) and 0.88 (t, 3H, $^3J_{H17\text{-}H16}$ = 7.3 Hz, methyl, C17–H). **^{13}C NMR** ($CDCl_3$): δ = 148.5 (C2, quaternary triazole); 142.7 (C9, quaternary olefinic); 132.1 (C5, quaternary olefinic); 123.5 (C8, CH olefinic); 119.8 (C1, CH triazole); 117.4 (C4, CH olefinic); 47.6 (C3, CH_2); 39.4 (C6, CH_2); 31.5 (C15, CH_2); 29.2 (C14, CH_2); 26.1 (C7, CH_2); 25.7 (C10, CH_3); 25.7 (C13, CH_2); 22.4 (C16, CH_2); 17.7 (C11, CH_3); 16.4 (C12, CH_3) and 14.1 (C17, CH_3).

Synthesis of (*Z*)-1-(3.7-dimethylocta-2.6-dien-1-yl)-4-octyl-1H-1.2.3-triazole (IT-10) and (*E*)-1-(3.7-dimethylocta-2.6-dien-1-yl)-4-octyl-1H-1.2.3-triazole (IT-15).

Following the general reaction conditions for the CuAAC reaction, a mixture of monoterpene azide (50 mg; 0.28 mmol) and 1-decyne (39 mg, 0.28 mmol) was dissolved in *t*BuOH:H_2O (1:1, 2 mL). Then, a solution 1M of $CuSO_4$ was added (12 μL, 0.01 mmol) followed by the addition of a solution 1M of sodium ascorbate (50 μL; 0.06 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 73 mg of white solid (isolated yield: 82%; ratio *E/Z*, 2:1).



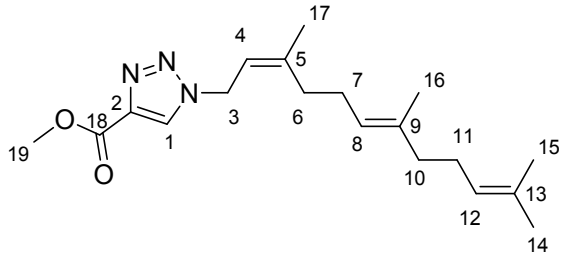
^{1}H NMR ($CDCl_3$): δ = 7.21 (s, 1H, H triazole, C1–H); 5.42 (t, 1H, $^3J_{H4\text{-}H3}$= 7.2 Hz, C4–H); 5.09 (m, 1H, C8–H); 4.90 (d, 2H, $^3J_{H3\text{-}H4}$=7.2 Hz, C3–H); 2.69 (t, 2H, $^3J_{H13\text{-}H14}$ = 7.7 Hz, C13–H); 2.11 (m, 4H, C6–H and C7–H); 1.80 (s, 3H, methyl, C12–H); 1.69 (s, 3H, methyl, C11–H); 1.68 (m, 2H, C14–H); 1.61 (s, 3H, methyl, C10–H); 1.26 (m, 10H, C15–H a C19–H) and 0.87 (t, 3H, $^3J_{H20\text{-}H19}$ = 6.8 Hz, methyl, C20–H). **^{13}C NMR** ($CDCl_3$): δ = 148.5 (C2, quaternary triazole); 142.5 (C9, quaternary olefinic); 132.6 (C5, quaternary olefinic); 123.2 (C8, CH olefinic); 119.8 (C1, CH triazole); 118.2 (C4, CH olefinic); 47.5 (C3, CH_2); 39.4 (C6, CH_2); 31.8 (C18, CH_2); 29.5, 29.3, 29.3 and 29.2 (C14 to C17, CH_2); 26.3 (C7, CH_2); 25.7 (C10, CH_3); 25.7 (C13, CH_2); 23.3 (C12, CH_3); 22.6 (C19, CH_2); 17.7 (C11, CH_3) and 14.0 (C20, CH_3). **HRMS** calculated for $C_{20}H_{36}N_3$ 318.2909. found m/z 318.2923.



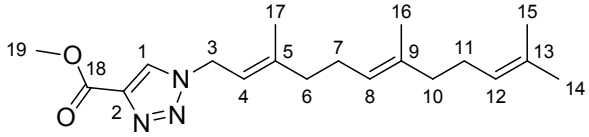
^{1}H NMR ($CDCl_3$): δ = 7.20 (s, 1H, H triazole, C1–H); 5.41 (t, 1H, $^3J_{H4\text{-}H3}$= 7.1 Hz, C4–H); 5.05 (m, 1H, C8–H); 4.92 (d, 2H, $^3J_{H3\text{-}H4}$=7.1 Hz, C3–H); 2.69 (t, 2H, $^3J_{H13\text{-}H14}$ = 7.7 Hz, C13–H); 2.10 (m, 4H, C6–H and C7–H); 1.76 (s, 3H, methyl, C12–H); 1.67 (s, 3H, methyl, C11–H); 1.66 (m, 2H, C14–H); 1.60 (s, 3H, methyl, C10–H); 1.26 (m, 10H, C15–H a C19–H) and 0.87 (t, 3H, $^3J_{H20\text{-}H19}$= 6.8 Hz, methyl, C20–H). **^{13}C NMR** ($CDCl_3$): δ = 148.5 (C2, quaternary triazole); 142.6 (C9, quaternary olefinic); 132.0 (C5, quaternary olefinic); 123.5 (C8, CH olefinic); 119.8 (C1, CH triazole); 117.4 (C4, CH olefinic); 47.7 (C3, CH_2); 32.9 (C6, CH_2); 31.8 (C18, CH_2); 29.6, 29.3, 29.3 and 29.2 (C14 to C17, CH_2); 26.1 (C7, CH_2); 25.8 (C10, CH_3); 25.7 (C13, CH_2); 22.6 (C19, CH_2); 17.7 (C11, CH_3); 16.4 (C12, CH_3) and 14.1 (C20, CH_3). **HRMS** calculated for $C_{20}H_{36}N_3$ 318.2909. found m/z 318.2924.

Synthesis of methyl 1-((2*Z*,6*E*)-3.7.11-trimethyldodeca-2.6.10-trien-1-yl)-1H-1.2.3-triazole-4-carboxylate (IT-16) and methyl 1-((2*E*,6*E*)-3.7.11-trimethyldodeca-2.6.10-trien-1-yl)-1H-1.2.3-triazole-4-carboxylate (IT-21).

Following the general reaction conditions for the CuAAC reaction, a mixture of sesquiterpene azide (50 mg; 0.20 mmol) and methyl propiolate (36 mg, 0.20 mmol) was dissolved in *t*BuOH:H_2O (1:1, 2 mL). Then, a solution 1M of $CuSO_4$ was added (10 μL, 0.01 mmol) followed by the addition of a solution 1M of sodium ascorbate (40 μL; 0.04 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 48 mg of white solid (isolated yield: 72%; ratio *E/Z*, 1.9:1).



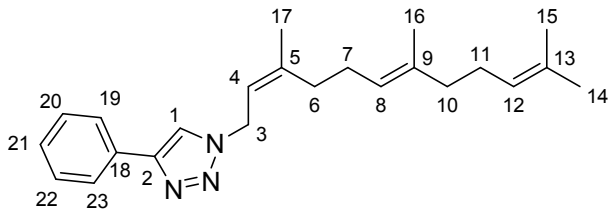
^{1}H NMR ($CDCl_3$): δ = 8.04 ppm (s, 1H, H triazole, C1–H); 5.43 (t, 1H, $^{3}J_{H4\text{-}H3}$=7.3 Hz, C4–H); 5.08 (m, 1H, C8–H); 5.06 (m, 1H, C12–H); 4.99 (d, 2H, $^{3}J_{H3\text{-}H4}$=7.1 Hz, C3–H); 3.94 (s, 3H, methyl, C19–H); 2.19 (m, 4H, C6–H and C7–H); 1.99 (m, 4H, C10–H and C11–H); 1.83 (s, 3H, methyl, C17–H); 1.67 (s, 3H, methyl, C16–H); 1.60 (s, 3H, methyl, C15–H) and 1.59 (s, 3H, methyl, C14–H). **^{13}C NMR** ($CDCl_3$): δ = 161.3 ppm (C18, carbonyl); 144.7 (C2, quaternary triazole); 139.9 (C9, quaternary olefinic); 136.6 (C5, quaternary olefinic); 131.5 (C13, quaternary olefinic); 126.8 (C1, CH triazole); 124.1 (C12, CH olefinic); 122.7 (C8, CH olefinic); 116.7 (C4, CH olefinic); 52.1 (C19, CH_3); 48.0 (C3, CH_2); 39.7 (C10, CH_2); 32.1 (C6, CH_2); 26.6 (C11, CH_2); 26.2 (C7, CH_2); 25.7 (C14, CH_3); 23.5 (C17, CH_3); 17.7 (C15, CH_3) and 16.0 (C16, CH_3). **HRMS** calculated for $C_{19}H_{30}N_3O_2$ 332.2338; found m/z 332.2343.



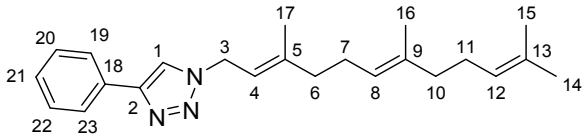
^{1}H NMR ($CDCl_3$): δ = 8.01 ppm (s, 1H, H triazole, C1–H); 5.44 (dt, 1H, $^{3}J_{H4\text{-}H3}$=7.3 Hz and $^{4}J_{H4\text{-}H17}$=1.0 Hz, C4–H); 5.06 (m, 2H, C8–H and C12–H); 5.00 (d, 2H, $^{3}J_{H3\text{-}H4}$=7.4 Hz, C3–H); 3.93 (s, 3H, methyl, C19–H); 2.12 (m, 4H, C6–H and C7–H); 2.00 (m, 4H, C10–H and C11–H); 1.78 (s, 3H, methyl, C17–H); 1.66 (s, 3H, methyl, C16–H); 1.58 (s, 3H, methyl, C15–H) and 1.58 (s, 3H, methyl, C14–H). **^{13}C NMR** ($CDCl_3$): δ = 161.2 ppm (C18, carbonyl); 144.8 (C2, quaternary triazole); 139.9 (C9, quaternary olefinic); 136.0 (C5, quaternary olefinic); 131.4 (C13, quaternary olefinic); 126.7 (C1, CH triazole); 124.2 (C12, CH olefinic); 123.1 (C8, CH olefinic); 116.0 (C4, CH olefinic); 52.1 (C19, CH_3); 48.1 (C3, CH_2); 39.7 (C10, CH_2); 39.6 (C6, CH_2); 26.6 (C11, CH_2); 26.0 (C7, CH_2); 25.7 (C14, CH_3); 17.7 (C15, CH_3); 16.6 (C17, CH_3) and 16.0 (C16, CH_3). **HRMS** calculated for $C_{19}H_{30}N_3O_2$ 332.2338; found m/z 332.2343.

Synthesis of 4-phenyl-1-((2*Z*,6*E*)-3.7.11-trimethyldodeca-2.6.10-trien-1-yl)-1H-1.2.3-triazole (IT-17) and 4-phenyl-1-((2*E*,6*E*)-3.7.11-trimethyldodeca-2.6.10-trien-1-yl)-1H-1.2.3-triazole (IT-22).

Following the general reaction conditions for the CuAAC reaction, a mixture of sesquiterpene azide (50 mg; 0.20 mmol) and methyl phenylacetylene (21 mg, 0.20 mmol) was dissolved in *t*BuOH:H_2O (1:1, 2 mL). Then, a solution 1M of $CuSO_4$ was added (10 μL, 0.01 mmol) followed by the addition of a solution 1M of sodium ascorbate (40 μL; 0.04 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 57 mg of white solid (isolated yield: 81%; ratio *E/Z*, 1.9:1).



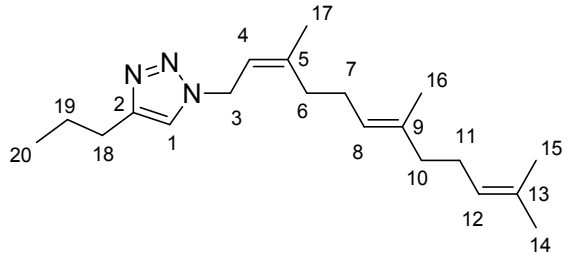
^{1}H NMR ($CDCl_3$): δ = 7.81 ppm (dt, 2H, aromatic proton *ortho*, Ar19–H and Ar23–H); 7.71 (s, 1H, H triazole, C1–H); 7.41 (tt, 2H, aromatic proton *meta* Ar20–H and Ar22–H); 7.31 (tt, 1H, aromatic proton *para* Ar21–H); 5.49 (t, 1H, $^3J_{H4\text{-}H3}$=7.3 Hz, C4–H); 5.31 (m, 1H, C12–H); 5.13 (m, 1H, C8–H); *5*.00 (d, 2H, $^3J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.20 (m, 4H, C6–H and C7–H); 2.02 (m, 4H, C10–H and C11–H); 1.84 (s, 3H, methyl, C17–H); 1.67 (s, 3H, methyl, C16–H); 1.62 (s, 3H, methyl, C15–H) and 1.59 (s, 3H, methyl, C14–H). **^{13}C NMR** ($CDCl_3$): δ = 147.8 ppm (C2, quaternary triazole); 143.3 (C9, quaternary olefinic); 136.4 (C5, quaternary olefinic); 131.5 (C13, quaternary olefinic); 130.8 (C18, aromatic *ipso*); 128.8 (C20 and C22, aromatic *meta*); 128.0 (C21, aromatic *para*); 125.7 (C19 and C23, aromatic *ortho*); 124.1 (C8, CH olefinic); 123.0 (C12, CH olefinic); 118.9 (C1, CH triazole); 117.8 (C4, CH olefinic); 47.8 (C3, CH_2); 39.8 (C10, CH_2); 32.1 (C6, CH_2); 26.6 (C11, CH_2); 26.3 (C7, CH_2); 25.7 (C14, CH_3); 23.4 (C17, CH_3); 17.7 (C15, CH_3) and 16.0 (C16, CH_3). **HRMS** calculated for $C_{23}H_{32}N_3$ 350.2596; found m/z 350.2595.



^{1}H NMR ($CDCl_3$): δ = 7.82 ppm (dt, 2H, aromatic proton *ortho*, Ar19–H and Ar23–H); 7.70 (s, 1H, H triazole, C1–H); 7.40 (tt, 2H, aromatic proton *meta* Ar20–H and Ar22–H); 7.31 (tt, 1H, aromatic proton *para* Ar21–H); 5.48 (t, 1H, $^3J_{H4\text{-}H3}$=7.3 Hz, C4–H); 5.10 (m, 1H, C12–H); 5.07 (m, 1H, C8–H); *5*.01 (d, 2H, $^3J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.15 (m, 4H, C6–H and C10–H); 2.00 (m, 4H, C7–H and C11–H); 1.82 (s, 3H, methyl, C17–H); 1.67 (s, 3H, methyl, C16–H); 1.60 (s, 3H, methyl, C15–H) and 1.58 (s, 3H, methyl, C14–H). **^{13}C NMR** ($CDCl_3$): δ = 147.8 ppm (C2, quaternary triazole); 143.4 (C9, quaternary olefinic); 135.8 (C5, quaternary olefinic); 131.4 (C13, quaternary olefinic); 130.8 (C18, aromatic *ipso*); 128.8 (C20 and C22, aromatic *meta*); 128.0 (C21, aromatic *para*); 125.7 (C19 and C23, aromatic *ortho*); 123.2 (C12, CH olefinic); 124.2 (C8, CH olefinic); 118.9 (C1, CH triazole); 117.0 (C4, CH olefinic); 48.0 (C3, CH_2); 39.7 (C6, CH_2); 39.4 (C10, CH_2); 26.7 (C11, CH_2); 26.0 (C7, CH_2); 25.7 (C14, CH_3); 17.7 (C15, CH_3); 16.5 (C17, CH_3) and 16.1 (C16, CH_3). **HRMS** calculated for $C_{23}H_{32}N_3$ 350.2596; found m/z 350.2595.

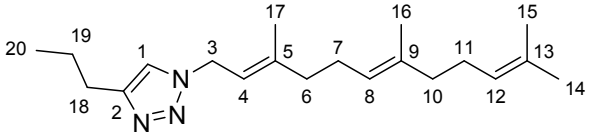
Synthesis of 4-propyl-1-((2*Z*,6*E*)-3.7.11-trimethyldodeca-2.6.10-trien-1-yl)-1H-1.2.3-triazole (IT-18) and 4-propyl-1-((2*Z*,6*E*)-3.7.11-trimethyldodeca-2.6.10-trien-1-yl)-1H-1.2.3-triazole (IT-23).

Following the general reaction conditions for the CuAAC reaction, a mixture of sesquiterpene azide (50 mg; 0.20 mmol) and 1-pentyne (40 mg, 0.40 mmol) was dissolved in *t*BuOH:H_2O (1:1, 2 mL). Then, a solution of 1M of $CuSO_4$ was added (10 μL, 0.01 mmol) followed by the addition of a solution 1M of sodium ascorbate (40 μL; 0.06 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 53 mg of white solid (isolated yield: 83%; ratio *E/Z*, 1.9:1).



^{1}H NMR ($CDCl_3$): δ = 7.21 ppm (s, 1H, H triazole, C1–H); 5.44 (dt, 1H, $^3J_{H4\text{-}H3}$=7.2 Hz and $^4J_{H4\text{-}H17}$=1.1 Hz, C4–H); 5.08 (m, 2H, C8–H and C12–H); 4.93 (d, 2H, $^3J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.65 (t, 2H, $^3J_{H18\text{-}H19}$=7.4

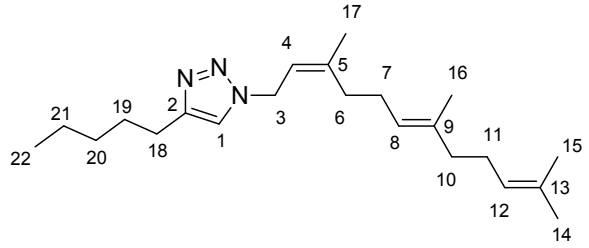
Hz, C18–H); 2.12 (m, 4H, C6–H and C7–H); 1.99 (m, 4H, C10–H and C11–H); 1.78 (s, 3H, methyl, C17–H); 1.68 (s, 3H, methyl, C16–H); 1.68 (q, 2H. $^{3}J_{H19\text{-}H20}$=7.4 Hz, C19–H); 1.61 (s, 3H, methyl, C15–H); 1.61 (s, 3H, methyl, C14–H) and 0.96 (t, 3H, $^{3}J_{H20\text{-}H19}$=7.3 Hz, methyl, C20–H). **^{13}C NMR** ($CDCl_3$): δ = 148.5 ppm (C2, quaternary triazole); 142.7 (C9, quaternary olefinic); 136.2 (C5, quaternary olefinic); 131.5 (C13, quaternary olefinic); 124.1 (C12, CH olefinic); 123.0 (C8, CH olefinic); 119.8 (C1, CH triazole); 118.2 (C4, CH olefinic); 47.6 (C3, CH_2); 39.7 (C10, CH_2); 32.1 (C6, CH_2); 27.8 (C18, CH_2); 26.6 (C11, CH_2); 26.3 (C7, CH_2); 25.7 (C14, CH_3); 23.4 (C17, CH_3); 22.4 (C19, CH_2); 17.7 (C15, CH_3); 16.0 (C16, CH_3) and 14.0 (C20, CH_3).



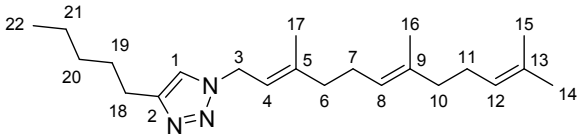
^{1}H NMR ($CDCl_3$): δ = 7.21 ppm (s, 1H, H triazole, C1–H); 5.41 (dt, 1H, $^{3}J_{H4\text{-}H3}$=7.2 Hz and $^{4}J_{H4\text{-}H17}$=1.1 Hz, C4–H); 5.08 (m, 2H, C8–H and C12–H); 4.93 (d, 2H, $^{3}J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.65 (t, 2H, $^{3}J_{H18\text{-}H19}$=7.4 Hz, C18–H); 2.12 (m, 4H, C6–H and C7–H); 1.99 (m, 4H, C10–H and C11–H); 1.78 (s, 3H, methyl, C17–H); 1.68 (q, 2H. $^{3}J_{H19\text{-}H20}$=7.4 Hz, C19–H); 1.67 (s, 3H, methyl, C16–H); 1.61 (s, 6H, methyls, C14–H and C15–H) and 0.96 (t, 3H, $^{3}J_{H20\text{-}H19}$=7.3 Hz, methyl, C20–H). **^{13}C NMR** ($CDCl_3$): δ = 148.5 ppm (C2, quaternary triazole); 142.7 (C9, quaternary olefinic); 135.7 (C5, quaternary olefinic); 131.4 (C13, quaternary olefinic); 124.2 (C12, CH olefinic); 123.3 (C8, CH olefinic); 119.8 (C1, CH triazole); 117.4 (C4, CH olefinic); 47.7 (C3, CH_2); 39.4 (C10, CH_2); 29.3 (C18, CH_2); 26.7 (C11, CH_2); 26.0 (C7, CH_2); 25.7 (C14, CH_3); 22.4 (C19, CH_2); 17.7 (C15, CH_3); 16.4 (C17, CH_3); 16.0 (C16, CH_3) and 14.0 (C20, CH_3).

Synthesis of 4-pentyl-1-((2*Z*,6*E*)-3.7.11-trimethyldodeca-2.6.10-trien-1-yl)-1H-1.2.3-triazole (IT-19) and 4-pentyl-1-((2*E*,6*E*)-3.7.11-trimethyldodeca-2.6.10-trien-1-yl)-1H-1.2.3-triazole (IT-24).

Following the general reaction conditions for the CuAAC reaction, a mixture of sesquiterpene azide (50 mg; 0.20 mmol) and 1-heptyne (50 mg, 0.40 mmol) was dissolved in *t*BuOH:H_2O (1:1, 2 mL). Then, a solution 1M of $CuSO_4$ was added (10 μL, 0.01 mmol) followed by the addition of a solution 1M of sodium ascorbate (40 μL; 0.06 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 63 mg of white solid (isolated yield: 89%; ratio *E/Z*, 1.9:1).



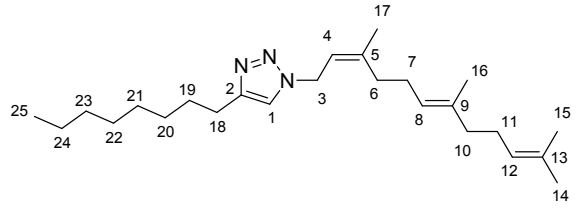
^{1}H NMR ($CDCl_3$): δ = 7.21 ppm (s, 1H, H triazole, C1–H); 5.41 (t, 1H, $^{3}J_{H4\text{-}H3}$=7.2 Hz, C4–H); 5.01 (m, 2H, C8–H and C12–H); 4.89 (d, 2H, $^{3}J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.67 (t, 2H, $^{3}J_{H18\text{-}H19}$=7.6 Hz, C18–H); 2.15 (m, 4H, C6–H and C7–H); 1.99 (m, 4H, C10–H and C11–H); 1.80 (s, 3H, methyl, C17–H); 1.67 (s, 3H, methyl, C16–H); 1.65 (m, 2H, C19–H); 1.61 (s, 6H, methyls, C14–H and C15–H); 1.32 (m, 4H, C20–H and C21–H) and 0.96 (t, 3H, $^{3}J_{H22\text{-}H21}$=7.3 Hz, methyl, C22–H). **^{13}C NMR** ($CDCl_3$): δ = 148.3 ppm (C2, quaternary triazole); 142.6 (C5, quaternary olefinic); 135.8 (C9, quaternary olefinic); 132.6 (C13, quaternary olefinic); 124.2 (C12, CH olefinic); 123.4 (C8, CH olefinic); 119.9 (C1, CH triazole); 118.2 (C4, CH olefinic); 47.6 (C3, CH_2); 32.4 (C6, CH_2); 27.8 (C18, CH_2); 26.2 (C11, CH_2); 26.0 (C7, CH_2); 25.7 (C14, CH_3); 23.4, 22.8 (C19 to C21, CH_2); 17.7 (C17, CH_3); 16.0 (C15 and C16, CH_3) and 13.8 (C22, CH_3).



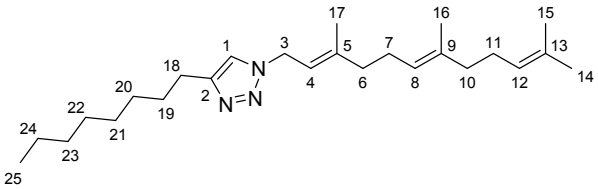
^{1}H NMR ($CDCl_3$): δ = 7.20 ppm (s, 1H, H triazole, C1–H); 5.41 (t, 1H, $^3J_{H8\text{-}H7}$=7.3Hz, C4–H); 5.01 (m, 2H, C8–H and C12–H); 4.92 (d, 2H, $^3J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.67 (t, 2H, $^3J_{H18\text{-}H19}$=7.6 Hz, C18–H); 2.10 (m, 4H, C6–H and C7–H); 1.99 (m, 4H, C10–H and C11–H); 1.76 (s, 3H, methyl, C17–H); 1.70 (s, 3H, methyl, C16–H); 1.65 (m, 2H, C19–H); 1.61 (s, 3H, methyl, C14–H); 1.59 (s, 3H, methyl, C15–H); 1.32 (m. 4H, C20–H and C21–H) and 0.96 (t, 3H, $^3J_{H20\text{-}H19}$=7.3 Hz, methyl, C22–H). **^{13}C NMR** ($CDCl_3$): δ = 148.2 ppm (C2, quaternary triazole); 142.7 (C5, quaternary olefinic); 135.8 (C9, quaternary olefinic); 131.4 (C13, quaternary olefinic); 124.2 (C12, CH olefinic); 123.4 (C8, CH olefinic); 119.9 (C1, CH triazole); 117.4 (C4, CH olefinic); 47.7 (C3, CH_2); 39.4 (C6 and C10, CH_2); 27.8 (C18, CH_2); 26.7 (C11, CH_2); 26.0 (C7, CH_2); 25.7 (C14, CH_3); 23.4, 22.8 (C19 to C21, CH_2); 17.7 (C17, CH_3); 16.4 and 16.0 (C15 and C16, CH_3) and 13.8 (C22, CH_3).

Synthesis of 4-octyl-1-((2*Z*,6*E*)-3.7.11-trimethyldodeca-2.6.10-trien-1-yl)-1H-1.2.3-triazole (IT-20) and 4-octyl-1-((2*E*,6*E*)-3.7.11-trimethyldodeca-2.6.10-trien-1-yl)-1H-1.2.3-triazole (IT-25).

Following the general reaction conditions for the CuAAC reaction, a mixture of sesquiterpene azide (50 mg; 0.20 mmol) and 1-decyne (28 mg, 0.20 mmol) was dissolved in *t*BuOH:H_2O (1:1, 2 mL). Then, a solution 1M of $CuSO_4$ was added (10 μL, 0.01 mmol) followed by the addition of a solution 1M of sodium ascorbate (40 μL; 0.06 mmol). After 8 h of continuous stirring at room temperature, the reaction was worked up and purified to afford 54 mg of white solid (isolated yield: 69%; ratio *E/Z*, 1.9:1).



^{1}H NMR ($CDCl_3$): δ = 7.21 ppm (s, 1H, H triazole, C1–H); 5.41 (t, 1H, $^3J_{H4\text{-}H3}$=6.8 Hz, C4–H); 5.01 (m, 2H, C8–H and C12–H); 4.91 (d, 2H, $^3J_{H3\text{-}H4}$=7.3 Hz, C3–H); 2.68 (t, 2H, $^3J_{H18\text{-}H19}$=7.8 Hz, C18–H); 2.15 a 1.90 (m, 8H, C6–H, C7–H, C10–H and C11–H); 1.80 (s, 3H, methyl, C17–H); 1.67 (s, 3H, methyl, C14–H); 1.61 (s, 6H, methyl, C15–H and C16–H); 1.25 (m, 12H, C19–H a C24–H) and 0.87 (t, 3H, $^3J_{H25\text{-}H24}$=6.7 Hz, methyl, C25–H). **^{13}C NMR** ($CDCl_3$): δ = 148.5 ppm (C2, quaternary triazole); 142.7 (C5, quaternary olefinic); 136.2 (C9, quaternary olefinic); 131.5 (C13, quaternary olefinic); 124.1 (C12, CH olefinic); 123.0 (C8, CH olefinic); 119.8 (C1, CH triazole); 118.1 (C4, CH olefinic); 47.6 (C3, CH_2); 32.1 (C6, CH_2); 31.8, 29.5, 29.3, 29.2, 23.4, 22.7 (C18 to C24, CH_2); 26.6 (C11, CH_2); 26.3 (C7, CH_2); 25.7 (C14, CH_3); 17.7 (C17, CH_3); 16.0 (C15 and C16, CH_3) and 14.1 (C25, CH_3). **HRMS** calculated for $C_{20}H_{36}N_3$ 318.2909; found m/z 318.2923.



H NMR ($CDCl_3$): δ = 7.20 ppm (s, 1H, H triazole, C1–H); 5.41 (t, 1H, $^3J_{H4\text{-}H3}$=7.2 Hz, C4–H); 5.41 (t, 1H, $^3J_{H8\text{-}H7}$=7.3Hz, C8–H); 5.07 (m, 2H, C8–H and C12–H); 4.91 (d, 2H, $^3J_{H3\text{-}H4}$=7.2 Hz, C3–H); 2.68 (t, 2H,

$^{3}J_{H18\text{-}H19}$=7.8 Hz, C18–H); 2.10 (m, 8H, C6–H, C7–H, C10–H and C11–H); 1.77 (s, 3H, methyl, C17–H); 1.67 (s, 3H, methyl, C14–H); 1.58 (s, 6H, methyl, C15–H and C16–H) 1.25 (m, 12H, C19–H a C24–H) and 0.87 (t, 3H, $^{3}J_{H25\text{-}H24}$=6.7 Hz, methyl, C25–H). **^{13}C NMR** ($CDCl_3$): δ = 148.5 ppm (C2, quaternary triazole); 142.7 (C5, quaternary olefinic); 135.7 (C9, quaternary olefinic); 131.4 (C13, quaternary olefinic); 124.2 (C12, CH olefinic); 123.3 (C8, CH olefinic); 119.8 (C1, CH triazole); 117.4 (C4, CH olefinic); 47.7 (C3, CH_2); 39.7 and 39.4 (C6 and C10, CH_2); 31.9, 29.6, 29.3, 29.2, 22.7 (C18 to C24, CH_2); 26.7 (C11, CH_2); 26.0 (C7, CH_2); 25.7 (C14, CH_3); 17.7 (C17, CH_3); 16.4 and 16.0 (C15 and C16, CH_3) and 14.1 (C22, CH_3). **HRMS** calculated for $C_{20}H_{36}N_3$ 318.2909; found m/z 318.2924

Biology

***In vitro T. cruzi* antiproliferative assays.**

Trypanosmoma cruzi epimastigotes from the CL-Brener strain were cultured in BHT medium at 28ºC. Trypanocidal activity of test compounds was measured as previously described.[1] Briefly, cultures (3-4 × 10^6 parasites/mL) were incubated with increasing amounts of each compound dissolved in DMSO (1% final concentration). Concentrations assayed ranged between 5 and 100 μg/mL with benznidazole used as positive control. Parasite growth was monitored by cell counting in a Neubauer chamber. Growth inhibition percentages were calculated as the ratio between parasite growth in the presence or absence of each compound after 72 hours of culture. Percentages of parasite growth inhibition for each concentration were plotted to determine the 50% inhibitory concentration (IC_{50}). Each experiment was conducted in triplicate and reported results correspond to the average of three independent experiments.

***In vitro* antileishmanial assays.**

Antileishmanial activity of the compounds was tested in vitroon, a culture of *Leishmania donovani* promastigotes (strain S1). Compounds with appropriate dilution were added to a 96 well microplate with promastigotes (2 × 10^6 cell/mL) reaching final concentrations of 40, 8 and 1.6 μg/mL. The plates were incubated at 26 ºC for 72 h and growth was determined by Alamar blue assay.[2] Pentamidine and Amphotericin B were used as standard antileishmanial agents.

All compounds were simultaneously tested for cytotoxicity against VERO (monkey kidney fibroblast) cells by Neutral Red assay,[3] and IC_{50} values were computed from the growth inhibition curve.

Inhibition Assay.

Sterol 14R-demethylase activity of TCCYP51 *in vitro* was reconstituted with cytochrome P450 reductase (CPR) from *Trypanosoma brucei* as an electron donor partner[4] and 24-methylenedihydrolanosterol (MDL) as a substrate.[5] The concentrated proteins were preincubated for 10 min at room temperature with dilauroyl-Rphosphatidylcholine (DLPC) at molar ratio TCCYP51:CPR:DLPC) 1:2:50. The final reaction mixture contained 1 μM TCCYP51 and 50 μM substrate (unlabeled and [^{3}H]-MDL were mixed to give ~2000 cpm/nmol and added from 1 mM stock solution in 45%, 2-hydroxypropyl-cyclodextrin) in 20 mM MOPS (pH 7.4), 50 mM KCl, 5 mM $MgCl_2$, 10% glycerol, 0.4 mg/mL isocitrate dehydrogenase, and 25 mM sodium isocitrate. For the inhibition assay, the reaction was performed in the presence of the increasing concentrations of the compounds tested as TCCYP51 inhibitors (concentration range 1-100 μM). After 5 min of preincubation with the inhibitors at 37 °C, the reaction was initiated with the addition of NADPH (5 μM). Sterols were extracted with ethyl acetate and analyzed by reverse phase HPLC in the linear gradient of methanol:acetonitrile:H_2O) 9:9:2 (solution A) and methanol (solution B) (0-100%) using a Waters C18

[1] Camargo, E.P. *Rev. Inst. Med. Trop. Sao Paulo*, **1964** (12), 93–100.
[2] Mikus, J.; Steverding, D. *Parasitol. Int*. 2000 (48), 265.
[3] Babich, H.; Borenfreund, E. *App. Envt. Microbiol.* 1991 (57), 2101.
[4] Lepesheva G.I., Nes W.D., Zhou W., Hill G.C., Waterman M.R. *Biochemistry*. 2004 (43), 10789–10799
[5] Lepesheva G.I., Zaitseva N.G., Nes W.D., Zhou W., Arase M., Liu J., Hill G.C., Waterman M.R. *J. Biol. Chem.* 2006 (281), 3577–3585

column and a β-RAM radioactivity detector. The inhibitory potency was estimated as molar ratio inhibitor/enzyme at which the activity decreased 2-fold (I/E2).[6]

Spectral Responses of TcCYP51.

The apparent affinities of ligand binding were evaluated by the spectral changes they induced in the TCCYP51.[6] The titration experiments were carried out at 24 °C in 2 mL tandem cuvettes, containing 2 μM TCCYP51 in buffer A in the wavelength range 350-500 nm using a Shimadzu UV-2401PC spectrophotometer. The tested compounds (1 or 10 mM stock solutions in DMSO, depending on the affinity of the interaction) were added in 1 μL aliquots to the test cuvette until the maximum in the TCCYP51 spectral response was reached. Equal volumes of DMSO were added to the reference cuvette. The apparent K_d's were determined from the equilibrium titration curves by plotting absorbance changes against the concentration of free ligand and fitting the data to a rectangular hyperbola using SigmaPlot Statistics.[7]

Cheminformatics Analysis

Computational modeling tools were used to estimate the bioavailability, aqueous solubility, mutagenicity, toxicity and clustering for the compounds using the ChemMineTools[8] and Osiris Property.[9]

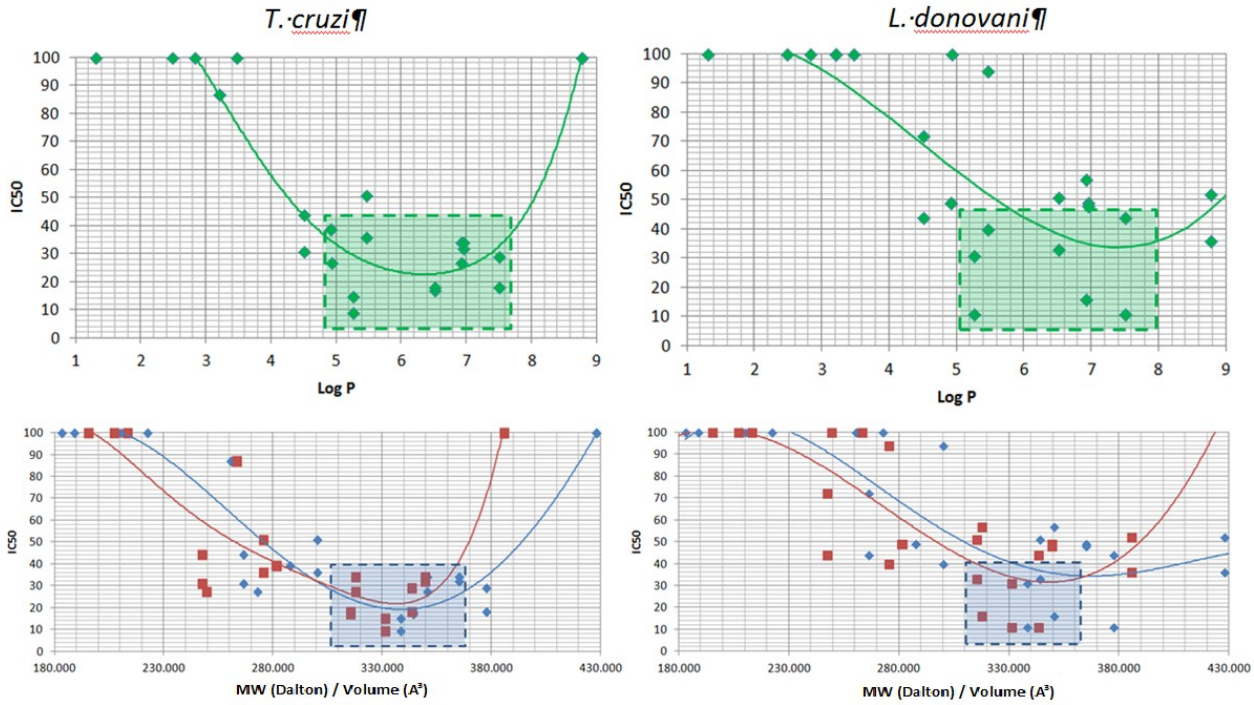
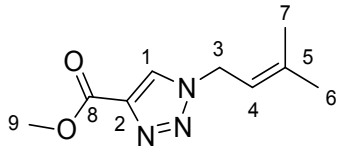
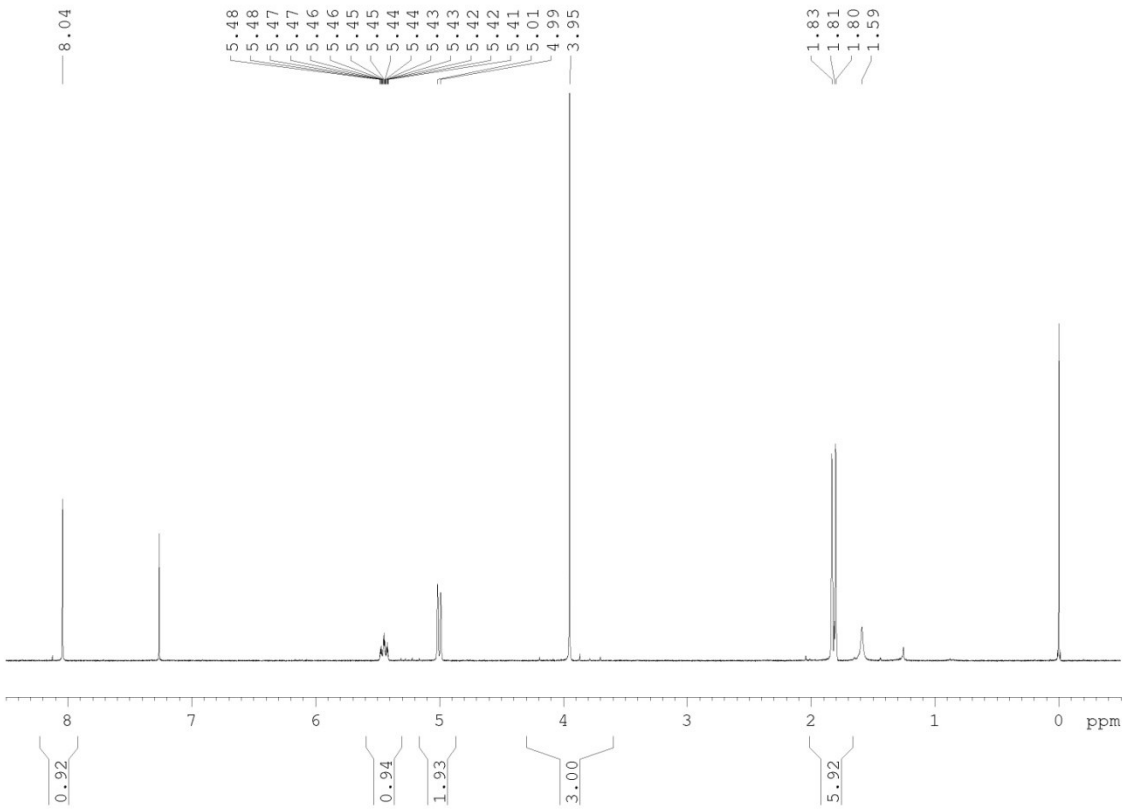


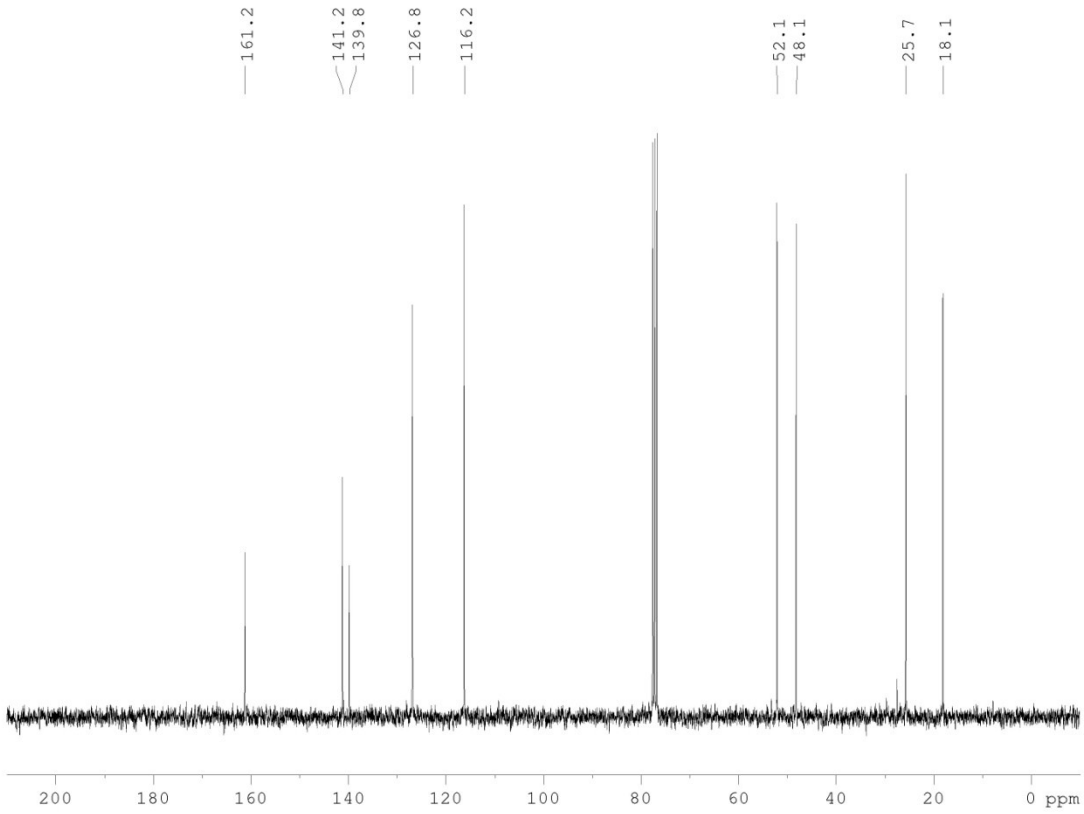
Figure S1. Analysis of activity depending on the physicochemical profiles of each trypanosomatid. (red=MW, blue=volume)

[6] Lepesheva G.I., Ott R.D., Hargrove T., Kleshchenko Y., Schuster I., Nes W.D., Hill G., Villalta F., Waterman M.W. *Chem Biol.* 2007 (14), 1283–1293.
[7] Lepesheva G.I., Virus C., Waterman M.R. *Biochemistry.* 2003 (42), 9091–9101.
[8] http://chemmine.ucr.edu/
[9] http://www.organic-chemistry.org/prog/peo/

Spectral data of IT-1



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139.8
126.8
116.2
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48.1
25.7
18.1
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180
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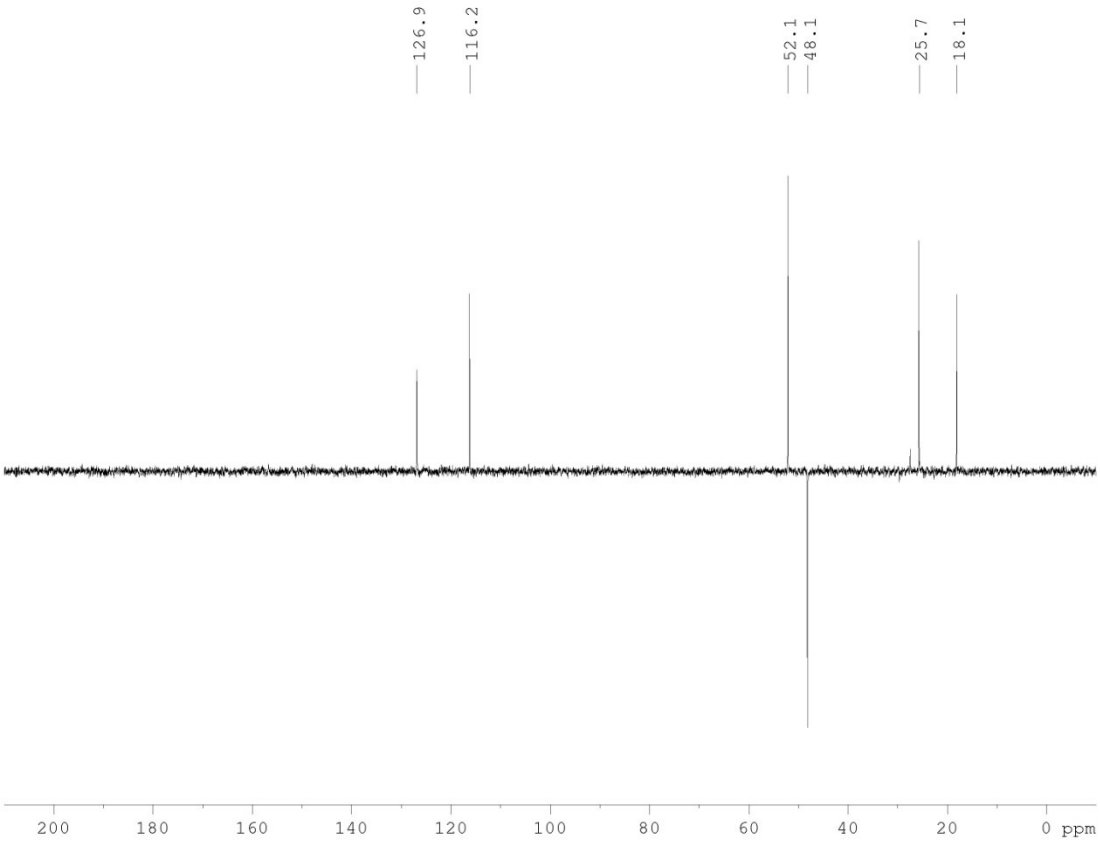
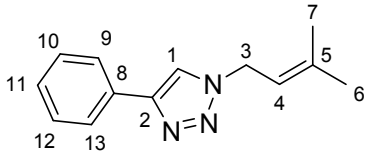
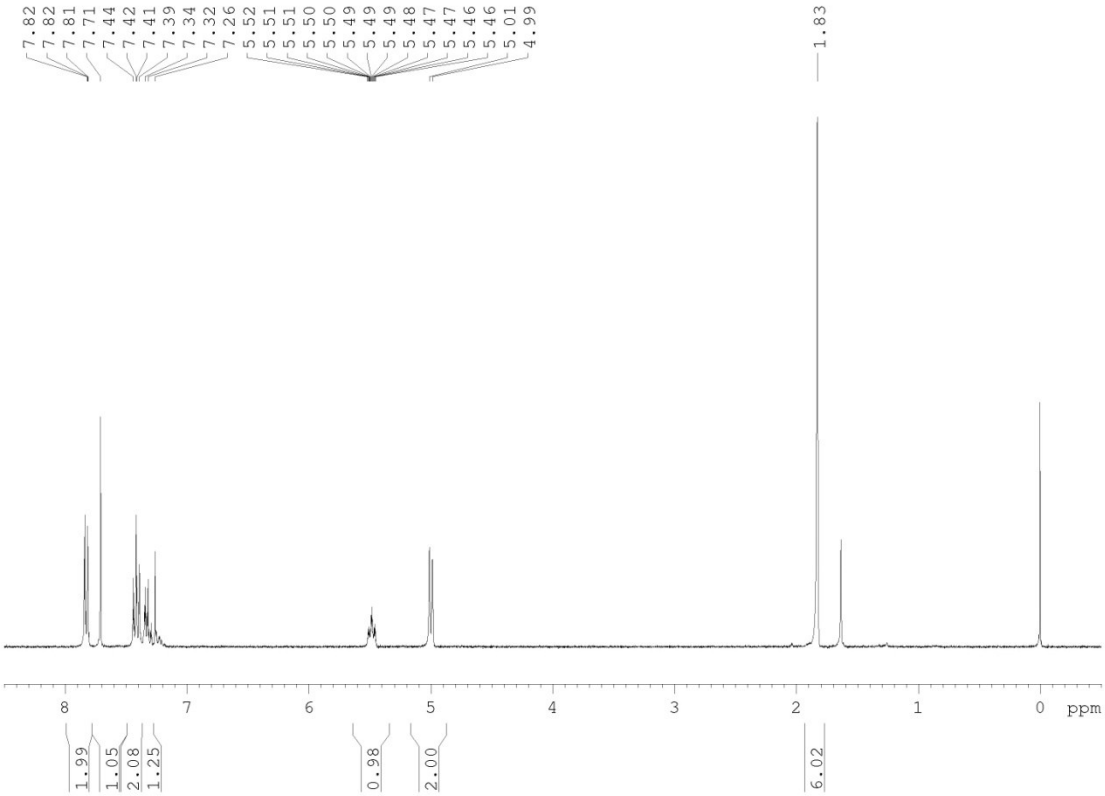
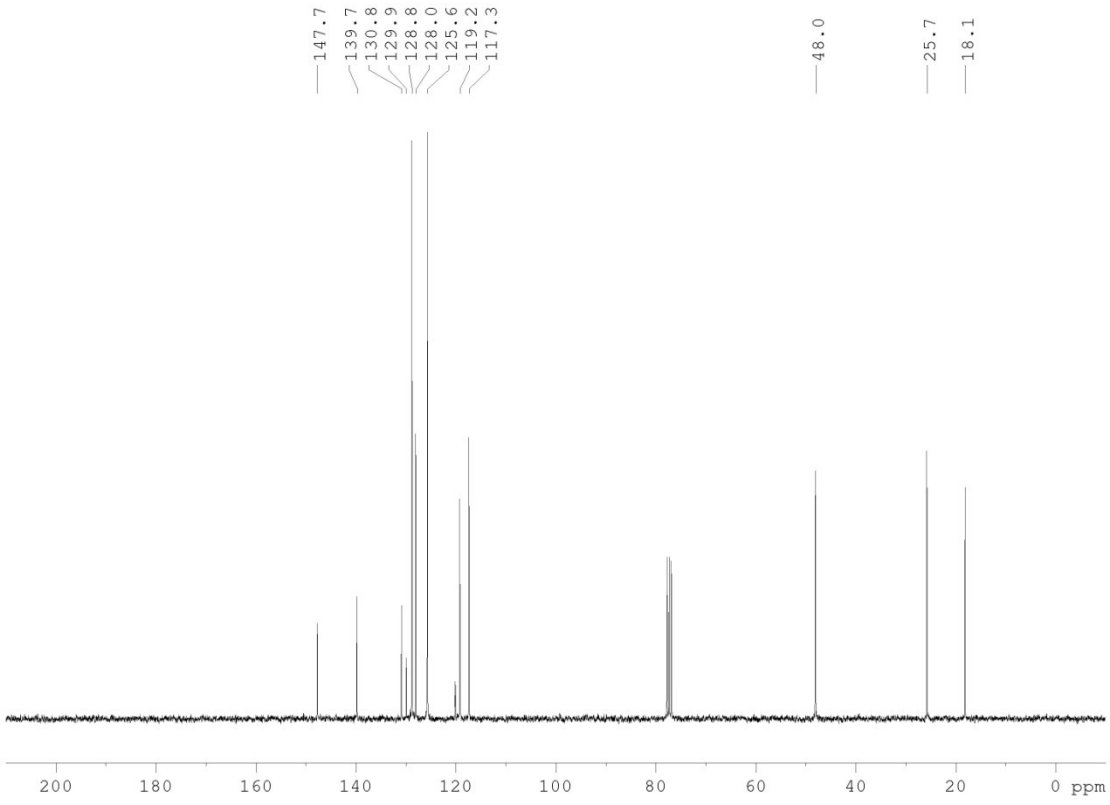
140
120
100
80
60
40
20
0 ppm

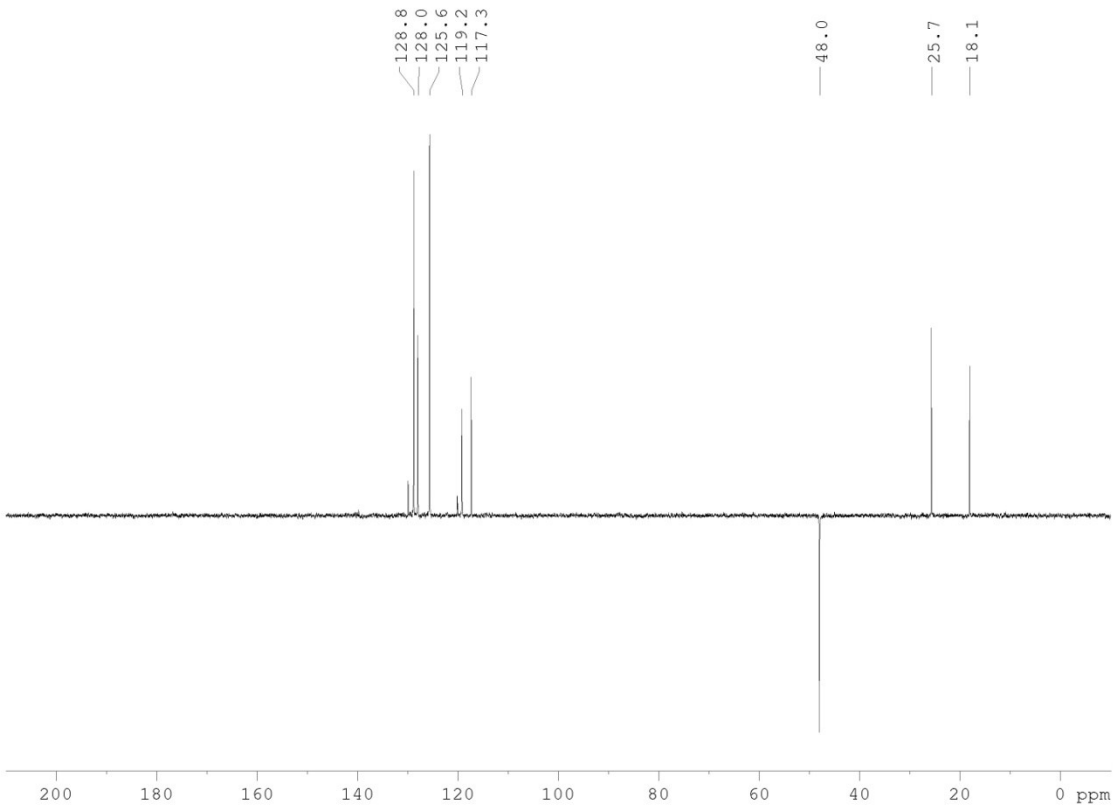

126.9
116.2
52.1
48.1
25.7
18.1
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-2

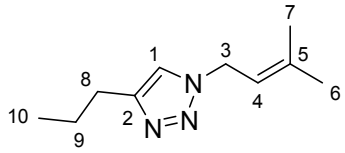


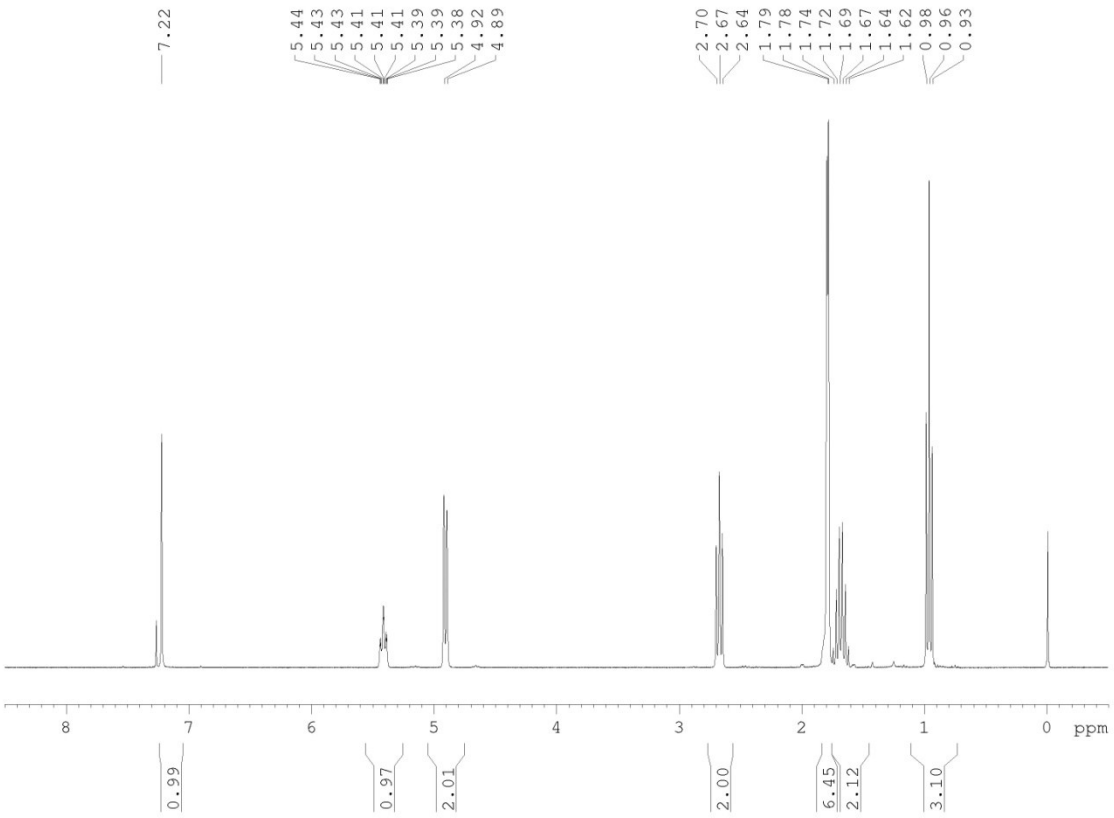


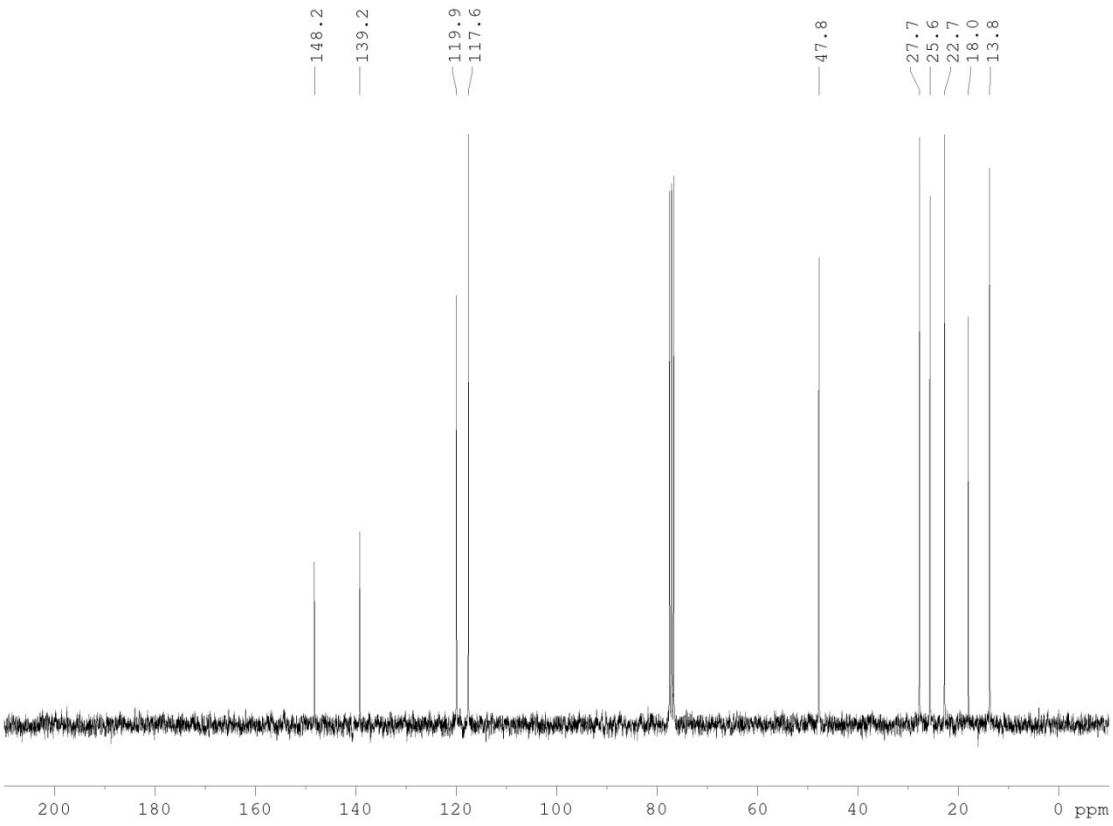

147.7
139.7
130.8
129.9
128.8
128.0
125.6
119.2
117.3
48.0
25.7
18.1
200
180
160
140
120
100
80
60
40
20
0 ppm

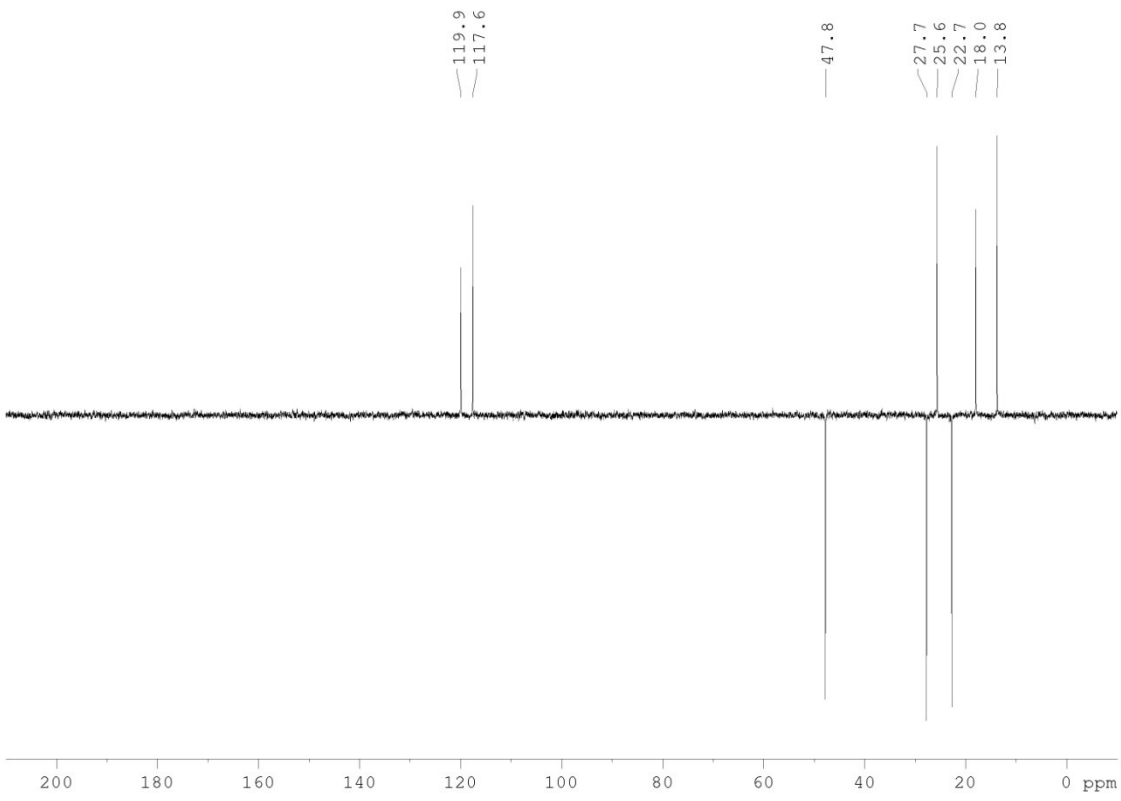

128.8
128.0
125.6
119.2
117.3
48.0
25.7
18.1
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-3

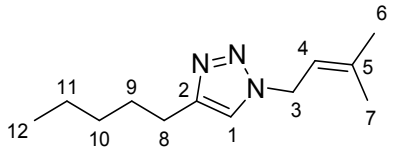


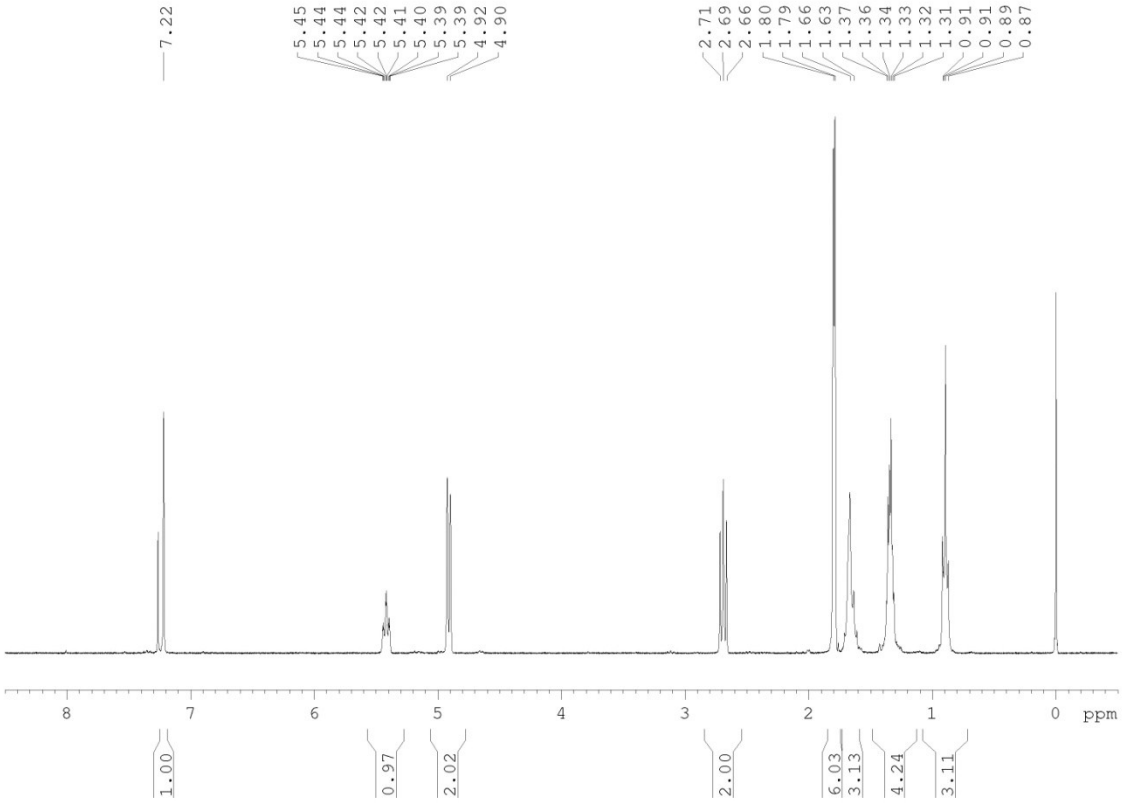


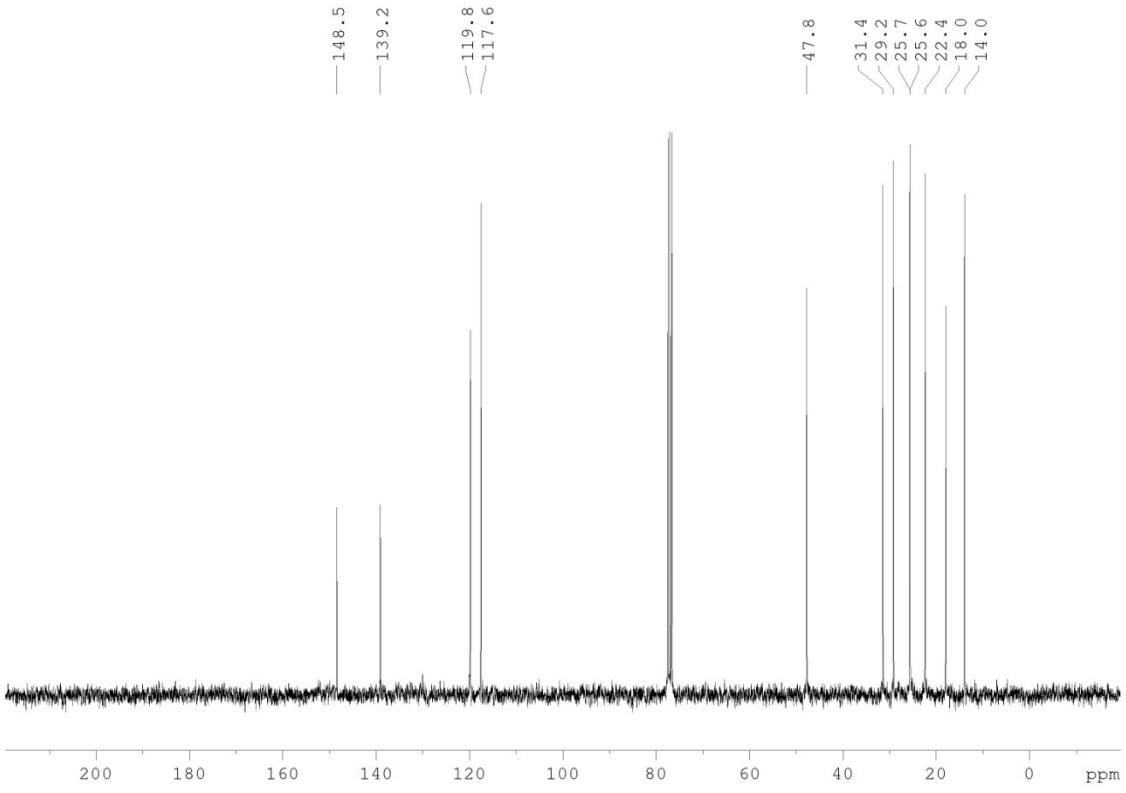

148.2
139.2
119.9
117.6
47.8
27.7
25.6
22.7
18.0
13.8
200
180
160
140
120
100
80
60
40
20
0 ppm

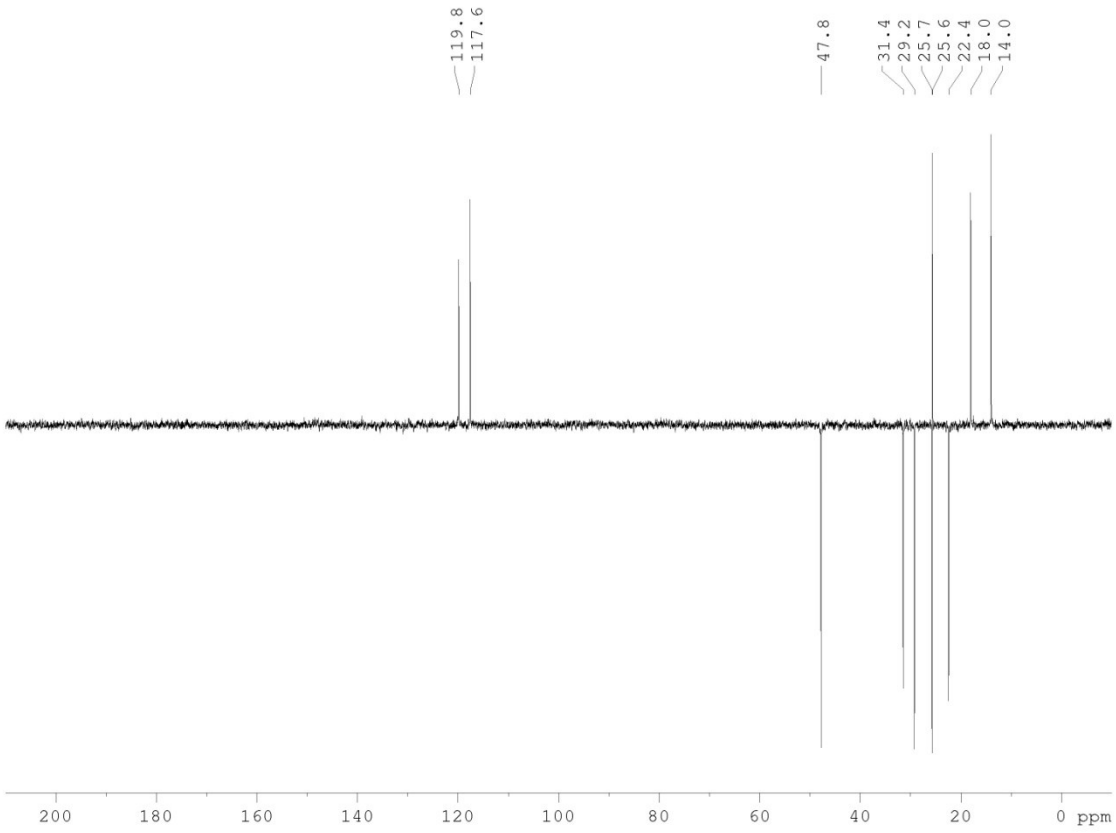

119.9
117.6
47.8
27.7
25.6
22.7
18.0
13.8
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-4

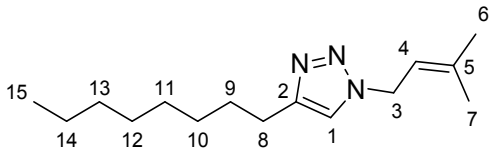


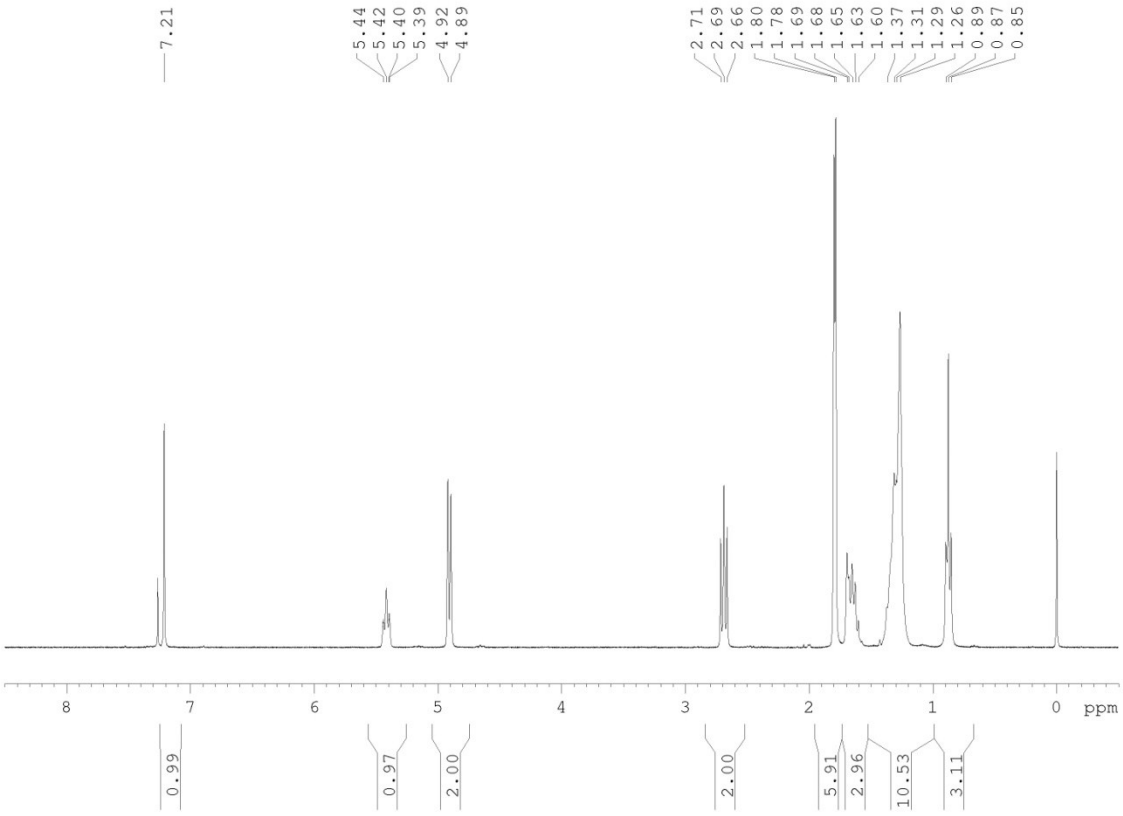


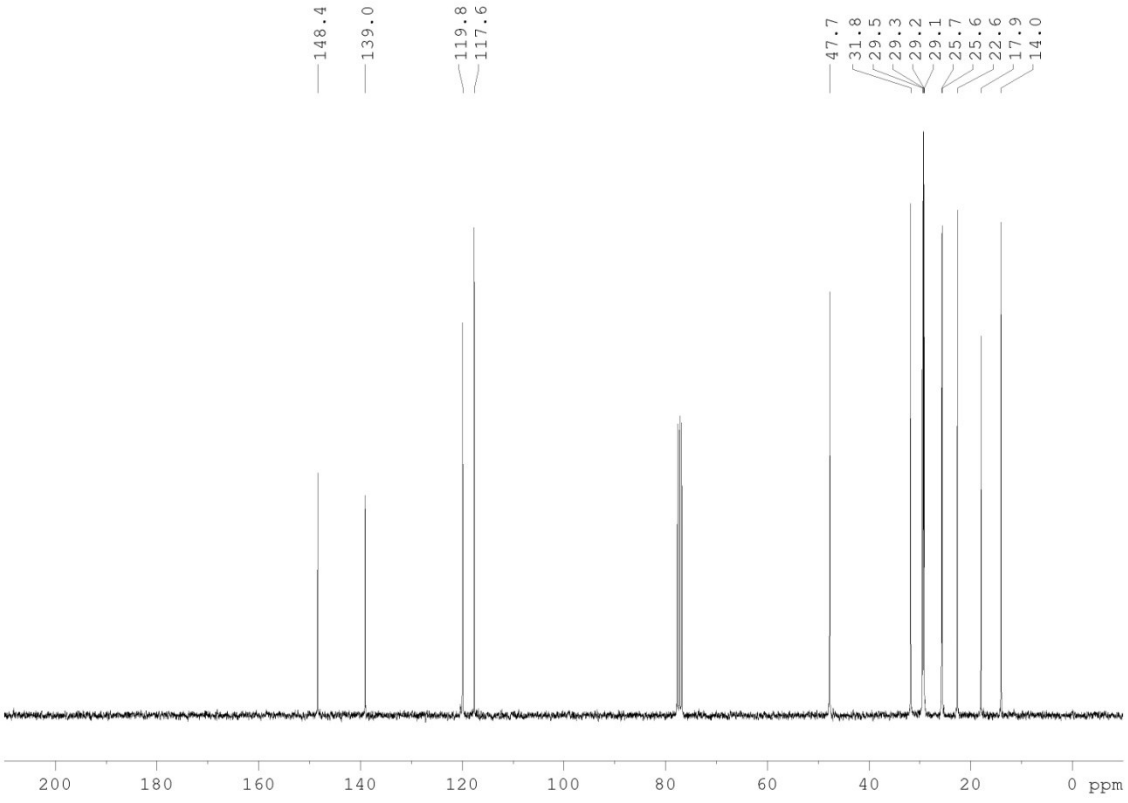

148.5
139.2
119.8
117.6
47.8
31.4
29.2
25.7
25.6
22.4
18.0
14.0
200
180
160
140
120
100
80
60
40
20
0
ppm

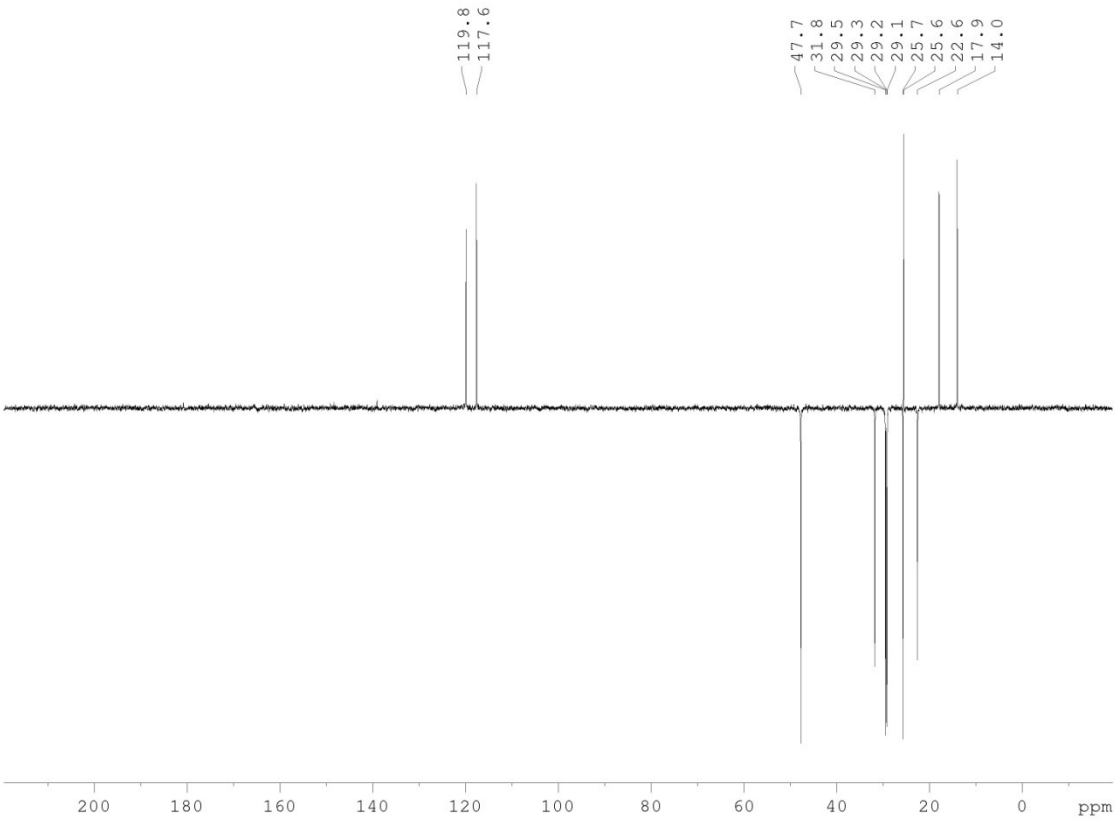

119.8
117.6
47.8
31.4
29.2
25.7
25.6
22.4
18.0
14.0
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-5






148.4
139.0
119.8
117.6
47.7
31.8
29.5
29.3
29.2
29.1
25.7
25.6
22.6
17.9
14.0
200
180
160
140
120
100
80
60
40
20
0 ppm


119.8
117.6
47.7
31.8
29.5
29.3
29.2
29.1
25.7
25.6
22.6
17.9
14.0
200
180
160
140
120
100
80
60
40
20
0
ppm

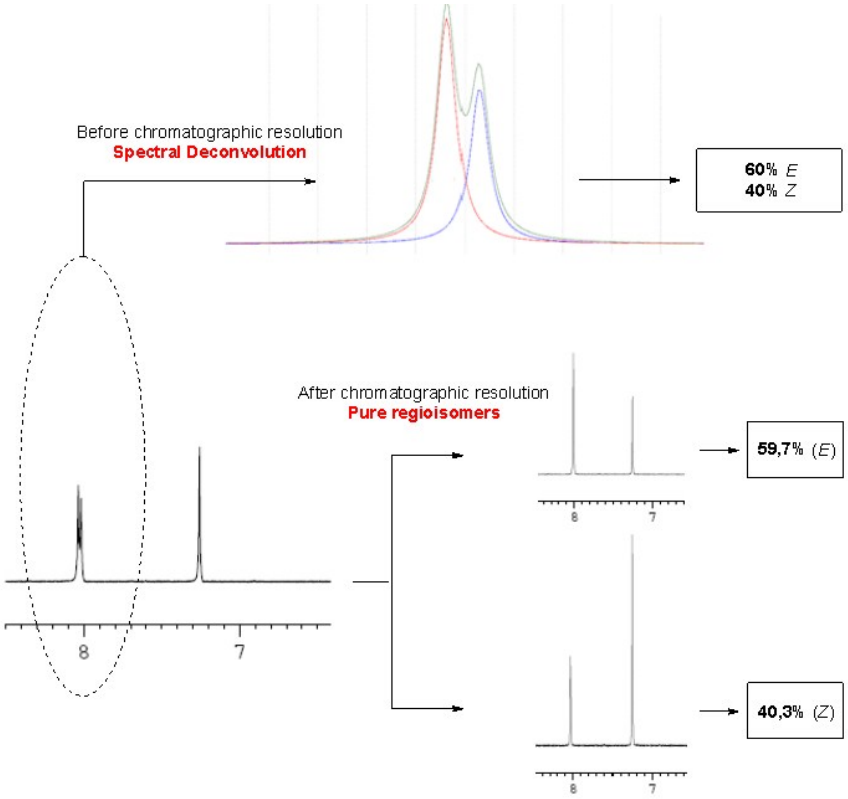
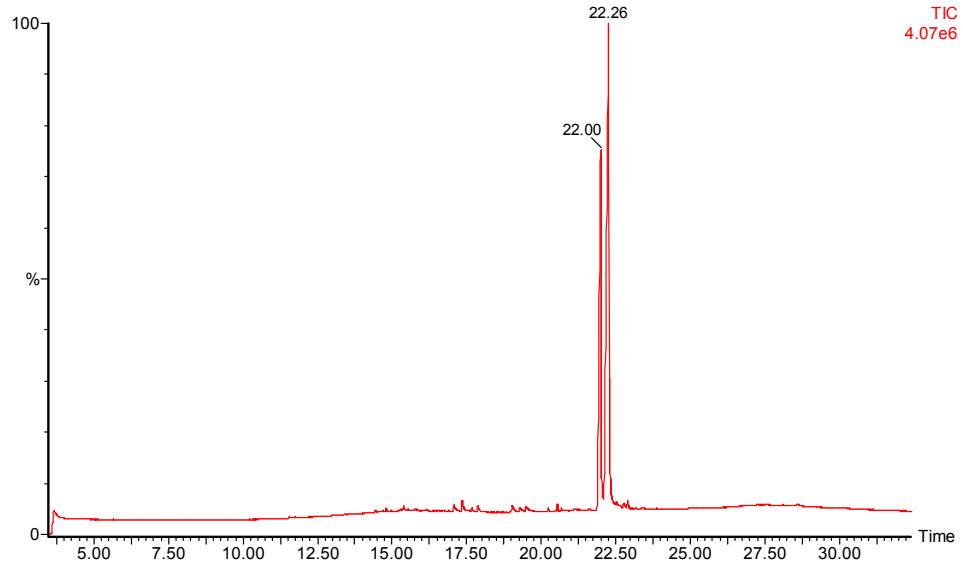
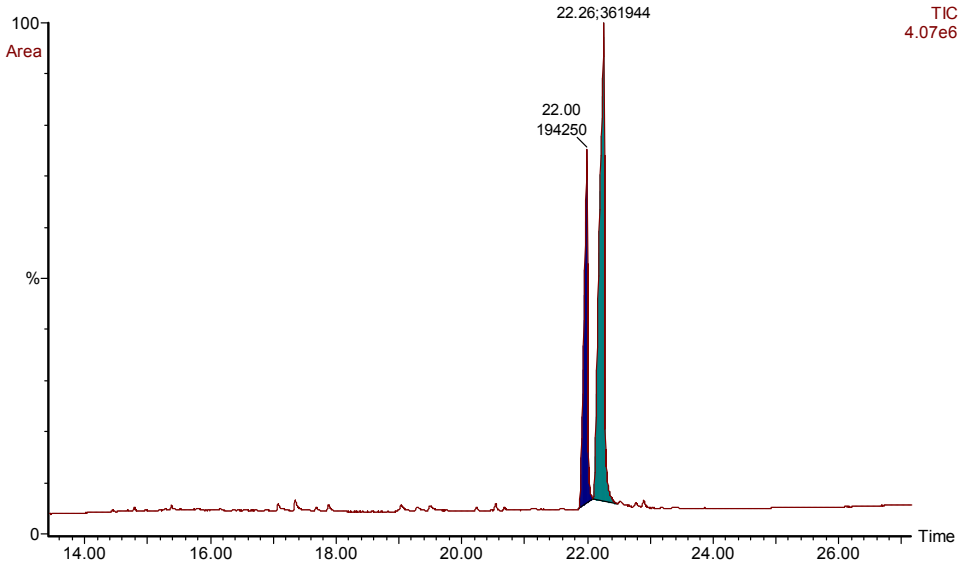


Figure S2 Chromatographic resolution of products. ^{1}H NMR signal of triazolic proton. The deconvolution spectra allow us to calculate the ratio between regioisomers.

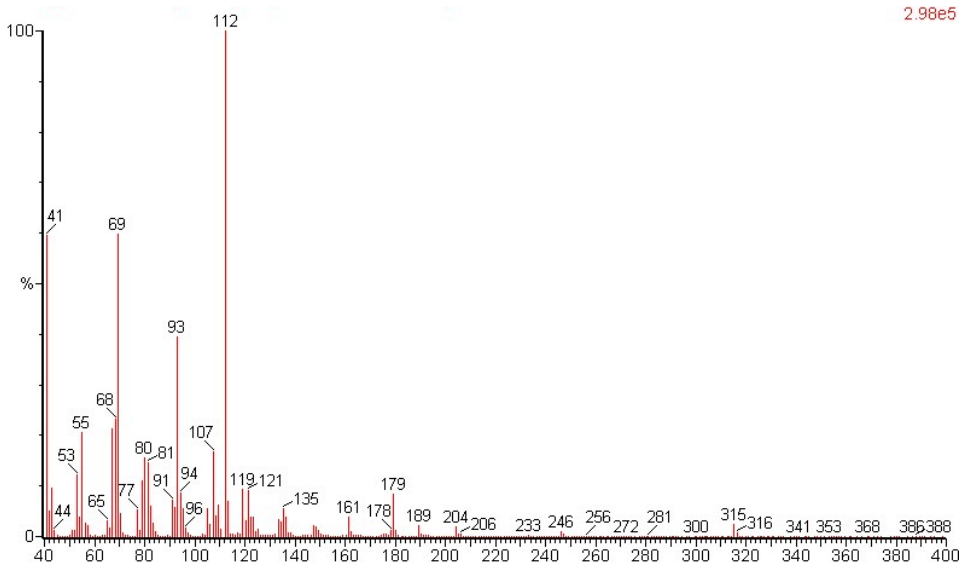
GC-MS chromatograms of mixture of reaction (before chromatographic separation)

IT-18 and **IT-23**

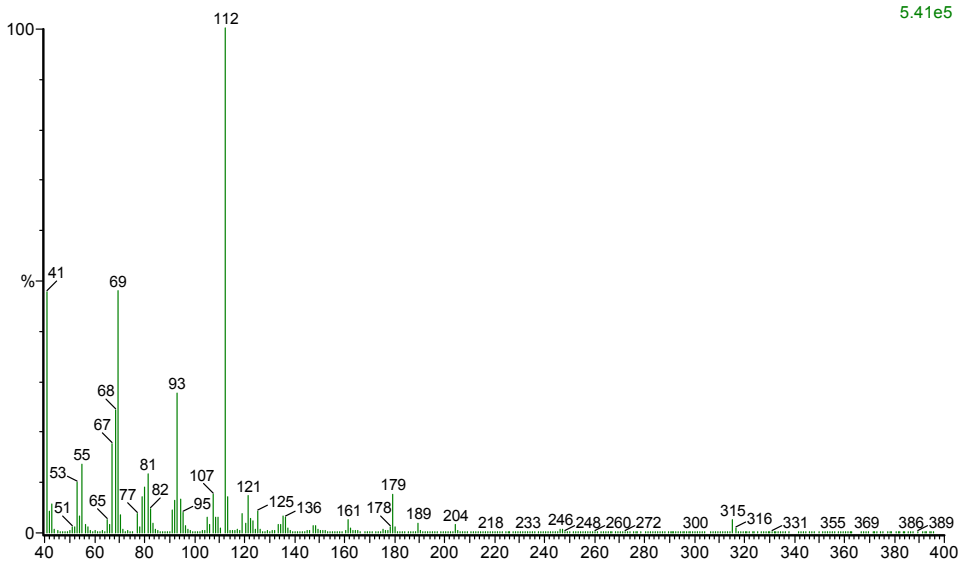




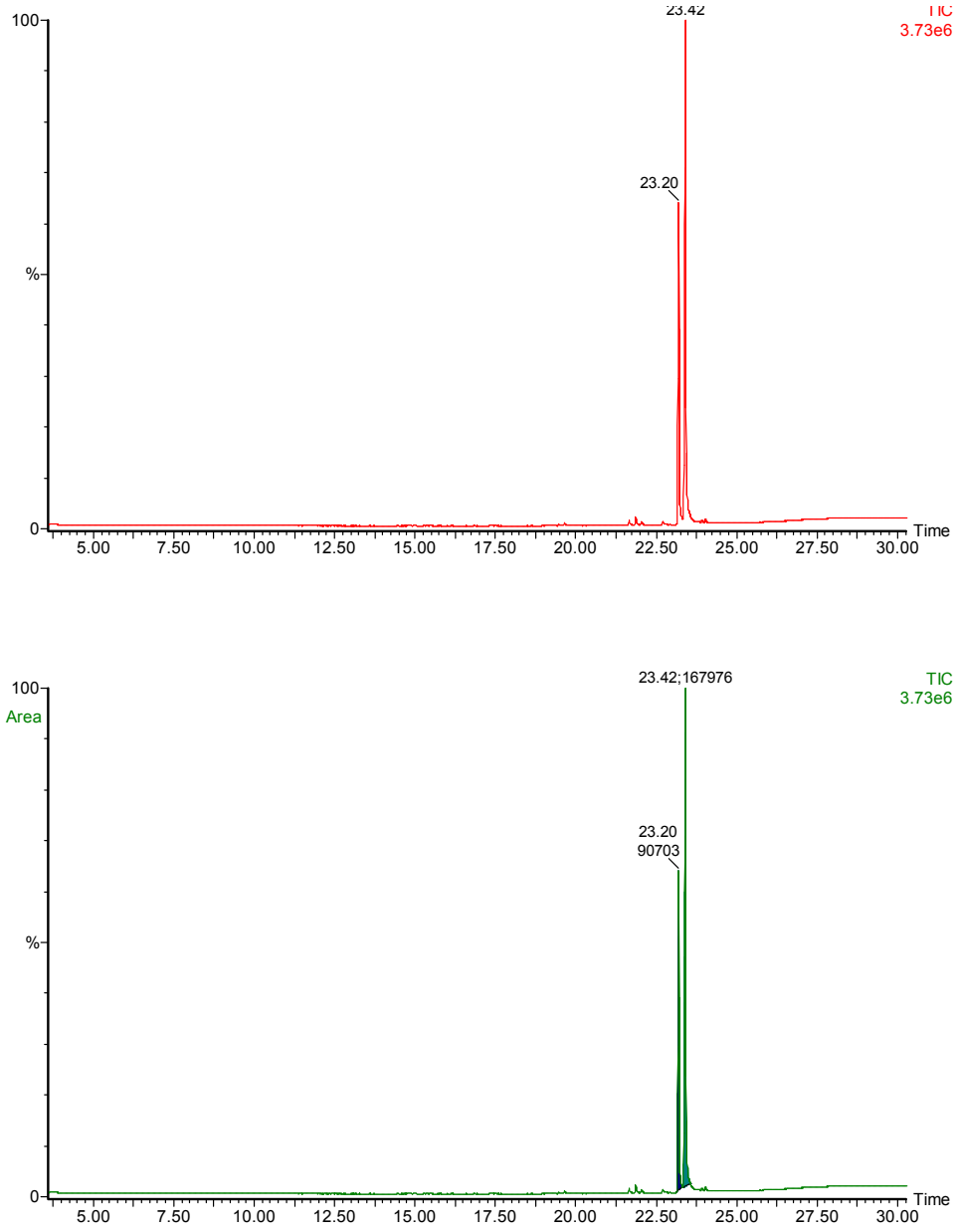
RT: 22’00



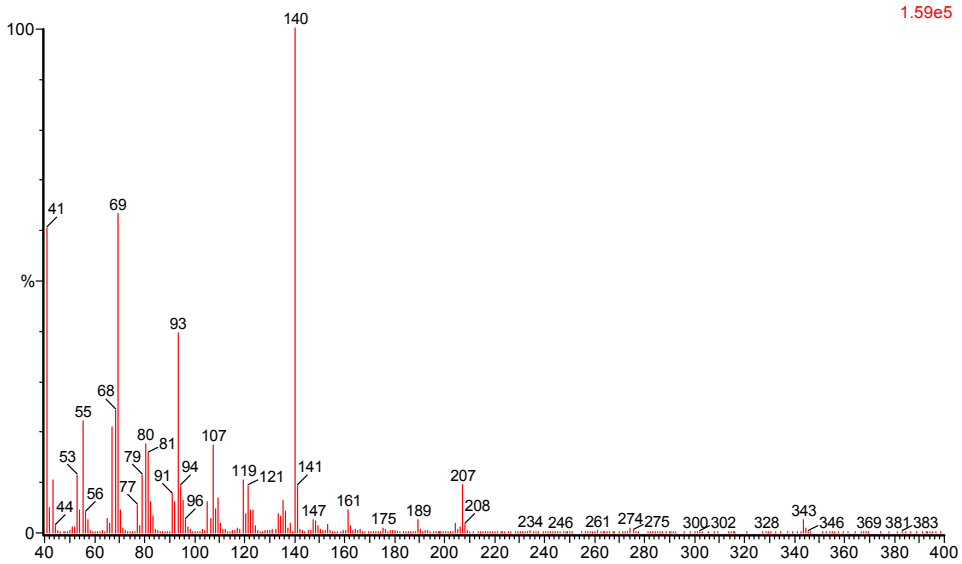
RT: 22.26’



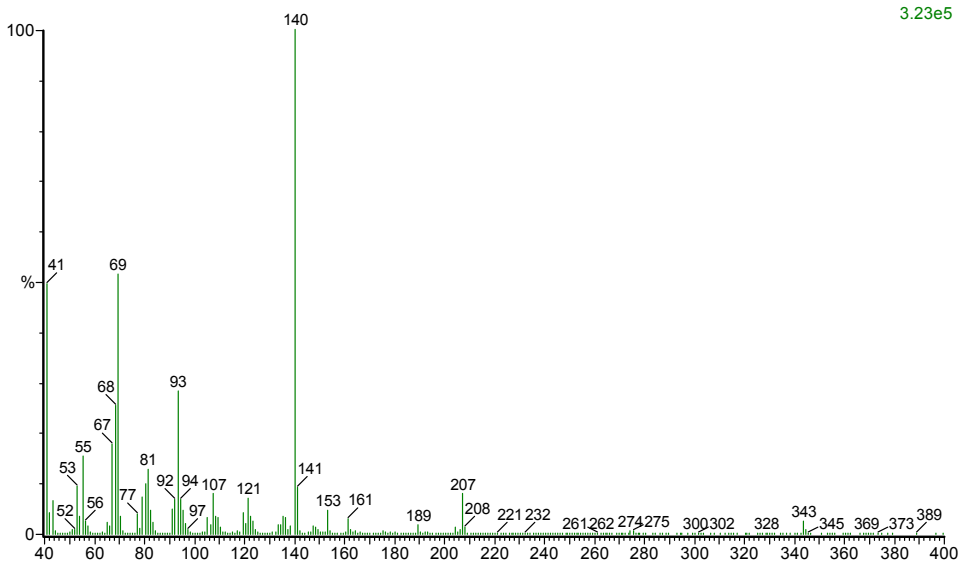
IT-19 and **IT-24**



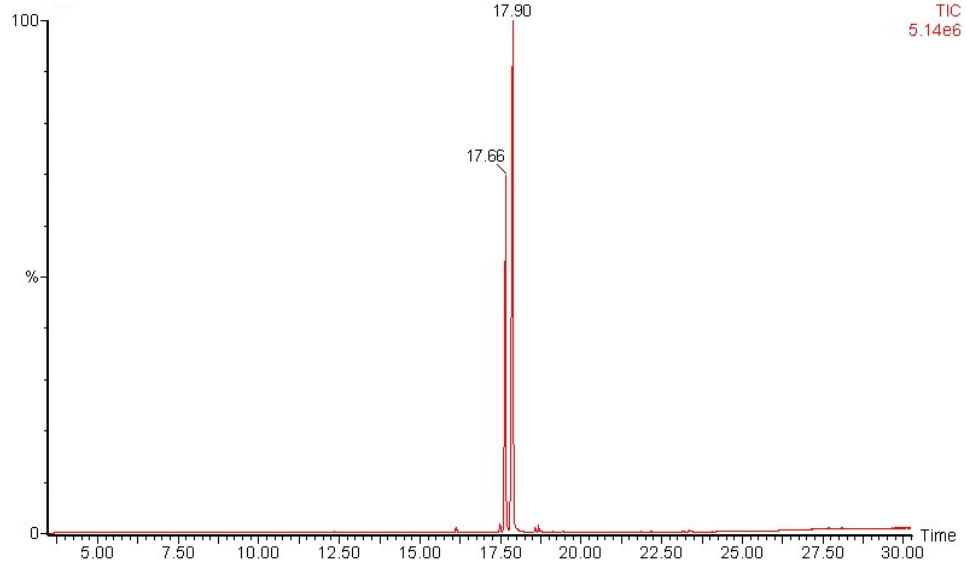
RT: 23.20’

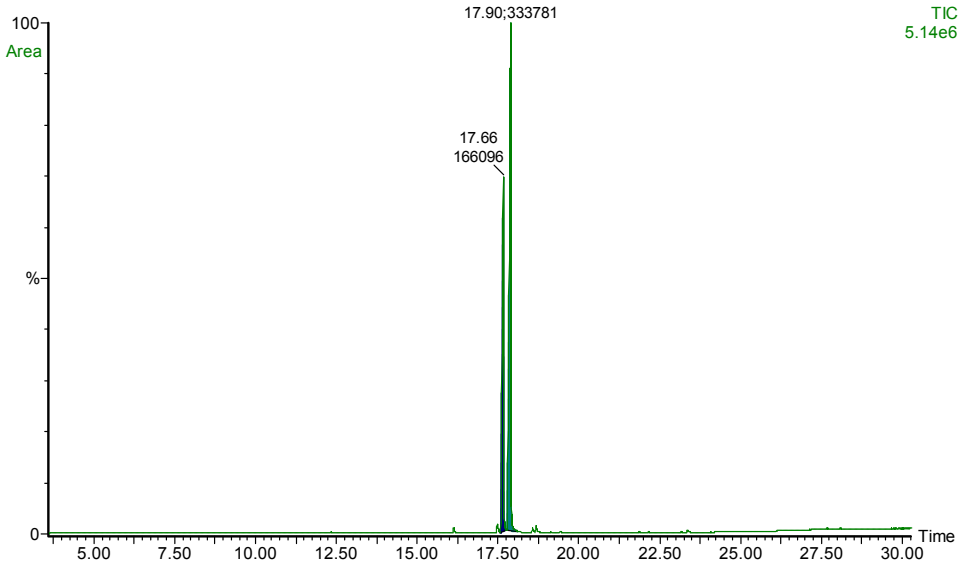


RT: 23.42’

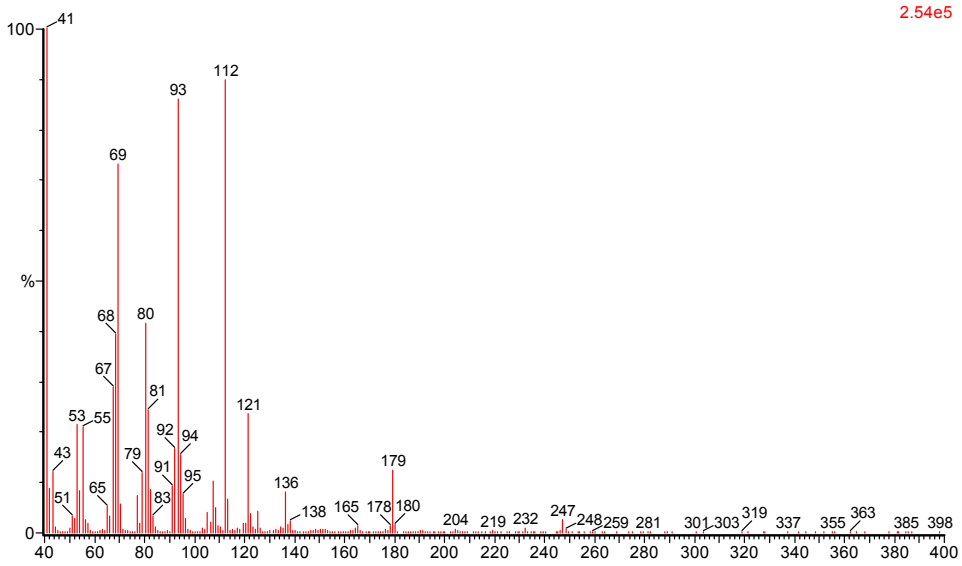


IT-8 and **IT-13**

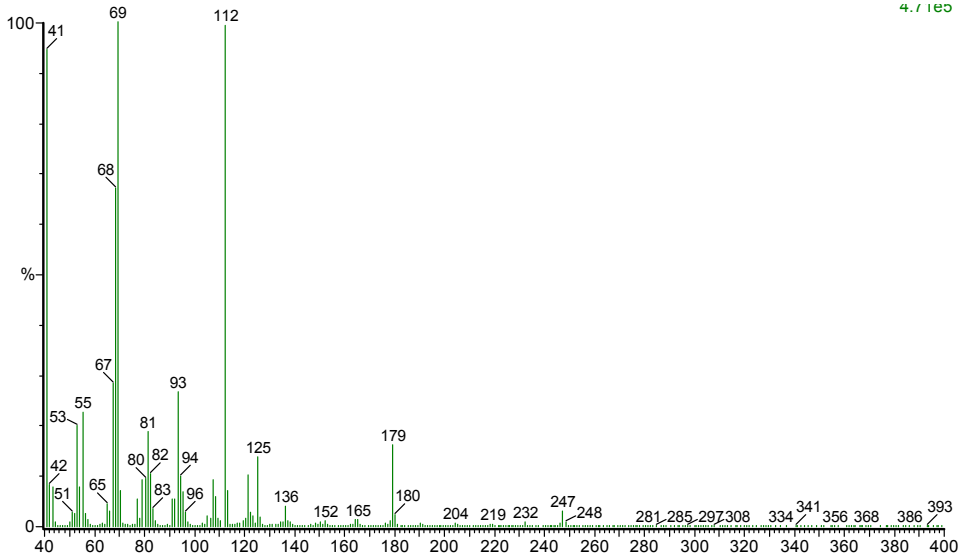

17.90
TIC
5.14e6
17.66
100
%
0
5.00
7.50
10.00
12.50
15.00
17.50
20.00
22.50
25.00
27.50
30.00
Time


17.90;333781
TIC
5.14e6
100
Area
17.66
166096
%
0
5.00
7.50
10.00
12.50
15.00
17.50
20.00
22.50
25.00
27.50
30.00
Time

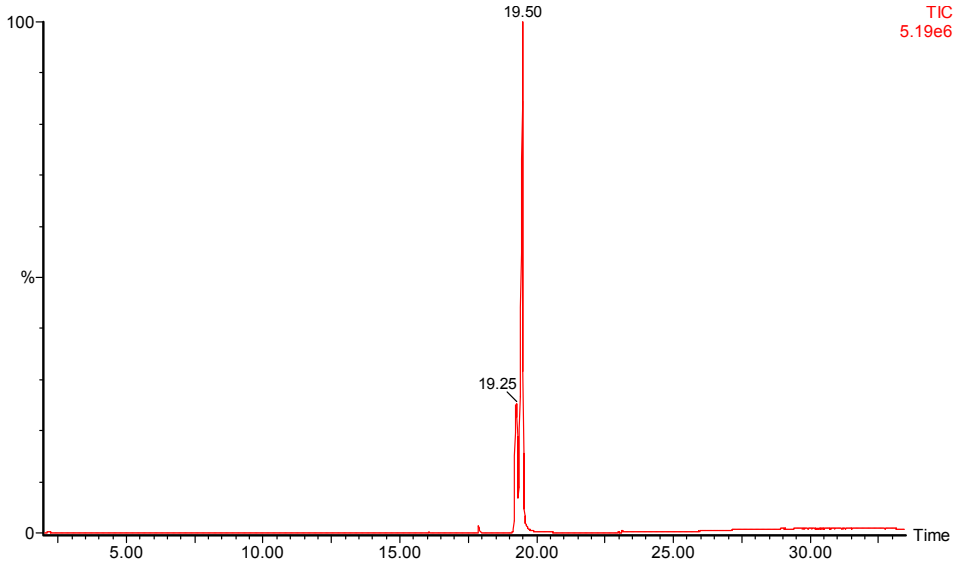
RT: 17.66’



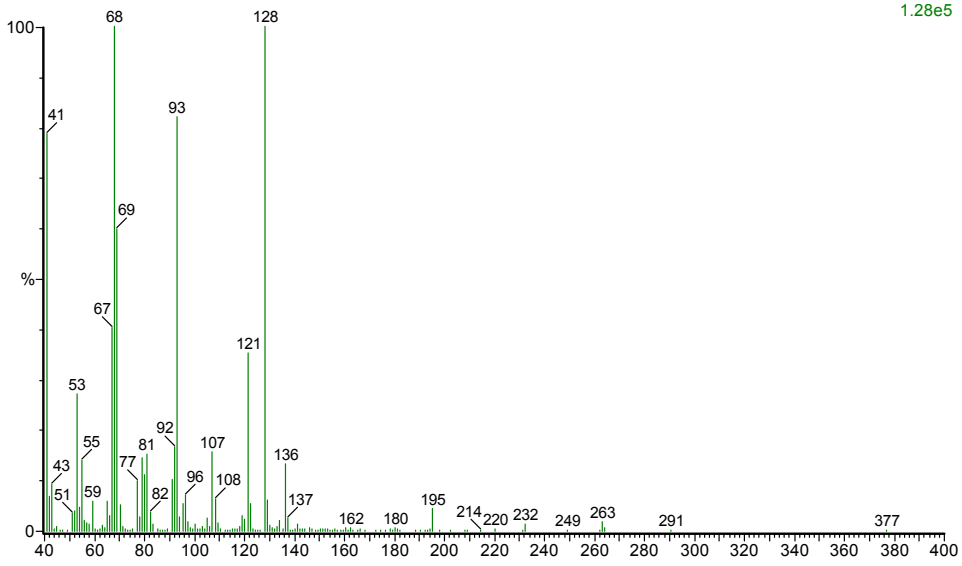
RT: 17.90’



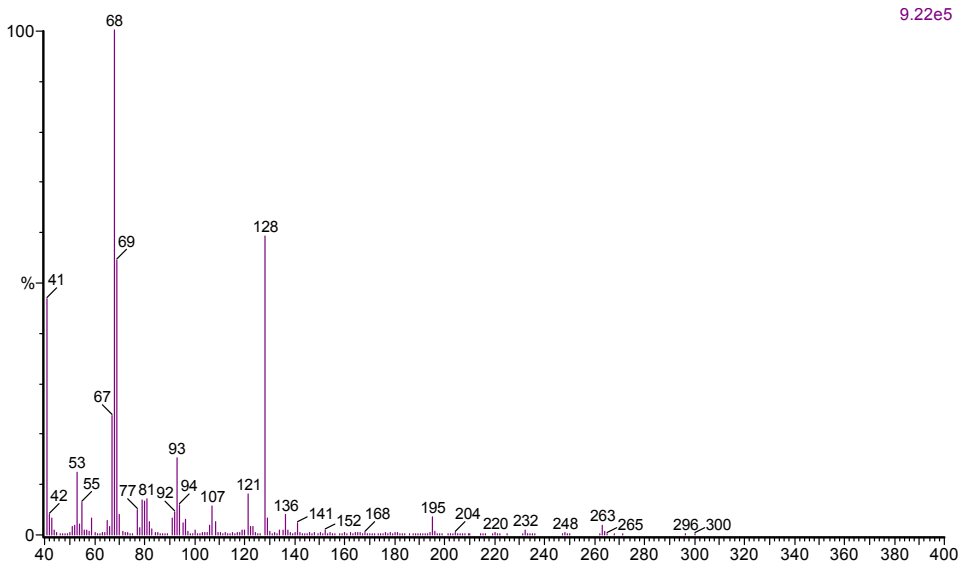
IT-7 and **IT-12**



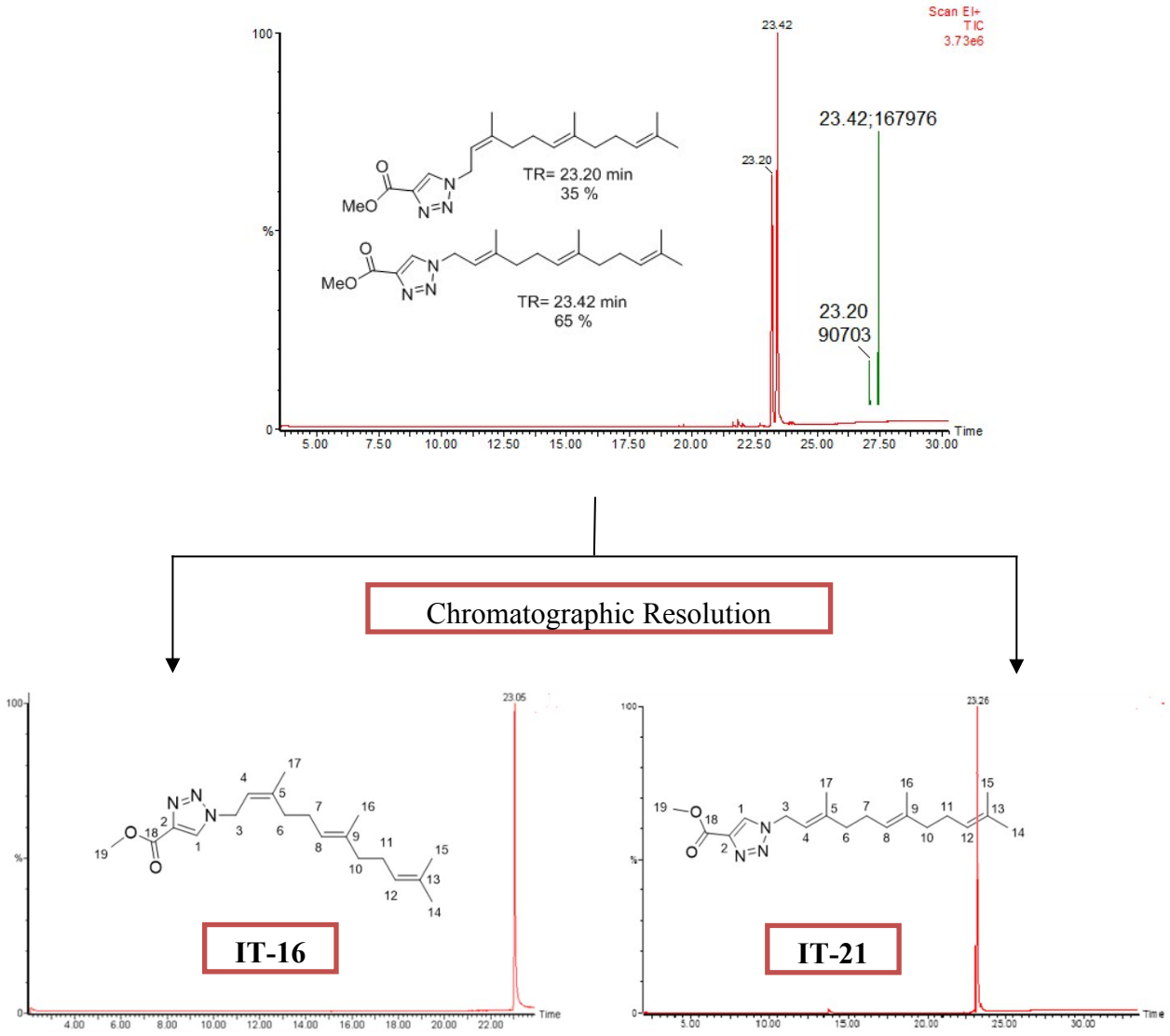
RT: 19.25'



RT: 19.49’


9.22e5
100
%
0
68
69
128
41
67
93
53
55
42
77
81
92
94
107
121
136
141
152
168
195
204
220
232
248
263
265
296
300
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400

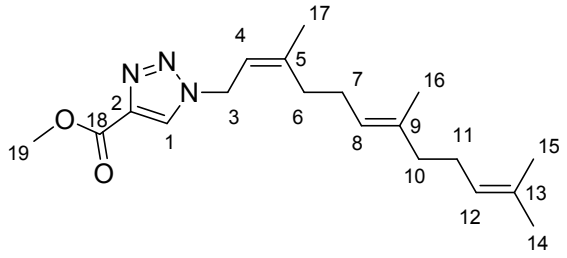
*Before chromatographic resolution: Mixture of products **IT-16** and **IT-21***

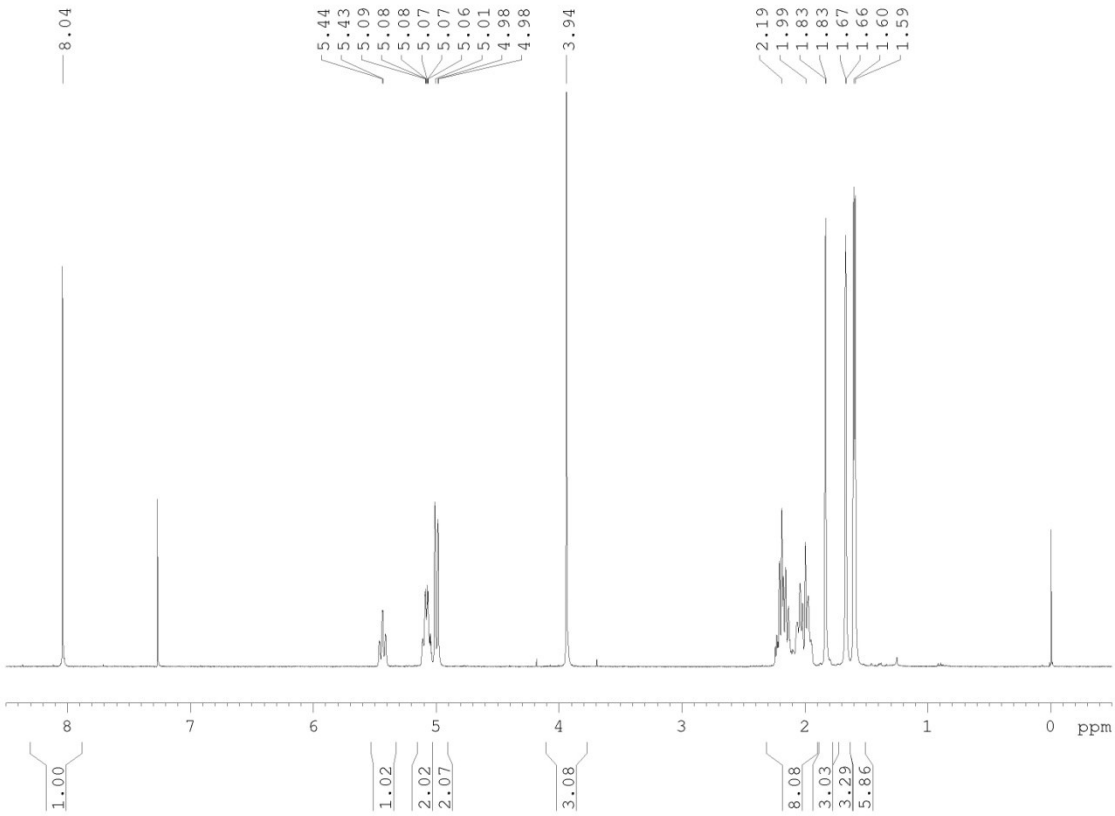


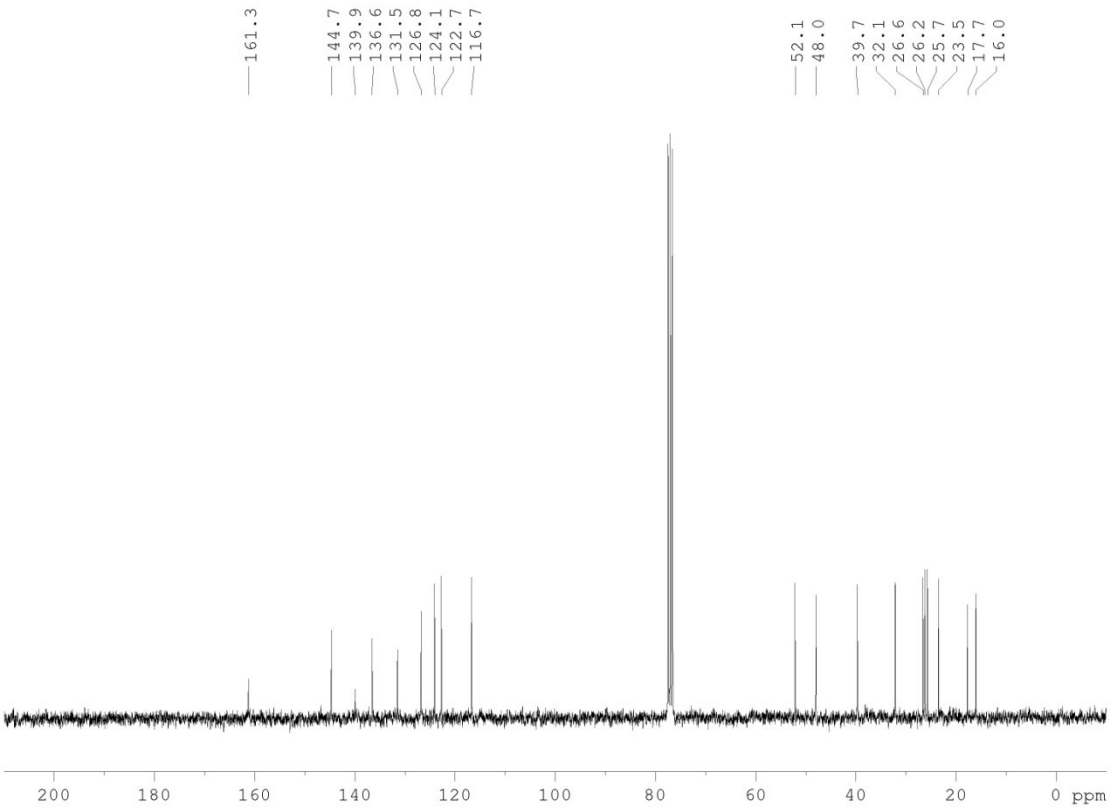
Pure Regioisomers fully characterized by NMR spectroscopy and HRMS

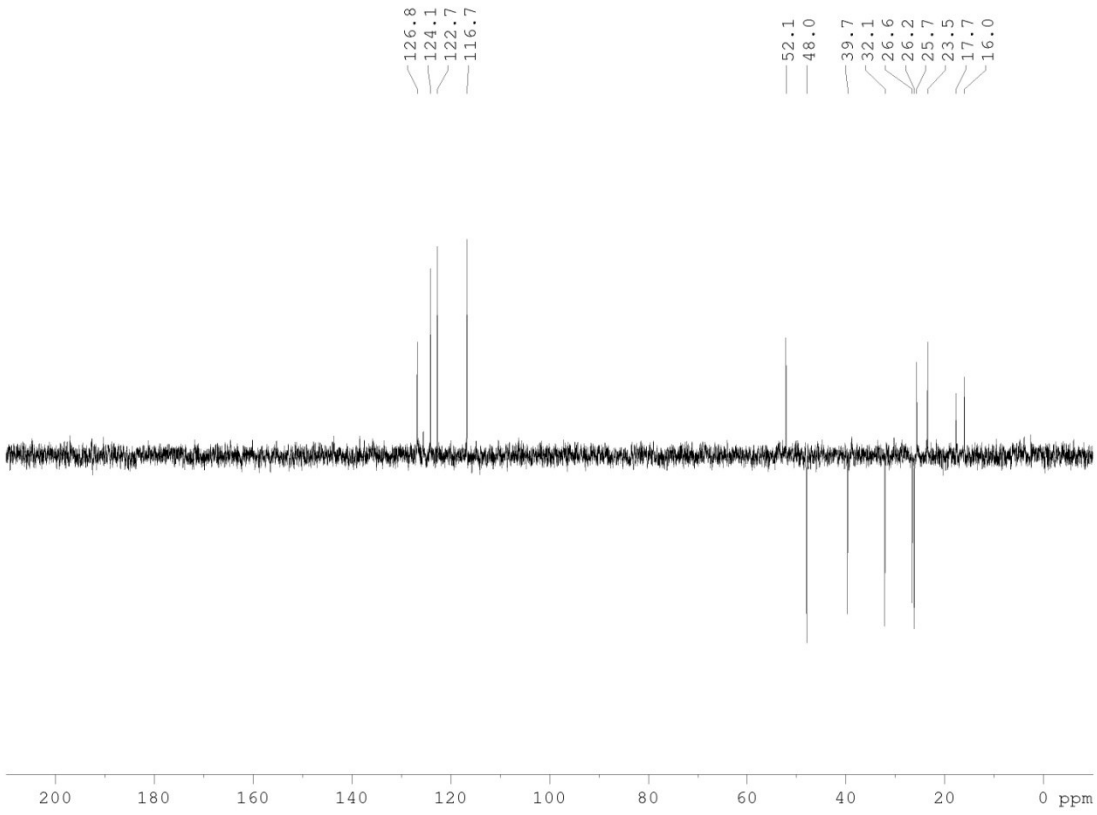
Figure S3 GC-MS chromatograms of the compounds **IT-16** and **IT-21** (before and after chromatographic resolution).

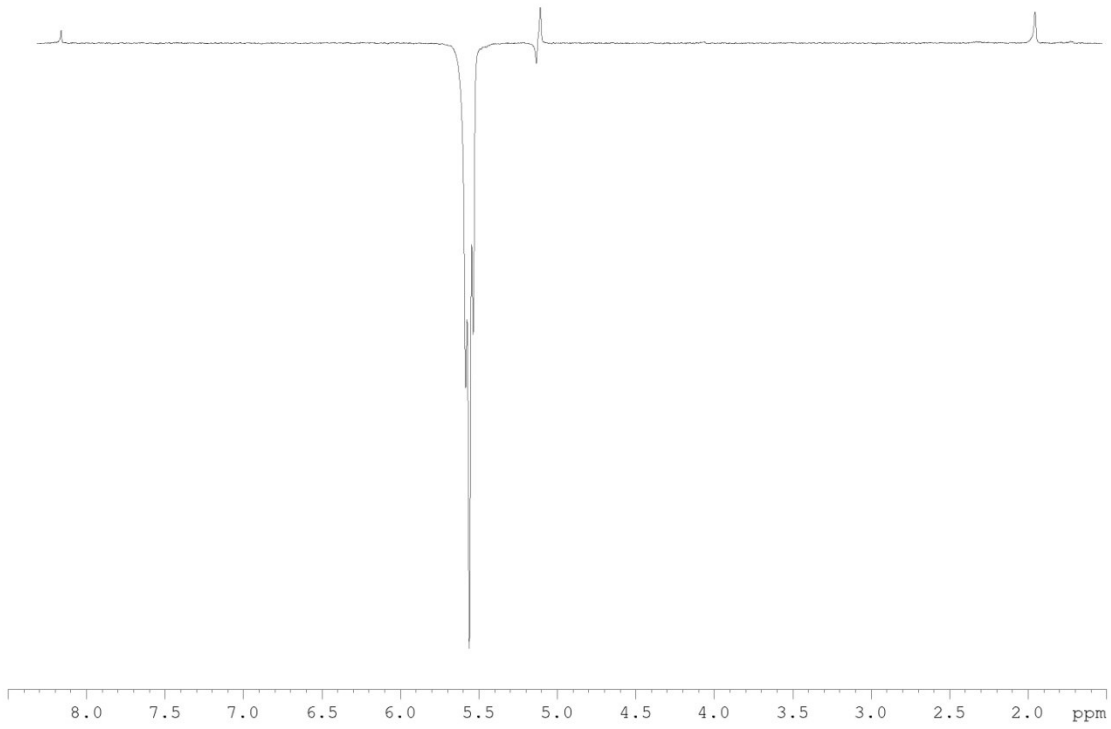
Spectral data of IT-16 (*Z*,*E*)

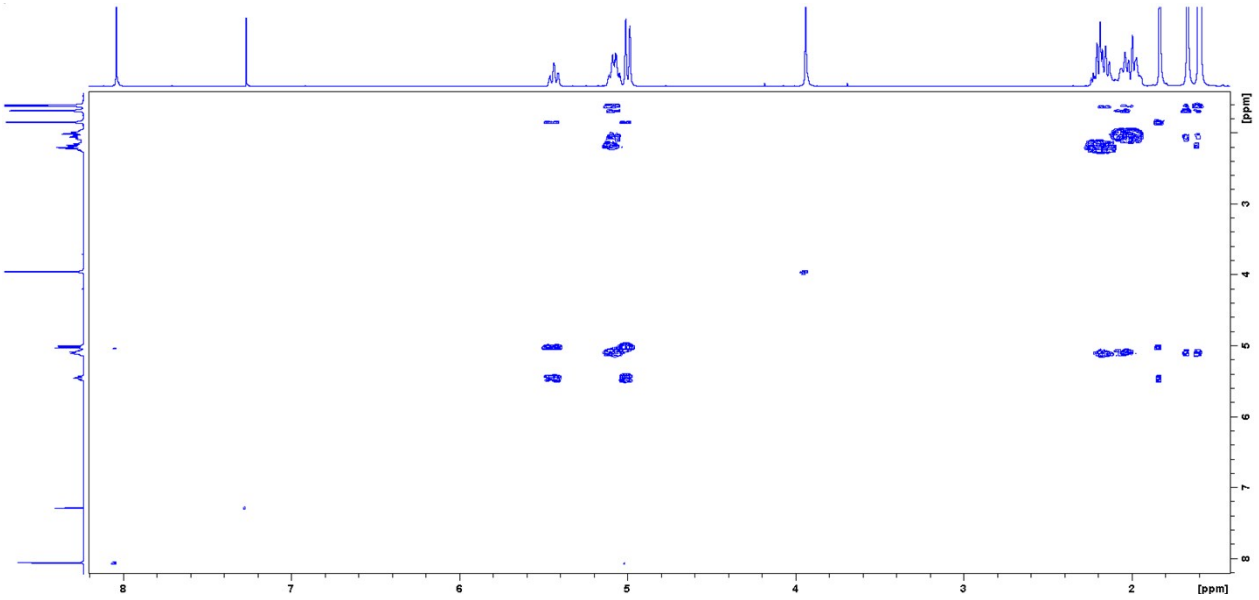


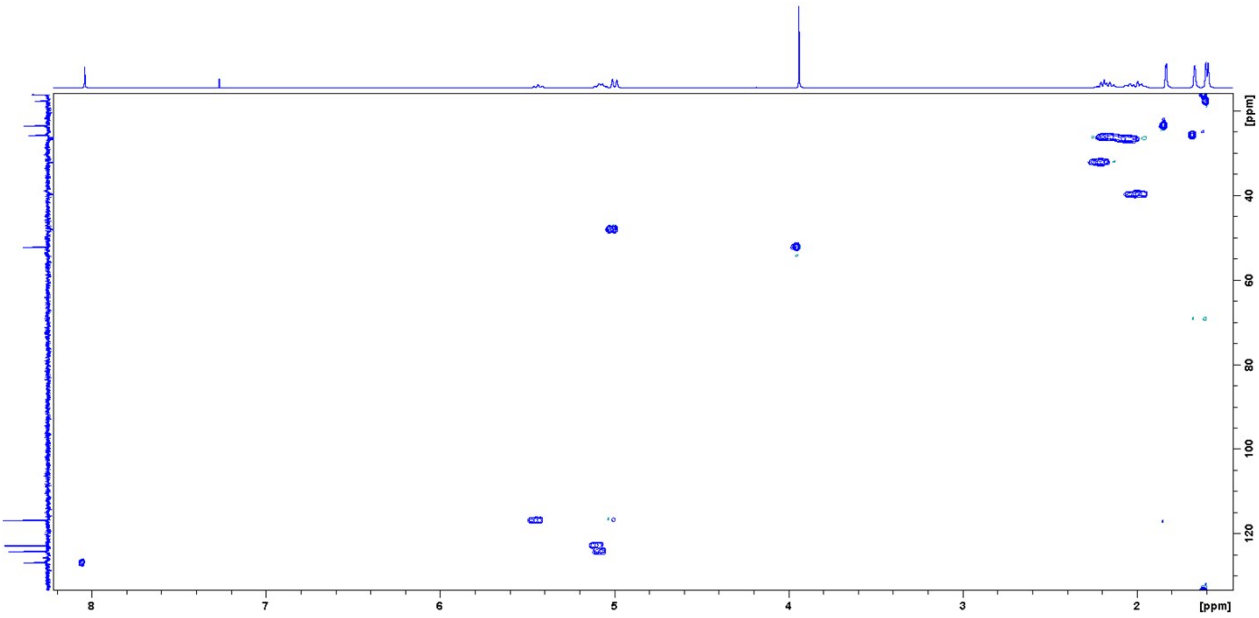


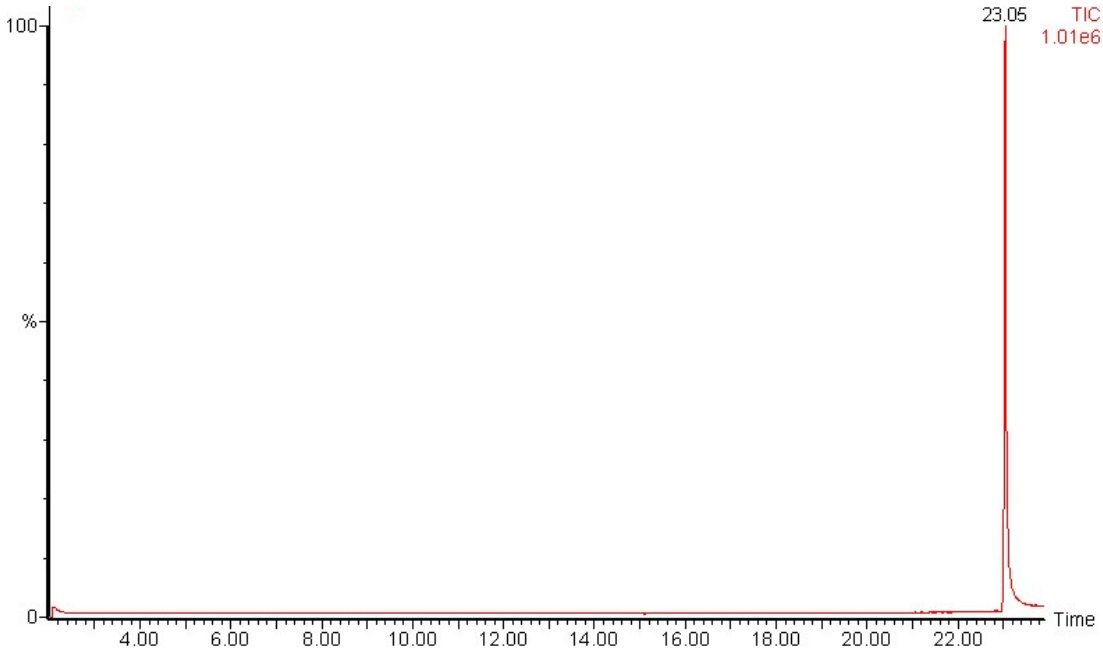

161.3
144.7
139.9
136.6
131.5
126.8
124.1
122.7
116.7
52.1
48.0
39.7
32.1
26.6
26.2
25.7
23.5
17.7
16.0
200
180
160
140
120
100
80
60
40
20
0 ppm

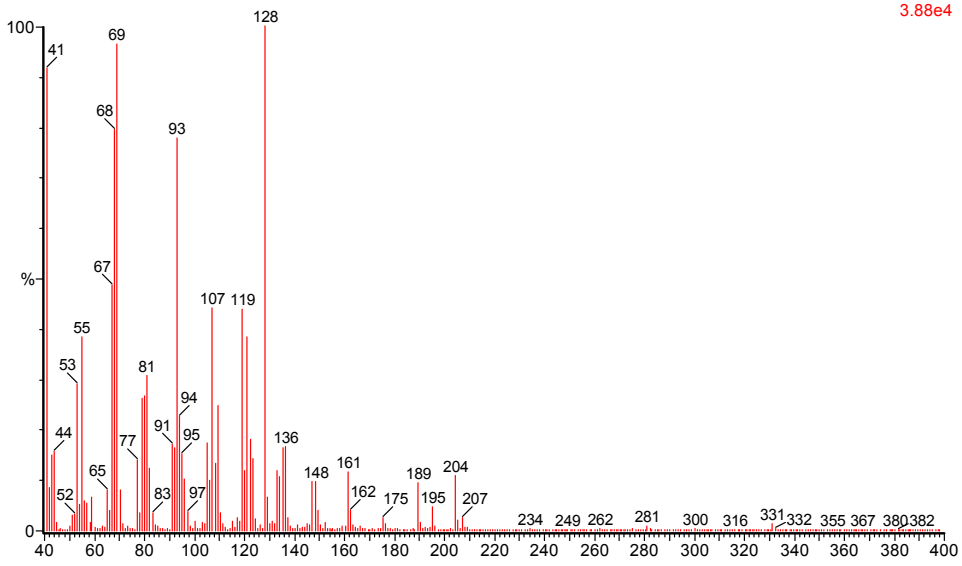

126.8
124.1
122.7
116.7
52.1
48.0
39.7
32.1
26.6
26.2
25.7
23.5
17.7
16.0
200
180
160
140
120
100
80
60
40
20
0 ppm


8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm

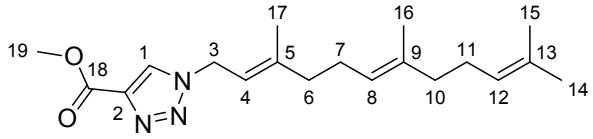

8
7
6
5
4
3
2
[ppm]

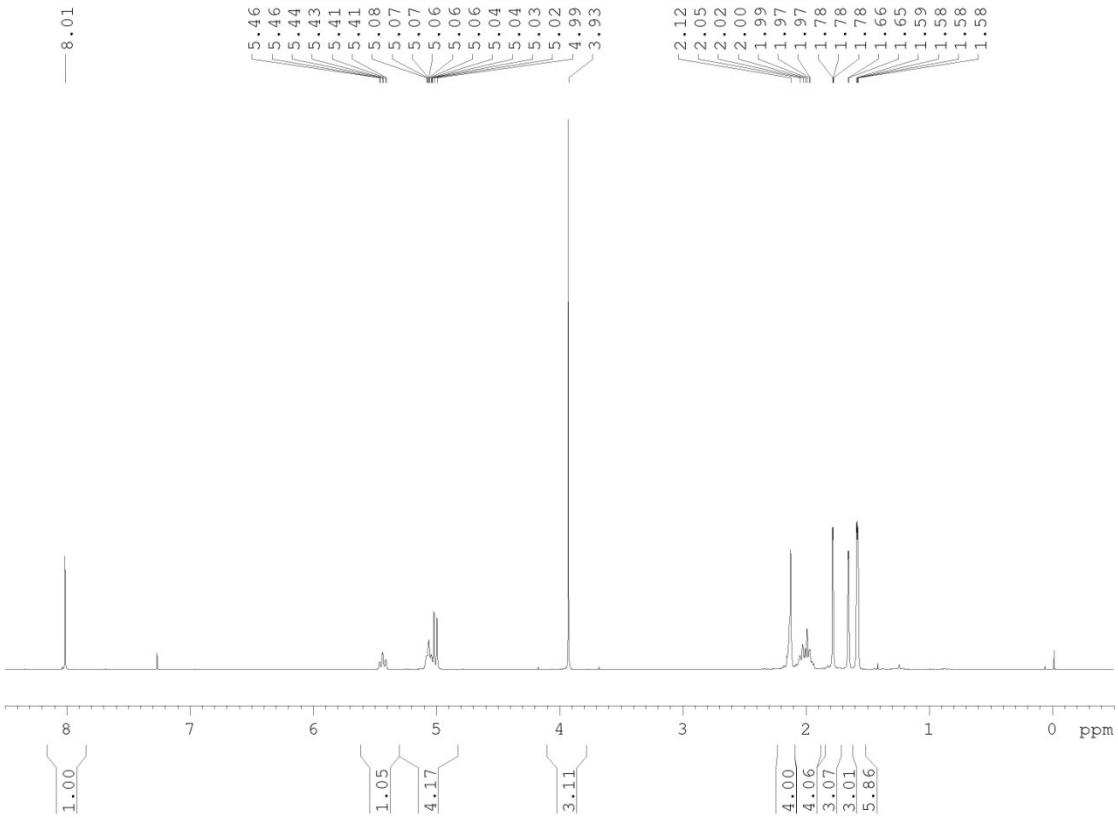

8
7
6
5
4
3
2
[ppm]
40
60
80
100
120

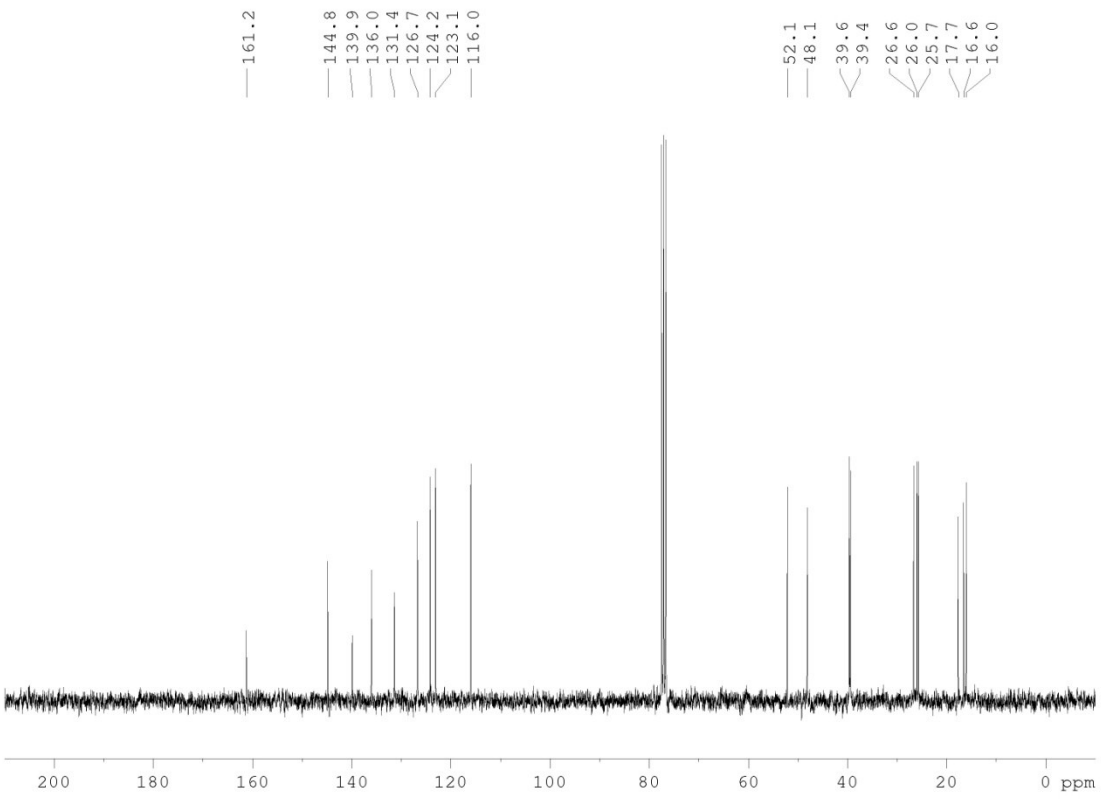

100
%
0
23.05
TIC
1.01e6
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
22.00
Time

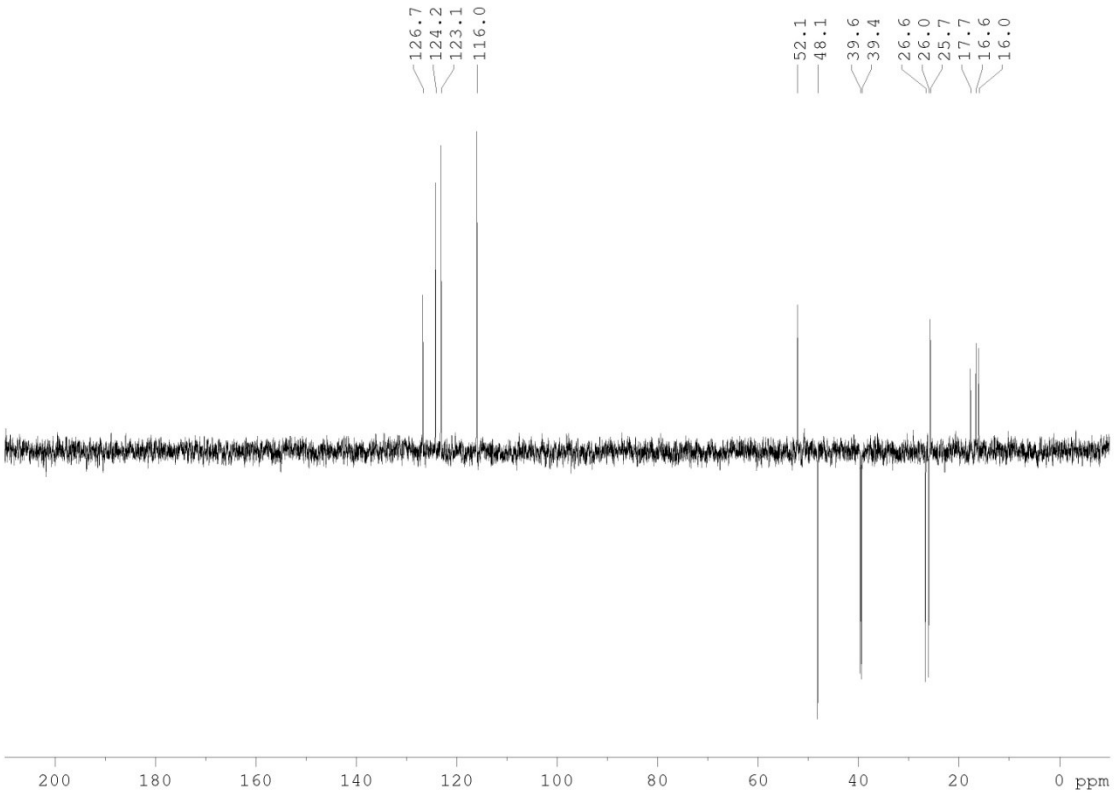

3.88e4
100
%
0
41
69
68
93
128
67
107
119
55
53
81
94
44
91
95
77
136
148
161
65
189
204
52
83
97
162
175
195
207
234
249
262
281
300
316
331
332
355
367
380
382
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400

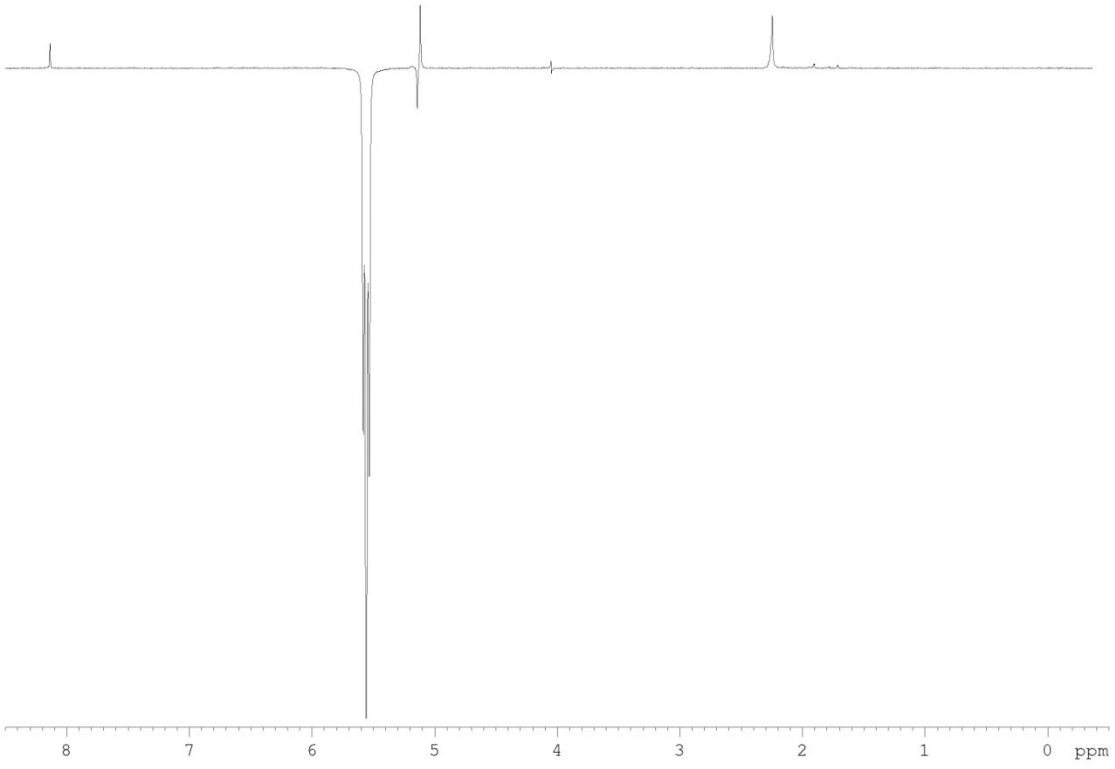
Spectral data of IT-21 (*E*,*E*)

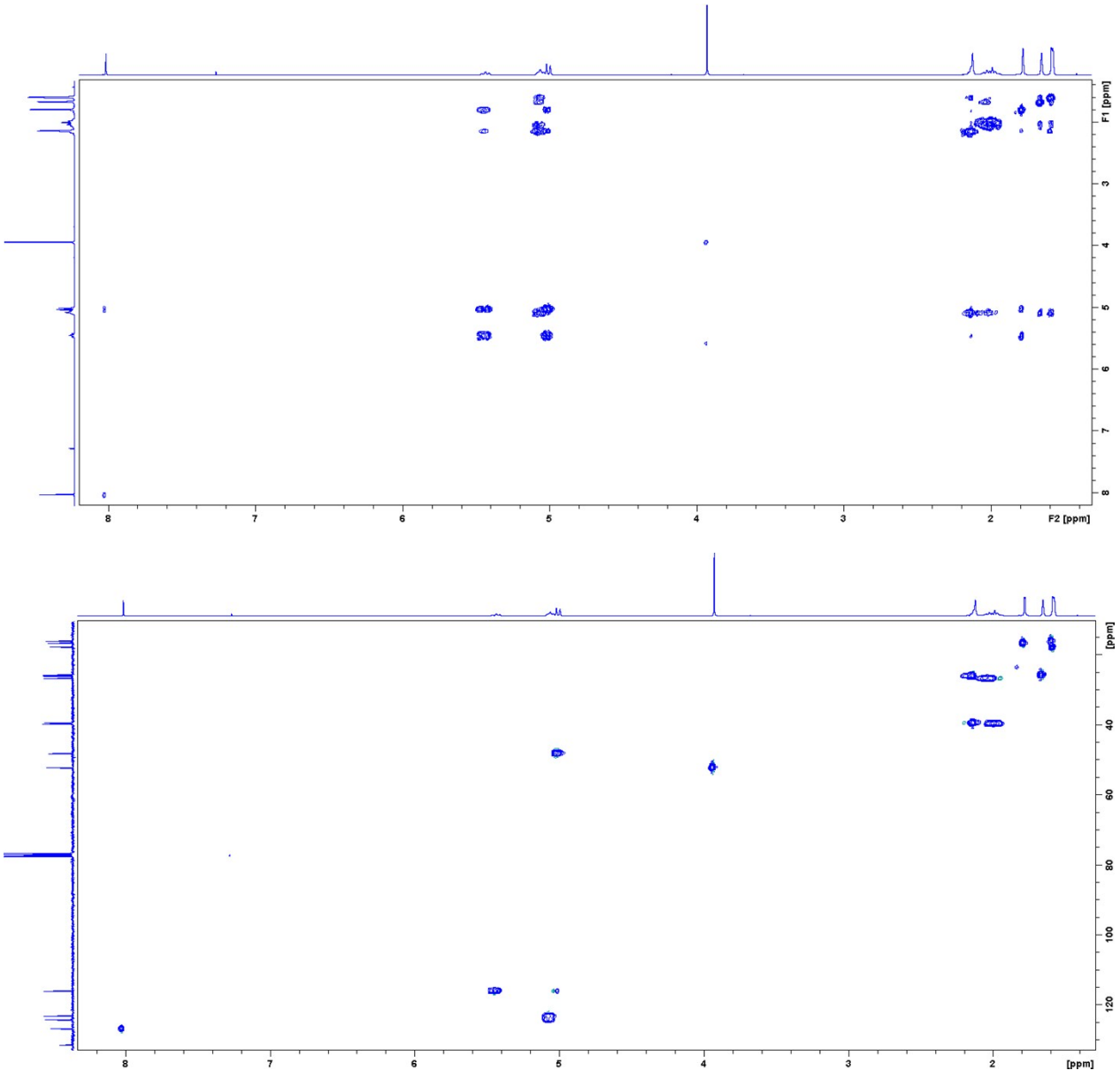


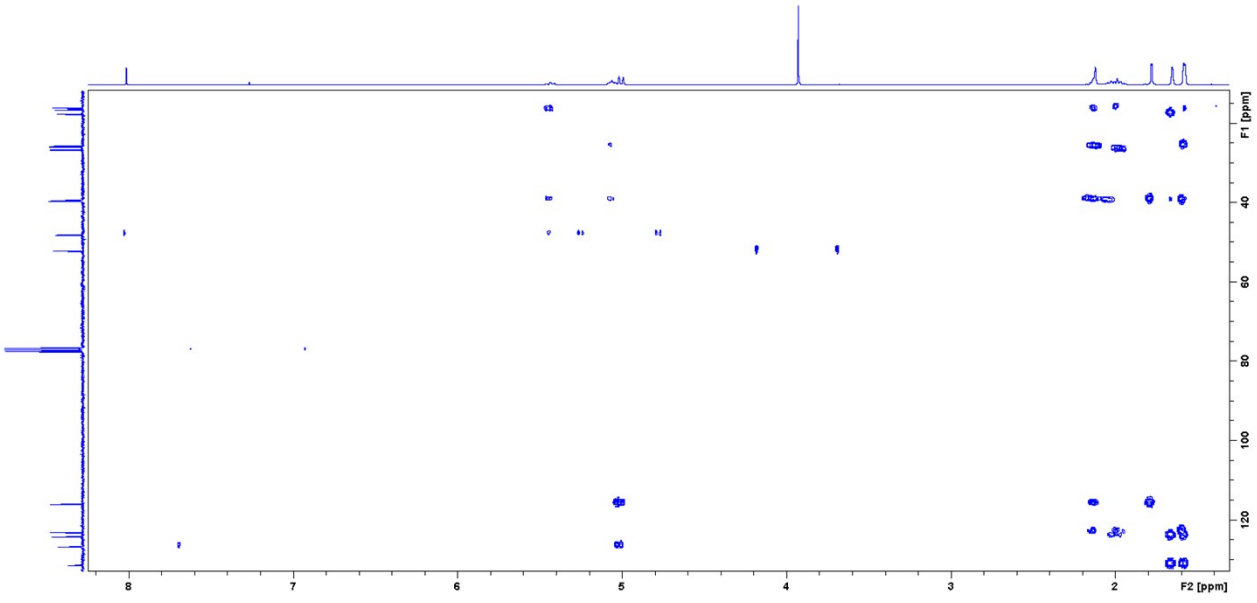


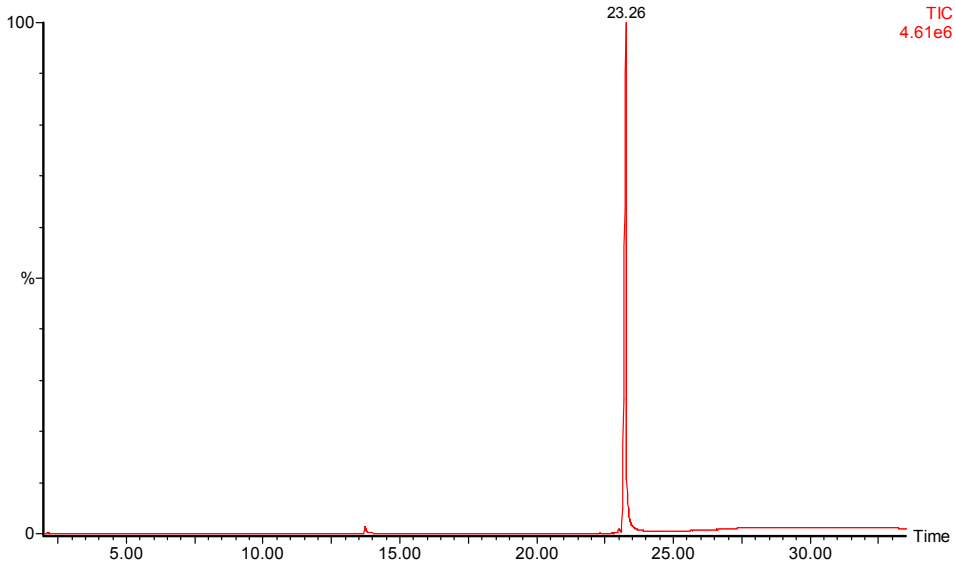

161.2
144.8
139.9
136.0
131.4
126.7
124.2
123.1
116.0
52.1
48.1
39.6
39.4
26.6
26.0
25.7
17.7
16.6
16.0
200
180
160
140
120
100
80
60
40
20
0 ppm

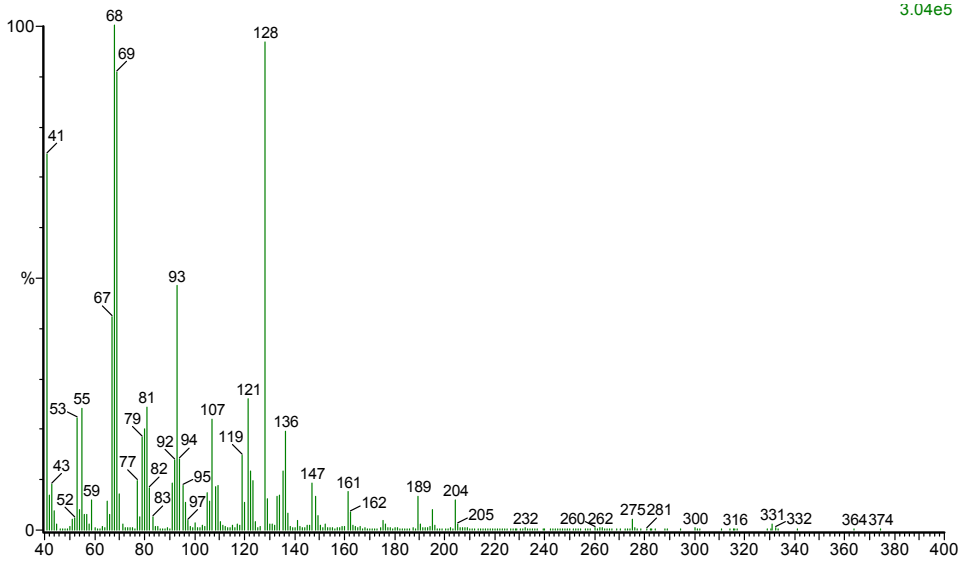

126.7
124.2
123.1
116.0
52.1
48.1
39.6
39.4
26.6
26.0
25.7
17.7
16.6
16.0
200
180
160
140
120
100
80
60
40
20
0 ppm


8
7
6
5
4
3
2
1
0
ppm

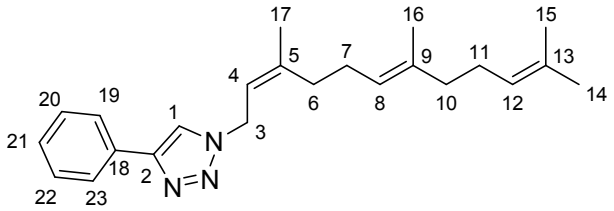

F1 [ppm]
F2 [ppm]
[ppm]
[ppm]

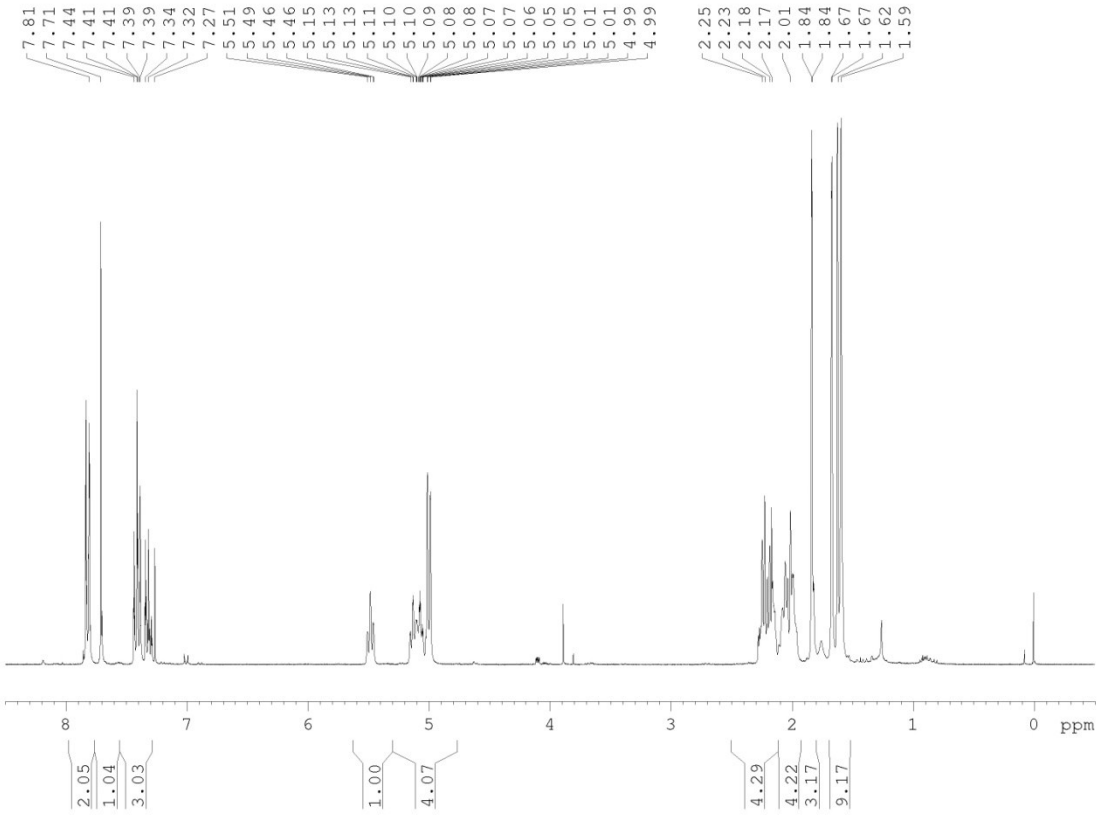

F1 [ppm]
40
60
80
100
120
8
7
6
5
4
3
2
F2 [ppm]

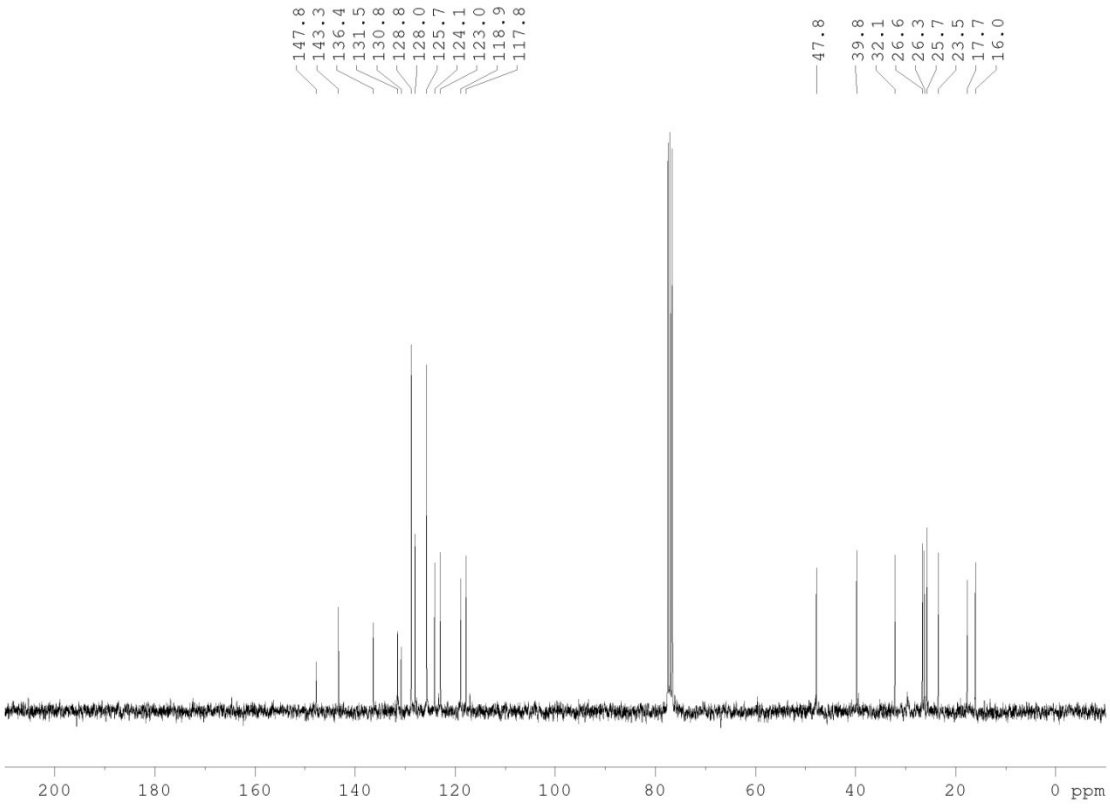

23.26
TIC
4.61e6
100
%
0
5.00
10.00
15.00
20.00
25.00
30.00
Time

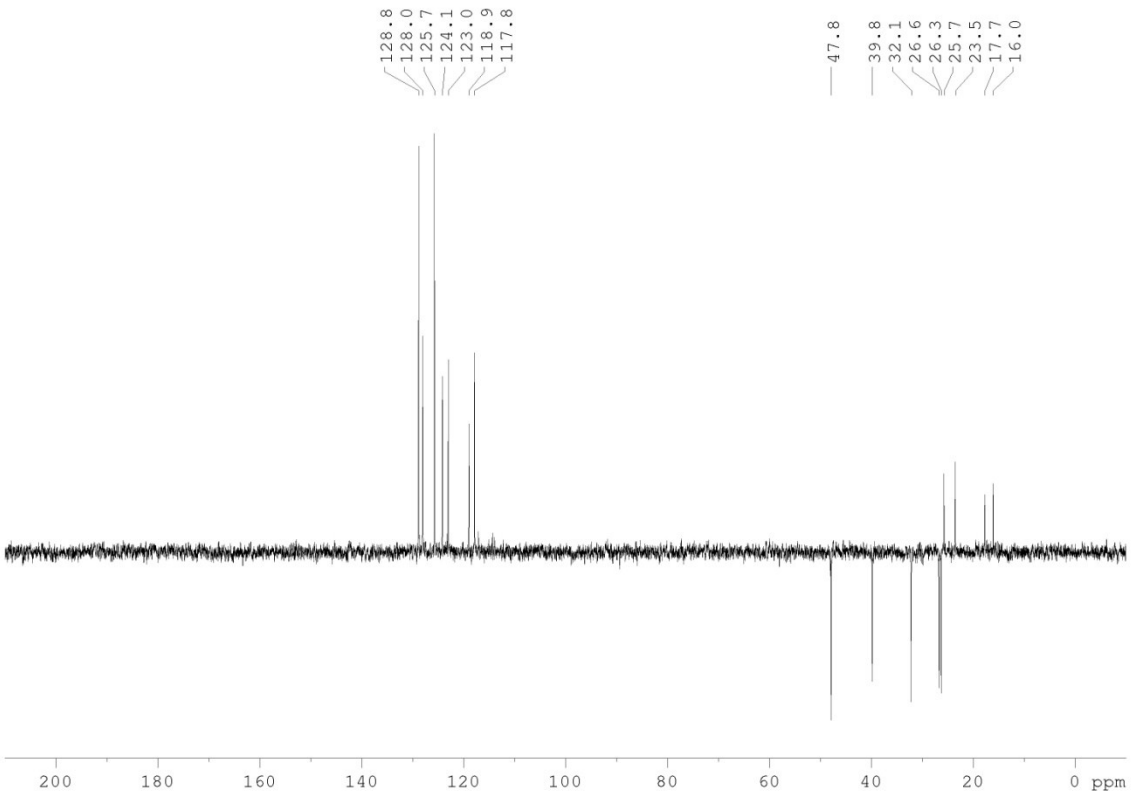

3.04e5
100
%
0
68
69
41
128
93
67
121
81
79
107
136
92
94
119
77
82
95
147
43
161
189
204
59
52
83
97
162
205
232
260
262
275
281
300
316
331
332
364
374
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400

Spectral data of IT-17

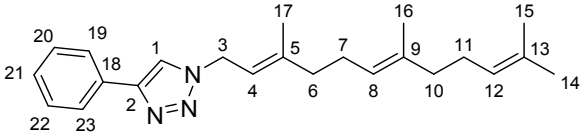


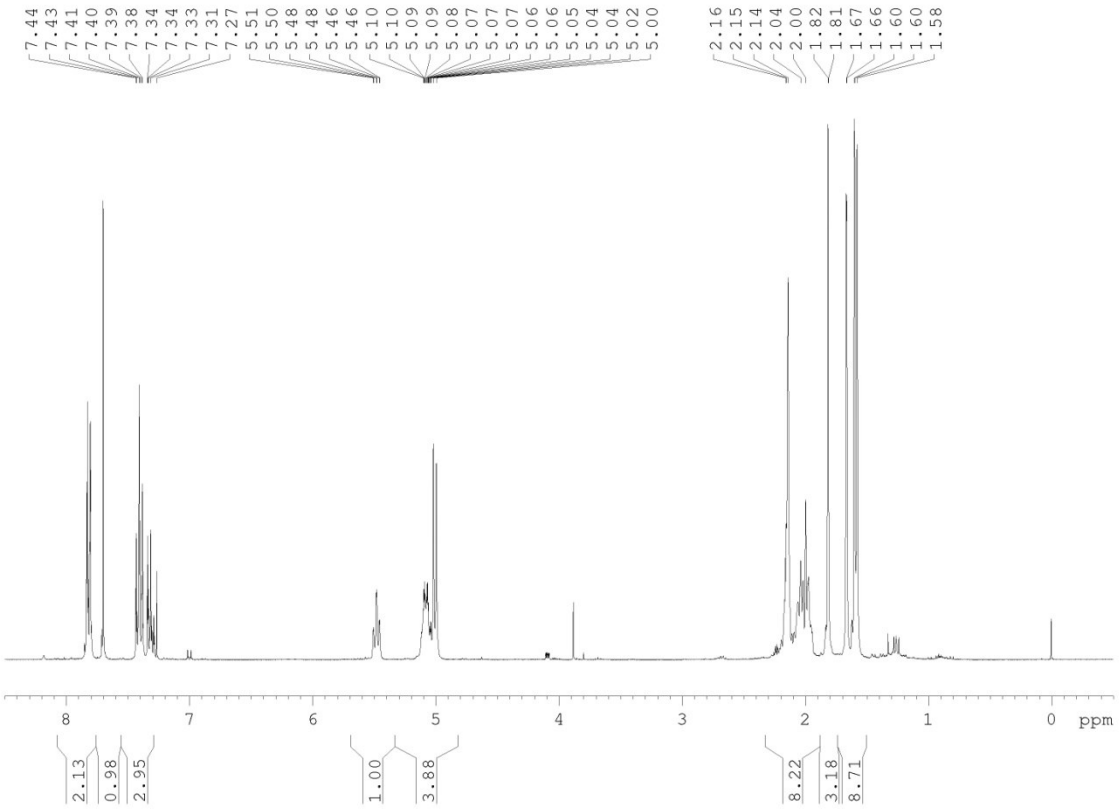


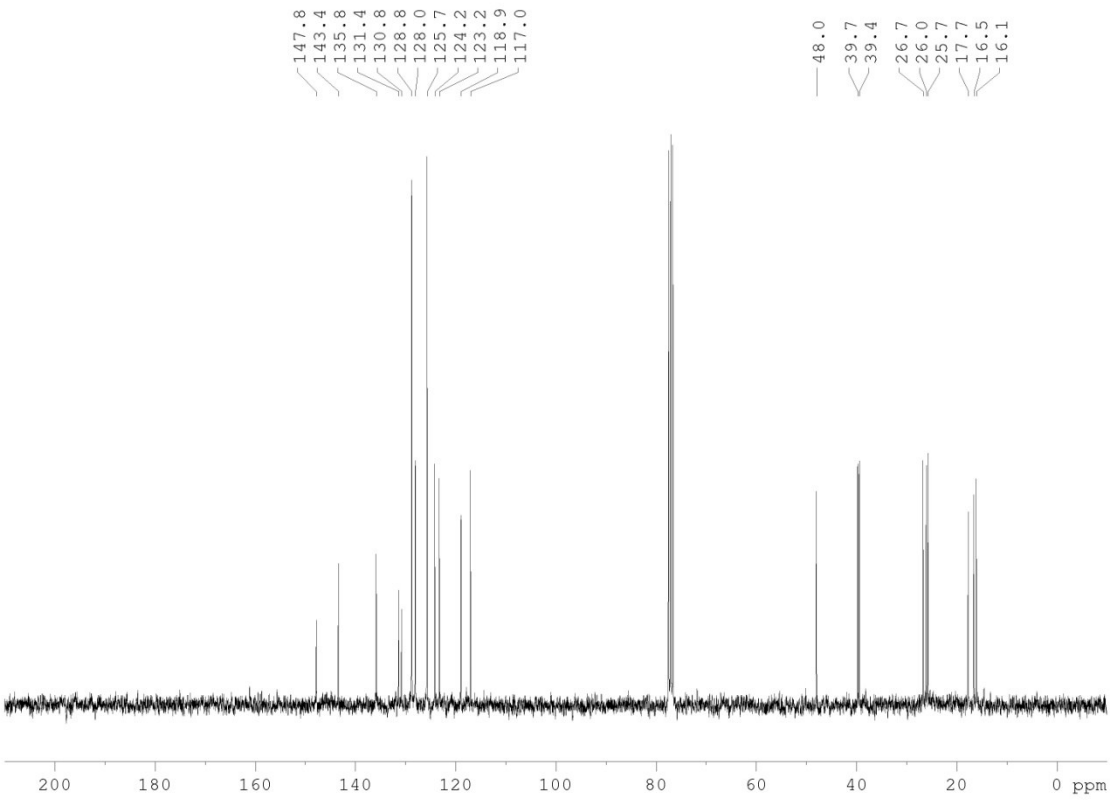

147.8
143.3
136.4
131.5
130.8
128.8
128.0
125.7
124.1
123.0
118.9
117.8
47.8
39.8
32.1
26.6
26.3
25.7
23.5
17.7
16.0
200
180
160
140
120
100
80
60
40
20
0 ppm

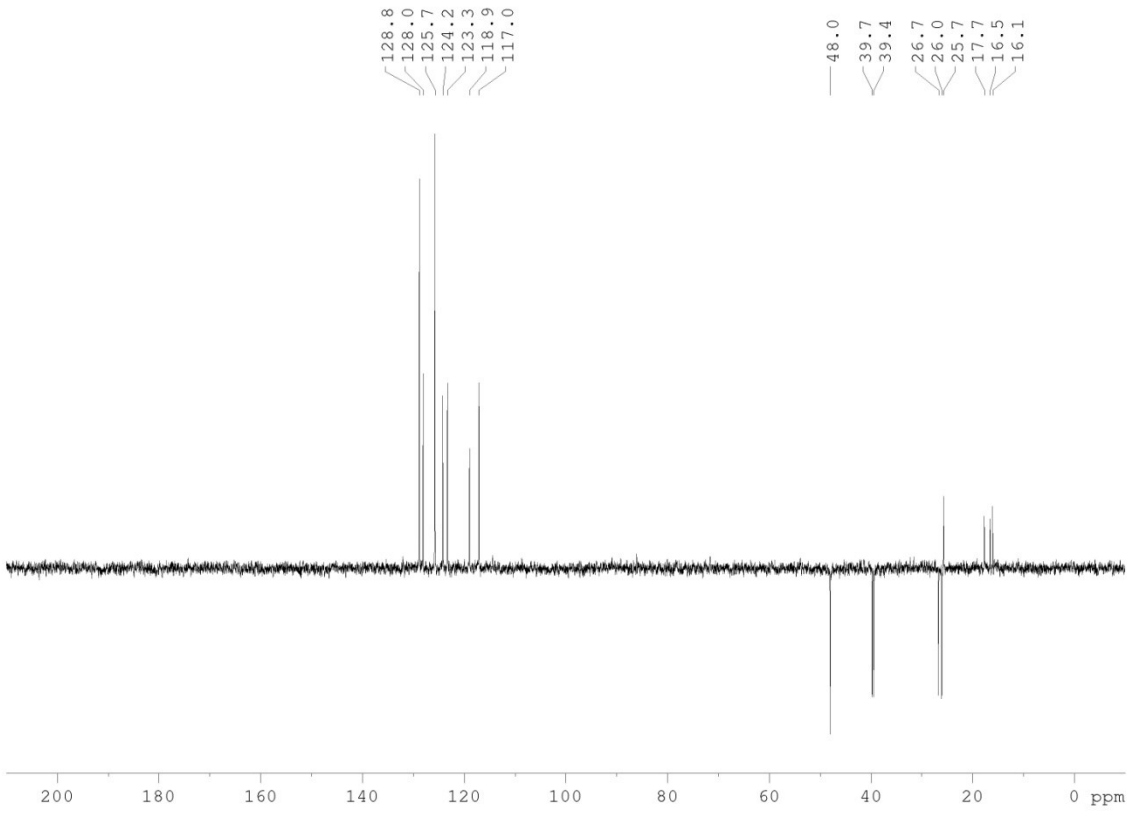

128.8
128.0
125.7
124.1
123.0
118.9
117.8
47.8
39.8
32.1
26.6
26.3
25.7
23.5
17.7
16.0
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-22

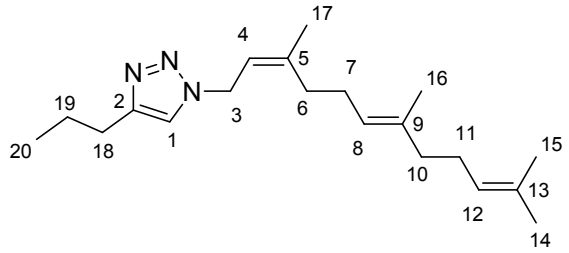


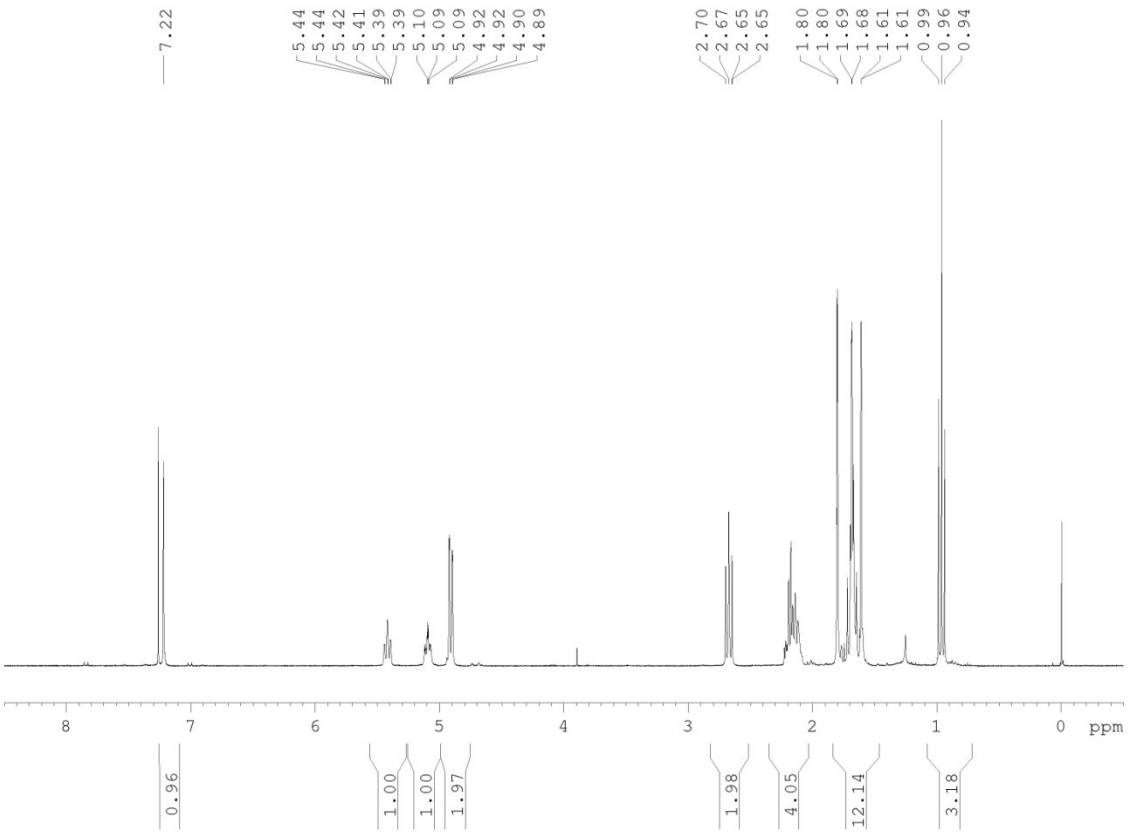


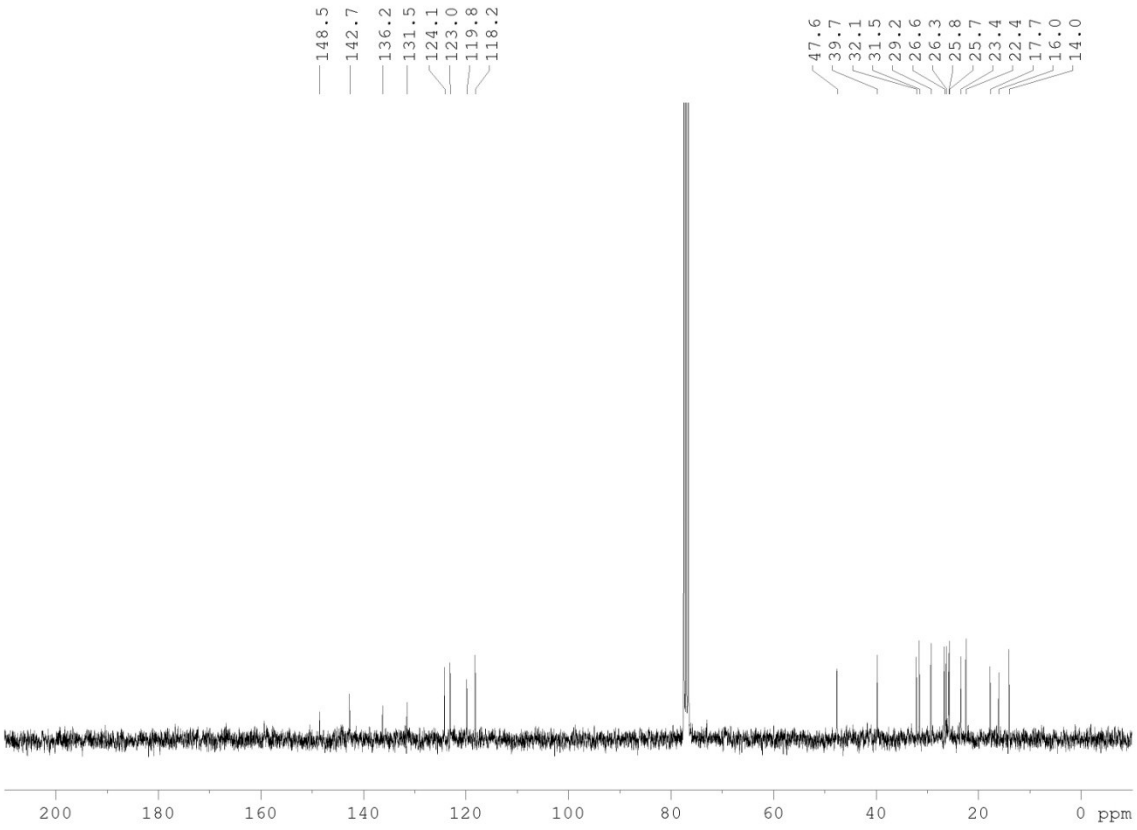

147.8
143.4
135.8
131.4
130.8
128.8
128.0
125.7
124.2
123.2
118.9
117.0
48.0
39.7
39.4
26.7
26.0
25.7
17.7
16.5
16.1
200
180
160
140
120
100
80
60
40
20
0 ppm

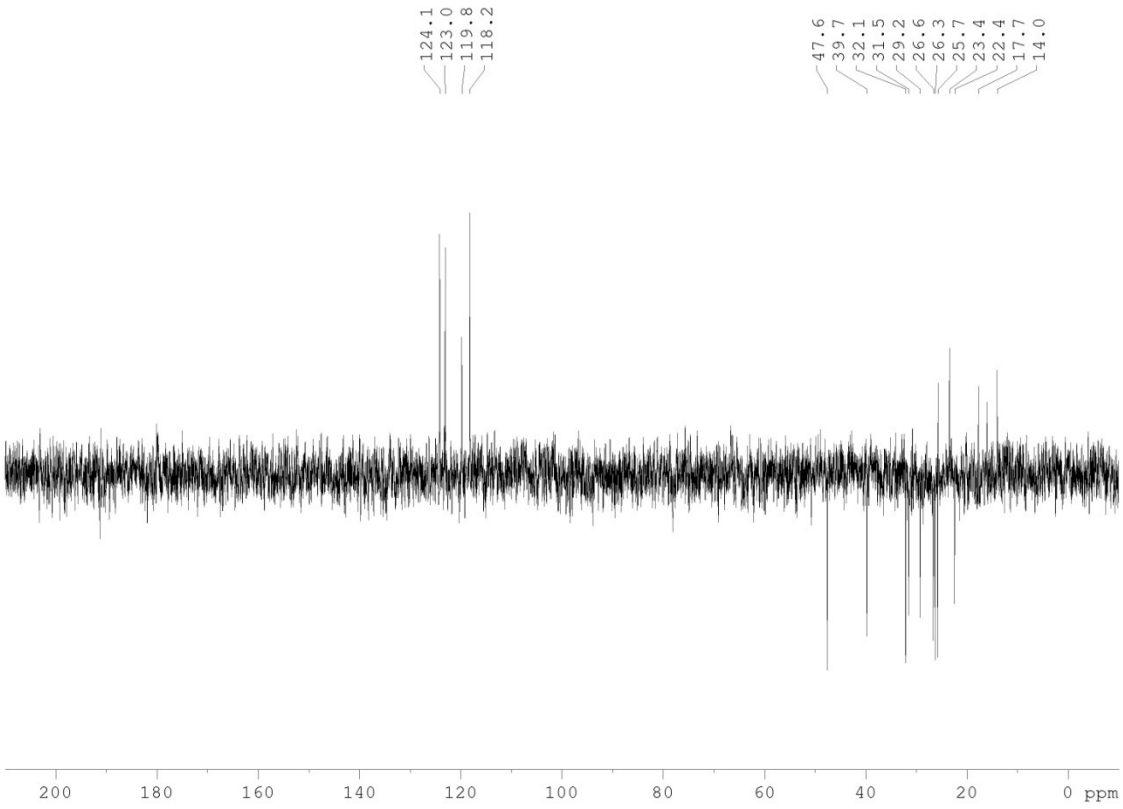

128.8
128.0
125.7
124.2
123.3
118.9
117.0
48.0
39.7
39.4
26.7
26.0
25.7
17.7
16.5
16.1
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-18

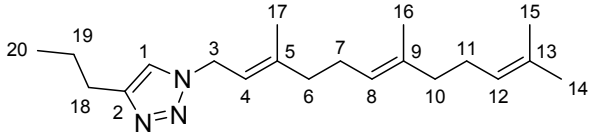


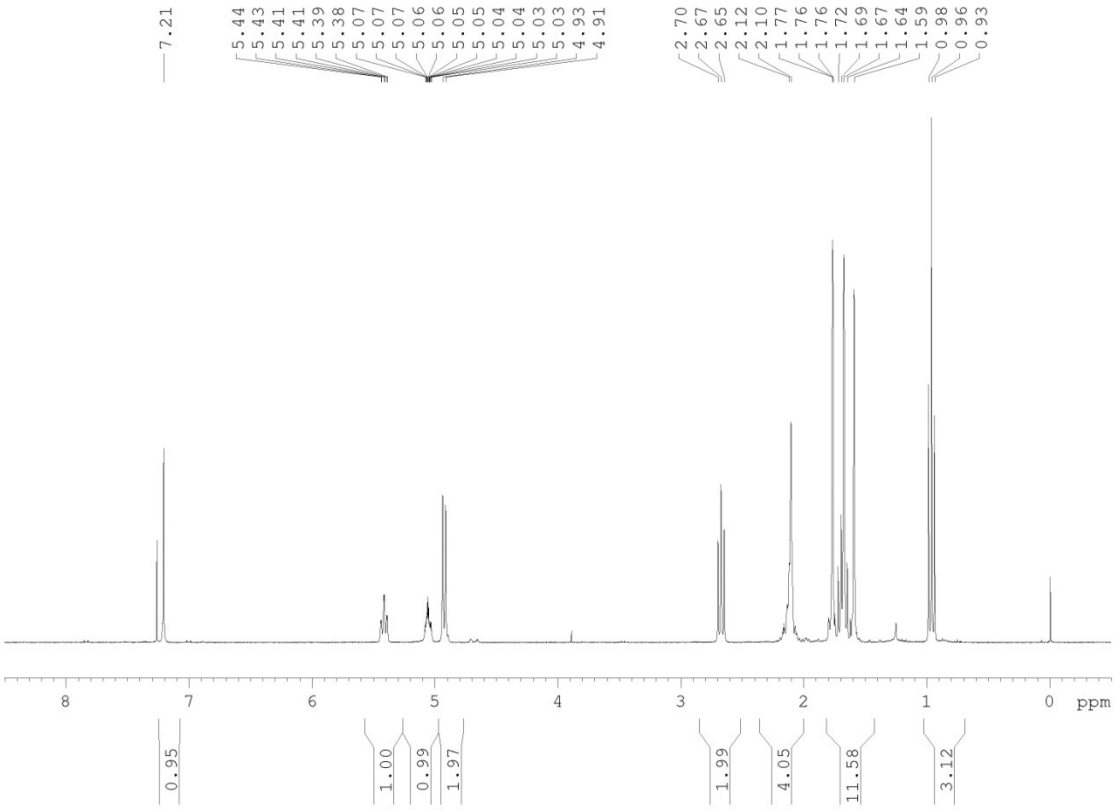


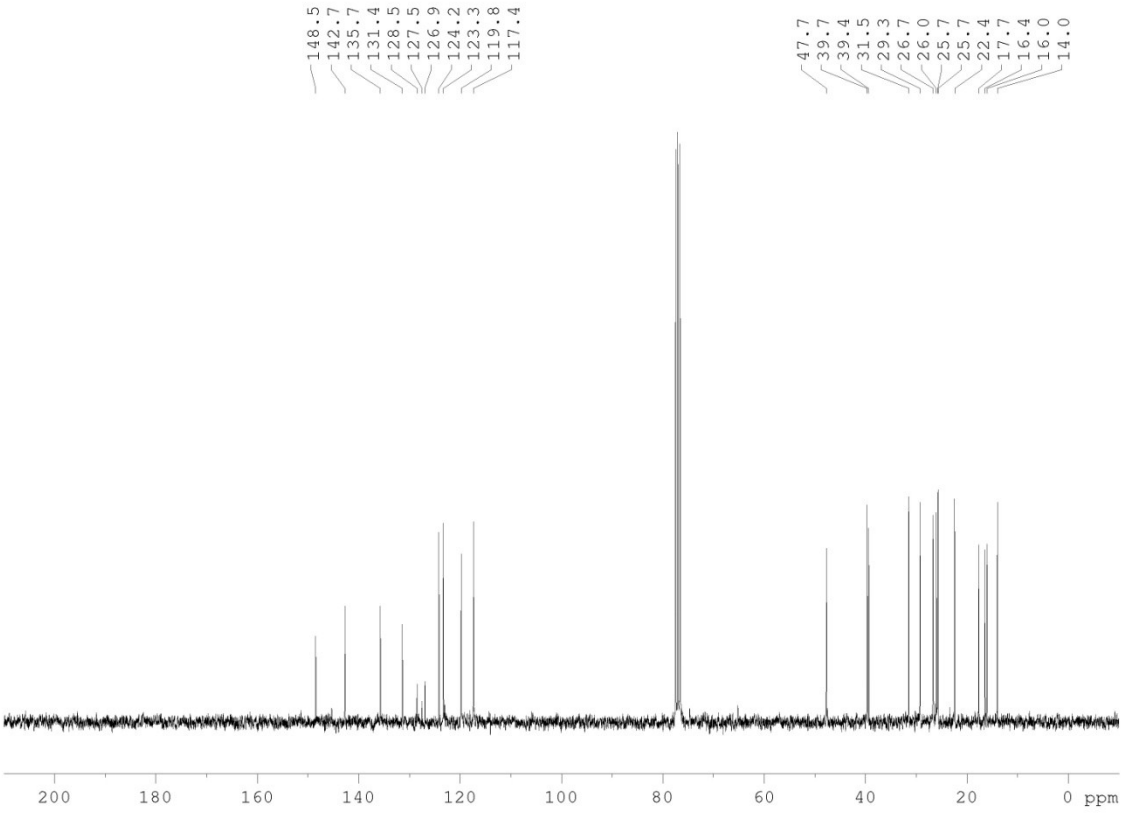

148.5
142.7
136.2
131.5
124.1
123.0
119.8
118.2
47.6
39.7
32.1
31.5
29.2
26.6
26.3
25.8
25.7
23.4
22.4
17.7
16.0
14.0
200
180
160
140
120
100
80
60
40
20
0 ppm

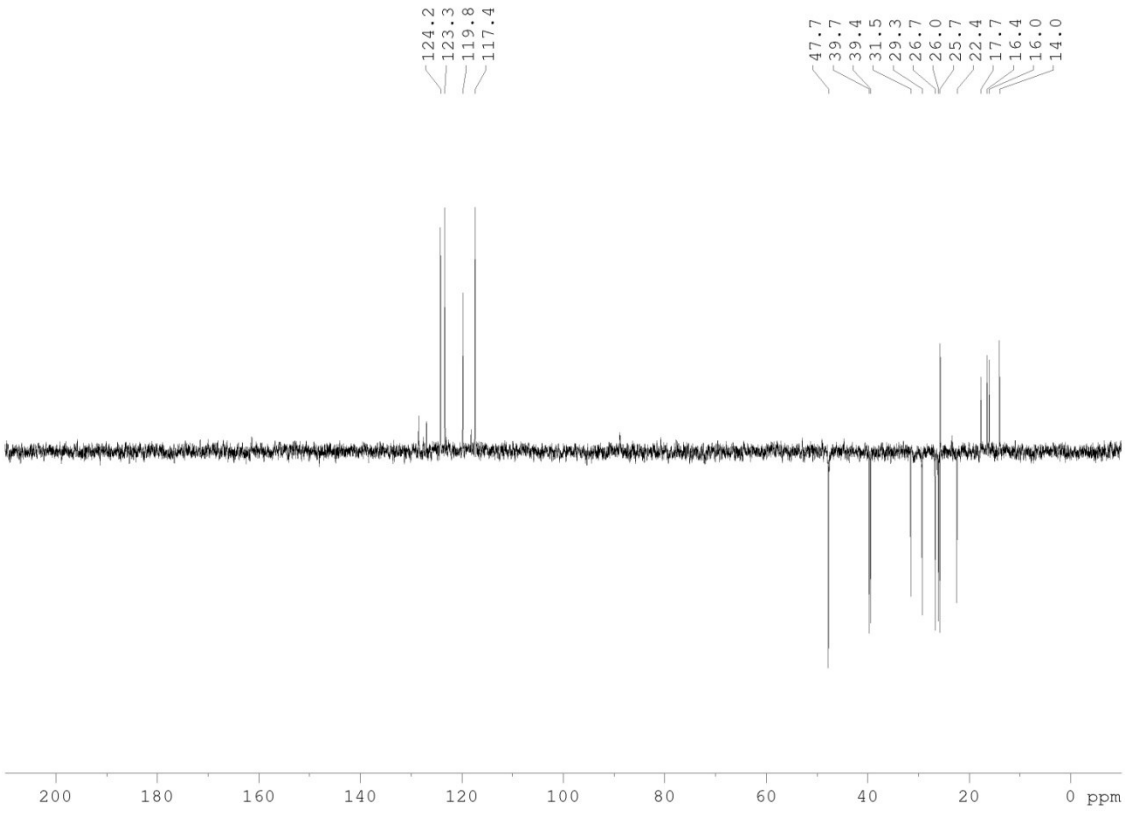

124.1
123.0
119.8
118.2
47.6
39.7
32.1
31.5
29.2
26.6
26.3
25.7
23.4
22.4
17.7
14.0
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-23

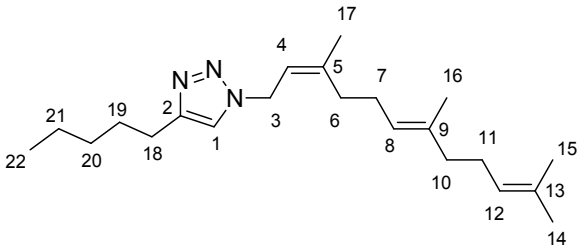


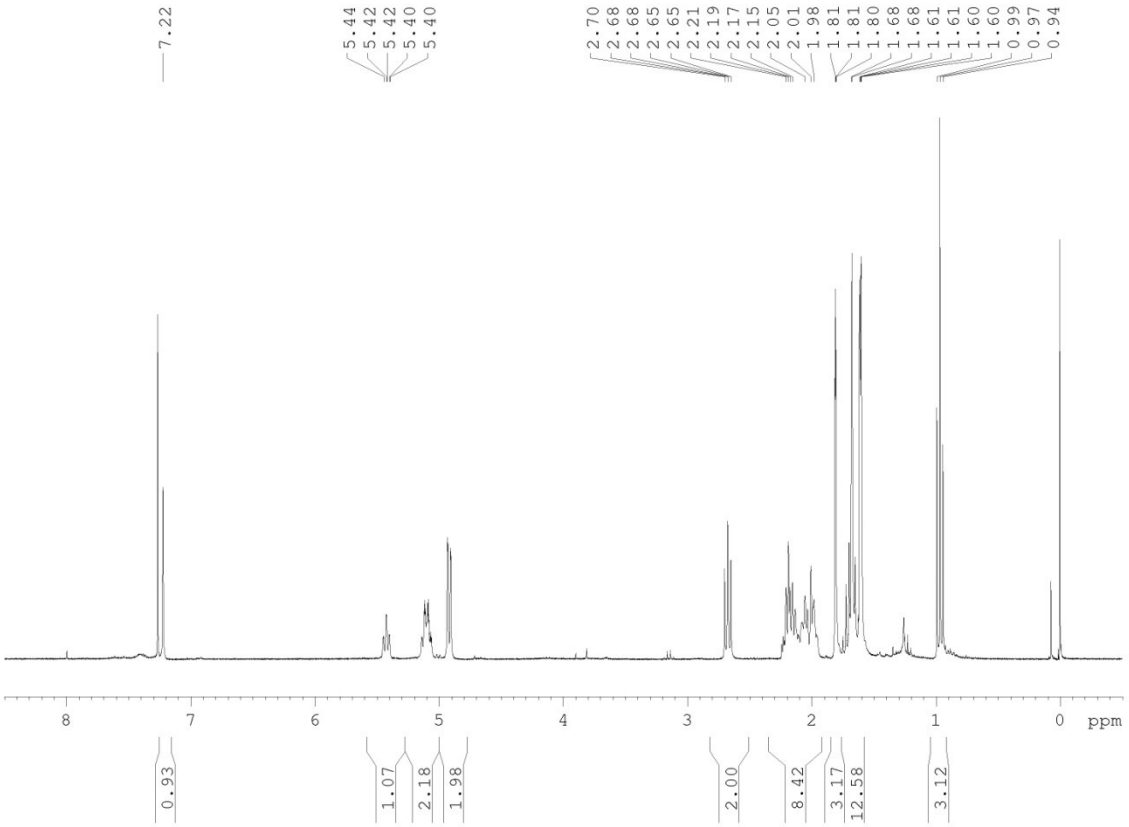


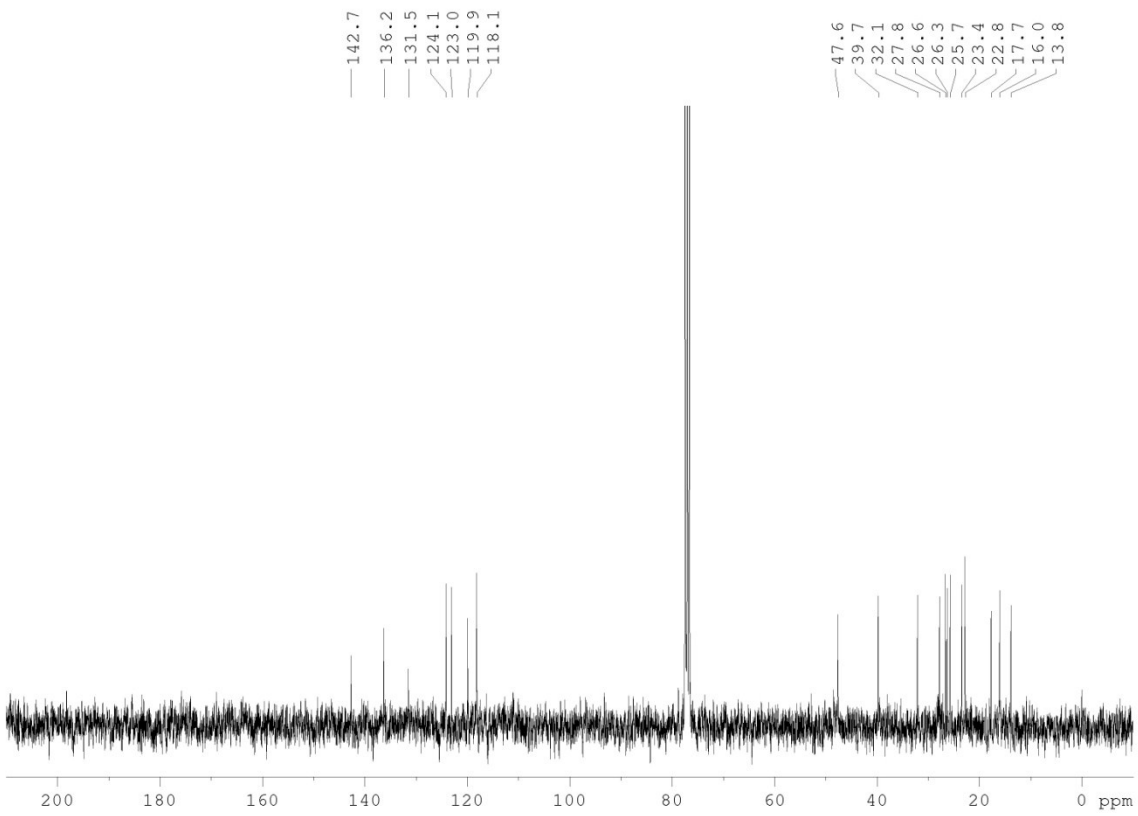

148.5
142.7
135.7
131.4
128.5
127.5
126.9
124.2
123.3
119.8
117.4
47.7
39.7
39.4
31.5
29.3
26.7
26.0
25.7
25.7
22.4
17.7
16.4
16.0
14.0
200
180
160
140
120
100
80
60
40
20
0 ppm

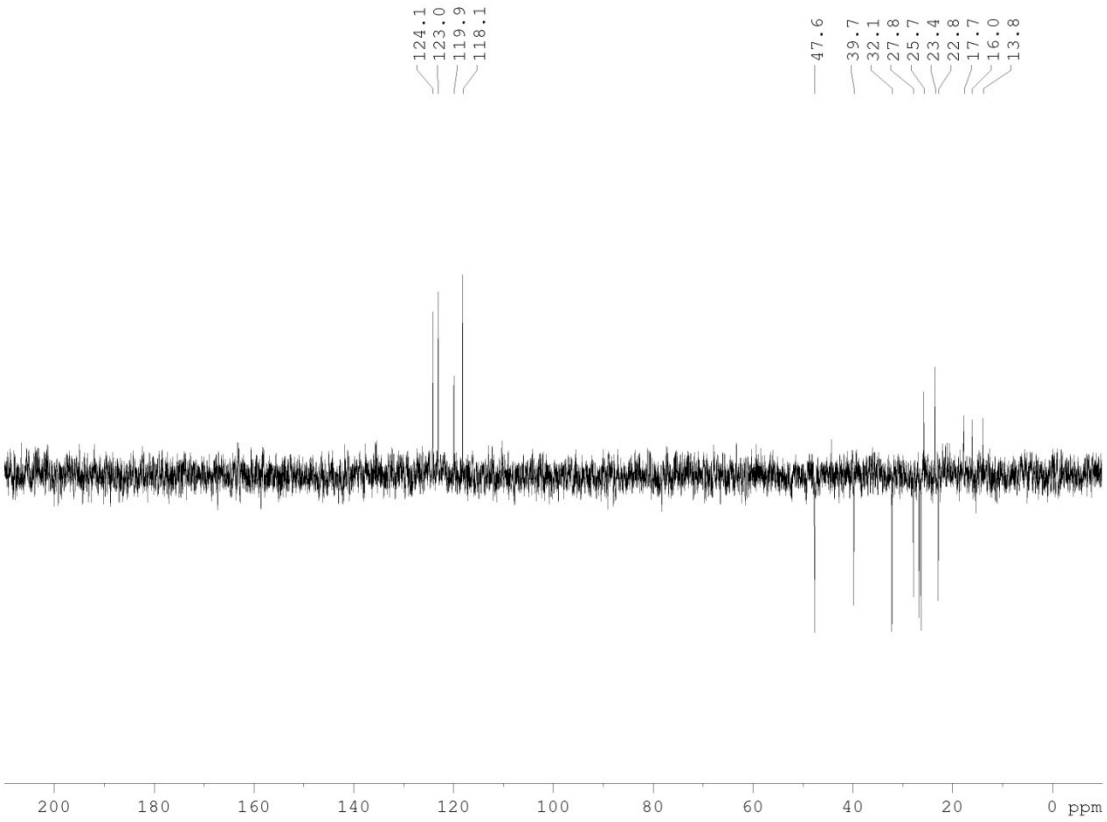

124.2
123.3
119.8
117.4
47.7
39.7
39.4
31.5
29.3
26.7
26.0
25.7
22.4
17.7
16.4
16.0
14.0
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-19

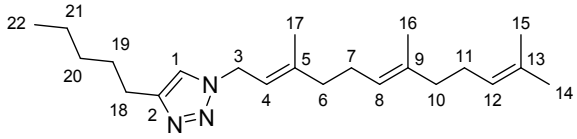


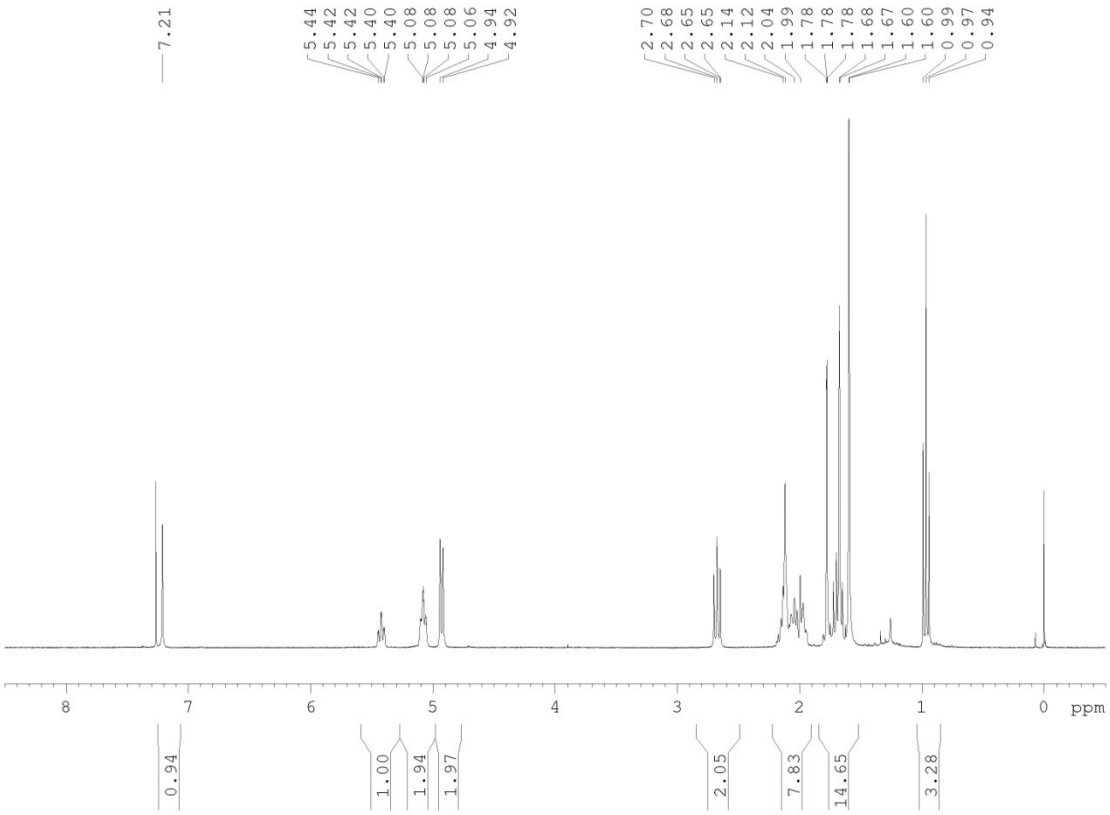


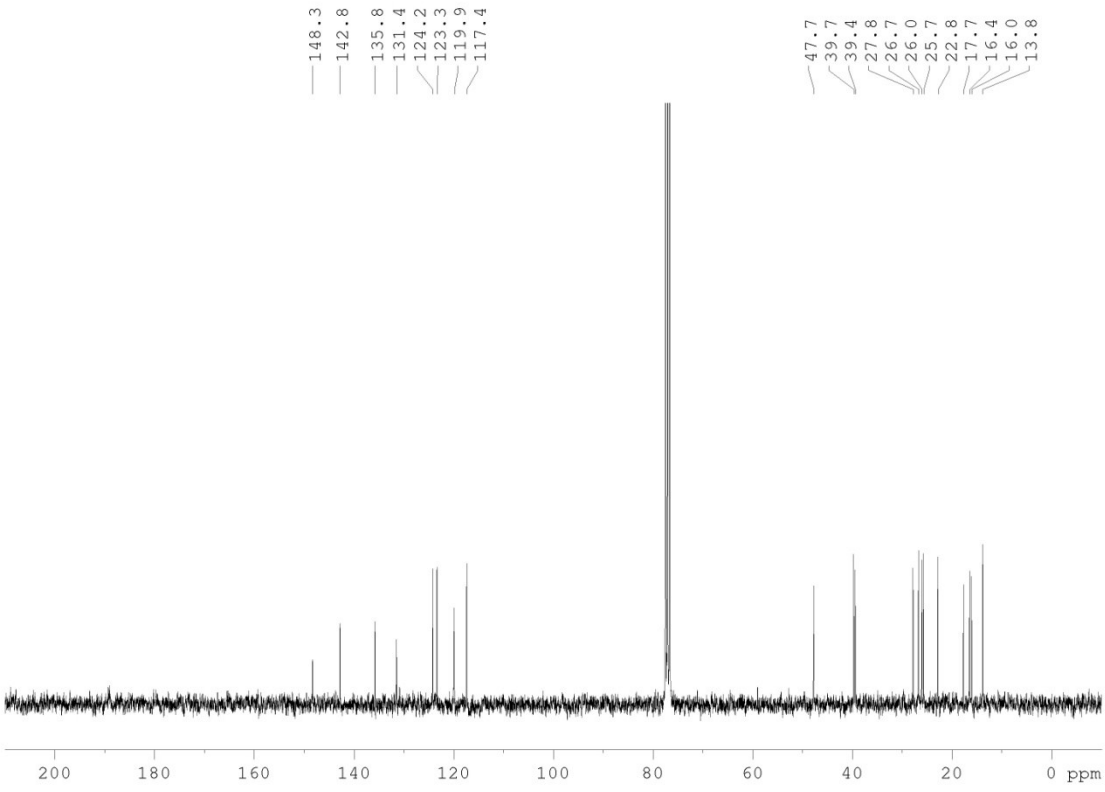

142.7
136.2
131.5
124.1
123.0
119.9
118.1
47.6
39.7
32.1
27.8
26.6
26.3
25.7
23.4
22.8
17.7
16.0
13.8
200
180
160
140
120
100
80
60
40
20
0 ppm

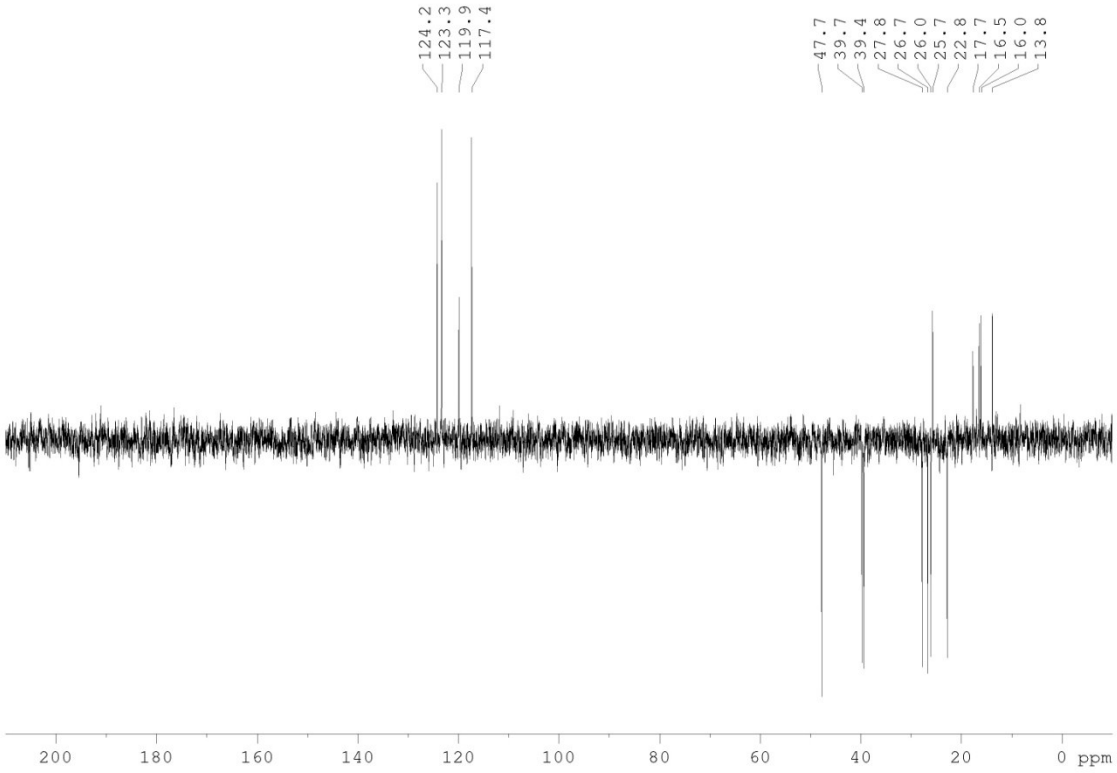

124.1
123.0
119.9
118.1
47.6
39.7
32.1
27.8
25.7
23.4
22.8
17.7
16.0
13.8
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-24

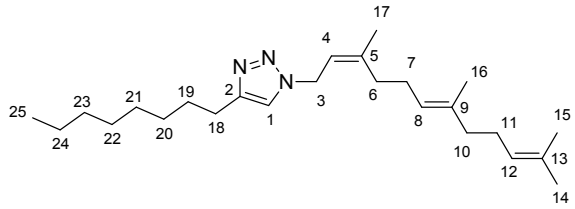


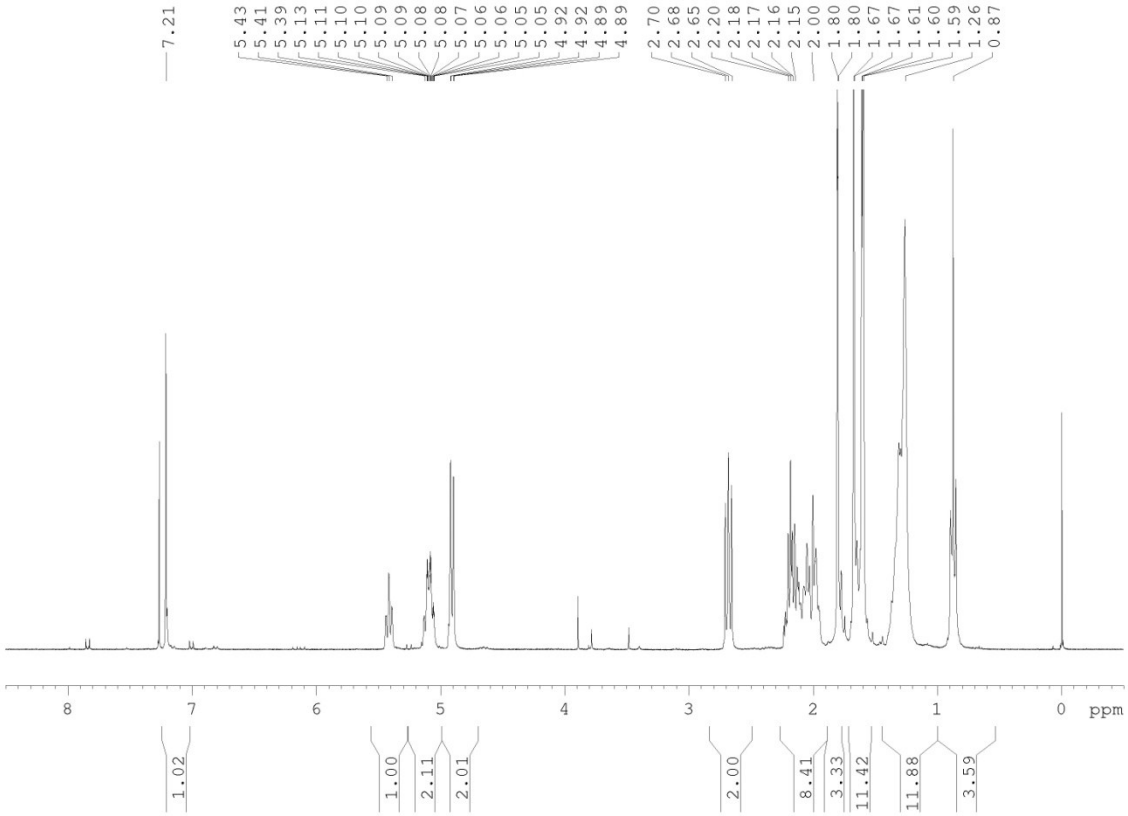


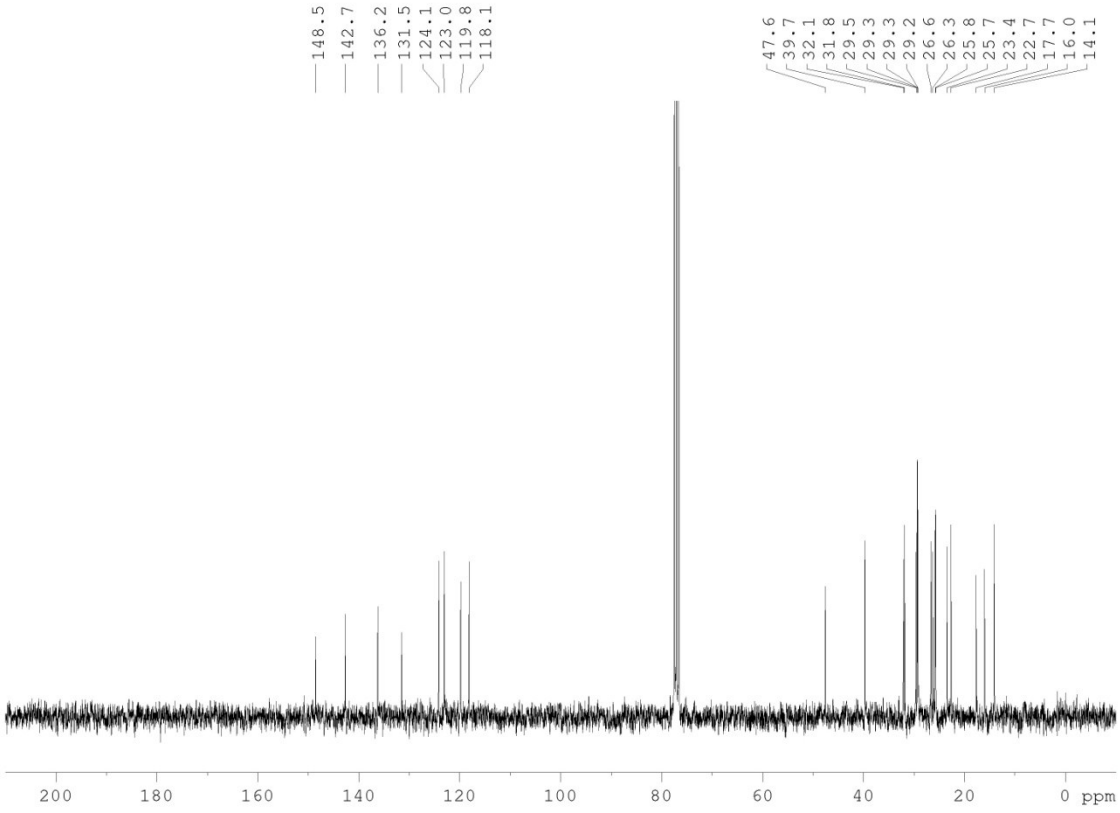

148.3
142.8
135.8
131.4
124.2
123.3
119.9
117.4
47.7
39.7
39.4
27.8
26.7
26.0
25.7
22.8
17.7
16.4
16.0
13.8
200
180
160
140
120
100
80
60
40
20
0 ppm

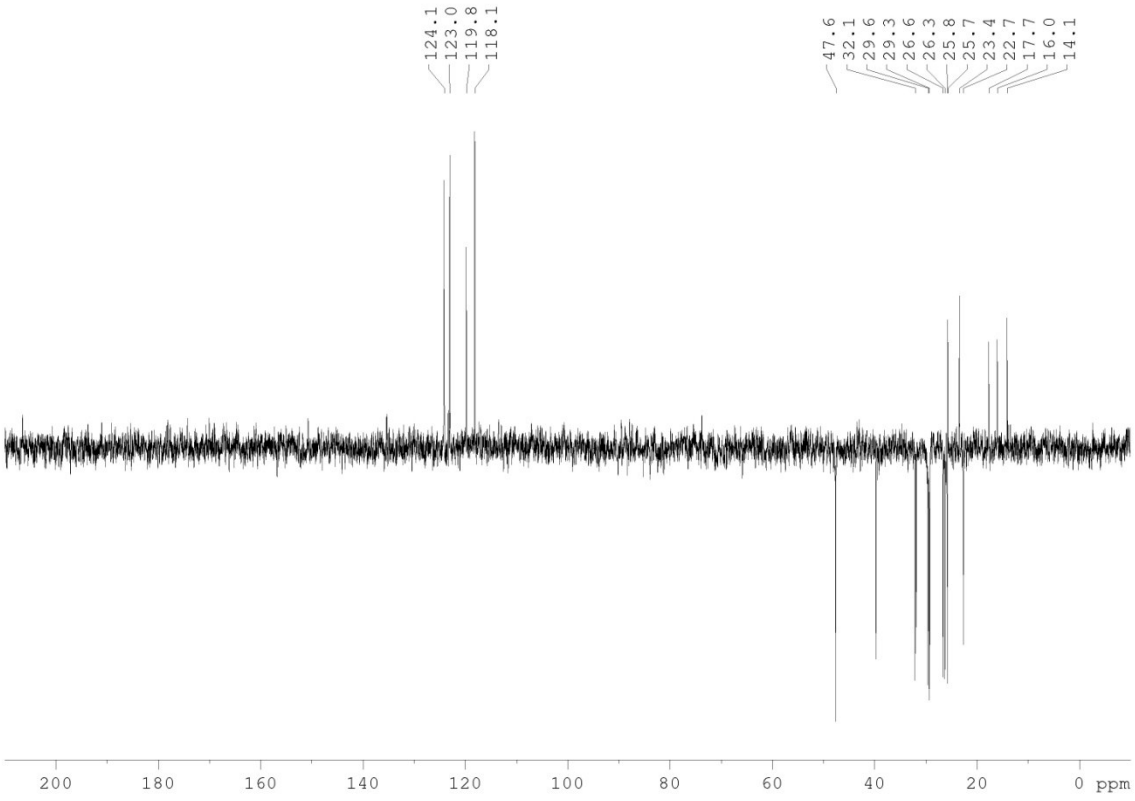

124.2
123.3
119.9
117.4
47.7
39.7
39.4
27.8
26.7
26.0
25.7
22.8
17.7
16.5
16.0
13.8
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-20

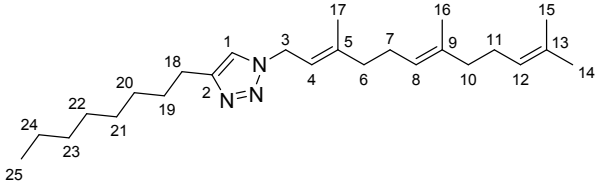


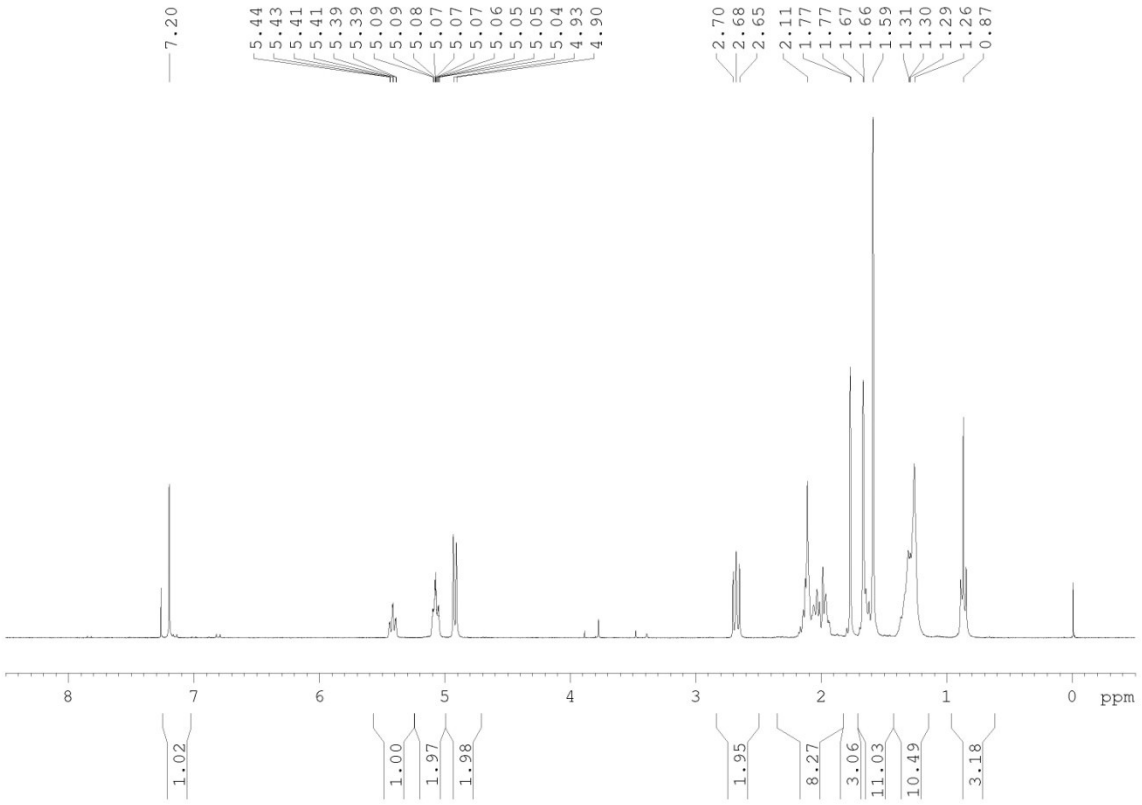


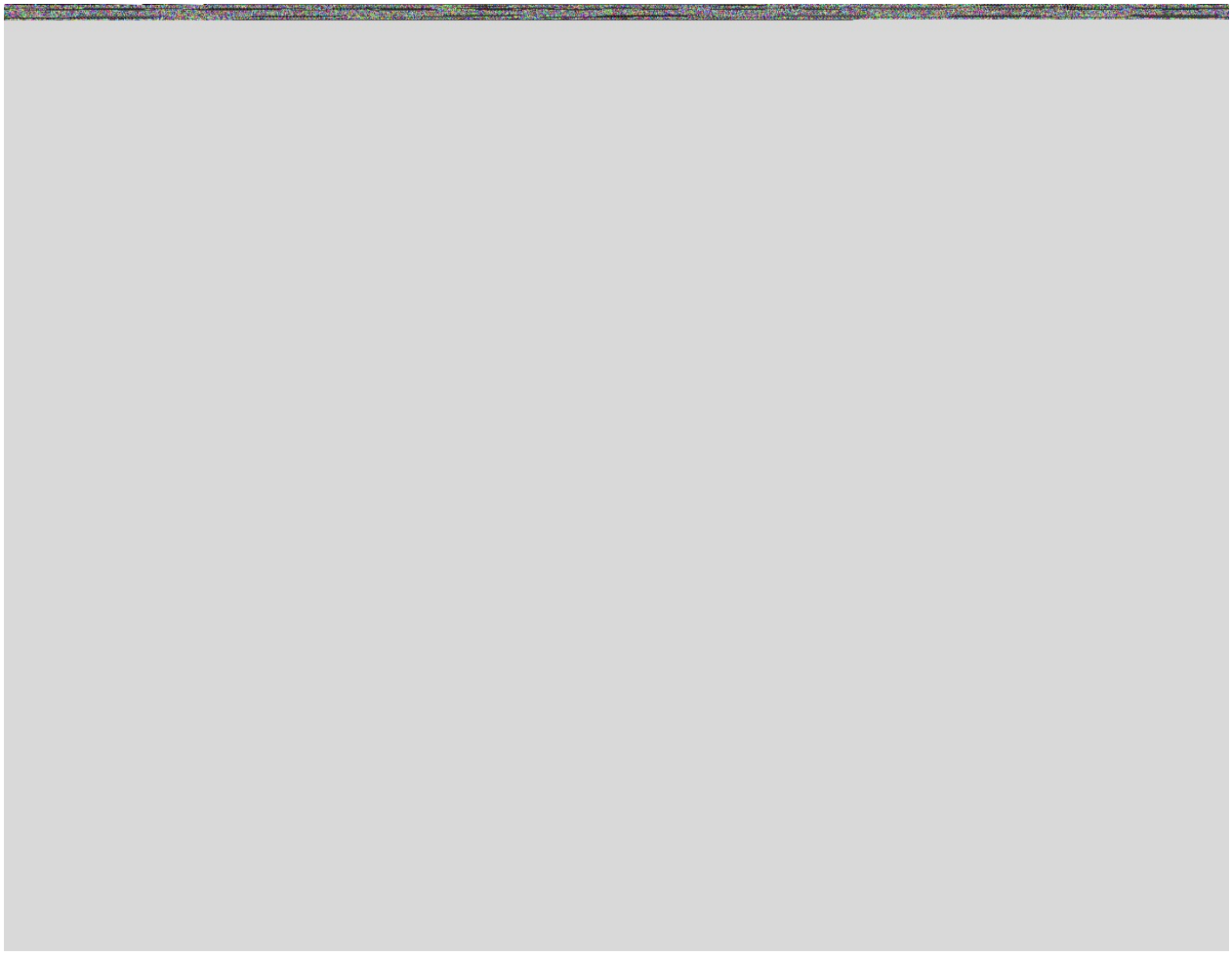

148.5
142.7
136.2
131.5
124.1
123.0
119.8
118.1
47.6
39.7
32.1
31.8
29.5
29.3
29.3
29.2
26.6
26.3
25.8
25.7
23.4
22.7
17.7
16.0
14.1
200
180
160
140
120
100
80
60
40
20
0 ppm


124.1
123.0
119.8
118.1
47.6
32.1
29.6
29.3
26.6
26.3
25.8
25.7
23.4
22.7
17.7
16.0
14.1
200
180
160
140
120
100
80
60
40
20
0 ppm

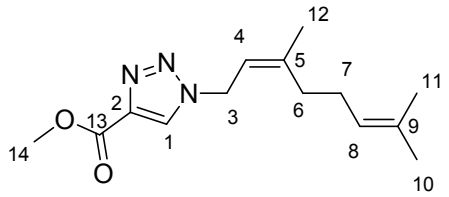
Spectral data of IT-25

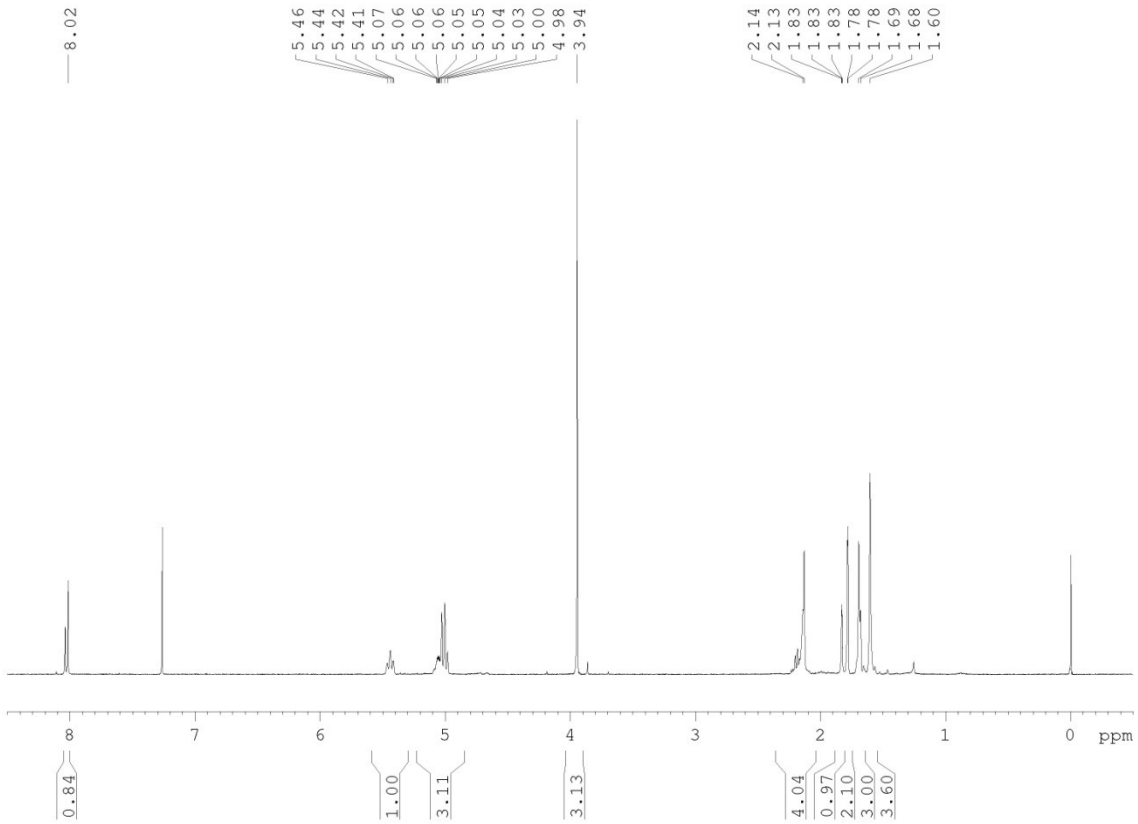


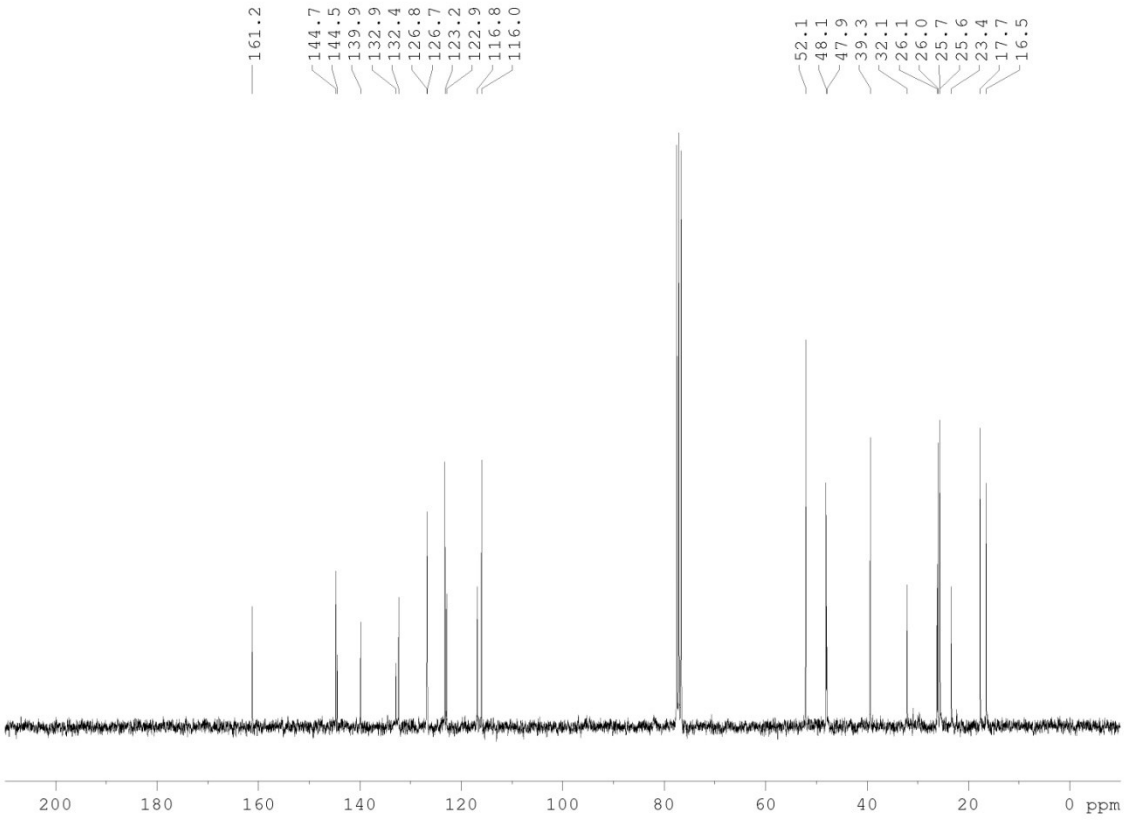


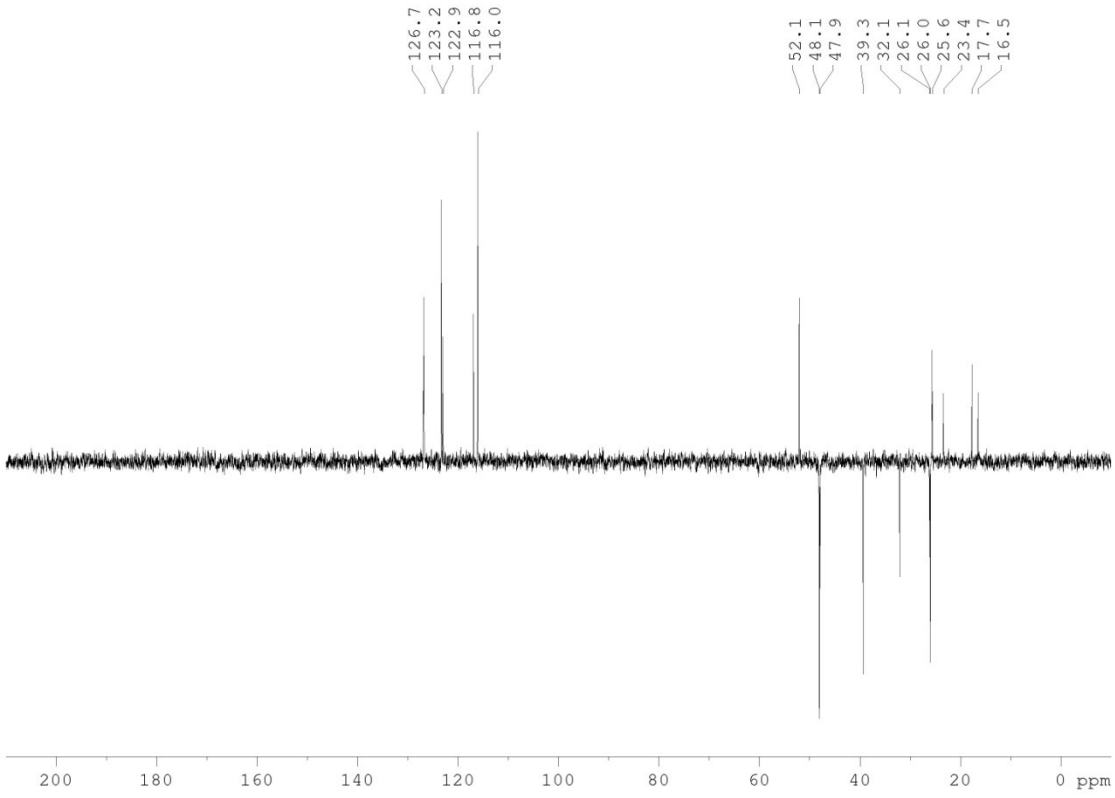


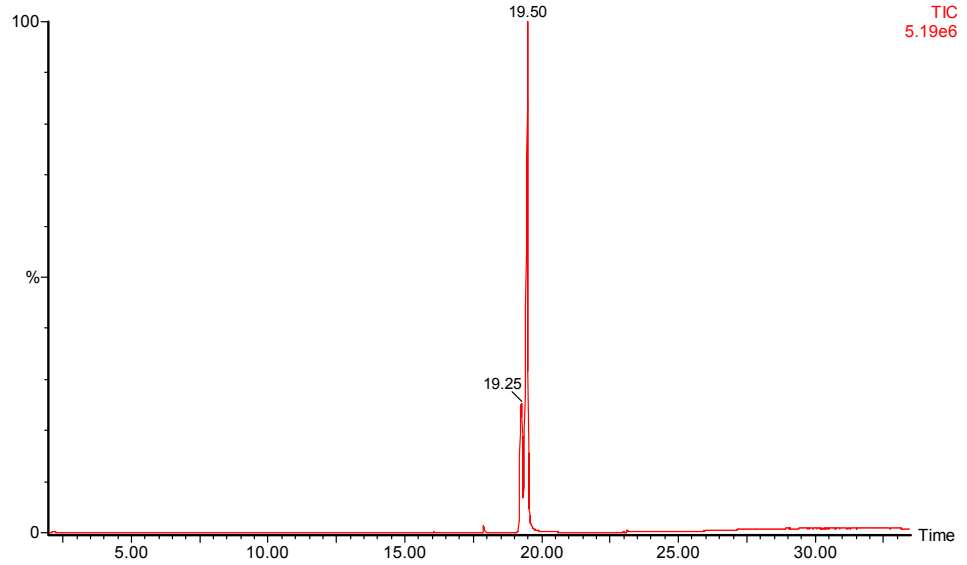
Spectral data of IT-6

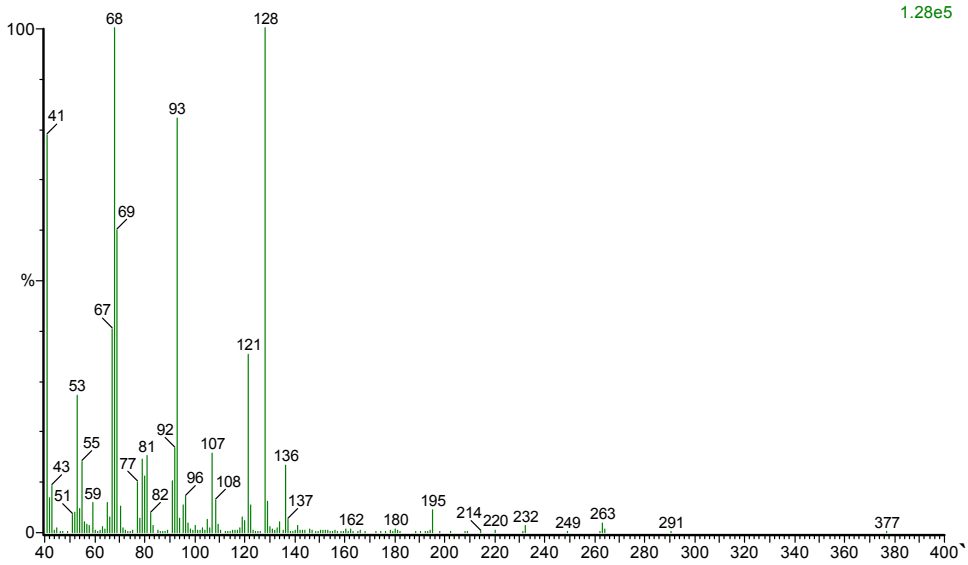





161.2
144.7
144.5
139.9
132.9
132.4
126.8
126.7
123.2
122.9
116.8
116.0
52.1
48.1
47.9
39.3
32.1
26.1
26.0
25.7
25.6
23.4
17.7
16.5
200
180
160
140
120
100
80
60
40
20
0 ppm


126.7
123.2
122.9
116.8
116.0
52.1
48.1
47.9
39.3
32.1
26.1
26.0
25.6
23.4
17.7
16.5
200
180
160
140
120
100
80
60
40
20
0 ppm


TIC
5.19e6
19.50
19.25
100
%
0
5.00
10.00
15.00
20.00
25.00
30.00
Time


1.28e5
100
%
0
68
128
41
93
69
67
121
53
55
92
81
107
43
77
136
96
108
51
59
82
137
162
180
195
214
220
232
249
263
291
377
40
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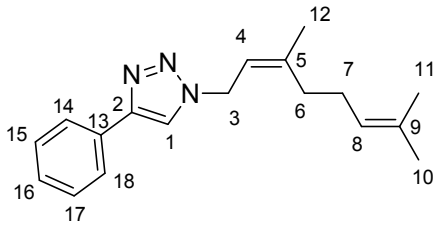
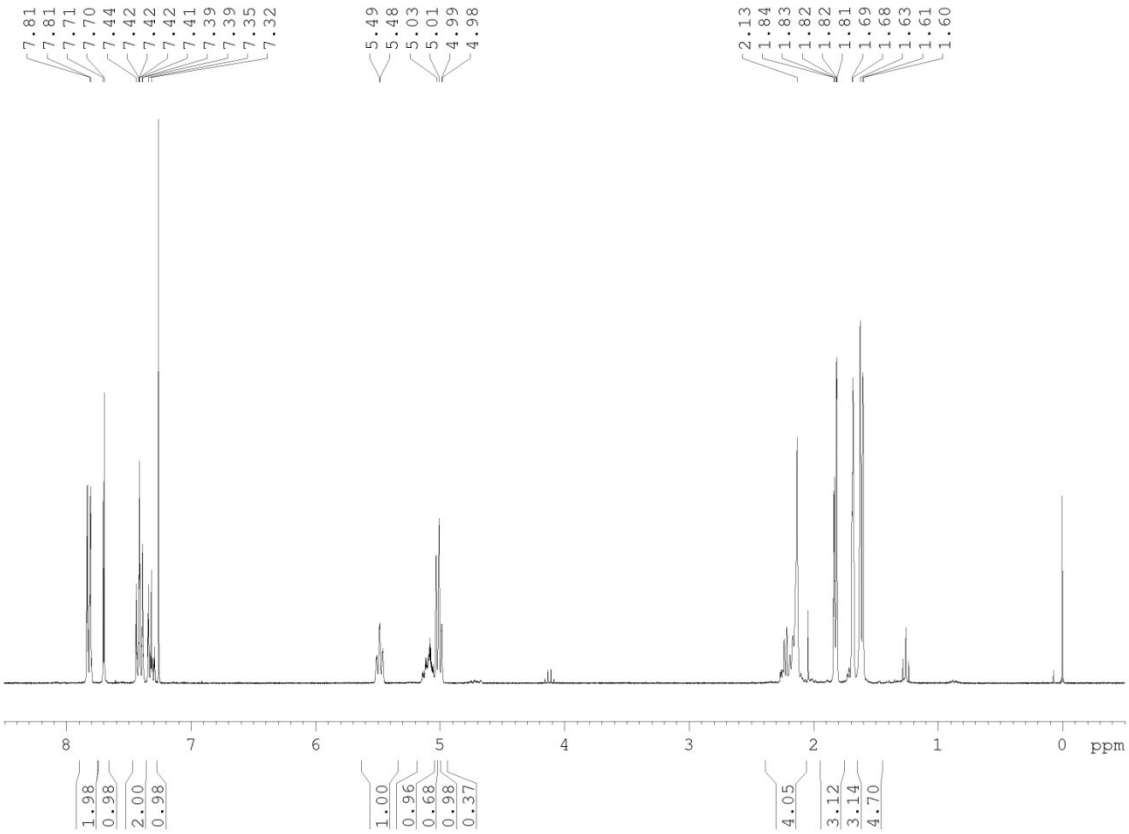
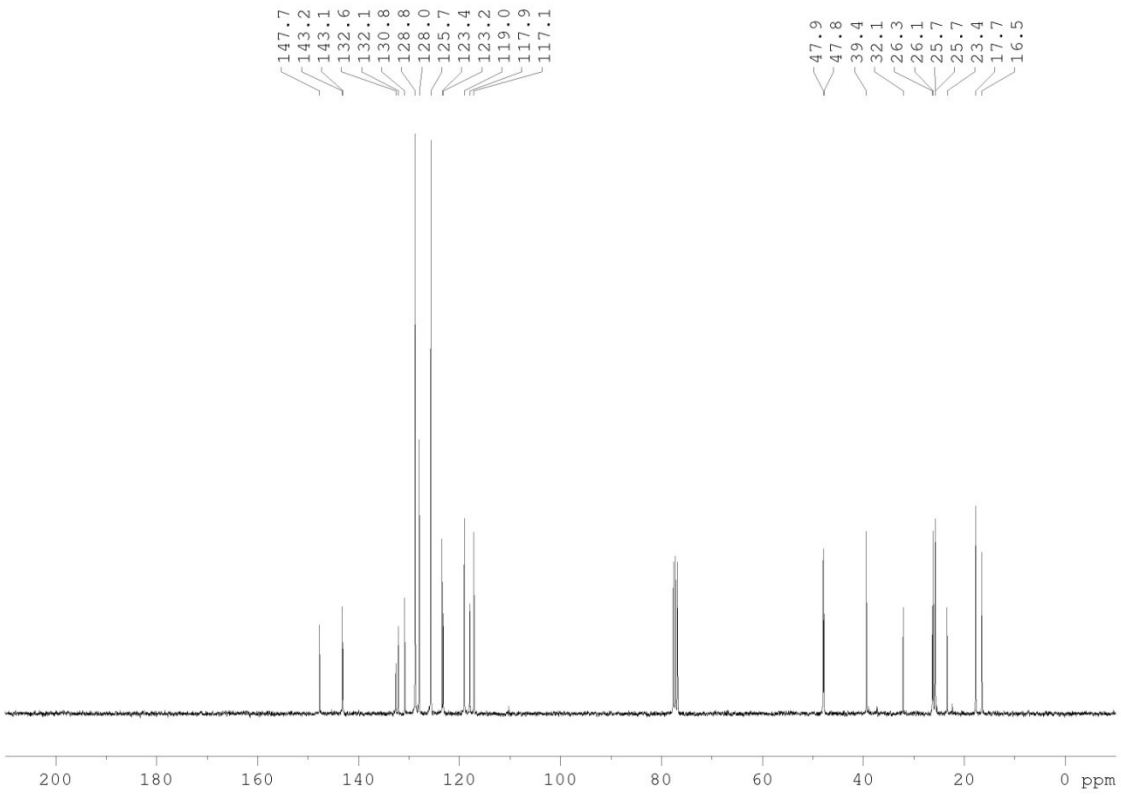
340
360
380
400

Spectral data of IT-7



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143.2
143.1
132.6
132.1
130.8
128.8
128.0
125.7
123.4
123.2
119.0
117.9
117.1
47.9
47.8
39.4
32.1
26.3
26.1
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23.4
17.7
16.5
200
180
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140
120
100
80
60
40
20
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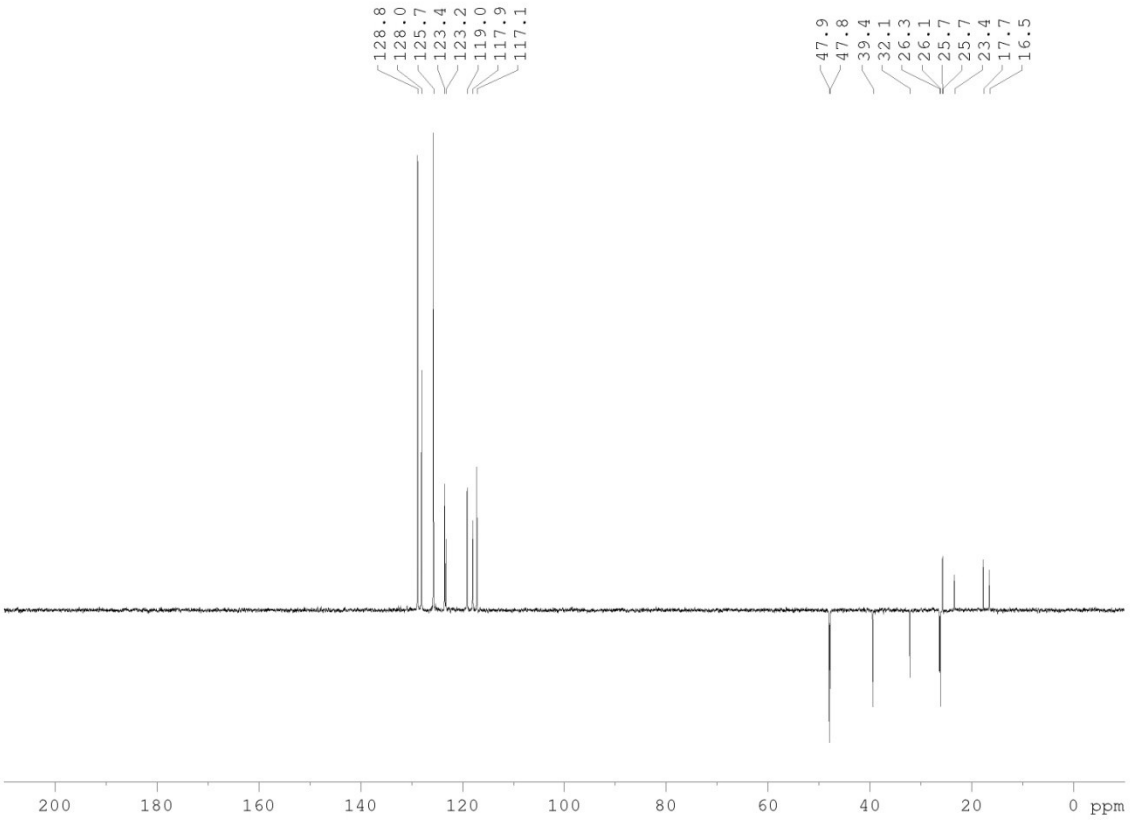
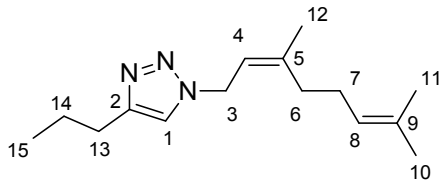
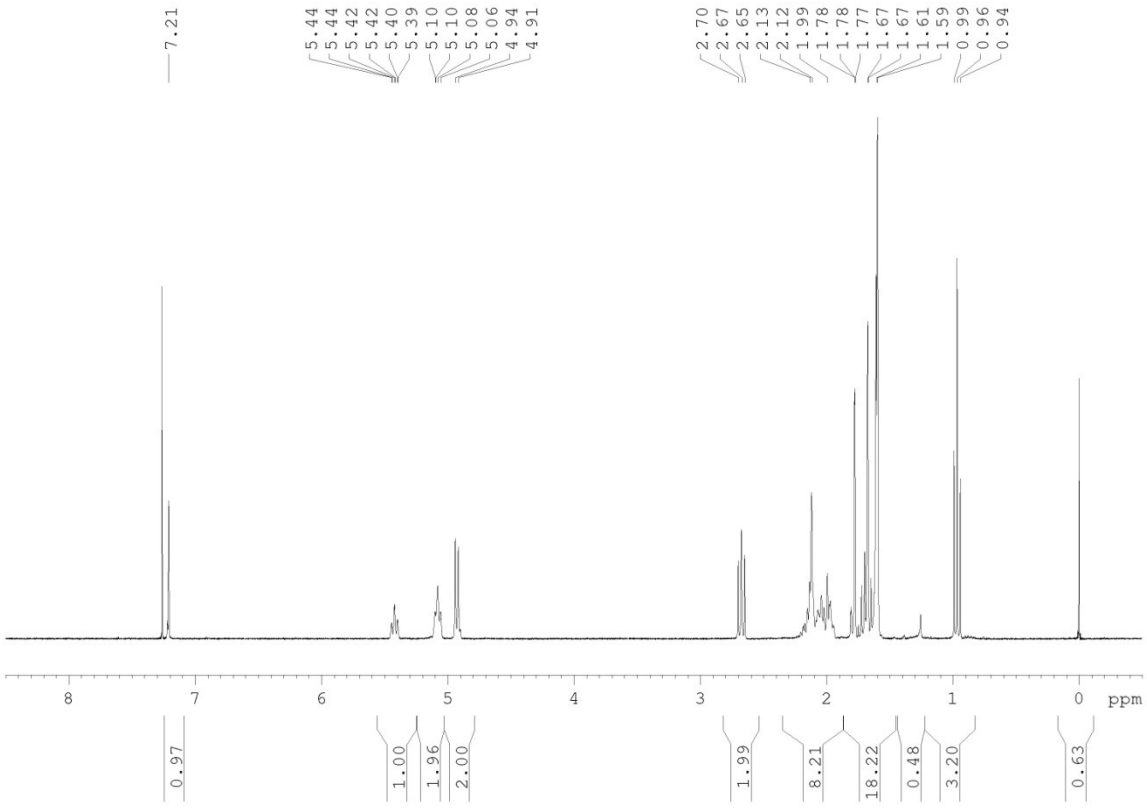
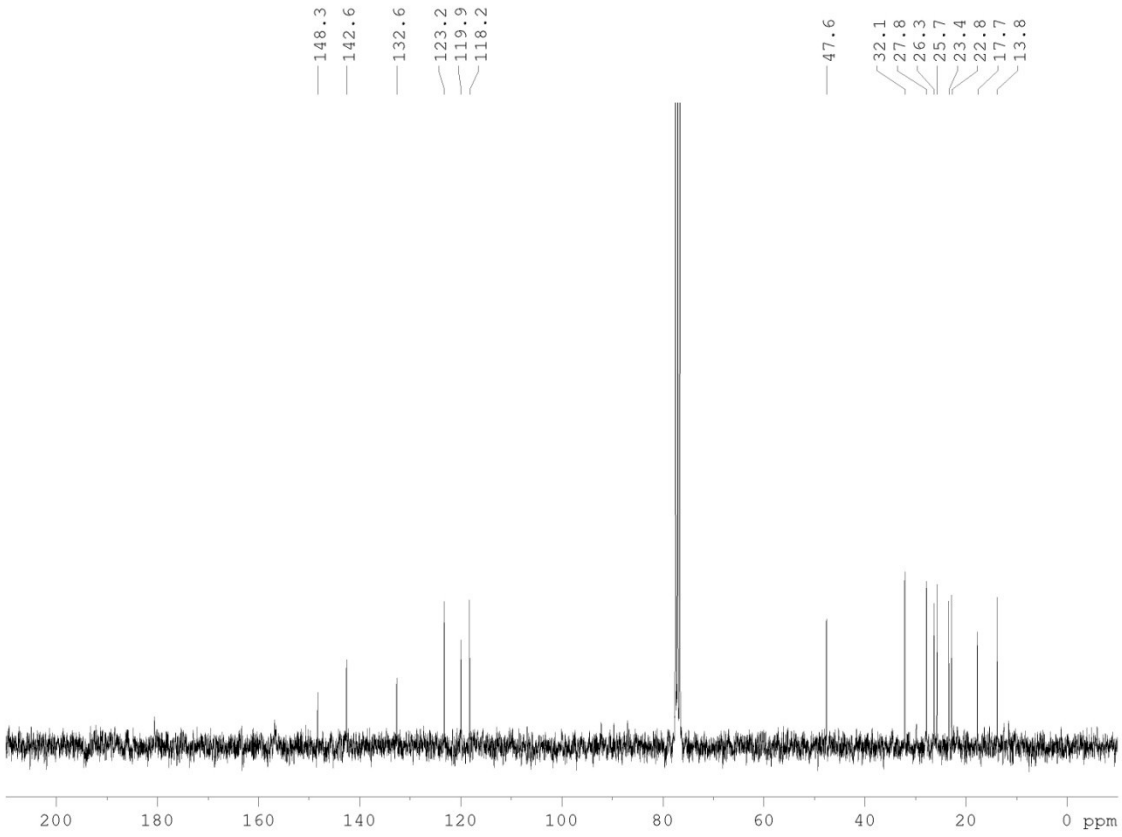

128.8
128.0
125.7
123.4
123.2
119.0
117.9
117.1
47.9
47.8
39.4
32.1
26.3
26.1
25.7
25.7
23.4
17.7
16.5
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-8



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132.6
123.2
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118.2
47.6
32.1
27.8
26.3
25.7
23.4
22.8
17.7
13.8
200
180
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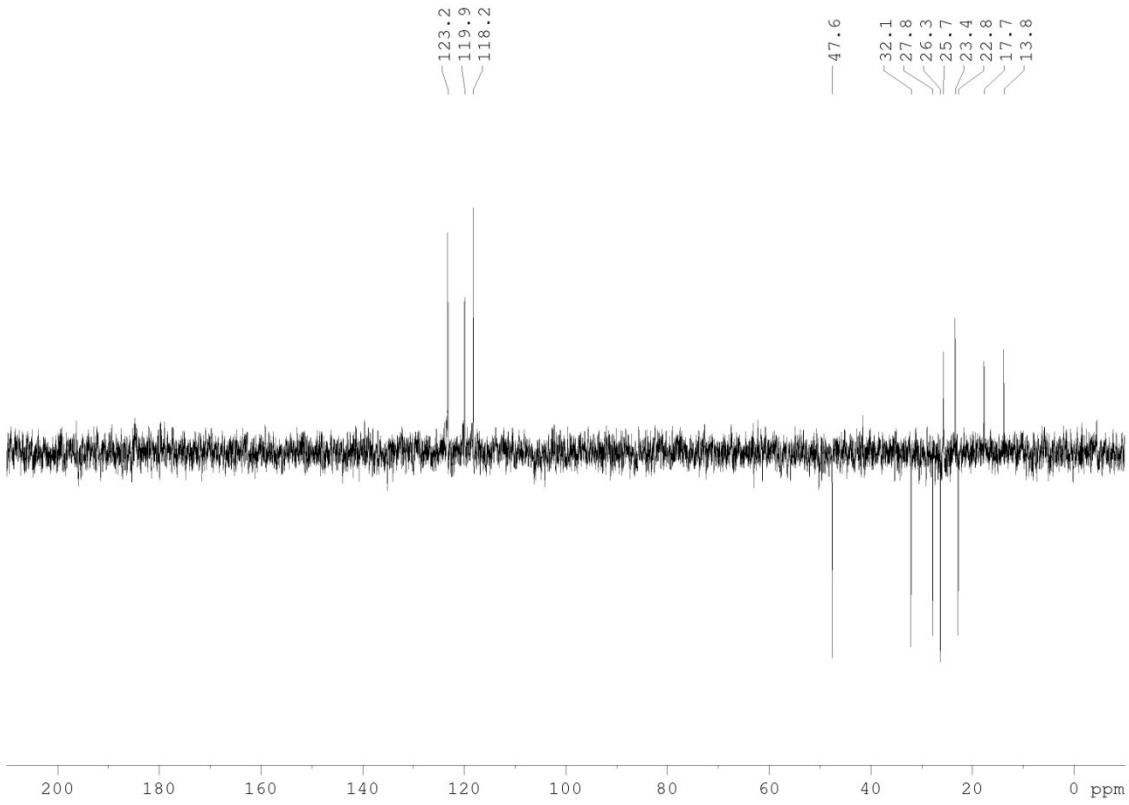
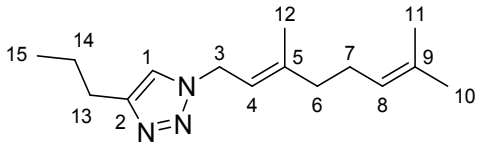
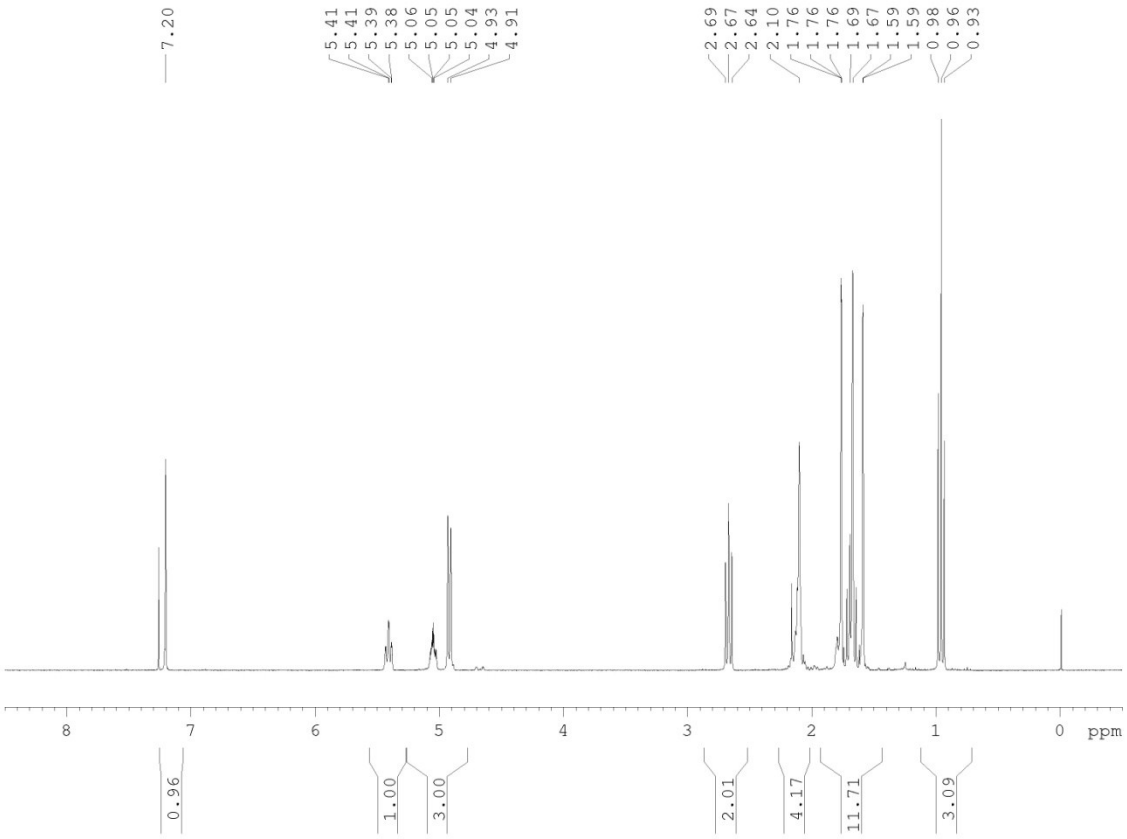
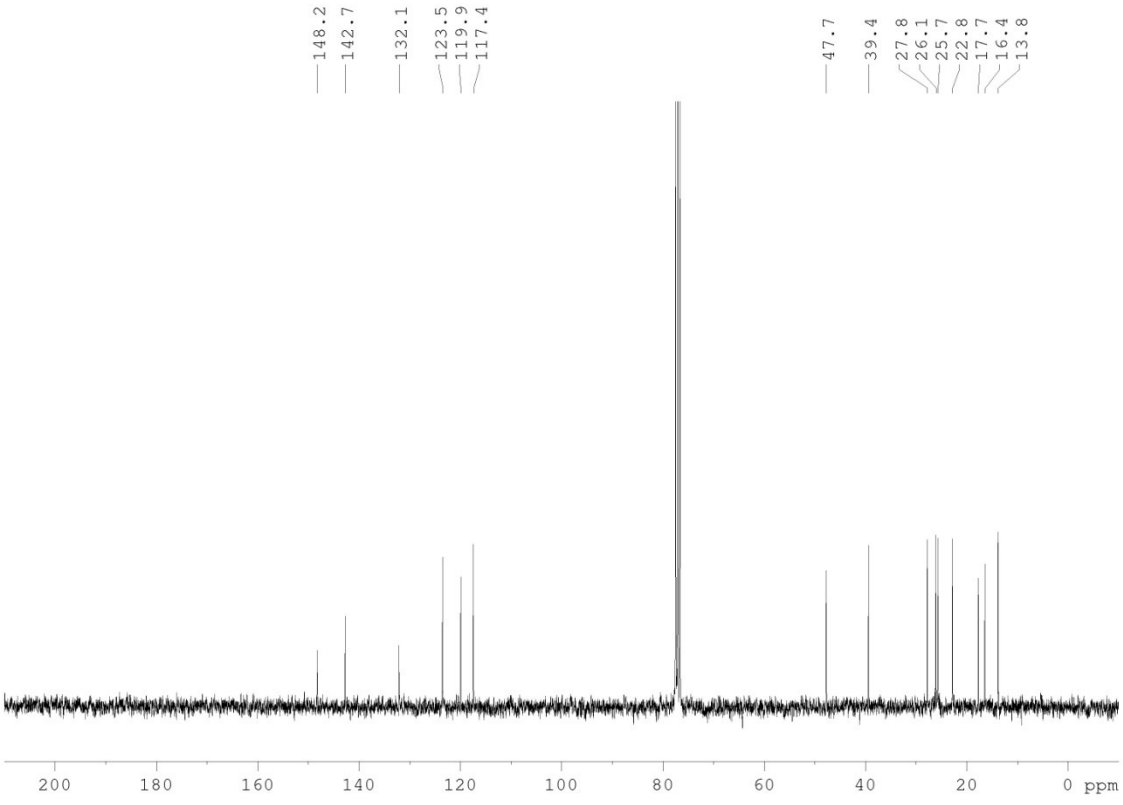
140
120
100
80
60
40
20
0 ppm


123.2
119.9
118.2
47.6
32.1
27.8
26.3
25.7
23.4
22.8
17.7
13.8
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-13



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142.7
132.1
123.5
119.9
117.4
47.7
39.4
27.8
26.1
25.7
22.8
17.7
16.4
13.8
200
180
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140
120
100
80
60
40
20
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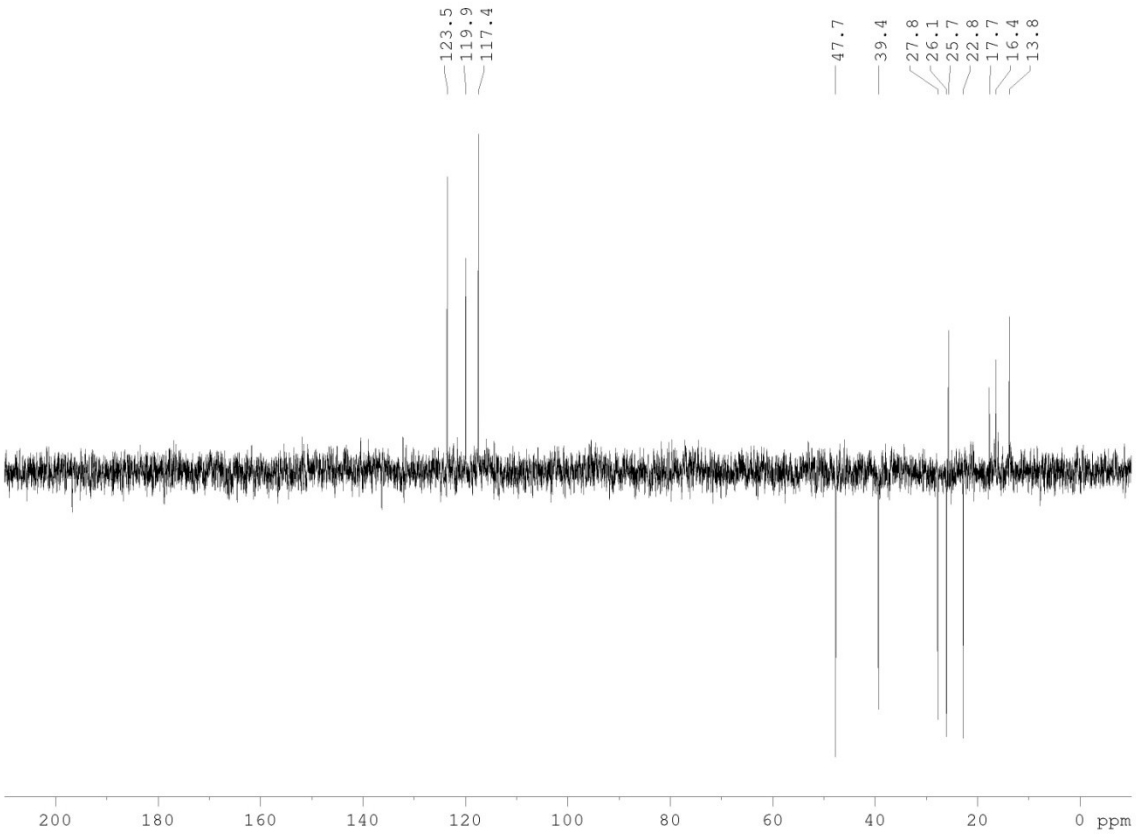
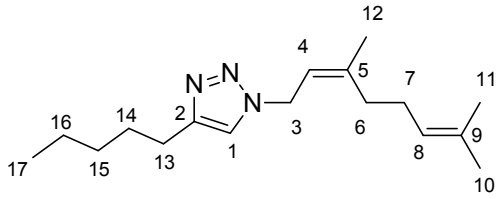
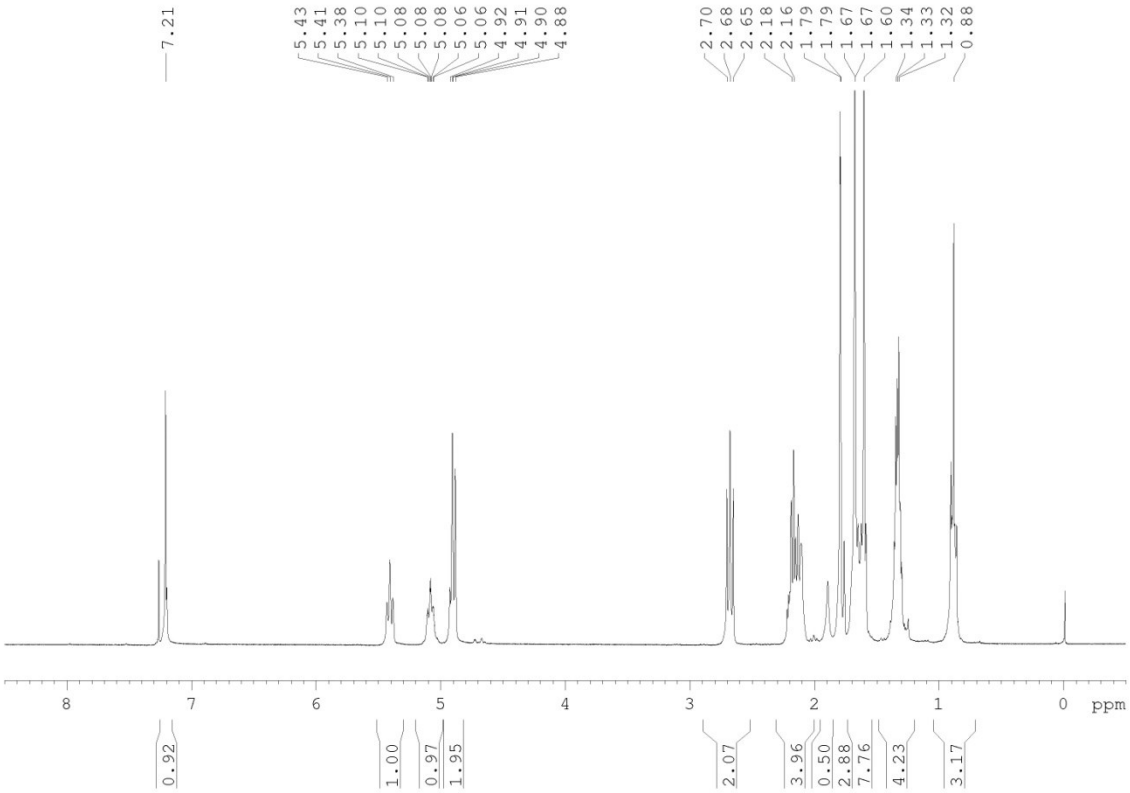
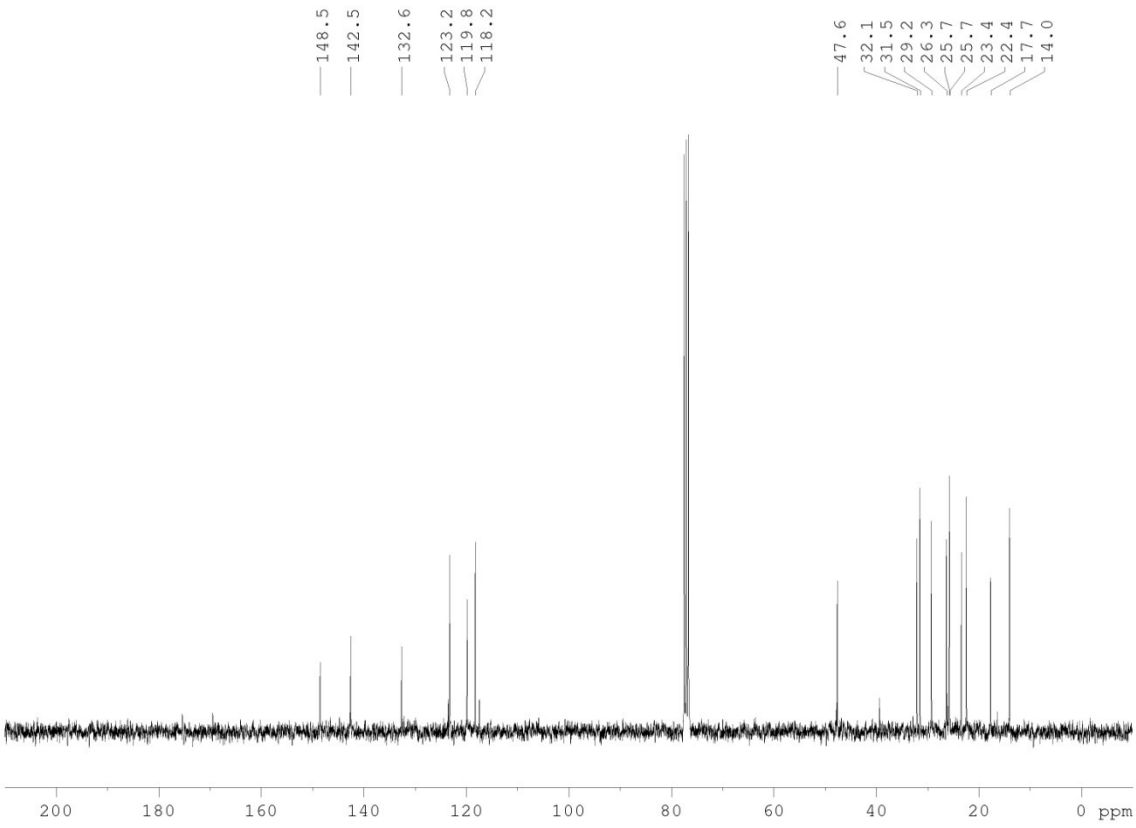

123.5
119.9
117.4
47.7
39.4
27.8
26.1
25.7
22.8
17.7
16.4
13.8
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-9



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142.5
132.6
123.2
119.8
118.2
47.6
32.1
31.5
29.2
26.3
25.7
25.7
23.4
22.4
17.7
14.0
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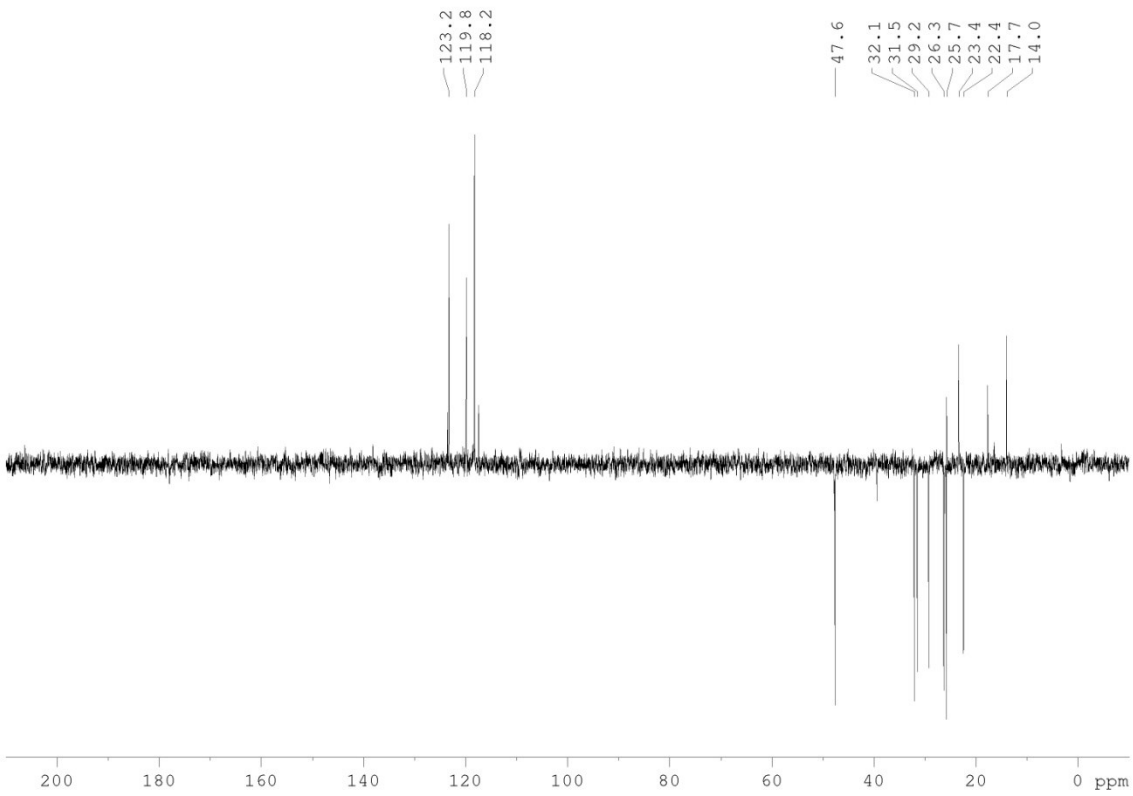
140
120
100
80
60
40
20
0 ppm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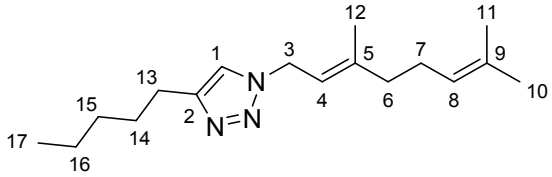
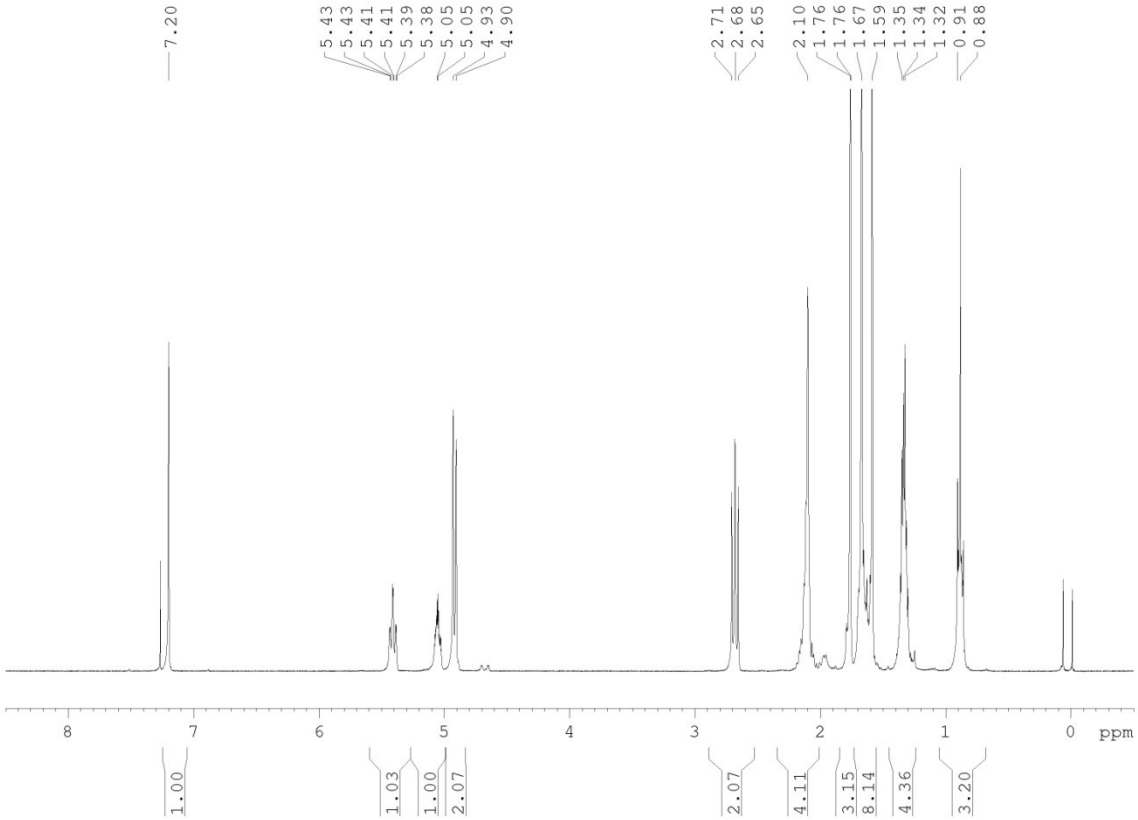
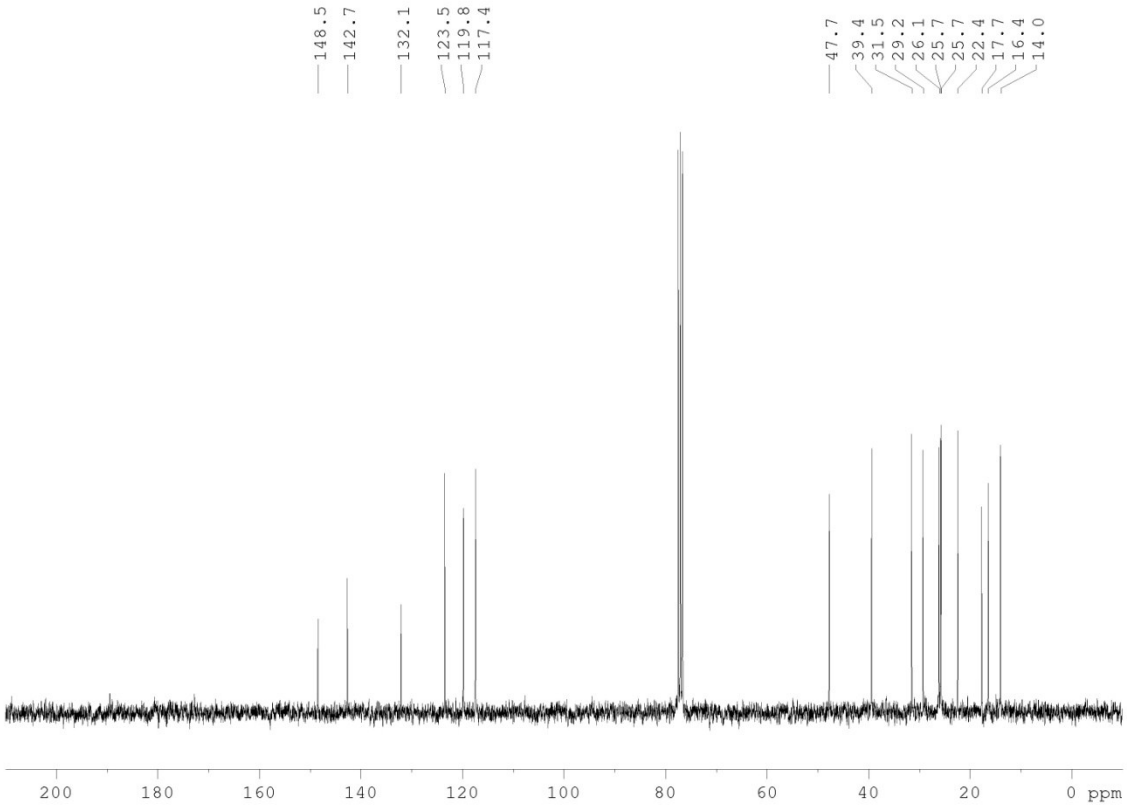
119.8
118.2
47.6
32.1
31.5
29.2
26.3
25.7
23.4
22.4
17.7
14.0
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-14



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39.4
31.5
29.2
26.1
25.7
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17.7
16.4
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140
120
100
80
60
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20
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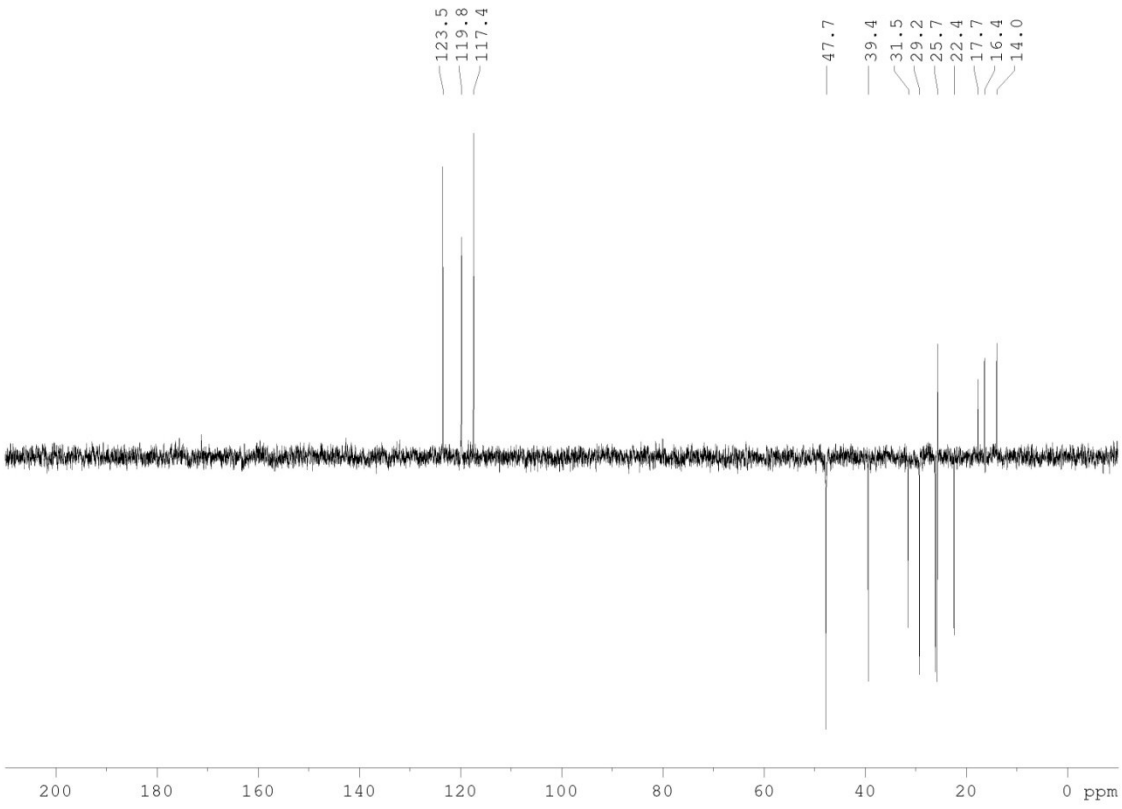
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117.4
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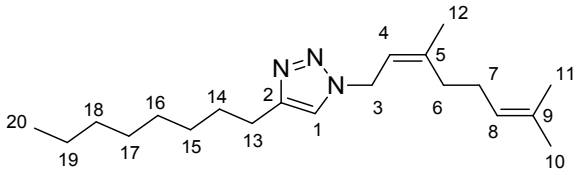
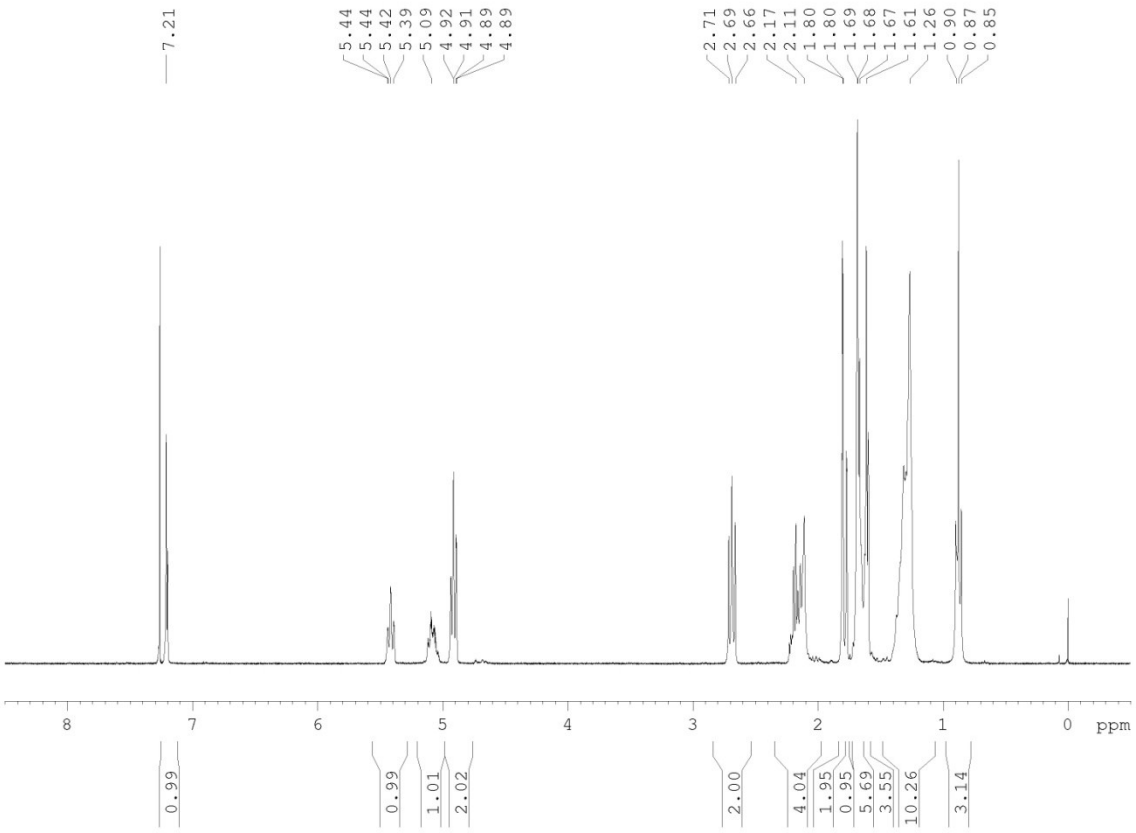
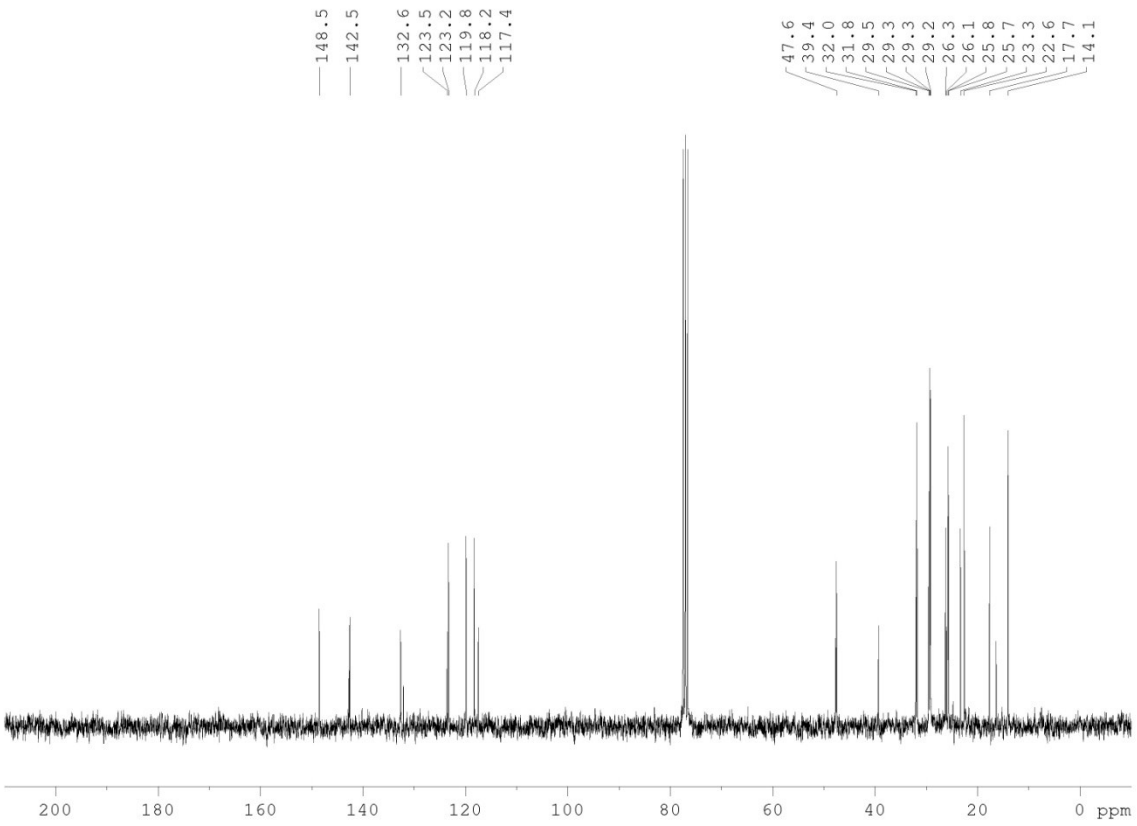
31.5
29.2
25.7
22.4
17.7
16.4
14.0
200
180
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-10



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118.2
117.4
47.6
39.4
32.0
31.8
29.5
29.3
29.3
29.2
26.3
26.1
25.8
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22.6
17.7
14.1
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100
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60
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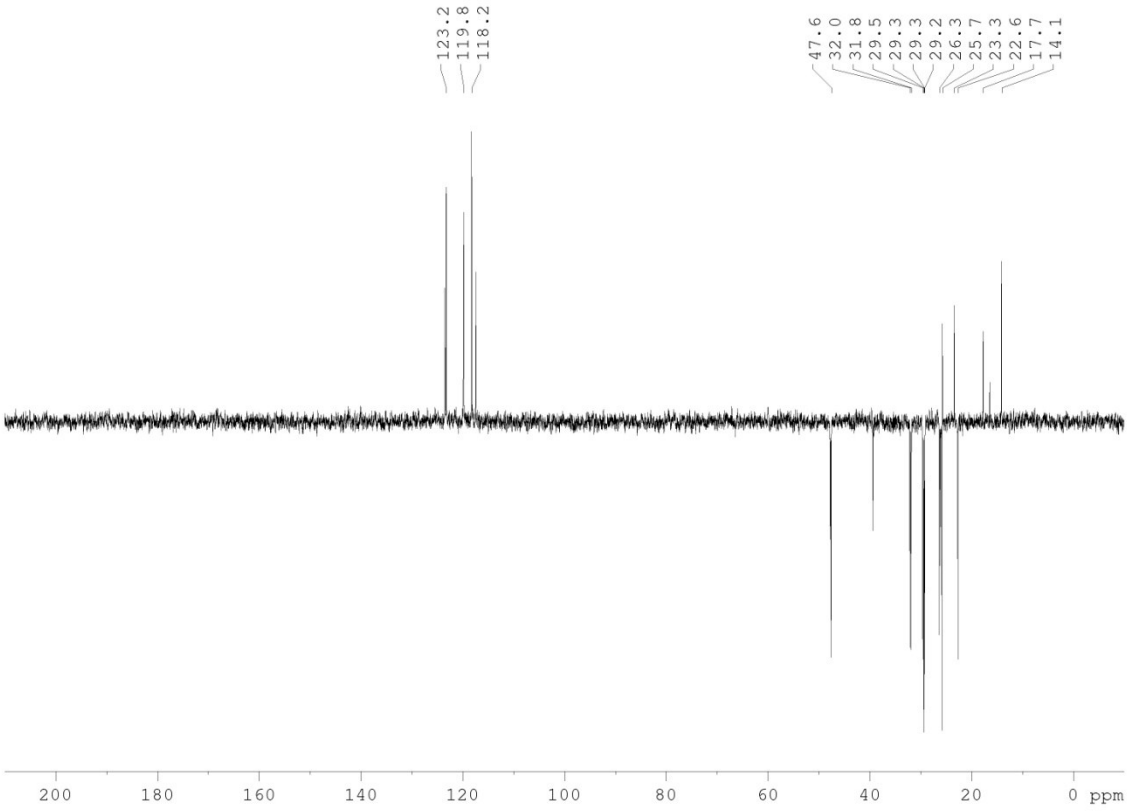
20
0 ppm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29.3
29.3
29.2
26.3
25.7
23.3
22.6
17.7
14.1
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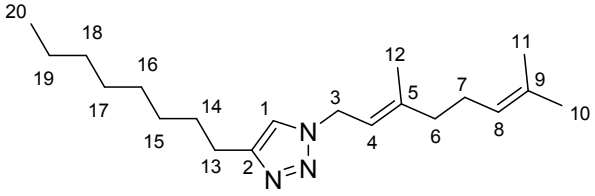
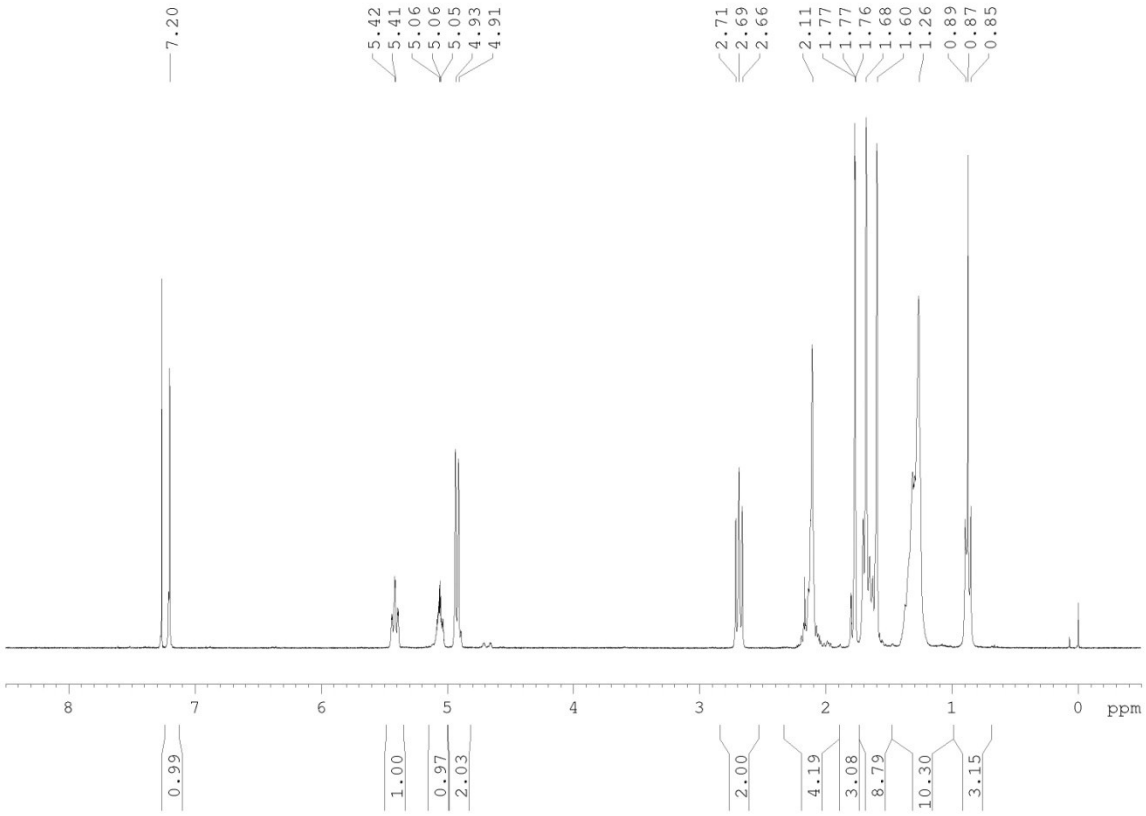
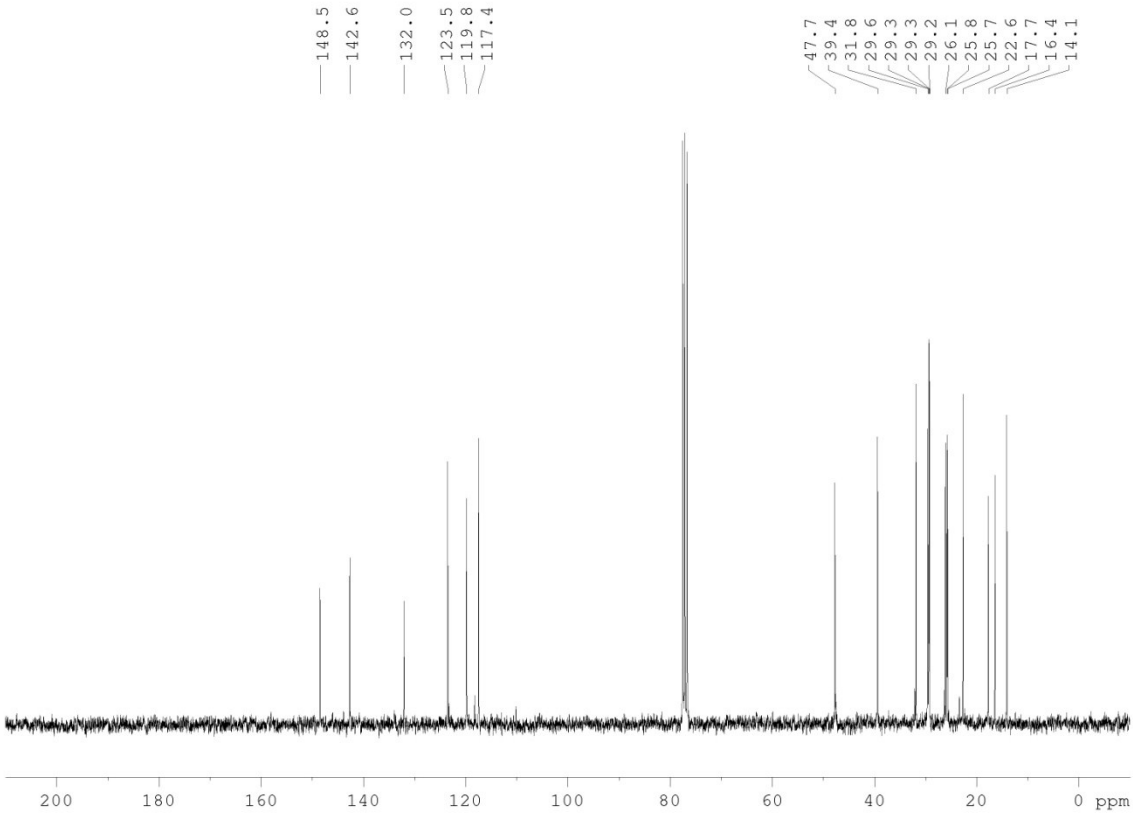
160
140
120
100
80
60
40
20
0 ppm

Spectral data of IT-15



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132.0
123.5
119.8
117.4
47.7
39.4
31.8
29.6
29.3
29.3
29.2
26.1
25.8
25.7
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17.7
16.4
14.1
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180
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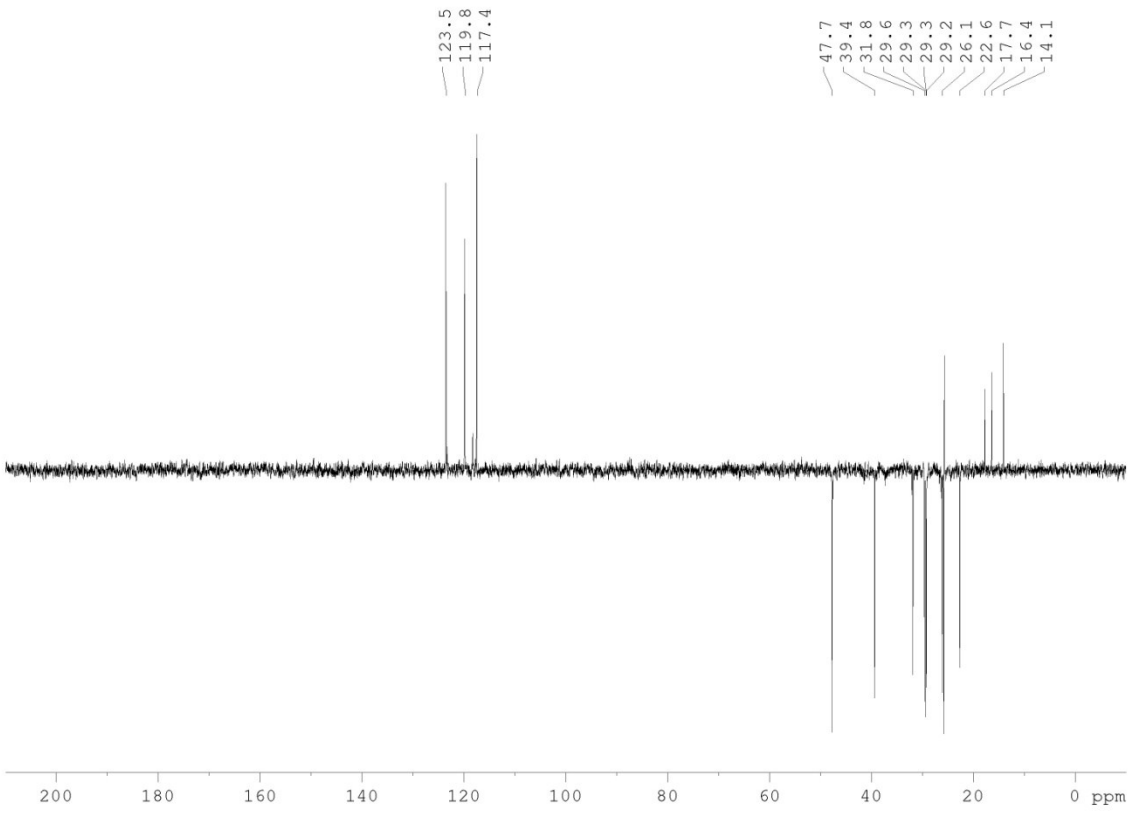
140
120
100
80
60
40
20
0 ppm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117.4
47.7
39.4
31.8
29.6
29.3
29.3
29.2
26.1
22.6
17.7
16.4
14.1
200
180
160
140
120
100
80
60
40
20
0 ppm